**DOCTORAL THESIS**

# The modulation of attention bias modification using transcranial electrical stimulation

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# The Modulation of Attention Bias Modification using Transcranial Electrical Stimulation

By

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# Abstract

Attention bias towards threat is implicated in the development, aetiology and maintenance of anxiety. Attention bias modification (ABM) is a cognitive training task which has been seen to manipulate the direction and magnitude of attention biases. ABM training to reduce threat bias has been effective in reducing anxiety. Transcranial electrical stimulation (tES) is a form of non-invasive brain stimulation which is known to modulate the effects of cognitive training. In the present research, two studies investigated the modulation of ABM with tES. In study 1, 172 participants (137 female) received transcranial random noise stimulation (tRNS) of the bilateral inferior frontal gyrus (IFG), anodal transcranial direct current stimulation (tDCS) of the left dorsolateral prefrontal cortex (DLPFC) or sham tES delivered concurrently with active, control or no-training ABM across three consecutive days to assess the effect on attention bias and state anxiety. State anxiety was reduced across participants irrespective of ABM or tES group. Threat bias was reduced for participants with a pre-existing threat bias and neutral bias was reduced for participants with a pre-existing neutral bias. In study 2, 39 participants (27 female) received ABM with anodal or sham tDCS of the left DLPFC during one session. As well as recording reaction times from the attention bias task, the N2pc component was measured as an electrophysiological indicator of attentional selection. The digit span task measured attentional control. State anxiety increased following ABM with sham (but not anodal) tDCS. N2pc suggested no modulation of ABM with anodal tDCS but reaction time data revealed reduced threat bias for participants with a pre-existing threat bias who received anodal (but not sham) tDCS. Digit span score was increased only for low trait anxious participants who received anodal tDCS. Overall, there was no evidence of superior

reductions in threat bias and anxiety for active ABM relative to non-active ABM or the enhancement of ABM effects with tES. Instead, findings suggested that, for each experiment, outcomes were determined by the interaction of pre-existing cognitive and neural state with task and tES-induced frontal cortex facilitation. Where ABM sufficiently enhanced frontal mechanisms associated with top-down control this resulted in down-regulation of emotional response to anxiety evoking stimuli and its aversive influence on attentional processes. Where training insufficiently recruited these mechanisms, they could be enhanced using tES.

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# Chapter 1

## Introduction

## 1.1 Anxiety

Speilberger et al. (1983) termed the 20th century the "age of anxiety". It was an era in which an increasing amount of work to conceptualise and research anxiety was motivated by a growing awareness of its pervasive and debilitating nature (Speilberger et al., 1983). Anxiety is an emotional and physiological state evolving from primal and automatic responses to perceived danger with the aim of promoting safety and survival (Beck, Steer & Brown 1996). Historically, such a response signalled the need to interrupt the task at hand and to prepare an 'escape' or 'confront' reaction (Bar-Haim et al., 2007; Bishop, 2007). The cognitive and physiological experiences associated with this signal are encapsulated in the modern characterisation of anxiety as "fear, worry and unease" in response to internal or external threats (Tian et al., 2016) or threatening circumstances (Eysenck & Calvo, 1992). Crucially, anxiety is a risk factor for both psychological disorder and physical illness (Tian et al., 2016; Yin et al. 2016).

### 1.1.1 Trait and State Anxiety

In 1983, an inventory was published to measure anxiety which comprised two scales (Speilberger et al., 1983). Each was designed to assess one of the two

related but distinct constructs of anxiety. These were trait anxiety and state anxiety. The trait anxiety inventory measures the tendency to experience negative affect such as fear, apprehension and tension across situations (Barnes, Harp & Jung, 2002). Trait anxiety is stable over time and situations (Leal et al., 2017). The highly trait anxious individual may consistently experience and report negative feelings along with associated physiological symptoms (Gidron, 2013) and be prone to perceiving mildly aversive events as dangerous or threatening (Spielberger et al., 1983). State anxiety refers to the level of tension, apprehension, nervousness and worry presently experienced (Eysenck, Santos, Derakshan & Calvo, 2007) and fluctuates as a factor of situational stressors (Barnes et al, 2002). Trait and state anxiety interact, with highly trait anxious individuals often experiencing state anxiety in circumstances which would not evoke state anxiety in low-trait-anxious individuals (Spielberger, 1972).

Anxiety is an adaptive phenomenon often necessary to protect an individual from harm and higher levels of state and trait anxiety are not necessarily of clinical concern (Steimer, 2002). Excessive anxiety may however be maladaptive and, in some circumstances represent an early warning or predisposition for anxiety disorder (Reidy & Richards, 1997).

### 1.1.2 Anxiety Disorders

Anxiety disorders are some of the most prevalent mental disorders (Craske & Zucker, 2002; MacDonald & Feifel, 2014) with an estimated 25% of adults experiencing an anxiety disorder across their lifetime (Angulo et al., 2017;

Bishop, 2007; Hill, Waite & Cresswell, 2016). Anxiety disorders may result in poor psychosocial functioning, mental and physical health, relationships and quality of life. There is a high rate of comorbidity with disorders such as major depressive disorder (MDD) and substance abuse (Angulo et al. 2017). Anxiety disorders are associated with excessive fear, worry and avoidance of perceived threat, largely due to a tendency to over-estimate its value (MacDonald & Feifel, 2014). The clinically anxious individual may also underestimate their own ability to cope with the threat (Beck et al. 1997). Associated physiological symptoms include increased heart rate, fast, shallow breathing, stomach or chest pain and sweating (Hill et al., 2016) and, in the long term, adverse impact upon cardiovascular health and mortality (Kizilcik et al., 2016). The economic burden of anxiety disorders is considerable with the cost to the UK in 2013 estimated at €11,687 million (Fineberg et al., 2013). There are also costs related to impaired workplace performance (Kizilcik et al., 2016). Of the ten anxiety disorders listed in the DSM-5 (Hill et al., 2016) generalised anxiety disorder (GAD) and social anxiety disorder (SAD) are amongst the most prevalent (Counsell et al., 2017).

#### 1.1.2.1 Generalised Anxiety Disorder

GAD is common, disabling and hard to treat (Fitzgerald et al., 2017). The disorder is characterised by extreme worry in daily life (Craske & Stein, 2016) which is difficult to control (Counsell et al., 2017). Often the worry and anxiety are not attached to a trigger or stimulus but are persistent (Tyrer & Balwin, 2006). Symptoms may include restlessness, psychological and muscular tension, nervousness, poor concentration, irritability, sleep problems (Craske & Stein,

2016), palpitations, sweating and dry mouth (Tyrer & Baldwin, 2016). First line treatment for GAD is psychological therapy such as cognitive behavioural therapy (CBT) or drug treatment (Tyrer & Baldwin, 2016). The most recent clinical guideline for the pharmacological treatment of GAD recommends treatment with a selective serotonin reuptake inhibitor (SSRI) such as Sertraline in the first instance (National Institute for Health and Care Excellence [NICE], 2011). However, symptoms persist in 50% or more of the patients who undertake CBT and up to 50% of GAD patients who use pharmaceuticals report no improvement (Fitzgerald et al., 2017)

#### 1.1.2.2 Social Anxiety Disorder

Social anxiety disorder is characterised by fear related to social events and scenarios. Specific fears are over social embarrassment, (Kizilik et al., 2016; Schmid, Kleiman & Amodio, 2015), scrutiny and negative evaluation (Bruhl et al., 2014; Spence & Rapee, 2016), rejection, offending others (Kizilcik et al., 2016) and inability to interact and cope in social situations (Beidel, Turner & Dancu, 1985). Typically, these fears are disproportionate to the potential social threat presented (Spence & Rapee, 2016). Consequently, individuals with SAD may avoid social situations (Bruhl et al., 2014; Rodebaugh et al., 2017) or experience them with intense anxiety (Spence & Rapee, 2016) and excessive physiological arousal (Beidel et al., 1985). Social avoidance exacerbates social anxiety and so the relationship between emotion and behaviour is cyclical (Rodebaugh et al., 2017). The socially anxious individual may also encounter impaired task performance (Schmid et al., 2015), poor advancement at work or

academically, loneliness and fewer romantic or sexual encounters (Beidel et al., 1985).

Anxiety disorders may run a chronic course if left untreated (Hill et al., 2016; MacDonald & Feifel, 2014) and it is essential to explore measures to intervene in their development.

### 1.1.3 Cognitive Models of Anxiety

Approximately 50 years ago influential models of anxiety began to emerge. Constructing such models enables identification of the point in anxiety formation at which intervention can occur. An aspect of cognition which models have consistently espoused as central to anxiety is the tendency to selectively attend to and process information which signals or is related to threat (Beard et al., 2012). This bias interferes with cognitive processes including memory (Reidy & Richard, 1997), interpretation of circumstances and attention allocation (Mogg & Bradley, 2016) and is held to maintain anxiety (Cody & Teachman 2010). As well as predicting the presence of cognitive bias in anxiety, information-processing models purported cognitive mechanisms via which they might arise.

#### 1.1.3.1 Williams, Watts, MacLeod and Matthews (1988, 1997) - Theory of Attention Bias and Anxiety

Williams et al. (1997, 1998) explained attentional bias in anxiety using a two-stage information processing model. Stage one involves the evaluation of the threat value presented by a stimulus or event. If a stimulus is deemed

sufficiently threatening, stage two, the attentional resource allocation system is triggered. Individuals with high level trait anxiety are thought to favour orientation towards stimuli deemed as threatening and low-level trait anxiety is associated with orientation away from mildly threatening stimuli. When state anxiety is elevated the relationship between trait anxiety and attention orientation is intensified with highly anxious individuals attributing higher levels of attention allocation to the perceived threat and low trait anxious individuals becoming more avoidant of the perceived threat (Mathews & Mackintosh, 1998).

#### 1.1.3.2 Mogg and Bradley (1998) - Cognitive Motivational Theory

Mogg & Bradley's (1998) cognitive motivational theory proposed the existence of two motivational systems which drive cognitive and behavioural outcomes to emotions. The first is a valance evaluation system (VES) which is responsible for surveying the environment and identifying potential threats. This is done rapidly and automatically via rudimentary assessment of the physical characteristics of the environment. However, the VES might also be influenced by contextual information, interoceptive signals and past experience. Importantly, this process occurs pre-attentively without effort or conscious awareness. The second is a goal engagement system which determines reaction to the perceived threat level in terms of the amount of attention allocated to it. In anxiety, a mildly threatening stimulus may be determined to be of moderate or high threat value by the valance evaluation system. This would trigger the allocation of increased attentional resources to the stimulus. In low anxiety, the stimulus might be valued as of low threat and disregarded in favour of more positive or goal relevant stimuli. However, even in low anxious individuals, increasing

threat value warrants increasing attention allocation to a stimulus. Thus, cognitive motivational theory suggests that everyone (not just high anxious individuals) orients towards stimuli which are considered threatening but that high anxious individuals have a lower threshold for threat appraisal (Mogg & Bradley, 1998).

#### 1.1.3.3 Eysenck, Santos, Derakshan and Calvo (2007) - Attentional Control Theory

Attentional control theory (ACT) proposes two attentional systems: a 'top-down' goal-directed system which is influenced by experience, knowledge and goals and a 'bottom-up' stimulus-driven system which responds to particularly salient information or stimuli (Corbetta & Shulman, 2002). Typically, the top-down system exerts control over the bottom-up system attenuating the influence of salient and, importantly, aversive stimuli. However, in anxiety, the balance between these two systems is disrupted and the stimulus-driven system has more influence over attentional allocation than the goal-directed system (Coombes et al., 2009). It is suggested furthermore that anxiety interrupts two specific functions of attentional control: inhibition and shifting. Effective 'inhibition' involves the ability to stop a pre-potent response or to resist interference from a task-irrelevant stimulus. 'Shifting' means directing attention between relevant stimuli or tasks (Derakshan & Eysenck, 2009).

The present thesis will not evaluate evidence which refutes or supports these models or seek to dissociate between them. However, these provide an important context for much of the work presented in the thesis.

### 1.1.4 Anxiety and Attention bias

Underpinning each of the above models is the idea that anxiety is associated with attentional bias towards threat relevant stimuli. Research has consistently shown that when threatening information or stimuli compete with neutral information or stimuli for attentional resources, anxious individuals will selectively attend to threat (Amir, Taylor & Donohue, 2011; for a review see Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg & van IJzendoorn, 2007).

Anxiety and vigilance of threatening stimuli possess an innate and privileged roles in human cognition (Bar Haim et al., 2007; Gilbert, 2000; LoBue & Rakinson, 2013). A functional fear system has been proposed, which has evolved to aid the survival [and gene transmission, Ohman & Mineka, (2001)] of individuals and species by protecting against aversive, dangerous and threatening situations (Misslin, 2003). This system is responsible for such defensive cognitive tendencies as visual attentional bias towards threat. In their 4-factor fear module model, Ohman and Mineka, 2001 suggested that this system is selective for stimuli which have posed a threat across time, is triggered automatically (outside of conscious awareness), is resistant to cognitive control and is associated with a specific neural circuitry centred around the amygdala. The proposed location of this neural circuit (subcortical regions of the medial anterior temporal lobe) indicates that behaviours elicited by the fear system have an adaptive basis as they are shared by mammals, including those with, in the words of Ohman & Mineka (2001), “more primitive brains”. In further support of an ‘innate’ model of fear response, studies have shown that children,

as early as their first year, respond quickly to threat even before learning threat-relevant fears (LoBue & Rakinson, 2013). The purpose of this fear system and the defensive mechanisms which it facilitates is to promote a state of mental preparedness and high arousal allowing for rapid response to potential threats (Gilbert, 1998). For early humans, such threats may have been in the form of potential predators or hostile conspecifics (Shulkin & Rosen, 1998). Rapid or selective engagement to threatening facial expressions would therefore have been advantageous in terms of motivating the individual to quickly fight or flee. This preferential attentional selection remains adaptive (Koster et al., 2006) although, in modern humans it may not promote the same responses. However, in anxiety disorders there is an overactive threat appraisal system and individuals are abnormally sensitive to threat-related stimuli. Anxious individuals are more likely to perceive stimuli, irrespective of their valence, as threatening (Barry, 2015).

The relationship between biased attention toward threat and anxiety has been explored and largely substantiated using a number of cognitive paradigms (see Bar-Haim et al., 2007 for a review). Early work utilised the emotional Stroop task and demonstrated that anxious participants take longer to name the colour of threat related words than of neutral words (e.g. Mathews & Macleod, 1985; Mogg, Mathews & Weinman, 1989). The prolonged latency of colour naming in this context is proposed to be due to attentional capture by emotionally salient words which delays response (Egloff & Hock, 2001). Similar evidence of attentional bias towards threat-related words in anxiety has been produced in studies using the visual search paradigm (e.g. De Voogd, Wiers, Prins &

Salemink, 2014) and the emotional spatial cuing task (e.g. Fox, Russo & Dutton, 2002).

#### 1.1.4.1 Attention Bias Assessment using the Emotional Dot-Probe Task

Much of the evidence for a relationship between attentional bias and anxiety has come from studies using the emotional dot probe paradigm (Macleod et al., 1986). In the emotional dot probe task two stimuli (typically words or faces), one neutral and one emotionally valenced, (e.g. a face with a neutral expression and a face with a threatening expression) appear simultaneously on a computer screen (e.g., Bar-Haim, 2010). Angry faces are often chosen as the negatively valenced stimuli as they represent potent social threat signals (Fox et al., 2002; Van Honk et al., 2002). Both cues disappear and one is replaced by a target letter or symbol that must be identified by the participant (e.g. Amir et al., 2008). The target replaces the neutral stimulus in 50% of trials and the threatening stimulus 50% of the time. More rapid responses to targets preceded by a threatening cue relative to targets preceded by a neutral cue reveals a threat bias (Bar-Haim, 2007). A critical factor of the emotional dot-probe task for assessing attention bias is that it is an implicit measure. Participants are asked to respond to targets following emotional or neutral stimuli and not to the stimuli per se.

#### 1.1.4.2 Evidence for Attention Bias using the Emotional Dot-Probe Task

Using the emotional dot-probe task, Macleod, Matthews and Tata (1986) were the first to show that when targets appeared in the location of negatively-valenced words, the targets would be detected more rapidly by clinically anxious participants. The authors suggested that when presented with a pair of threat-neutral words on a screen, attention would shift automatically and unconsciously to threat-related words and thus targets replacing these stimuli would be detected more rapidly invoking a faster response (Macleod et al., 1986). The emotional dot-probe task has revealed enhanced vigilance for threat compared to neutral stimuli in enhanced state anxiety (Bradley, Mogg & Millar, 2000). However, Broadbent and Broadbent (1988) reported that trait anxiety predicted attention bias towards threat to a greater extent than state anxiety and that at high levels, trait anxiety was particularly predictive of greater threat bias (Broadbent & Broadbent, 1988). In studies involving participants with clinical anxiety, patients with generalised social phobia responded more rapidly to targets replacing socially or physically threatening words than neutral words (Asmundson & Stein, 1994). Individuals with GAD have also shown greater attention bias towards threatening faces relative to neutral faces compared to individuals who did not have GAD. This was irrespective of whether stimuli were presented for 500ms or 1250ms (Bradley, Mogg, White, Groom & de Bono, 1999). Since the publication of these early findings, a wealth of evidence in support of the prioritised processing of threat-related stimuli in anxiety has been produced (Bar-Haim et al., 2007; Beard et al., 2012; Rinck & Becker, 2007).

Although the emotional dot-probe task has highlighted faster responses to targets following threatening stimuli in anxiety, there is some debate regarding the mechanism of this facilitation (Koster et al., 2004). Some have argued that it arises as a result of speeded detection of threat (Williams et al., 1997). Others have suggested that faster responses to threat-replacing targets could be explained by difficulty in disengaging from threat which causes attention to remain at the location of the threatening stimulus when the target appears (Fox et al., 2002). Koster et al. (2004) provided evidence for difficulty disengaging from threatening stimuli by showing that participants were slower to respond to targets replacing neutral images paired with threatening images compared to targets replacing neutral images paired with neutral images. However, Vassilopoulus (2005) revealed that attention in social anxiety was marked by a pattern of rapid engagement (at 200ms) followed by avoidance (at 500ms).

#### 1.1.4.3 Attention bias findings from EEG studies

Evidence of attention biases to threat in anxious and non-anxious individuals also comes from studies measuring neural activity in response to threatening and non-threatening visual stimuli. Event related potentials (ERPs) are recordings of electrical brain processes (waves of electro-cortical activity), time and phase-locked to specific events. They offer a detailed electrophysiological representation of the time-course of neural processes associated with an event (Helfinstein et al., 2008). ERPs are measured by placing electrodes on the surface of the scalp during electroencephalography (EEG), a non-invasive imaging technique. ERPs associated with attentional processes are often observed within the first 500ms after the appearance of a stimulus in attention

experiments (Bar Haim et al., 2005). It is suggested that early ERPs such as the C1 (a negative component between 50 and 100ms post-stimulus; Miller et al., 2015), P1 (a positive deflection between 120ms and 140ms; Fu et al., 2010) and N170 (a negative ERP between 130ms and 210ms post-stimulus; Blau et al., 2007), which are recorded within the first 200ms after stimulus presentation reflect bottom-up, automatic engagement. Later ERPs such as the P2 (a positive voltage in the latency range of 100ms to 250ms after stimulus; Sur & Sinha, 2009), P3 (a positive deflection between 300 and 650ms post stimulus; Salti, Bar-Haim & Lamy, 2012) and late positive component (LPP; a sustained positivity also beginning around 300ms; Kujawa et al., 2013) observed after 200ms post-stimulus, represent top-down, post-perceptual actions such as categorisation, response selection (Harrewijn et al., 2017) and the post-perceptual processing of emotional stimuli (Richards, Holmes, Pell & Bethel, 2013). Interestingly, ERPs have supported the presence of attentional bias to threat even where behavioural measures were taken but failed to evince threat related bias (e.g. Thomas, Johnstone & Gonsalvez, 2007). Given that ERPs are believed to provide specific temporal indices of visual spatial attention allocation and stimulus processing (Bar Haim et al., 2005) they may provide a more sensitive measure of attentional bias and attentional processes than reaction time data.

Many ERP studies have used the dot-probe paradigm to pinpoint the time course of attentional processes. In a study using a dot-probe task with angry-neutral or angry-positive faces pairs, behavioural data revealed a bias towards angry faces (Eldar et al., 2010). ERP data also supported the presence of a threat bias with an enhanced C1 to threat cues in anxious relative to non-anxious participants (Eldar et al., 2010). High anxious participants but not low anxious participants

have also exhibited an enhanced N2PC (a negative component between 170ms and 270ms post-stimulus) for angry faces compared to neutral faces during a dot probe task (Fox, Derakshan & Shoker, 2008) and an augmented, and shorter latency of P2 for angry faces relative to neutral faces (Bar-Haim, Lamy & Glickman, 2005). Evidence that ERPs reveal threat biases so soon after stimulus presentation support the view that attention is automatically deployed towards threatening stimuli, prior to conscious perception. There are also findings of enhanced ERP amplitudes for threatening stimuli later than 300ms from stimulus presentation. Socially anxious participants had elevated P3/LPPs for angry faces relative to reassuring faces in an adapted Erikson Flanker task (Moser et al., 2008). Furthermore, in an adapted dot-probe task, aversive images elicited an amplified LPP compared to neutral images across participants but the difference in ERP amplitude was more pronounced in participants with GAD (MacNamara & Hajcak, 2010).

Despite evidence from ERP studies which corroborates the presence of threat bias in anxious participants, studies comparing ERPs in anxious and non-anxious participants have suggested that attention bias is not modulated by anxiety. For example, Santesso et al. (2008) reported elevated P1 for angry faces relative to neutral faces for all participants which was unrelated to anxiety level. An enhanced N170, EPN (Morel et al., 2014) and N2PC (Kappenman et al., 2014) for aversive relative to neutral stimuli across participants, irrespective of anxiety level has also been reported. Furthermore, in non-anxious participants, elevated C1 (Eldar et al., 2010; Pourtois et al., 2004), P1 (Pourtois et al., 2004; Santesso et al., 2008), N2pc (Holmes et al., 2009) and P3 (Thomas, Johnstone &

Gonsalvez, 2007) amplitudes for aversive relative to neutral stimuli have been reported suggesting that elevated anxiety is not a prerequisite for threat bias.

### 1.1.5 Targeting Anxiety

The theory and evidence presented so far suggests that anxiety is pervasive and is associated with an attentional bias towards threat related stimuli. Currently, first line treatments for anxiety disorders are cognitive behavioural therapy (CBT) and pharmacological treatments, mainly selective serotonin reuptake inhibitors (SSRIs; Craske & Stein, 2016; Mogg et al., 2004; Hill, Waite & Creswell, 2016). However, neither treatment targets the threat bias which is characteristic of anxiety. CBT is a psychotherapeutic treatment which is the most supported for treating anxiety disorders (Craske & Stein, 2016). The method assumes that maladaptive cognitions maintain emotional distress and behavioural difficulties (Hoffman et al., 2012). CBT includes therapeutic strategies which challenge and attempt to adapt dysfunctional cognitions as a way of reducing emotional distress in ways which encourage the patient to be a participant in their own treatment (Hoffman et al., 2012; Jonhson, Hoffart, Nordahl & Wampold. 2017). Meta-analyses reveal CBT to be efficacious with medium to large effect sizes when compared to control condition in children (Crowe & McKay, 2016) and compared to control, waitlist or no-treatment conditions in adults (Hofmann et al. 2012). However, one systematic review of 87 studies gave a response rate of only 49.5% across anxiety disorders immediately following treatment and 53.6% at follow-up (Loerinc et al., 2015). SSRIs including Venlafaxine, Paroxetine, Fluoxetine and Citalopram, block the reuptake of serotonin in the brain (Farach et al., 2012). This means that more

serotonin is available in the synaptic cleft which can bind to post-synaptic receptors (Farach et al., 2012). This activation is thought to play an important role in the modulation of emotional processes (Olivier, 2015). SSRIs are safe and tolerable compared to alternative psychopharmacological treatments for anxiety (Popovic et al., 2015). However, one third to a half of patients with anxiety disorder treated with SSRIs fail to achieve long-term remission (Farach et al., 2012). Moreover, there is a growing list of side-effects associated with SSRIs including drowsiness, attentional deficit, lack of concentration, memory impairment and apathy (Popovic et al., 2015), nausea, diarrhoea, insomnia, headache, restlessness, reduced libido, suicidal ideation (Farach et al., 2012) and sexual dysfunction (Isaac, 1999). This information indicates that there are shortfalls in existing anxiety interventions and highlights the need for novel treatments.

## 1.2 Attention bias Modification

Recently, a cognitive paradigm called attention bias modification (ABM) has been developed to specifically target the implicit attention bias associated with anxiety. ABM is non-invasive, simple to administer and easily accessible. It avoids the effortful participation required for CBT and the potential side effects linked to SSRIs. Previously, a cognitive task based on a dot-probe design was described which assessed the direction and level of attentional bias towards neutral and emotionally valanced stimuli. In this task, participants are required to respond to a target which replaces either the neutral or the emotionally valenced stimulus by indicating its identity, gender etc. Faster responses to targets replacing the emotional stimulus suggest an attentional bias towards that

emotion (Beard et al., 2012). ABM paradigms are modifications of the emotional dot probe paradigm and have been recently developed with the aim of reducing attentional biases (Hayes, Matthews & Hirsch, 2010). In those ABM training paradigms designed to modify bias away from threat a contingency is introduced and the target typically replaces the neutral stimulus in all (or nearly all) trials. This encourages participants to implicitly attend away from threatening stimuli (usually towards neutral stimuli; Boettcher, Berger & Renneberg, 2012).

### 1.2.1 Attention Bias Modification and Anxiety

ABM towards neutral stimuli has been repeatedly demonstrated to reduce threat bias and often this reduction is accompanied by a reduction in anxiety (see Beard et al., 2012, for a review), particularly when training is carried out over a number of days (e.g. Amir et al., 2009b; Bar-Haim, 2010; Li, Tan, Qian & Liu, 2008). In contrast, ABM training which augments biased attention towards threat stimuli has been shown to increase anxiety (Bar-Haim, 2010). These findings support the suggestion that attentional threat bias may not simply arise from anxiety but may be causally related to its development and maintenance (Van Bockstaele et al., 2012).

Early ABM studies produced robust findings in healthy samples. Using neutral-threat word pairs, Macleod et al. (2002) sought to augment attention bias towards threat or away from threat in non-anxious participants. Attention was successfully manipulated in the intended direction. Additionally, anxiety ratings in response to an anagram stress task were lower for participants who had been trained towards neutral targets compared to those who had been trained

towards threat-related targets (Macleod et al., 2002). Van Bockstaele et al. (2012) reported a reduction in threat bias in neuro-typical participants following ABM towards neutral faces. This reduction in threat bias did not generalise to an interference task in which participants responded to a target following a single neutral or angry face. In a separate study, participants who were due to leave their home to study overseas were allocated to either 'attend neutral' ABM training spanning 15 days just prior to leaving, or no training (See, MacLeod & Bridle, 2009). The active training group demonstrated a reduction in attentional bias towards threat following ABM training 17 days after initial assessment of attentional bias which was not present in the no-training group. Participants who demonstrated the greatest reductions in attention bias towards threat also had the largest reductions in trait and state anxiety in response to the study's naturalistic stressor (moving to Australia). More recently neuro-typical participants received active (towards neutral) or control ABM training with neutral/social-threat word pairs (Chen et al., 2015). Following training, participants in the active ABM group had a greater attentional bias away from threat relative to the control ABM group.

In clinical samples, ABM training toward neutral faces seems to have been effective, not only in attenuating attention bias, but also in reducing the number of participants meeting the diagnostic criteria for clinical anxiety (Amir et al., 2009b; Amir, Taylor & Donohue., 2011; Hazen, Vasey & Schmidt, 2009; Schmidt, Richey, Buckner & Timpano, 2009).

#### 1.2.1.1 ABM and Generalised Anxiety

ABM studies have been carried out in populations with generalised anxiety. In one study, eight sessions of word-based ABM training towards non-threat or control ABM training were delivered to individuals with generalised anxiety disorder (GAD; Amir et al., 2009a). Participants in the active ABM group but not in the control group had a reduction in threat bias and in both self-report and clinician-rated anxiety following ABM training compared to before ABM training. Similar results were reported in Hazen et al. (2009) with participants who received five sessions of ABM training towards neutral words (away from threat words) demonstrating significantly greater reductions in threat bias and in anxious and depressive symptoms relative to participants who received control training.

#### 1.2.1.2 ABM and Social Anxiety

ABM protocols have also been used with socially anxious participants and have demonstrated reductions in both attentional bias and social anxiety symptoms following ABM away from threat (e.g. Amir et al., 2009b; Amir, Taylor & Donohue, 2011; Li et al., 2008; Schmidt et al., 2009). In one study with socially phobic participants, Amir et al. (2009b) demonstrated reduced attentional bias post training in those who received ABM away from threat and subsequent reduction in self-report and clinician-assessed social anxiety relative to participants who received control ABM. Additionally, only 50% of the active ABM group met the diagnostic criteria for generalised social phobia after ABM compared to 86% in the control ABM group and symptom reduction was

maintained for the active training group at a 4-month follow-up assessment (Amir et al., 2009b). In a separate study, participants with social phobia were allocated to receive active 'attend neutral' ABM training or control ABM (Amir et al., 2011). Those in the active training group who had the greatest level of attentional bias towards threat before ABM training had the greatest reductions in clinician rated social anxiety after ABM relative to participants in the control training group (Amir et al., 2011). In a recent study, participants with sub-clinical social anxiety received ABM training towards neutral stimuli or control ABM in which stimuli were presented for either 100ms or 500ms. Both the 100ms training group and the 500ms training group had greater reduction in threat bias and social anxiety following training compared to their respective control group (Liang, Tsai & Hsu, 2016).

However, several studies focusing on ABM in social anxiety have produced weaker effects in terms of attention bias modulation and anxiety reduction. Internet-based active ABM away from threat or control ABM was delivered to socially anxious participants over 4 weeks (Boettcher et al., 2012). Post-treatment there were significant reductions in social anxiety symptoms in both ABM and control groups (Boettcher et al., 2012). This finding was replicated in another study of internet-delivered ABM in social anxiety (Carlbring et al., 2012).

### 1.2.2 Inconsistency in ABM Research

Despite encouraging results, findings related to the efficacy of ABM have been variable (Emmelkamp, 2012). Some studies have failed to replicate the

successes of ABM from early research in terms of reducing attention bias and anxiety (e.g. Bunnell, Beidel & Mesa, 2013; Boettcher et al., 2012; Everaert et al., 2015; Fitzgerald, Rawdon & Dooley, 2016; Julian et al., 2012). Recently the evidence for ABM has been labelled 'disappointing' (Koster & Bernstein, 2015).

Moreover, meta-analyses have reported inconsistent effect sizes for ABM outcomes. Beard et al. (2012) and Hakamata et al. (2010) reported large effect sizes for change of attention bias in the trained direction. However, Mogoase et al. (2014) reported medium effect sizes and Hallion and Ruscio (2011) reported small effect sizes although the latter meta-analysis included studies which sought to manipulate interpretation bias as well as ABM studies. Hakamata et al. (2010) reported medium effects sizes for anxiety reductions but Beard et al. (2012) and Mogoase et al. (2014) reported small effect sizes for symptom related outcomes including anxiety, depression and alcohol craving reductions. Hallion and Rusco (2011) and Cristea et al. (2015) also reported small effect sizes for anxiety and depression reduction and in the latter meta-analysis, effect sizes became non-significant once the authors removed outliers and adjusted for publication bias. Such variation between meta-analyses findings might be explained by differences in inclusion criteria (Mogoase et al., 2015). For example, Hakamata et al. (2010) included studies which looked at the impact of ABM on anxiety in healthy and clinically anxious participants. Beard et al. (2012) on the other hand, incorporated ABM studies with varying outcome measures including anxiety, depression, alcohol dependency and smoking. Notably, none of the earlier meta-analyses including Beard et al. (2012); Hakamata et al. (2010) and Hallion et al. (2011) included recent studies which have produced

negative findings (e.g. Boettcher et al., 2012; Bunnell, Beidel & Mesa, 2013; Everaert et al., 2015; Fitzgerald, Rawdon & Dooley, 2016; Julian et al., 2012).

Inclusion criteria might explain different findings between meta-analyses. However, researchers have begun to explore other factors which might explain inconsistency in findings from individual ABM studies.

#### 1.2.2.1 Pre-existing Attention Bias Towards Threat

A potential factor underlying inconsistent results is baseline level of attention bias in participants. As attentional bias towards threat is implicated in a number of anxiety related pathologies, the mechanism via which ABM aims to reduce the associated symptoms is the reduction of threat bias. In this context, ABM may be more effective where there is pre-existing threat bias (Mogoase, David & Koster, 2014). However, a number of ABM studies did not find attentional bias towards threat in anxious participants prior to ABM training (e.g. Carleton et al., 2015, Enock et al., 2014, McNally et al., 2013, see Mogg et al., 2017). Given that the capacity of ABM for manipulating attention bias in a particular direction has been shown to be restricted to individuals with an existing attention bias in the opposite direction (e.g. O'Toole & Dennis, 2012) then pre-existing attention bias of participants should be considered during participant selection and when interpreting results from ABM studies. O'Toole and Dennis (2012) did not observe a change in attention bias from before to after ABM training when data from all participants was analysed. However, when analysis was constrained to participants with a pre-training attentional bias either towards or away from threat, a significant change in bias in the opposing direction was revealed after

ABM training. In other studies, participants with greater levels of threat bias have been seen to display larger reductions in social anxiety following ABM (Amir, Taylor & Donohue, 2011). Some researchers have chosen to include pre-existing attentional bias as a selection criterion (e.g. Eldar et al., 2012). Eldar et al. (2012) justified this pre-selection criterion by arguing that there might be a risk in inducing avoidance of threat in anxiety where there is no baseline threat bias to levels below what might be considered a healthy level of vigilance. However, from a research perspective inconsistent results, stemming from varying levels of attention bias across ABM studies, may lead to lack of consensus regarding the outcomes and mechanisms of ABM training.

#### 1.2.2.2 Pre-existing anxiety

In the same way that the reduction of attentional bias towards threat may be dependent upon a pre-existing threat bias, the alleviation of anxiety or anxiety symptoms may only occur (and in fact be necessary) in cases of unhealthy levels of anxiety. A large proportion of ABM studies have therefore selected for participants with clinical or high-level anxiety (e.g. Amir et al., 2011; Amir et al., 2009; Amir et al., 2010; Baert et al., 2010; Boettcher et al., 2012; Carlbring et al., 2012; Hayes et al., 2010; Heeren et al., 2012; Li et al., 2008; Neubauer et al., 2010; Schmidt et al., 2010; Wells et al., 2010). Review articles have identified larger effect sizes for successful ABM outcomes in individuals with high-level or clinical anxiety than for neuro-typical participants (Bar Haim et al., 2007; Beard et al., 2012; Hakamata et al., 2010). Nevertheless, some ABM studies have used non-anxious samples, particularly when experimental designs have involved inducing threat bias by training participants to attend towards

threat stimuli (e.g. Cret et al., 2013; Eldar et al., 2008; Krebs et al., 2010; MacLeod et al., 2007; Suway et al., 2013). The use of a neuro-typical sample still allows the investigation of the relationship between anxiety and attentional bias and how the manipulation of attention bias impacts anxiety.

#### 1.2.2.3 Variability in Methodology

Another proposed explanation for inconsistent results in ABM research is the large variability in stimulus parameters across studies (Hakamata et al., 2010). These include stimulus type, stimulus alignment and positioning, size of stimuli and length of training in terms of number of trials and sessions (see chapter 2 for a full discussion). A number of meta-analyses have examined methodological elements of ABM studies which may be influential in determining the success of ABM at modulating attention bias and symptoms. When looking at the impact of ABM on both attention bias reduction and anxiety, Hakamata et al. (2010) found higher effect sizes for studies using word stimuli than those which used face stimuli in the ABM paradigm. Beard et al. (2012) also found that stimulus type moderated ABM effect on symptoms with greater effect sizes for words compared to pictures. However, for ABM effect on attention bias change, effect sizes were larger for pictures than for words (Beard et al., 2012). Both studies reported larger effect sizes for vertically aligned stimulus pairs than for horizontally aligned stimulus pairs when considering ABM's effect on both attention bias and symptoms. The number of ABM training sessions has also been found to moderate the effect of ABM on attention bias change (Hallion & Rusco., 2011) with more sessions resulting in higher effect sizes for reduction in threat bias (Hakamata et al., 2010). However, there are reports that number of

training sessions does not modulate the impact of ABM on symptoms (Hakamata et al., 2010; Hallion & Rusco, 2011) and meta-analyses have in fact, reported lower effects of ABM training on symptom reduction with a greater number of training sessions (Cristea et al., 2015). Another methodological factor which has been shown to have an impact on how ABM modifies attention bias is experimental setting with laboratory based studies generating larger effect sizes than studies conducted outside of the laboratory (Mogoase et al., 2014).

Research is yet to define the optimal paradigmatic format for ABM. Until there is a better understanding of the contribution of aspects of the ABM design to efficacy, they are a potential source of variability within ABM research. Despite mixed findings, ABM has produced beneficial results in terms of promoting more healthy allocation of attention and reducing anxiety and remains a candidate future treatment for anxiety symptoms (Clarke et al., 2014). Further ABM research is needed to cast light on the mechanisms of ABM training.

## 1.3 Transcranial Electrical Stimulation (TES)

Transcranial electrical stimulation (tES) is a non-invasive form of brain stimulation involving the application of a small current of electricity to selected areas of the cortex via scalp electrodes (Coffman, Clark & Parasuraman, 2014; Kuo & Nitsche, 2012). Forms of stimulation which fall under the tES umbrella term include transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS), transcranial random noise stimulation (tRNS; Bikson, Edwards & Kappenman, 2014) and non-invasive deep brain stimulation via temporally interfering electric fields (TI; Grossman et al., 2017).

Each form of tES is proposed to have a distinct mechanism for achieving a neuromodulatory effect.

### 1.3.1 TDCS

In tDCS a weak electrical current is applied on the scalp via a pair of electrodes, one anodal and one cathodal (Kuo & Nitsche, 2012). The current passes into the cortex and modulates cortical excitability in a polarity dependent manner. Anodal stimulation is generally used to increase cortical excitability in a targeted cortical region and cathodal stimulation to inhibit neuronal excitability within a given area (Javadi & Cheng, 2013). TDCS during training has been demonstrated to improve performance in tasks of visual perception (Bolognini et al., 2010), motor control (Nitsche & Paulus, 2000) and memory and language (Cattaneo, Pisoni & Papagno, 2011) and this improvement has been seen to be present at up to 12 months after training (Dockery, 2009). For example, Ditye, Jacobson, Walsh and Lavidor (2012) reported that anodal tDCS over the right inferior frontal gyrus (rIFG), alongside cognitive training on four consecutive days generated better behavioural inhibition during a Stop Signal task versus training alone. Anodal tDCS over the left posterior temporoparietal junction has been shown to produce better learning when applied during training for novel item naming over multiple days than sham tDCS (Meinzer et al., 2014). Parietal anodal tDCS (atDCS) or cathodal tDCS (ctDCS) was delivered whilst participants learned the magnitude of artificial numerical symbols (Cohen Kadosh et al., 2010). A double dissociation was demonstrated related to polarity with anodal tDCS resulting in enhanced learning which was maintained at 6 months after training and ctDCS leading to deficient learning (Cohen Kadosh et

al., 2010). Despite the wealth of findings in support of the modulation of cognitive training with tDCS, the methodology (or at least its implementation) has its detractors. Medina and Cason (2017), for example, reported that studies which have researched tDCS-modulated cognitive training have been underpowered. Meta-analyses have also reported that tDCS induced little or no enhancement of cortical excitability (as measured by motor evoked potentials; Horvath et al., 2015a) and had no significant effect on the outcomes of working memory or language training (Horvath et al., 2015b). However, the latter of these meta-analyses has been criticised for inconsistent data selection and statistical approach (Price & Hamilton, 2015).

The mechanisms of tDCS are not fully understood but it is thought that by inducing a shift in resting membrane potential, anodal stimulation brings neurons closer to their point of excitation thus rendering them more receptive to incoming excitatory input (Brunoni et al., 2012). The longer term (learning) effects induced by tDCS are proposed to be NMDA receptor dependent (Stagg & Nitsche, 2011). When pre- and post- synaptic neurons are activated simultaneously, excitation of the already depolarised post-synaptic cell relieves NMDA receptors of magnesium allowing for the influx of calcium (Luscher & Malenka, 2012). This triggers a cascade which ultimately leads to an increase in synaptic efficiency via protein synthesis in a process which shares features of long-term potentiation (LTP) and long-term depression (LTD; Cohen Kadosh, 2010). The effects of tDCS are also proposed to be dependent on GABA receptors with anodal tDCS linked to reductions in GABA concentration (Antonenko et al., 2017; Bachtiar et al., 2015; Kim et al., 2014) and cathodal

tDCS associated with reductions in both GABA and glutamate concentration (Cohen Kadosh et al., 2010; Kim et al., 2014).

Nitsche and Paulus (2000) first demonstrated that tDCS increased cortical excitability more than 15 years ago. Since then tDCS has been used frequently in studies and has been shown to be easy and safe to use with no reported seizures (Harvey et al., 2015). Arguably, the main advantage of using tDCS over other forms of neuro-stimulation is that it is the most well-known form of TES (Cohen Kadosh, 2013) with a success and safety profile over a greater amount of time than other forms of tES. A key disadvantage of tDCS is that active stimulation can be uncomfortable, likely due to shunting of current at the scalp (Zaghi et al., 2009). The sensations most regularly reported are itching and tingling of the skin (Ambrus et al., 2010). In addition to potentially rendering the receipt of tDCS unpleasant this might also make it difficult to maintain experimental blinds (Zaghi et al., 2009). It is possible that in the future this problem might be mitigated by altering the size or montage of electrodes (Fertonani et al., 2015).

#### 1.3.1.1 The impact of tDCS on functional connectivity

In addition to modulating neural activity in the brain structures below stimulating electrodes, tES is known to induce changes across functionally connected regions (e.g. Keeser et al., 2011, Krause et al., 2017, Meinzer et al., 2012, Pena-Gomez et al., 2012, Polania et al., 2012, Weber et al., 2014, Wörsching et al., 2017). Studies which have examined the effect of tES on functional connectivity have used fMRI to measure changes in cerebral blood

flow across distributed brain networks following tDCS relative to before tDCS. In a study by Keeser et al., 2011 participants received active or sham tDCS (anode over left DLPFC, cathode right supra-orbital) for 20 minutes at 2mA. FMRI data were taken prior to and following tDCS and independent component analysis was used to assess the effects of active versus sham stimulation on resting state network connectivity. The study examined connectivity within the default mode network (DMN) and the fronto-parietal network (FPN). The DMN incorporates brain areas spanning the medial prefrontal cortices, medial and lateral parietal cortices and lateral temporal cortices (Garrison, 2015). It is engaged during rest and is associated with self-referential thinking, autobiographical memory and theory of mind (Pena-Gomez et al., 2012). The fronto-parietal network includes structures in the frontal and parietal cortices of the brain and is engaged during cognitive tasks requiring attentional control (Hossain, Myers and Kozma, 2018). Active, as compared to sham tDCS resulted in increased coactivation in regions of the default mode network and fronto-parietal network close to the site of stimulation and at more distal sites during rest. There was also coactivation of the site of stimulation (left DLPFC) and the left middle frontal gyrus and of the left DLPFC and left superior frontal gyrus (Keeser et al., 2011). Pena-Gomez et al. (2012) also investigated the effects of tDCS on resting-state DMN activation and on the anticorrelated network (AN) which has a strong negative correlation with DMN. There was stronger spatial and temporal activation correlation between areas of AN (including superior parietal cortex and lateral prefrontal cortex) and reduced activation synchrony for areas of the DMN following active tDCS relative to sham tDCS. The authors suggested that these effects might be implicated in improvements in cognitive function following tES (Pena-Gomez et al., 2012). Attempts to understand how tDCS affects functional connectivity and

how might modulate cognitive functioning have been made (e.g. Meinzer et al., 2012, Weber et al., 2013, Krause et al., 2017). In one such study fMRI data were recorded during anodal or sham tDCS of the left inferior frontal gyrus (IFG) applied at rest or during performance of a semantic word retrieval task (Meinzer et al., 2012). Superior word-recall in the task during anodal tDCS relative to sham tDCS corresponded with reduced activity in the left ventral IFG. During task performance with concurrent anodal tDCS there was increased functional connectivity between the left IFG and the anterior insula, the bilateral inferior parietal cortices and also between the FPC and the left middle temporal gyrus. Seed-based analysis of fMRI data showed activation correlations within the pre-supplementary motor area (pre-SMA), SMA, basal ganglia and cerebellum. Krause et al. (2017) recorded local field potential, multi-unit activity and single neuron activity at multiple sites in the macaque neocortex during active and sham tDCS of the right PFC at rest and during active and sham tDCS delivered concurrently with a foraging paradigm. There was a reduction in low-frequency local field potential coherence and an increase in high frequency coherence between distant sites (across prefrontal cortex and inferotemporal electrodes). Increased gamma frequency coherence was associated with faster task acquisition (Krause et al., 2017).

These results indicate a relationship between tES induced changes in functional connectivity and task performance modulations and suggest that tDCS produces neuromodulatory effects which are not restricted to the site of stimulation but which are distributed across functional brain networks. This neural mechanism may be implicated in tES-induced behavioural changes.

### 1.3.2 TACS

TACS delivers an alternating current into the cortex at a specific frequency. These bands represent the frequencies at which oscillations naturally occur within neural circuits (Cohen Kadosh, 2013). TACS is thought to influence this intrinsic oscillatory activity (Wach et al., 2013) by synchronising or 'entraining' cortical oscillations (Antal & Paulus, 2013) or by adapting the amplitude of given frequencies (Hermann et al., 2013). A frequency-task interaction is proposed with neural oscillations of a specific frequency linked with specific cognitive functions. Enhancing oscillations at a given frequency therefore, should have a predictable effect on behaviour (Brem et al., 2014). TACS delivered at 10Hz for 7 minutes over the motor cortex has been seen to improve implicit motor learning (Antal et al., 2008). Additionally, theta tACS delivered parietally for 15 minutes can improve working memory storage capacity (Jausovec & Jausovec, 2014; Jausovec, Jausovec & Pahor, 2014). To date, the application of TACS in the theta and gamma ranges has been shown promising effects in terms of improving working memory capacity (Jausovec et al., 2014; Meiron & Lavidor, 2014) and enhancing fluid intelligence (Pahor & Jausovec; Santarnecchi et al., 2013). However, recently, Braun, Sokoliuk and Hanslmayr (2017) reported that tACS delivered in the beta range failed to ameliorate performance in a verbal and non-verbal material encoding task and did not modulate cortical excitability. The authors questioned the effectiveness of tACS to entrain beta oscillations and modulate cognition (Braun et al., 2017). Using tACS researchers have recently begun to explore the cortical rhythms which characterise attentional processes and attentional training. By applying tACS at 10hz, 40hz or sham to the right parietal lobe during a spatial cueing task Hopfinger et al.

(2016) discovered that gamma oscillations in the right parietal cortex may support disengagement from task irrelevant stimuli and re-orienting to task relevant stimuli. tACS in the alpha range (10hz) appeared to slow down responses to invalid targets (Hopfinger et al., 2016). The findings suggested a role for parietal gamma and alpha oscillations in visual attention processes. Van Schouwenburg et al. (2017) applied alpha tACS with the electrodes placed at F4 and P4 (10-20 system of electrode placement) simultaneously and in-phase during a spatial attention task. Alpha tACS but not sham tACS had an impact upon visual attentional processes by abolishing a laterality bias (faster responses for targets in the right hemifield; Van Schouwenburg et al.,2017). This supported previous assertions that fronto-parietal alpha cohesion is integral to attentional processing (Sauseng et al., 2005).

An advantage of tACS over tDCS is that it targets neurons which oscillate at a specific frequency within a neural region rather than exciting or inhibiting all neurons within a precise space. It may therefore be less likely to stimulate neurons with competing functions, for example, excitatory and inhibitory neurons (Bestmann et al., 2015). However, because TACS synchronises neurons to a given frequency (Cohen Kadosh, 2012) it may not lend itself to the enhancement of a dynamic neural system.

### 1.3.3 TRNS

TRNS involves the application of an alternating electrical current at random frequencies into the cortex (Fertonani et al., 2011) which can increase cortical excitability for up to an hour after stimulation (Moliadze et al., 2012). The

efficacy of low frequency (0.1-100Hz) tRNS for modulating cortical excitability has been explored (e.g. Terney et al., 2008) but it is high frequency tRNS, delivered at frequencies between 101 and 640Hz (Kuo & Nitsche, 2012), which has proven most proficient in this regard (e.g. Snowball et al., 2013). In tRNS, bursts of current, at random amplitudes are delivered as samples, usually at a rate of 1280 samples per second (Moliadze et al., 2012). Each sample is normally distributed around a mean of 0mA thus creating the 'noise' associated with transcranial random noise stimulation (Cohen Kadosh, 2013). The mechanisms of tRNS have yet to be elucidated. However, one theory is that tRNS generates small, consistent bursts of neural excitation which trigger the repeated polarisation of sodium channels (Paulus, 2011), bringing neurons closer to their threshold of activation (Fertonani et al., 2011). Another way of explaining the facilitatory effects of tRNS is via the concept of stochastic resonance (Miniussi et al., 2013). Stochastic resonance occurs in a noisy system when random noise is at an optimal level to render certain neurons more sensitive to weak incoming signals (Miniussi et al., 2013). The weak signals are generated during performance of a cognitive task or cognitive training (Miniussi et a., 2013). Thus, the principal of stochastic resonance does not propose that random noise causes neuronal firing per se but that it provides a platform for task-relevant brain activity, pushing naturally sub-threshold signals above their threshold of polarisation (Bestmann et al., 2015).

As well as being responsible for short term modulation of cortical activity, the concurrent application of tRNS and cognitive training is known to elicit long lasting learning enhancements which suggests that the combined methodologies may be capable of inducing neuro-plastic changes (Medeiros et al., 2012). The

consensus regarding the neural mechanisms of these long-term alterations is that, when high-frequency tRNS is applied during performance or learning of a cognitive task the resultant repeated neuronal firing activates NMDA channels, increasing intra-cellular calcium levels (Cohen Kadosh, 2012; Nitsche et al., 2003). This leads to synaptic plasticity of the type observed in long-term potentiation (LTP; Brunoni et al., 2012). However, a study using pharmacological agents to investigate the neuronal effect of tRNS reported that neither the partial NMDA agonist D-cycloserine nor the NMDA antagonist dextromethorphan had any significant effect on tRNS induced neural excitability (Chaieb et al., 2015). This suggests that the lasting effects of tRNS may be independent of NMDA warranting further investigation of these mechanisms.

TRNS is more recent and less commonly used in research than tDCS (Cohen Kadosh, 2013) but has produced some robust findings in terms of its ability to enhance task performance when applied during cognitive training. The application of high frequency tRNS to the dorso-lateral prefrontal cortex (DLPFC) during arithmetic training over 5 consecutive days, increased calculation speed and led to superior 'rote' learning of arithmetic rules compared to sham tRNS (Snowball et al., 2013). This enhanced learning effect was still present after 6 months (Snowball et al., 2013). Elsewhere, high-frequency tRNS over the visual cortex led to better performance in an orientation discrimination task than sham stimulation, anodal tDCS and cathodal tDCS when delivered during training (Fertonani, Pirulli & Miniussi, 2011). In contrast to these findings, Mulquiney et al. (2011) reported that performance in a 2-back task was enhanced following training in working memory tasks with concurrent anodal tDCS above the DLPFC but not following training with high frequency tRNS. Nevertheless, favourable

findings (e.g. Ambrus, Paulus & Antal, 2010; Cappalletti et al., 2013; Fertonani et al., 2011; Snowball et al., 2013) present tRNS as a promising, emerging neuro-modulation technique.

There are advantages to using tRNS over tDCS or TACS as a means of enhancing the effects of training. Firstly, relative to tDCS, tRNS is reported to have a higher cutaneous perception threshold (Ambrus et al., 2010). The use of tRNS therefore results in less discomfort for participants and reduces the detection of experimental condition (Cohen Kadosh, 2013). Secondly, random noise stimulation does not engage the neuronal homeostatic mechanisms associated with direct current stimulation (Miniussi, Harris & Ruzzoli, 2013). During the application of anodal tDCS, neurons may adapt to compensate for continuous excitatory input. In tRNS, the alternating nature of the applied current means that neurons are not subject to a constant electrical field but are subject to repeated sub-threshold stimulations and therefore ionic adjustments are less likely to be made (Fertonani et al., 2011). Another consequence of the direct nature of the electrical current applied in tDCS is that it provides no subtlety if the process of learning involves the differential activation of a network of facilitatory and inhibitory neurons. TRNS involves the generation of samples of positive and negative going current at random frequencies and amplitudes (Cohen Kadosh, 2012). This is a more accurate representation of intrinsic oscillatory activity and therefore perhaps a more appropriate 'overlay' for intrinsic activity. Another purported advantage of tRNS over tDCS is that tRNS current is not direction sensitive (Paulus, 2011). Typically, in tDCS, a positive electrode (anode) is placed over a specific target site of the left or right cortical hemisphere and electrical current flows from this to a negative electrode

(cathode) often mistermed the 'reference' electrode (Biksom, Datta, Rahman & Scaturro, 2010; Horvath, Forte & Carter, 2015). The possibility of ionic changes in the brain area beneath the return electrode therefore cannot be repudiated and it is possible that modulations of a specific cognitive function are not solely attributable to changes in cortical activity in the targeted brain region (Moliadze, Antal & Paulus, 2010). TRNS avoids this complication by means of its operation. Whilst advantageous in the sense that this circumvents the uncertainty associated with unknown effects at the cathode (during anodal stimulation) this also poses a disadvantage where the aim is to stimulate a brain structure in one specific hemisphere. However, this has been attempted resulting in the successful modulation of training. Fertonani et al. (2011) placed the tRNS active electrode above V1 and the return electrode on the right arm (Fertonani et al. 2011). It is postulated that increasing the distance between the active and return electrode reduces the magnitude and duration of tDCS and tRNS induced after-effects (Moliadze et al., 2010). Focality might be achieved by reducing the size of the active electrode and increasing the size of the return electrode thus increasing the density of the current delivered by the active electrode relative to the return (e.g. Fertonani et al. 2011). Another way to potentially target a specific brain region would be to apply high definition tES (HD tES; Villamar et al., 2013). In HD tES smaller (high definition) gel-based electrodes, approximately 25mm$^2$ in size (Kuo et al., 2013) are applied to the scalp inside plastic electrode holders (e.g. Kuo et al., 2013) or are inserted into an EEG cap (e.g. Villamar et al., 2013). The smaller electrode increases the current density at the target stimulation site (Roy et al., 2014). Focality is achieved by surrounding a single 'active' electrode with multiple return electrodes between which the return current is split (Edwards et al., 2015). In

the 4 x 1 high definition montage, a single stimulating electrode is positioned above the target brain region with 4 return electrodes positioned concentrically around it (e.g. Edwards et al., 2013; Kuo et al., 2014; Roy et al., 2014; Villamar et al., 2013). In addition to increasing focality of stimulation, this montage should reduce the extent to which neural activity is altered below the return electrode as the current density which, with the traditional montage would have been allocated to one electrode, is divided between four electrodes (Roy et al., 2014). To date, the high definition approach to tES has been examined predominantly with tDCS (e.g. Edwards et al., 2013; Kuo et al., 2013; Roy et al., 2014). Research which has modelled current flow following HD tDCS revealed that, using this method current is relatively confined to the stimulated area (Edwards et al., 2013). Few studies have examined the potential use of a HD montage with tRNS. Heise et al. (2016) compared cortico-spinal activity change following 10 minutes of low-frequency tRNS with the stimulating electrode above M1 and the return electrode above the right supra-orbital area with high definition low-frequency tRNS of M1 using a ring montage. There was an increase in corticospinal activity during and following HD tRNS but not following tRNS with the conventional montage. Additionally, participants reported less discomfort with the high definition montage than with the 2-electrode montage (Heise et al., 2016). These findings suggest that it may be possible to apply more focal tRNS in the future to target a specific brain region.

## 1.4 Neural Structures and Processes Associated with ABM (Selecting Site of Stimulation)

Studies which have employed tES as a means of influencing cognitive processes, have applied stimulation above a well-defined neural region, often the area of the brain most associated with performance or modulation of that function (Cohen Kadosh, 2012). In selecting a site of stimulation for enhancing the effects of ABM therefore it is necessary to identify which neural regions are most associated with the cognitive processes implicated in ABM training. This is a complex assay however, given that attentional processes recruit a frontoparietal network including areas such as the anterior insula, ventral pre-frontal cortex (vPFC), dorsolateral pre-frontal cortex (DLFPC), the temporoparietal junction (TPJ; Corbetta and Shulman, 2002) and the pulvinar (the largest thalamic nucleus (Pessoa and Adophs, 2010). Connectivity between these areas as well as activation of these structures in isolation is known to impact the efficacy of ABM training. For example, Hakamata et al., 2018 reported a greater increase in connectivity between the pulvinar and transverse gyrus, along the temporoparietal junction following active ABM towards positive stimuli than following control ABM. This increase in connectivity was correlated with decrease in self-report 'fatigability', a subscale of the temperament and anxiety inventory. Furthermore, there was a reduction in connectivity between post-central gyrus and ventral frontoparietal network for the active ABM group which was not associated with anxiety modulation (Hakamata et al., 2018).

Although the attention network recruits an array of neural structures, cognitive models of attentional processes emphasise the role of two specific brain

regions. They propose that selective attention is dependent on the influence of bottom-up salience driven mechanisms involving the amygdala and top-down attentional control mechanisms associated with the frontal cortices (Bishop, 2007). As such fMRI studies of ABM have focused on these areas. One study by Britton et al. (2015) reported differences in amygdala activation between participants who had received ABM training across 4 weeks and participants who had received control ABM for the same period of time. Bilateral amygdala activation for the threat bias contrast (reaction time for threat incongruent targets > reaction time for threat congruent targets) was increased for participants who had received active ABM group and reduced for control ABM group. This result was complicated however by between group differences in amygdala activation prior to ABM training. Greater reduction in social anxiety symptoms following ABM training was associated with greater baseline left amygdala activation, irrespective of ABM group and with allocation to the active ABM group (Britton et al., 2015). Another study reported that ABM effects were mediated by neuroplastic changes in the extended amygdala-PFC network (Aday and Carlson, 2017). For participants who received mobile phone-based ABM training towards neutral stimuli across 6 weeks, ABM was associated with reduced grey matter volume in the basal forebrain/extended amygdala and the medial PFC. These grey matter volume reductions were positivity correlated with reductions in threat-related bias. There were also increases in grey matter volume in the ventral PFC and dorso-lateral PFC however these changes were not associated with behavioural outcomes (Aday and Carlson, 2017). These studies support a role for the amygdala in ABM processes and also emphasise the importance of functional connectivity between nodes of the attention network including the amygdala and the PFC. Despite being strongly implicated in ABM

processes, as a subcortical structure the amygdala is not a viable target for transcranial electrical stimulation. Therefore, studies with the aim of modulating the amygdala-prefrontal pathway have done so via tES to the PFC (e.g. Ironside et al., 2018, Mungee et al., 2014).

The prefrontal cortex (PFC) is considered central to cognitive control (Miller, 2000). As such, tES research with the aim of modulating cognitive outcomes has typically attempted to manipulate cortical excitability in this location. One of the most commonly selected sites of stimulation of the PFC is the dorsolateral prefrontal cortex (DLPFC). Located in the upper region of the PFC, the DLPFC has functional projections to the thalamus (Wagner et al., 2013), basal ganglia (Scharmuller et al., 2014), hippocampus (Meyer-Lindenberg et al., 2005) and areas of the parietal (Hughes et al., 2014) and occipital lobes (Kundu et al., 2015). Anodal tDCS above the left DLPFC during training has enhanced learning in memory (e.g. Javadi & Cheng, 2013), attentional control (Vanderhasselt et al., 2013; Wolkenstein et al., 2013) and executive planning (Dockery et al., 2009) relative to sham tDCS or cathodal tDCS.

Another sub-region of the PFC with notable links to executive function (Hampshire et al., 2010) is the inferior frontal gyrus (IFG). The IFG is in the lower region of the PFC and has connections to areas of the motor cortex (Greenlee, 2004), parietal cortex (Asplund et al., 2010) and sub-cortical regions (Cieslik et al., 2015). Anodal tDCS above the left IFG has produced training enhancements in face-name association learning (Pisoni et al., 2014) and picture naming (Holland et al., 2011) relative to sham tDCS of the same location. tDCS

above the right IFG has elicited augmentation of response inhibition in a stop signal task (Ditye et al., 2012; Jabobson et al., 2011).

### 1.4.1 Cognitive Functions associated with ABM - Attentional control

ABM is predominantly a form of attention training and a widely supported view of ABM is that it achieves its intended results via the enhancement of attentional control (Heeren, Coussement & McNally, 2016). Efficient attentional control involves the ability to focus attention upon task relevant stimuli and to ignore non-relevant information (Eysenck & Derakshan, 2011). Basanovic et al., 2017 demonstrated that individuals with greater inhibition and selection capacity (two facets of attentional control) exhibited greater magnitude of change in attention bias in the trained direction (Basanovic et al., 2017). From a neural perspective, attentional control is associated with a fronto-subcortical/basal ganglia network (Verbruggen et al., 2008) in which the frontal cortices exert attentional control over a system responsible for valence evaluation (Heeren, de Raedt, Kosta & Phillippot, 2013). FMRI studies using a variety of paradigms to explore the neural correlates of attentional control have consistently implicated the inferior frontal cortex in this process (e.g. Asplund et al., 2010; Hopfinger, Buonocore & Mangun, 2000; Milham et al., 2001) or have focused their analysis on the IFG (e.g. Erickson et al., 2005). However, attention bias research which is predicated on the principal that biased attention towards threatening material reflects inefficient top-down attentional control of salience evaluation mechanisms, has tended to emphasise the role of the DLPFC (e.g. Peers, Simons & Lawrence, 2013; Telzer et al., 2008). Some researchers have emphasised that attentional control is not just a function of the frontal cortices but that it is

modulated by a network of neural regions across the frontal, temporal, parietal and occipital cortices (Scolari et al., 2015). Within this network, the posterior parietal cortex (PPC) has also been identified as having an important role in spatial attention shifting (Shomstein, 2012).

#### 1.4.1.1 Attentional control and the IFG

Milham et al., (2001) acquired BOLD data from participants while they performed a Stroop task in which participants were required to name the colour in which a word was printed in some trials but not in others. Relative to no-response trials, when a response was required, activation of the right inferior frontal gyrus was observed. This suggests that the rIFG is activated when responding to stimuli but not while passively observing them. Also, increased BOLD signal in the left inferior frontal gyrus was noted during incongruent trials (when the colour of the word contrasted its semantic meaning). It is possible that this activation represented the inhibition of distracting information. fMRI evidence appears to stress the role of the inferior frontal gyrus in attentional control. However, there is an indication that the nature of its involvement may be hemisphere specific with the left inferior frontal gyrus dedicated to the resolution of attentional conflict and the right inferior frontal gyrus devoted to goal-directed attention (Milham et al., 2001).

#### 1.4.1.2 Attentional Control and the DLPFC

Evidence from fMRI studies has indicated that biased attention towards threatening stimuli is related to excessive activation of the amygdala reflecting an enhanced emotional response towards the detection of threat related stimuli

(see Etkin & Wager, 2007 for review). It has also been associated with impoverished functioning of the PFC which may be suggestive of inefficient attentional control and hence impaired down-regulation of limbic system response (e.g. Taylor et al., 2013). One study with a cohort of children and adolescents revealed that more pronounced activity in the DLPFC in response to threatening faces was positively associated with greater attentional bias towards threat (Telzer et al., 2008). Elevated activity in the DLPFC has been observed in threat trials for participants with higher attentional control scores (Peers et al., 2013). In a cohort of highly socially anxious participants fMRI data was recorded during attentional bias assessment which took place before and after ABM training towards neutral faces (Taylor et al., 2013). There was reduced activation in the limbic system following ABM training and increased activity in the PFC in response to threatening faces (Taylor et al., 2013).

#### 1.4.1.3 Attentional Control and the PPC

Human lesion studies have demonstrated that lesions of the PPC are associated with spatial attention deficits. Syndromes such as visual neglect and extinction are characterised by a difficulty in detecting stimuli in the visual hemifield contralateral to parietal lesion (Nachev & Hussain, 2006). Studies have shown that TMS-induced virtual lesions produce similar effects. In research by Hilgetag et al, (2001), inhibitory TMS was applied to P3 or P4 prior to a rectangle detection task. Participants were to detect small rectangles presented for 40 milliseconds in the periphery of the visual field. The detection of visual stimuli was impaired for stimuli in the contralateral hemifield with greater impairment for right hemisphere TMS (left hemifield stimuli). Attention to stimuli in

ipsilateral hemifield improved relative to normal level demonstrating that visual stimulus detection efficiency is modulated by the balance between left and right PPC activation (Hilgetag et al., 2001). The ability to direct visual attention is therefore impaired by damage to or downregulation of the PPC.

A wealth of neuroimaging studies have implicated the PPC in attentional control processes (e.g. Beauchamp et al., 2001; Esterman et al., 2009; Hopfinger et al., 2000; Ikkai and Curtis, 2007; Thakral & Slotnick, 2009). Hopfinger et al. (2000) collected event-related fMRI data during a cued spatial cueing task. When participants responded to a cue directing attentional to a specific locus of the visual display, activation of the superior frontal, inferior parietal and superior-temporal cortices was observed (Hopfinger et al., 2000). These results highlighted the involvement of the parietal cortex in top-down attentional control. A further study recorded fMRI data during tasks requiring sustained focused attention (Thakral & Slotnick, 2009). The intraparietal sulcus, right middle frontal gyrus and right superior temporal gyrus were consistently activated during sustained attention (Thakral & Slotnick, 2009). This suggests that, as part of an attentional network, the PPC may be involved in maintaining attentional focus on specific stimuli as well as shifting attention to task-relevant stimuli.

#### 1.4.1.4 TES studies of Attentional Control - DLPFC

Research which has explored the enhancement of working memory training with tES have highlighted the role of attentional control in effective performance of these tasks. One study reported that participants receiving 20 minutes of 2mA anodal tDCS above the left DLPFC whilst training in a 3-back task provided

significantly faster and more accurate responses in a subsequent paced, auditory serial addition task (PASAT) than participants who had received sham tDCS (Gill, Shah-Basak & Hamilton, 2015). This effect was not seen when participants had trained in a 1-back task whilst receiving atDCS or sham tDCS. This suggests that extent to which attentional control can be enhanced via atDCS of the DLPFC may be dependent upon the attentional demand of the training task.

Attentional control is often conceptually divided into two functional processes: 'inhibition' of aversive or task-irrelevant stimuli and 'shifting' of attention to relevant stimuli (Miyake et al., 2000; Posner & Rothbart, 1998, Eysenck & Derakshan, 2011). These processes are two key mechanisms of ABM which requires the inhibition of aversive stimuli and engagement to non-threatening stimuli (Heeren et al., 2015a). Inhibitory control is often afforded a special role in the modification of attentional processes with ABM literature emphasising the importance of inhibiting the engagement of threat related stimuli in reducing threat bias (Bar-Haim et al., 2010; Beard et al., 2012; Heeren, Lievens & Philippot, 2011).

#### 1.4.1.5 TES studies of Attentional Control - PPC

Recently, research using tES has investigated whether modulation of activity in the PPC impacts upon behavioural outcomes in visual attention tasks (Bolognini et al., 2010; Dueker et al., 2017). In one study, participants received anodal or sham tDCS of the left or right PPC during an auditory and visual exploration task (Bolognini et al., 2010). Anodal tDCS of the right but not of the left PPC led to greater increases in training-related improvement in a visual exploration task relative to sham tDCS. Anodal tDCS of the right PPC was also associated with

improvement in covert visual spatial orienting. Furthermore, right hemisphere stimulation *without* concurrent training was also associated with an improvement in visual exploration task performance. The authors suggested that the modulation of right PPC activity had an effect on top-down visual processing capacity and that this modulation (in the absence of training) impacted upon visual attentional control capacity (Bolognini et al., 2010).

### 1.4.2 Cognitive Functions associated with ABM - Inhibitory control

Inhibitory control refers to the stopping of a response which has been initiated (Jacobson et al., 2011) or which is overlearned or conditioned (Stramaccia et al., 2015). It has been suggested that the right IFG (rIFG) has functional specificity for inhibitory control (Aron, Robbins & Poldrack, 2004; Rubia et al., 2003) and this notion has received empirical support from brain imaging studies (Aron et al.,2004; Menon et al., 2001, Rubia et al., 2003). However, previous studies have also implicated the DLPFC (Krug & Carter; 2012) and the pre-SMA (Floden & Stuss, 2006) in inhibitory control function. Two main paradigms have been used to evaluate inhibitory control of motor response. The first is the go/go-no task in which participants are instructed to respond to a stimulus if it is in one format (e.g. in a particular colour) and to withhold response if it is in a different format (Georgiou & Essau, 2011). The second is the stop signal task (SST) in which participants must respond to a stimulus unless it is proceeded by a signal (audio or visual) which indicates that the participant must refrain from responding (Aron et al., 2003). Inhibitory control also describes the control of pre-potent attentional and/or emotional responses (Meule, 2017). This might be resisting distractor interference from emotionally salient stimuli (Friedman &

Miyake, 2004). One example of a task which assesses attentional inhibitory control is the emotional Stroop task in which participants must supress the processing of emotionally valenced words in order to report the colour in which they are presented (Wingenfeld et al., 2009).

#### 1.4.2.1 Inhibitory Control and the IFG

Evidence in support of an IFG influence in inhibitory control is ubiquitous. FMRI studies have reported an increase in BOLD signal in rIFG during response inhibition tasks at the point that stopping is required (Aron et al.,2004; Menon et al., 2001, Rubia et al., 2003). In Brown et al. (2012), healthy adults performed an emotional Go/No Go task which used aversive and neutral stimuli. Response inhibition in both neutral and aversive trials elicited IFG activation greater than in the simple response baseline (neutral go trials; Brown et al., 2012). Another study scanned participants whilst they underwent a number of inhibitory control tasks including the go/no-go paradigm, the stop signal task and the conventional Stroop task (Cieslik et al., 2015). Throughout these tasks there was consistent activation the inferior frontal gyrus. Using the emotional Stroop task, Mohanty et al. (2005) reported increased activation in both the IFG and the DLPFC when naming the colour of negative words relative to neutral words.

#### 1.4.2.2 Inhibitory control and the DLPFC

In a study by Krug and Carter (2012), participants performed a facial Stroop task in which fearful or neutral faces were presented with the word 'fearful' or 'neutral' visible across the middle of the face image. Participants were required to indicate the facial expression. The researchers reported sustained activation

of the DLPFC when words were incongruent with facial expression (Krug & Carter; 2012). Whilst the researchers highlighted the activity of the DLPFC during trials in which word meaning conflicted with facial expression, their results also indicated that there was enhanced activation of the IFG in these trials (Krug & Carter; 2012).

#### 1.4.2.3 Inhibitory control and the Pre-SMA

A number of accounts of the neural mechanisms sub-serving inhibitory control stemming from ERP source localisation and fMRI studies suggest that these are spread across a network or regions including the DLPFC, IFC, inferior parietal cortex, the basal ganglia and the pre-supplementary motor cortex (pre-SMA; Albert et al., 2013). The pre-SMA forms part of the dorsomedial frontal cortex and is positioned anterior to the primary motor cortex (Juan and Muggleton, 2012). It is an area associated with the inhibition of motor response (Aron and Poldrack, 2006).

Evidence from lesion studies suggests that damage to the pre-SMA is linked with impaired response inhibition (e.g. Floden and Stuss, 2006; see Mostofsky and Simmonds, 2008 for review). Research which has examined or proposed a role for the pre-SMA in response inhibition has often used the stop signal task (SST; e.g. Albert et al,. 2013; Chao et al., 2009; Chen et al., 2009; Coxon et al., 2014; Hsu et al., 2011; Li et al., 2006). A number of these studies have studied pre-SMA activation during the SST using fMRI (e.g. Albert et al., 2013; Chao et al., 2009; Coxon et al., 2014; Li et al., 2006). Albert et al. (2013) reported that participants who responded more quickly in 'go' trials of the SST had greater pre-SMA activation during successful infrequent no-go trials. This suggests that

participants with greater pre-potent response tendency required greater inhibitory resources to inhibit motor response (Albert et al., 2013). A further study reported that participants with shorter stop signal reaction time (an indication of the time taken to elicit the withholding of response, estimated using the distribution of 'go' reaction times and the probability of responding in stop trials) had greater activation in the superior medial frontal cortices (including the pre-SMA) than participants with longer stop signal reaction time). Neuromodulation techniques have also been used to investigate the role of the pre-SMA in response inhibition (e.g. Chen et al., 2009; Hsu et al., 2011). In the study by Chen et al. (2009), inhibitory rTMS to the pre-SMA, to the vertex or no rTMS was applied prior to completion of the stop signal task. Participants who had received rTMS above the pre-SMA showed increased error rates. Specifically, the number of 'stop' trials in which response was withheld was lower for participants who received rTMS of the pre-SMA compared to those who had received rTMS to the vertex and those who had not received rTMS (Chen et al., 2009). When single pulse TMS was applied to the pre-SMA but not when it was applied above the vertex during a stop switch task, inhibition was impaired (Obeso et al., 2013). However, this only occurred when sham continuous theta burst stimulation was applied to the rIFG prior to the task and not when active continuous theta burst stimulation (cTBS) had been applied to the rIFG. This suggests that the effects of single pulse TMS over the pre-SMA were modulated by cTBS. This indicates a functional connectivity between the pre-SMA and rIFG in relation to inhibitory function (Obeso et al., 2013).

#### 1.4.2.4 TES Studies of Inhibitory Control - IFG

In a study by Chambers et al. (2006), low frequency repetitive (inhibitory) TMS to the rIFG resulted in impaired performance in a go-no-go task. In Jacobson et al. (2011) 10 minutes of offline atDCS above the rIFG led to significantly better response inhibition in a stop signal task than sham tDCS, ctDCS or control tDCS over the right angular gyrus. In a further study, after receiving atDCS over the rIFG for 4 consecutive days during training in a stop signal task, participants demonstrated a greater linear improvement in response inhibition across trials relative to those who received training with sham stimulation (Ditye et al., 2012). Leite et al. (2017) examined whether inhibition of prepotent response is lateralised to the rIFG or a function of inter-hemispheric balance between the left and right IFG. Participants received unihemispheric tDCS (anode of $35cm^2$ above the rIFG and a cathode of $100cm^2$ above the lIFG), bihemispheric tDCS (anode of $35cm^2$ above the rIFG and a cathode of $35cm^2$ above the lIFG), or sham tDCS during a proactive control task. In the task, participants indicated the direction in which an arrow was pointing if the arrow was green or indicated the opposite direction is the arrow was red. Accuracy was increased but response time reduced following unihemispheric tDCS but not for bihemispheric or sham tDCS (Leite et al., 2017). This signals that the inhibition of prepotent response is dependent on the interaction between left and right IFG activity (Leite et al., 2017).

### 1.4.2.5 TES Studies of Inhibitory Control - DLPFC

Anodal tDCS of the left DLPFC has been seen to ameliorate attentional inhibition in a Stroop colour-word matching task (Loftus et al., 2015). TDCS was delivered offline however, between two administrations of the Stroop task and not during training for the task (Loftus et al., 2015). In another study, anodal or sham tDCS over the left DLPFC was delivered prior to a Cued Emotional Control Task (Vanderhasselt et al., 2013). Participants received the cue word 'opposite' or 'actual' followed by a sad or happy face image. They then had to press a button corresponding to the actual or opposite emotion (sad or happy) to the face image dependent upon the cue preceding the stimulus. Response times were faster for opposite/happy trials relative to opposite/sad trials for the atDCS group but not the sham tDCS group. The authors suggested that anodal tDCS improved the ability to inhibit a habitual response towards positive relative to negative face images (Vanderhasselt et al., 2013).

### 1.4.2.6 TES Studies of Inhibitory Control - Pre-SMA

Hsu et al. (2011) applied anodal or cathodal tDCS at 1.5mA above pre-SMA for 10 minutes to participants before they completed the stop signal task. The authors reported reduced non-cancelled response rates following anodal tDCS and increased non-cancelled response rated following cathodal tDCS. There were no such effects when participants received tDCS to a control site (the primary motor cortex; M1).

The pre-SMA is associated with the inhibition of pre-potent motor response, potentially via it's links to the basal ganglia which exerts influence over the

primary motor cortex (Juan and Muggleton, 2012) or connection to the subthalamic nucleus and striatum which are associated with behavioural inhibition (Aaron and Poldrack, 2006; Li et al., 2008b). However, there is little evidence of pre-SMA involvement in emotional response inhibition which may be of particular relevance to ABM training. Therefore, it might not be optimal candidate site for active stimulation if the aim is to modulate ABM training effects.

## 1.5 ABM with TES

To my knowledge only a few studies have reported the use of tES delivered alone or concurrently with ABM for manipulating attention bias. In the study reported by Ironside, O'Shea, Cowen and Harmer, (2015) participants received active tDCS for 20 minutes at 2mA or sham tDCS offline (while the participant was at rest and not during training). Active tDCS was delivered using two different montages. Some participants received bilateral tDCS to the DLPFC with the anode placed over the left DLPFC (F3) and cathode over the right DLPFC (F4). Other participants received anodal tDCS with the anode above the left DLPFC and the cathode placed over the right supra-orbital ridge. Stimuli were happy-neutral, neutral-neutral or fearful-neutral face pairs and were presented for 100ms or 1000ms before participants indicated the orientation of a pair of dots which replaced one of the faces. For trials in which stimuli were presented for 100ms there was an effect of tDCS group. Relative to the sham tDCS group participants in the bilateral tDCS group had significantly reduced (smaller) attentional bias towards fearful faces. Whereas participants who received sham

tDCS had an attentional bias towards fearful faces during subsequent attention bias assessment, those in the bilateral tDCS group did not. Participants who received anodal tDCS with the return electrode above the right supra-orbital ridge did not have reduced threat bias relative to the sham group (Ironside et al., 2015). In the study by Ironside et al., (2015), no measure of attention bias was taken before tDCS and vigilance towards threatening faces in the sham tDCS group was used as the baseline measure of bias. Consequently, it is not possible to state with certainty that the disparities in attentional bias between groups arose from stimulation group and not simply the result of baseline differences in bias levels. In order to elucidate differential roles for the left and right DLPFC in attentional processes, Sagliano et al. (2017) delivered tDCS offline following and prior to attention bias assessment using a Modified Posner task. TDCS or sham tDCS was delivered for 15 minutes at 1mA with the anode above the left DLPFC (F3) and the cathode above the right DLPFC (F4) or with the anode above the right DLPFC (F4) and the cathode above the left DLPFC (F3). During attention bias assessment, threatening or non-threatening images were presented before a target for 100ms, 200ms or 500ms. STAI score at baseline (high or low) was used as a between participants factor to examine whether the impact of tDCS stimulation was modulated by STAI score. When stimuli were presented for 200ms, threat bias was revealed for participants who received anodal tDCS of the right DLPFC and cathodal tDCS of the left DLFPC. Participants in this group with low anxiety showed delayed disengagement from threatening stimuli. Participants in this group with high anxiety showed facilitated engagement to threatening stimuli (Sagliano et al., 2017). Heeren et al. (2017) assessed whether anodal tDCS, delivered at 2mA for 25 minutes above the left DLPFC with the cathode on the ipsilateral arm, reduced threat bias in

socially anxious participants. Anodal tDCS or sham tDCS was delivered online (during attention bias assessment). No ABM took place. Attentional bias towards threat was significantly lower in the anodal tDCS group compared to the sham tDCS group. The authors concluded that direct augmentation of activity in the DLFPC facilitated attenuation of bias towards threat related stimuli (Heeren et al., 2017). Another study compared the impact of ABM training towards neutral stimuli (away from threatening stimuli) combined with atDCS, ctDCS or sham tDCS of the left DLPFC on indices of attention bias (Heeren et al., 2015b). Response time data revealed no decrease in attention bias towards threat from pre- to post ABM in any of the conditions. However, eye-tracking revealed that the amount of time that gaze fixated upon threatening faces was reduced after ABM with anodal tDCS but not in the other two tDCS groups (Heeren et al., 2015b). Clarke et al., (2014) reported that both ABM away from and ABM towards threat with anodal tDCS concurrently applied to the DLPFC induced an attention bias in the trained direction which was greater than that attained via ABM with sham tDCS (Clarke et al., 2014).

Each of the above studies comprised only one experimental session. There are mixed findings concerning how the length of ABM training (the number of ABM sessions delivered or the number of trials per session) effects the outcomes of ABM training. Beard et al., (2012) suggested that ABM training over a number of sessions is more effective than single-session ABM training for improving symptomology (Beard et al., 2012). Other meta-analyses have reported that number of sessions was not a significant moderator of the impact of ABM on anxiety (Hakamata et al., 2010; Hallion & Rusco, 2011) but that a greater number of ABM sessions resulted in greater modulation of attention bias

(Hakamata et al., 2010). In contrast an inverse relationship between the length of training and the level of symptom change has been reported in ABM studies (Cristea et al., 2015; Price et al., 2017). Price et al. (2017) reported greater effect on symptoms for shorter training relative to longer training (Price et al., 2017). The moderating influence of number of sessions has not been explored for ABM with tES and so a potential progression from these studies would be to study the impact of ABM with tES across a number of sessions.

Although ABM seeks to target threat related bias with the aim of reducing anxiety, studies using tES to modulate ABM training (Clarke et al., 2014; Heeren et al., 2015b) included no measure of anxiety. It is therefore impossible to know whether threat bias reductions mediated anxiety attenuation. Further investigation is needed to establish whether attentional bias modulations which occur when tES is delivered concurrently with ABM are accompanied by alterations in anxiety level.

## 1.6 Summary

Early cognitive models of anxiety predict that information processing biases play a crucial part in elevated anxiety (e.g. Williams et al., 1988; Mogg & Bradley, 1998). Subsequent research demonstrated that attentional bias towards threat related stimuli is implicated in the development, aetiology and maintenance of anxiety (Bar Haim, 2010). In particular, a high level of anxiety is associated with more rapid engagement to threatening than to neutral information (Rinck & Becker, 2007) and greater difficulty disengaging from threatening material (Fox, Russo & Dutton, 2002). Recent years have seen the emergence of attention bias

modification (ABM), a cognitive training paradigm (often computerised) which reduces or induces attention bias by directing attention away from or towards aversive stimuli (McLeod & Holmes, 2012). Promisingly, ABM represents a new technique for intervening in the formation and consolidation of anxiety. It can produce efficacious results at a sub-clinical level (e.g. Van Bockstaele et al., 2012), and in clinical populations ABM has been reported to attenuate attention bias and to reduce symptoms of general anxiety disorder (e.g. Amir et al., 2009b) and social anxiety disorder (Schmidt et al., 2009).

Transcranial electrical stimulation (TES) is a non-invasive form of brain stimulation involving the application of a small current of electricity to selected areas of the brain via electrodes (Cohen Kadosh, 2013). TES modulates cortical excitability within defined regions of interest (Brunoni et al., 2012). The technique is currently receiving considerable attention in light of its ability to augment performance in cognitive tasks when applied during training (Cohen Kadosh, 2013). ABM represents a form of cognitive training and it is therefore possible that its mechanisms are susceptible to modulation via TES. To date few studies have examined the impact of tES delivered concurrently with ABM training reporting an enhancement of ABM training (Clark et al., 2014; Heeren et al., 2015b). These studies delivered tDCS above the left DLPFC during one session of ABM training. There is therefore the opportunity to explore the use of other forms of tES and to target other sites of stimulation. Additionally, future studies can investigate whether ABM training with tES across a number of days is able to produce superior results to ABM with tES on one occasion.

## 1.7 Research Aims

### 1.7.1 Study 1

The aim of study 1 was to explore whether tES could modulate the impact of ABM training in terms of reducing attentional bias towards threat and reducing anxiety. It was anticipated that ABM training towards neutral face images (active ABM) would prove more effective at reducing both threat bias and anxiety than control ABM. It was further predicted that active online tES would enhance the effects of active ABM only training relative to sham tES.

#### 1.7.1.1 Experiment 1

In experiment 1 participants received high frequency (active) tRNS or sham tRNS to the bilateral IFG for 20 minutes at the beginning of three active or control ABM training sessions. Attention bias was assessed at the beginning of day 1, at the end of day 3 and at a 30 day follow up. State anxiety was measured at the beginning and end of each experimental session. It was predicted that participants receiving active ABM would have reduced threat-related attention bias and anxiety as compared with those receiving control ABM. It was further predicted that these reductions in attention bias and anxiety would be more pronounced in those receiving active tRNS relative to sham tES.

#### 1.7.1.2 Experiment 2

Experiment 2 extended experiment 1 and studies which have reported indistinguishable reductions in anxiety following both ABM training towards neutral stimuli and control ABM training (e.g. Carlbring et al., 2012; Cristea et al., 2015; Carleton et al., 2015; Enock et al., 2015; Heeren et al., 2013; Heeren et al., 2015a; Klumpp & Amir, 2010; McNally, Enock, Tsai & Tousian, 2013). Early proponents of ABM training (e.g. Macleod et al., 2002) suggested that the mechanism of active ABM training is the contingency (more or all targets replacing neutral relative to threatening cues). This seeks to implicitly train the automatic engagement of neutral stimuli and reduce orientation towards threat which contributes to the formation and maintenance of anxiety. However, this mechanism does not explain anxiety reduction following control ABM. One suggestion is that cognitive training, irrespective of the inclusion of contingency, increases attentional control and thus the capacity for attention regulation (Enock et al., 2014; Heeren et al., 2013; Klumpp et al., 2010; Taylor, Cross & Amir, 2015). Experiment 2 replicated experiment 1 except that all participants underwent a simplified version of the ABM training paradigm which was designed to minimise enhancement of attentional control in lieu of active or control ABM. Participants were required to press a single key if a target appeared and to withhold response where there was no target. It was hypothesised that 'no-training' ABM would induce no improvement in attention bias and anxiety relative to the active ABM and control ABM groups of experiment 1 which each had the capacity to augment attentional control. This would support the theory

that attentional control enhancement is the mechanism via which anxiety reduction occurs following ABM training irrespective of training group.

#### 1.7.1.3 Experiment 3

Previous studies have reported successful modulation of ABM using anodal tDCS above the DLPFC (Clarke et al., 2017; Heeren et al., 2015b). This has not been examined across 3 consecutive days however. Previous studies also failed to investigate the impact of ABM with concurrent tDCS on anxiety levels (Clarke et al., 2017; Heeren et al., 2015b). In experiment 3 anodal tDCS replaced active TRNS as the mode of tES and was delivered consecutively with active or control ABM. It was predicted that the experiment would support the findings from Clarke et al. (2014) and Heeren et al. (2015b) that anodal tDCS enhances ABM training towards neutral faces.

### 1.7.2 Study 2

Findings from studies which have used the emotional dot-probe task to measure attentional bias have been mixed (Bantin et al., 2016). Recent work has suggested that the task lacks sensitivity as a measure of attention bias (Sigurjonsdottir et al., 2015). It has been shown to have poor internal consistency and test-retest reliability (Rodebaugh et al., 2016; Schmukle, 2005). Moreover, ABM induced attention bias reduction, as measured using the emotional dot-probe task, has been found not to transfer to other tasks which assess attentional bias (Van Bockstaele et al., 2017). This may be attributable to the poor psychometric properties of the assessment task (Van Bockstaele et al., 2017). Kappenman et al. (2014) reported that reaction time, as assessed by

the modified dot-probe task, did not show any indication of automatic engagement of threat, demonstrated poor internal consistency and was not correlated with trait anxiety. The inconsistency and unreliability reported (Schmukle, 2005) might have less to do with the dot-probe task per se and more to do with its reaction time-based output. Conversely, an event related potential index of attention (the N2PC component) measured using EEG did reveal an initial shift towards threat related stimuli and was internally reliable (Kappenman et al., 2014). ERPs are considered accurate temporal markers of visual spatial attention allocation and stimulus processing (Bar Haim et al., 2005). In study 2 anodal or sham tDCS above the left DLPFC was applied during one session of active ABM training towards neutral stimuli. Attention bias was measured immediately before training and directly afterwards using the modified dot probe task. During assessment EEG recording was taken. The N2PC was isolated as a measure of attention bias in addition to recording reaction times. The aim was to capture a more detailed indication of the impact of anodal tDCS versus sham tDCS with ABM on attention bias than could be provided by reaction time alone. It was hypothesised that there would be greater attenuation of N2pc amplitude to angry faces following ABM with anodal tDCS than following ABM with sham tDCS.

# Chapter 2

**Modulation of Attention Bias Modification using Transcranial Random Noise Stimulation of the Bilateral Inferior Frontal Gyrus.**

**Experiment 1**

## 2.1 Introduction

Attentional bias towards threat-related stimuli is implicated in the development, aetiology and maintenance of anxiety (Amir, Taylor & Donohue, 2011). ABM is a computerised cognitive training task which has been seen to manipulate the direction and magnitude of attentional biases (Bar-Haim, 2010). ABM paradigms which are intended to reduce attentional bias towards threat have also been effective in reducing anxiety (Beard et al., 2012). TES is a form of non-invasive brain stimulation which is known to modulate the effects of cognitive training (Cohen Kadosh, 2013). Since the start of the current project two studies have reported successful modulation of ABM using tES (Clark et al., 2014; Heeren et al., 2015b). However, these studies represent the very early stages of ABM with tES research. tES research is still in its infancy and questions remain regarding which type, electrode montage and stimulation parameters are best suited to the modulation of certain types of cognitive training. Much is to be done in terms of finding the optimal design for ABM and tES as stand-alone methodologies. Yet more is needed to identity the ideal combination of ABM and tES for modulating attentional bias and anxiety. Experiment 1 aimed to investigate the modulation of ABM training using tRNS. ABM and tES procedures have, individually, been subject to enormous variability in methodology. Careful

consideration of the design aspects which have created methodological variance was necessary to inform procedure.

### 2.1.1 ABM Design

Although early studies using the emotional dot-probe task to modify attention bias were promising (e.g. Macleod et al., 2002), recent reports suggest that findings have been variable and have questioned the reliability of the task (Mogg et al., 2017). It has been suggested that this inconsistency of findings is attributable to aspects of the ABM task which have been presented differently between studies (Hakamata et al., 2010).

#### 2.1.1.1 Stimulus Type

The first designs of the modified dot probe task used to modify attentional bias employed negative and positive words as the stimuli (e.g. Macleod et al., 2002) and this design has been replicated since with successful outcomes (e.g. Baert et al., 2010; Chen et al., 2015; Cret et al., 2013). However, a review of ABM research reported larger effect sizes for faces over words (Bar Haim et al., 2010). More recent versions of the emotional dot-probe have typically used face stimuli (e.g. Amir et al., 2011; Boettcher et al., 2012; Carlbring et al., 2012; Eldar et al., 2008; Heeren et al., 2015a; Li et al., 2008; Suway et al., 2013). Browning et al. (2012) suggested that face-based ABM elicits a more emotion-centred response than word-based training. They directly compared the impact of using face stimuli and word stimuli in ABM training and reported a greater decline in depressive symptoms and anxiety symptoms with face-based ABM

compared to word-based ABM, with the effect on anxiety maintained at a 4-week follow-up (Browning et al., 2012). Traditionally, ABM protocols for use in social anxiety have utilised neutral-disgust faces (e.g. Amir et al., 2009b; Boettcher et a., 2012; Carlbring et al., 2012; Heeren et al., 2015a; Klumpp & Amir, 2010). Evidence suggests that individuals with social anxiety rate disgust faces as more negative compared to angry faces (Amir et al., 2010). This is perhaps because disgust faces represent rejection and aversion, constructs which are relevant in social anxiety (Amir et al., 2008). ABM paradigms designed to target generalised anxiety or non-anxious individuals have, however, tended to use angry faces (e.g. Eldar et al., 2008; O'Toole et al., 2012; Suway et al., 2013). Angry faces, which represent potent threat cues, are known to disrupt attention in cases of generalised anxiety and in non-anxious individuals (Monk et al., 2008).

#### 2.1.1.2 Stimulus Alignment and Size

Another source of variability within ABM designs is stimulus orientation. Some researchers have selected vertical alignment of stimuli (e.g. Amir et al., 2009b; Klumpp et al., 2010; Krebs et al., 2010; McNally et al., 2013) whereas others have presented stimuli horizontally (e.g. Heeren et al., 2012; Li et al., 2008; Wells & Beavers, 2010). Meta-analyses have reported larger effect sizes for studies using vertical orientation (Beard et al., 2012; Hakamata et al, 2010). Face stimuli presented horizontally have tended to be larger e.g. 11cm tall by 8cm wide (e.g. Amir et al., 2011); 11cm tall by 7.6cm wide (e.g. Heeren et al., 2012) compared to vertical face stimuli e.g. 3.75cm tall by 5cm wide (e.g. Amir et al., 2008); 4cm tall by 5.3cm wide (e.g. Van Bockstaele et al., 2012). ABM

training is an implicit process which aims to manipulate early, pre-conscious engagement to stimuli (Bar-haim et al., 2010). It could be that larger horizontal stimuli are more easily visually engaged than smaller vertical stimuli and therefore become processed at a conscious, explicit level rather than at an automatic level.

#### 2.1.1.3 Length of Presentation of Stimuli

There is little consensus regarding the optimal length of presentation for stimuli in ABM protocols. ABM training for depressive symptoms has tended to present stimuli for longer durations e.g. 1500ms (Baert et al., 2010), 3000ms (Wells & Beavers, 2010) with successful outcomes. O'Toole et al. (2012) revealed that, for neuro-typical participants who had a pre-existing bias before ABM training, ABM in which face stimuli were presented for 100ms before the onset of the target letter resulted in effective manipulation of attentional bias in the trained direction (towards threat or towards neutral). Nevertheless, the large majority of ABM paradigms for use with anxious or non-anxious individuals have presented stimuli for 500ms (e.g. Amir et al., 2008; Boettcher et al., 2012; Carlbring et al., 2012; Heeren et al., 2015a; Klumpp & Amir, 2010; Li et al., 2008).

#### 2.1.1.4 Length of training

The number of training sessions in ABM protocols is also purported to be influential in research outcomes (Heeren et al., 2015c). This number ranges from 1 (e.g. Amir et al., 2008; Chen et al., 2015; Cret et al., 2013; Klumpp et al., 2010; Macleod et a., 2012) to 15 training sessions (See, Macleod & Bridle.,

2009). In addition, sessions have varied in length (number of trials). For example, as few as 160 trials (e.g. Amir et al., 2008; Klumpp et al., 2010) and as many as 600 trials (Suway et al., 2013) have been included in 1-session studies. Where ABM training has comprised a greater number of training sessions, the sessions have generally been shorter [e.g. 8 sessions of 160 trials (Amir et al., 2009b) and 15 sessions of 192 trials (See et al., 2009)]. Early meta-analyses of ABM studies have reported that a greater number of sessions produces greater effect sizes in terms of post-treatment reduction in attentional bias towards threat (Hakamata et al., 2010) and reduction in symptoms (Beard et al., 2012). However, number of training has also been found not to modulate the impact of ABM on symptoms (Hakamata et al., 2010; Hallion & Rusco, 2011). Recent meta-analyses have, in fact, reported lower effects of ABM training on symptom reduction with a greater number of training sessions (Cristea et al., 2015) or longer training as calculated by number of sessions multiplied by length of sessions (Price et al., 2017). There is, to date, no consensus regarding the optimal number of ABM sessions or session length or whether multi-session ABM is more effective than single session ABM necessitating further research.

### 2.1.2 Transcranial Electrical Stimulation

Chapter 1 includes a comprehensive review of different types of tES and what is known of the benefits and potential challenges of each for modulating cognitive training. There is a wealth of evidence in support of the modulation of cognitive training using tDCS as outlined in chapter 1 and anodal tDCS has been shown to enhance the effects of ABM training towards neutral faces (Clarke et al., 2014; Heeren et al., 2015b). However, tDCS is known to induce discomfort in some

participants including itching and tingling of the skin (Ambrus et al., 2010). This might render the receipt of tDCS unpleasant and studies using tDCS may be subject to higher rates of attrition. TDCS-generated discomfort might also create difficulties in terms of maintaining experimental blinds (Zaghi et al., 2009). TRNS is more recent and less commonly used in research than tDCS (Cohen Kadosh, 2013). However, there is robust evidence that tRNS effectively modulates the effects of cognitive training (e.g. Fertonani, Pirulli & Miniussi, 2011; Snowball et al., 2013). TRNS is reported to have a higher cutaneous perception threshold compared to tDCS (Ambrus et al., 2010). The use of tRNS therefore results in less discomfort for participants and facilitates the maintenance of experimental blinds (Cohen Kadosh, 2013). In addition, tRNS, in which neurons receive repeated sub-threshold stimulations (Fertonani et al., 2011), may not result in engagement of the neuronal homeostatic mechanisms associated with tDCS whereby membrane potentials adapt to accommodate a continuous excitatory or inhibitory input (Miniussi, Harris & Ruzzoli, 2013). TRNS involves the generation of samples of positive and negative going current at random frequencies and amplitudes (Cohen Kadosh, 2012). It may therefore enhance the intrinsic oscillatory activity associated with cognitive training with greater subtlety than tDCS in which excitatory and inhibitory neurons are held within a constant excitatory or inhibitory electrical field. Furthermore, unlike tDCS, tRNS is not direction sensitive (Paulus, 2011). For a full discussion regarding the advantages and disadvantages of tDCS and tRNS see chapter 1.

#### 2.1.2.1 Methodological Considerations in tES Application

##### Stimulation Dose (Safety)

Dosage is determined by the density of the current (which is a factor of current amplitude and electrode size), tES montage (including the positioning of the electrodes; Peterchev et al., 2012; Poreisz et al., 2007) and length of the stimulation period (Brunoni et al., 2012). The recommended dosage safety regimen has been set out through work at the University of Gottingen (e.g. Boggio et al., 2007; Nitsche et al., 2003a), and outlined in Bikson et al. (2009). This protocol stipulates that if current density does not exceed 25.46A/$m^2$ then stimulation can be applied for 20 minutes with little or no sensation and without damage to skin (Bikson et al., 2009). Typically studies which have used transcranial electrical stimulation for neuromodulatory purposes have administered current at a density far below the endorsed stimulation density limit. Electrode size has ranged from 9$cm^2$ (e.g. Cohen Kadosh et al., 2010) to 35$cm^2$ (e.g. Bolognini et al., 2010; Stagg et al., 2011) and stimulation amplitude has been between 0.2mA (e.g. Nitsche & Paulus, 2000) and 2mA (e.g. Cattaneo et al., 2011; Holland et al., 2011). These parameters would result in maximum stimulation density of 1.25A/$m^2$. In studies using tRNS, Fertonani et al. (2011) safely delivered current densities of between .25A/$m^2$ and .6A/$m^2$ for 22 minutes and Snowball et al. (2013) delivered a current density of .4A/$m^2$ for 20 minutes. The use of tES within the recommended density guidelines has not been associated with injury and the most aversive side-effect arising from studies using this protocol is skin irritation beneath the electrode, incidents of which are rare (Dundas et al., 2007; Poreisz et al., 2007).

### 2.1.2.2 The Impact of Stimulation Dose on Cortical Excitability and Behavioural Outcomes

A number of studies have used TMS to measure motor evoked potentials (MEPs), a measure of corticospinal excitability, following the application of tES at different dosages. In a series of experiments Nitsche and Paulus (2000) applied anodal or cathodal tDCS to the motor cortex (return electrode at the contralateral supraorbital ridge) with both electrodes measuring 35cm$^2$. TDCS was applied for between 0 and 5 minutes at intensities ranging from 0.2mA (.0057mA/cm2) to 1mA (.029mA/cm2). At least 3 minutes of tDCS at 1mA or 5 minutes of tDCS at 0.6mA were needed to induce aftereffects. The authors found larger increases in MEP amplitude following tDCS at higher intensities compared to tDCS at lower intensities (Nitsche & Paulus, 2000). Bastani et al. (2013) delivered anodal tDCS for 10 minutes at densities of .013mA/cm$^2$, .029 mA/cm$^2$, .058 mA/cm$^2$ or .083 mA/cm$^2$. Corticospinal excitability was increased compared to baseline following tDCS for all densities. Like Nitsche and Paulus (2000) the relationship between the highest three intensities and corticospinal excitability followed a linear pattern with higher intensities associated with higher corticospinal excitability. However, the lowest density (.013mA/cm$^2$) resulted in MEPs which were greater than those generated for .029 mA/cm$^2$ and .058 mA/cm$^2$. Comparable findings were reported by Jamil et al., (2017). For anodal tDCS, there was a non-linear relationship between current intensity and cortical excitability with the lowest intensity (.5mA) and the highest intensity (2mA) producing greater effects following stimulation than 1mA or 1.5mA. In another study, anodal tDCS at 2mA and cathodal tDCS at 2mA resulted in increased corticospinal activity but cathodal tDCS at 1mA resulted in decreased

corticospinal excitability (Batsikadze et al., 2013). Kidgell et al. (2013) reported equivalent increases in cortical excitability following 10 minutes of anodal tDCS at .8mA, .1mA and 1.2mA. Evidence from MEP studies therefore suggests a complex, non-monotonic relationship between tES application parameters and effect on cortical excitability (Esmaeilpour et al., 2017).

Another way to study the impact of differing tDCS dose regimens is to examine their impact on behavioural outcomes of training where tDCS has been used to modulate the effects of training. Evidence from such investigations has also been varied. A meta-analysis looked at the effect of tDCS parameters in studies on accuracy and reaction time in cognitive tasks for neuropsychiatric and neurotypical participants (Dedoncker et al., 2016). It reported that higher densities and density charge [density x stimulation duration (Bikson, 2009)] were associated with higher task accuracy in neurotypical participants. There was no such finding for neuropsychiatric participants (Dedoncker et al., 2016). Teo et al. (2011) delivered atDCS 1mA, 2mA or sham tDCS of the left DLPFC for 20 minutes during working memory training. Response times were faster for 2mA tDCS compared to the sham tDCS during the last 5 minutes of stimulation but there was no difference between the 1mA and the 2mA groups. In contrast, following 20 minutes of sham, 1mA or 2mA atDCS to the left DLPFC, faster reaction times in the n-back task were observed following 1mA anodal tDCS compared to sham or 2mA anodal tDCS (Hoy et al., 2013). In a study by Nikolin et al. (2018) participants received bifrontal tDCS with the anode above the left DLPFC (F3) and the cathode above the right DLPFC (F4). TDCS was delivered for 15 minutes during the 3-back task at intensities of 2mA (.125mA/$cm^2$), 1mA (.0625mA/$cm^2$), .034mA (.0021mA/$cm^2$), .016mA (.001mA/$cm^2$) or 0mA

(0mA/cm$^2$). EEG data were recorded and the P3 component (positive deflection between 220ms and 420 post stimulus) was calculated as an indication of attention and memory updating (Nikolin et al., 2017). There was no effect of tDCS intensity on task performance. However, P3 was reduced following training with 0mA tDCS and increased following training with 1mA tDCS suggesting that tDCS delivered at 1mA during training was associated with the enhancement of working memory processing. Furthermore, increased working memory accuracy was associated with increased P3 amplitude following tDCS compared to baseline (Nikolin et al., 2017). Similar to the results from studies examining dose dependent effects on cortical excitability, evidence related to behavioural outcomes suggests a non-linear relationship between tES dose and effects. It may therefore not possible to predict neurophysiological and behavioural outcomes by considering tES dosage in isolation. Instead a complex interaction between tES dosage, neural anatomy, and underlying neural state (Esmaeilpour et al., 2017) is indicated. However, studies which have used tES to modulate training have tended to apply current at between 1mA and 2mA (Cohen Kadosh, 2013) using electrodes of between 25cm$^2$ and 35cm$^2$ in size (Turi et al., 2014). Despite suggestions that even higher current densities might be tolerable (Nitsche & Bikson, 2017), this dosage continues to be the gold standard.

### 2.1.3 ABM with tES Studies

Since the start of the present study, two studies have modulated the effects of ABM using tES (Clarke et al., 2014 & Heeren et al., 2015b). Both studies selected the left DLPFC as the site of stimulation and cited its involvement in attentional control processes as the reason for targeting this site (Clarke et al.,

2014 & Heeren et al., 2015b). Clarke et al. (2014) pointed to the role of the DLPFC in the attentional inhibition as a key factor in its selection. When experiment 1 was commenced, neither Clarke et al. (2014) nor Heeren et al. (2015b) had been published and they were therefore not available to inform tES procedure. The DLPFC and IFG were therefore both considered as potential target sites of stimulation for the present experiment.

Although tES studies have demonstrated the enhancement of attentional inhibitory control with tES of the DLPFC and the modulation of attentional control via tES of the PPC, the IFG was selected as the site of stimulation in the current experiment due to evidence from FMRI studies which have focused predominantly on the role of the IFG in both motor and attentional (emotional) inhibitory control. TRNS rather than tDCS was chosen as the form of stimulation as it was felt that it might, from a mechanistic perspective, be suited to facilitation of the cognitive processes involved in ABM training.

### 2.1.4 Aims

The aim the current study was to explore whether tES could enhance the effects of ABM training towards neutral stimuli (and away from angry faces) to produce greater reductions in threat bias and anxiety than ABM training alone. Participants underwent ABM training away from threat or control ABM training on three consecutive days whilst receiving high frequency tRNS or sham tES. It was predicted that participants who received active ABM would have a greater reduction in attentional bias towards threat and a greater diminution of anxiety than those who received control ABM. Given evidence for lasting effects of ABM

(e.g. Amir et al., 2009b) it was expected that these reductions would be maintained at 30-day follow-up assessment. Further it was predicted that in the active ABM group, participants who received active tRNS would demonstrate enhanced reductions in attentional bias towards threat and in anxiety relative to participants who received sham tES. Based on findings that tRNS-enhanced training effects are lasting (e.g. Snowball et al., 2013) maintenance of these effects at follow-up assessment was projected. For the control ABM group, differences between the active and sham tES groups in terms of threat bias and anxiety reduction, were not anticipated.

## 2.2 Method

### 2.2.1 Design

A 2 x 2 x 3 mixed methods design was employed. There were 2 between subjects factors of ABM (active ABM, control ABM) and tES (active tRNS and sham tES).

ABM training with concurrent tES was delivered on 3 consecutive days. A 30-day follow-up was also included to assess longer-term effects. Attention bias was assessed and self-report measures were administered at three principal time points: before ABM training on day 1, following ABM training on day 3 and at a follow-up session on day 30. Between day 3 and day 30 there were no experimental sessions. The within subjects factor was assessment [before training (Assessment 1), after training (Assessment 2), at 30-day follow up (Assessment 3)].

### 2.2.2 Participants

Participants were 88 students from the University of Roehampton (66 female, mean age = 20.99 years, *SD* = 3.70, range = 18 to 41). All participants were right-handed and had normal or corrected to normal vision. Four participants did not attend their 30-day follow-up appointment and therefore their data was not included in the analysis. This left 84 participants (61 female, mean age = 21.14 years, *SD* = 3.76, range = 18 to 41) whose data were analysed.

The number of participants recruited was based on previous studies using tES to modulate cognitive functioning e.g. Ditye et al. (2012), Fertonani, Pirulli & Miniussi, (2011) and Snowball et al. (2013). Participants were divided across two ABM groups (active ABM, control ABM) and within each ABM group there were two tES groups (active tRNS, sham tES). This resulted in four sub-groups (active ABM with active tRNS, active ABM with sham tES, control ABM with active tRNS and control ABM with sham tES). The number of participants per sub-group was 21.

Participants were recruited for the study via posters which included the experimenter's email address and on the university's online booking system for research participation. Participants who expressed an interest in taking part were emailed the tES safety screen (Appendix 5) adapted from the transcranial magnetic stimulation adult safety screen (TASS) questionnaire (Keel et al., 2000). This was to exclude anyone with an existing neurological condition or metal implants which might affect, or who might be affected by the tES

procedure. Participants were asked to reply to the email indicating whether they answered 'yes' to any of the questions on the screening form. To ensure consistent cerebral lateralization amongst participants, only right-handed individuals were selected for the study. Participants were therefore also asked to confirm that they were right handed in their email reply. Participants who did not answer 'yes' to any of the tES screen questions and who indicated that they were right handed were invited to participate in the study.

Allocation to ABM group was single blinded and allocation to tES group was double blinded. See section 2.2.5 (Procedure) for details.

### 2.2.3 Ethics

The study was approved by the University of Roehampton ethics committee (approval code PSYC 14/ 116; see Appendix 1). Written informed consent was provided by all participants before participation (Appendix 3). Participants were compensated for their participation with course credits. Participants who did not require course credits as they were not part of the University of Roehampton undergraduate psychology program were paid £20 for attending the three days and follow-up.

### 2.2.4 Materials

#### 2.2.4.1 Measures

State and trait anxiety scale (Appendix 7)

The state and trait anxiety inventory (STAI: Spielberger et al., 1983) is a widely used measure comprising a state anxiety and trait anxiety sub-scale (Quigley et al., 2012). Each sub-scale contains 20 questions rated on a Likert scale from 1 to 4. Higher scores indicate higher levels of anxiety (Rossi & Pourtois, 2012). The STAI was not designed as a diagnostic tool for the categorisation of individuals as high or low in anxiety and therefore its manual does not provide an indication of what scores might suggest high or low anxiety. It does however stipulate that the normative mean state anxiety scores for university students under stressful circumstances (e.g. an exam) are 54.99 for males and 60.51 for females (Spielberger et al., 1983). Internal consistency for the STAI is high with a median alpha of .87 for the state anxiety scale and .89 for the trait anxiety scale (Spielberger et al., 1983).

Attentional Control Scale (Appendix 8)

The Attentional Control Scale (Derryberry & Reed, 2002) has 20 items each scored on a Likert scale from 1 and 4 with higher scores indicating higher attention control. The questionnaire comprises 2 subscales which are proposed to assess attentional focusing and attentional shifting (Olafsson et al., 2011). The scale has been shown to have strong internal consistency ($a$ = .88) and to

correlate strongly with measures of positive emotionality e.g. extroversion ($r$ = .40) and is negatively associated with indices of negative emotionality e.g. trait anxiety ($r$ = -.55; Derryberry & Reed, 2002).

Fear of Negative Evaluation scale (Appendix 9)

The Fear of Negative Evaluation (FNE: Watson & Friend, 1969) scale measures social anxiety. It has 30 items which are responded to with "true" or "false". Internal reliability is reported to have a Cronbach alpha of .94 to .98 and a test-retest reliability of .78 to .94 (Watson & Friend, 1969).

Centre for Epidemiological Studies Depression scale (Appendix 10)

The Centre for Epidemiological Studies Depression scale is a 20 item self-report questionnaire used to measure depressive symptoms in the general population (Radloff, 1977). Participants are required to answer questions regarding their feelings or behaviours, selecting from 4 time-related responses ranging between "Rarely or none of the time (less than 1 day)" and "Most or all of the time (5-7 days)". Higher scores indicate a higher level of depression. A score of 16 or above is indicative of depression (Radloff et al., 1977). Internal consistency for the general population sample was reported as .85 and the alpha for psychiatric patients was $\alpha$ = .9. Test-retest reliability over a 2 to 8-week period ranged from $r$ = 0.51 and $r$ = .67 (Radloff et al., 1977).

TES intensity scale (from Meinzer et al., 2014; Appendix 11)

Participants were asked to rate on a scale of 1 to 5 with 1 signifying 'none' and 5 being 'very intense' the extent to which they experienced headache, neck pain, aching scalp, tickling, itching, burning, skin irritation, tiredness, loss of concentration and mood swings.

Experimental Condition Questionnaire (Appendix 12)

Participants were asked to indicate whether they believed they had been allocated to the real ABM or control ABM group and whether they believed they were in the active tRNS or sham tES group.

#### 2.2.4.2 Stimuli

The experiment was programmed using E-Prime software (Schneider, Eschman & Zuccolotto, 2002). Face images were from the NimStim Face Stimulus set (Tottenham et al., 2009). Photographs of 16 different individuals were selected (8 female and 8 male). A pair of photographs of each actor was used, one with an angry expression and one with a neutral expression.

Two photographs of the same individual were presented simultaneously in their neutral-angry pairs and were aligned vertically. Each face image subtended a visual angle of 3.44$^{o}$ by 4.58$^{o}$. The angle between the fixation point and the centre of each image was 4$^{o}$. Photographs were centred horizontally. The photographs were trimmed to remove the white background.

#### 2.2.4.3 Attention Bias Assessment

Attention bias was assessed via a dot-probe paradigm which had been modified to measure attention bias using socially relevant stimuli (MacLeod, Mathews & Tata, 1986). At the beginning of each trial, a fixation cross appeared in the middle of the screen for 500ms followed by two faces of the same identity, one neutral and one threatening for 500ms. The faces disappeared and a target letter (p or q) appeared in the position of one of the faces until the participant responded by pressing the p or q on the computer keyboard or until 2000ms elapsed. Participants were asked to use the same finger of each hand (index finger or middle finger) to press the two keys. Participants were instructed to respond to the target letter as quickly and accurately as possible. The target letter replaced the neutral cue in 50% of trials. Attention bias assessment comprised 2 blocks of 96 trials. Figure 2.1 illustrates an example trial.


*Figure 2.1.* Paradigm used for attention bias assessment and ABM training. During attention bias assessment the probe replaced the neutral cue in 50% of trials. During ABM training, the probe replaced the neutral cue in 95% of trials.

Face identity, target letter (q or p) and target location (top or bottom) were randomised. Each face identity had an equal probability of being presented as did each target letter. There was an equal chance of a target letter appearing in each of the target locations.

#### 2.2.4.4 Attention Bias Modification

The paradigm used for ABM training was the same as that employed during attention bias assessment with the exception that the target letter appeared in the position of the neutral probe in 95% of trials. In the control ABM group, the target letter replaced the neutral face 50% of the time and the angry face 50% of the time (as per ABM assessment). In the absence of the contingency, it was

considered that attention was not being directed toward a cue of particular valence and therefore no training was taking place. Active ABM or control ABM lasted approximately 30 minutes and consisted of 6 blocks of 96 trials with a short break between each block.

#### 2.2.4.5 tES

Participants received either active tRNS or sham tES. TRNS was administered through a DC-Stimulator Plus (neuroConn©). Two electrodes with an area of 5cm x 7cm (35cm$^2$), each placed inside a saline soaked sponge were attached to the scalp and held in place using a rubber headband. The anodal electrode was positioned over the right inferior frontal gyrus (rIFG) which was identified as the intersection between the line joining T4 and Fz and the line joining F8 and Cz based on the 10-20 EEG system (Ditye et al., 2012; see Appendix 18). The cathode was placed over the left IFG, symmetrical to the anode. A current consisting of high frequency (100-640Hz) random noise was generated at a sample rate of 1280 per second and applied at 1500μA (-750 μA to 750 μA). This was normally distributed around a mean of 0. Stimulation lasted for 20 minutes at the beginning of a 30-minute ABM training period. The current was ramped up and down for 20 seconds at the beginning and end of active stimulation. Conditions for sham tES matched those for active tRNS except that the hfTRNS current was ramped up for 20 seconds and then stopped.

### 2.2.5 Procedure

As part of the screening process for the study, participants completed a tES safety screening form and the Edinburgh Handedness Inventory (Oldfield, 1971; Appendix 6). Participants were invited to participate if they met the safety criteria outlined in the safety form and if they were right handed. At the start of day 1, participants were allocated to either active ABM or control ABM. The first 44 participants were allocated to active ABM and the second 44 participants allocated to control ABM. Allocation to tES group was randomised and double blind. A list was provided to the experimenter which contained 5-digit codes to generate either active tRNS or sham tES. These were taken from the NeuroConn DC-Stimulator Plus manual. Twenty codes relating to each stimulation group had been selected and randomised within one list by a member of the experimenter's supervisory team. One stimulation code was allocated to each participant and the same code was used for that participant on each of the 3 days of training. The first participant to commence the study was allocated the first code on the list. Each time a new participant attended the study they were allocated the next code on the list. Once all 40 codes had been allocated, the experimenter began again at the beginning of the list.

The study procedure is outlined in figure 2.2. On day 1, all participants completed the ACS, FNE, CES-D and STAI. Following this, with the computer monitor at approximately 50cm from the participant and the keyboard within effortless reach, participants commenced the attention bias assessment lasting approximately 10 minutes. Participants were then fitted with the tES montage. The experimenter began stimulation by keying the 5-digit code into the tES

machine. Participants received active tRNS or sham tES for 20 minutes at the beginning of a 30-minute active ABM or control ABM training period. Participants then completed the SAS.

On day 2 of the study, participants completed the State Anxiety Scale (SAS) of the STAI. They then completed 30 minutes (6 blocks x 96 trials) of active ABM or control ABM with active tRNS or sham tES for the first 20 minutes. Following this, participants again completed the SAS.

On day 3, participants completed the SAS and then 6 blocks of active ABM or control ABM with 20 minutes of active or sham tES from the beginning. At the end of the 6 blocks, participants completed 2 blocks of ABM assessment. These 2 blocks continued from the 6 training blocks in order that the training and assessment blocks would appear part of the same task and participants would remain unaware of the transition from training to assessment. Participants then completed the SAS and tES intensity questionnaire. The researcher then made an appointment with the participant for their follow-up appointment.

At 30-day follow-up participants were administered the SAS. They then completed 2 x 96 block trials of attention bias assessment. This was followed by the SAS, ACS and experimental condition questionnaire. Participants were then allocated their credits for taking part and debriefed (see Appendix 17 for example debrief form).

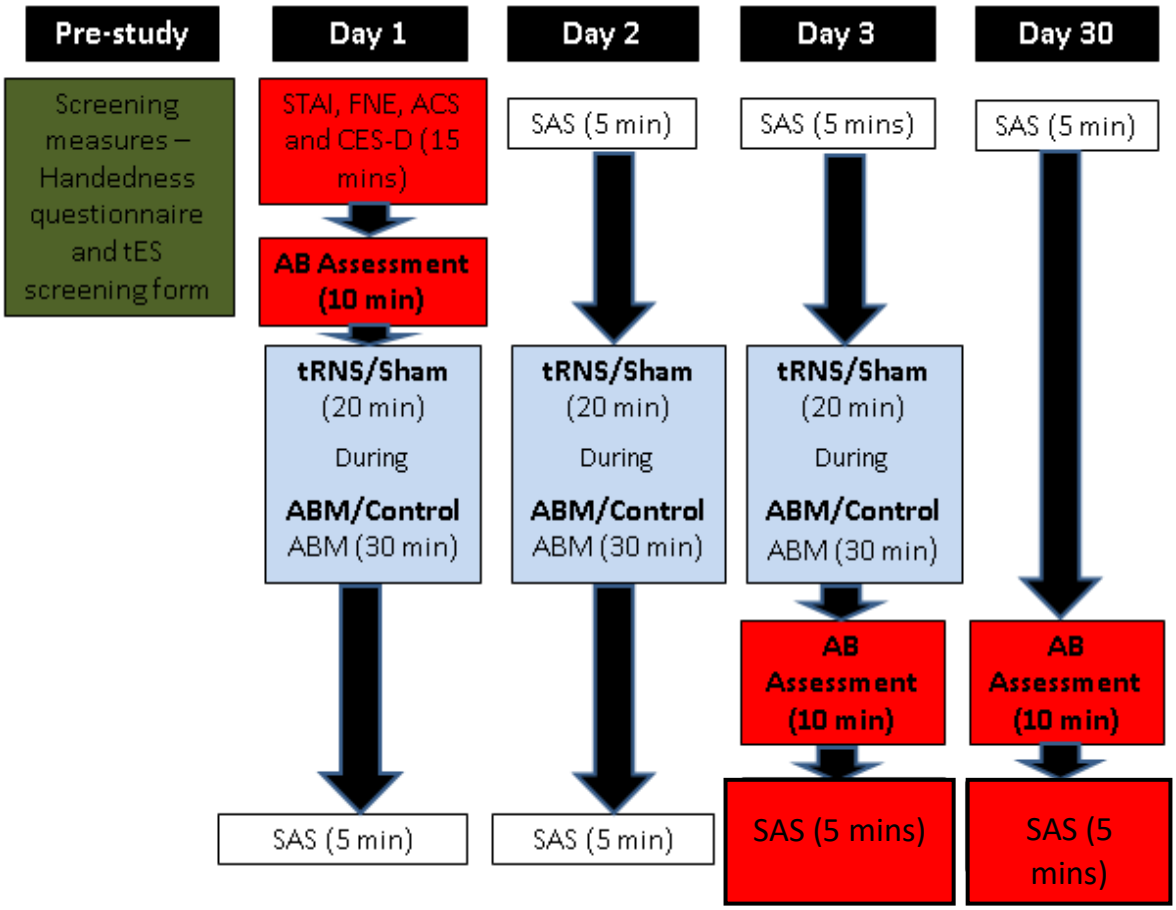



Figure 2.2: Experimental procedure by day

### 2.2.6 Data Preparation

Prior to analysis, Data from inaccurate trials were removed. Mean accuracy across attention bias assessments was 94.54% (*SD* = .047). Reaction times below 200ms as well as outlying reaction times which were more than 2.5 standard deviations from each participant's mean reaction time were excluded as per Brown et al. (2014). This led to the rejection of a further 1.69% of the total number of trials. This was in order to remove the effect of outlying data upon analysis and to preclude responses which may have been generated before the onset of the stimulus or delayed by an attentional distraction. Attentional bias was calculated by subtracting the mean response time to threatening faces from

mean response time to neutral faces for each participant. Greater bias towards threatening faces compared to neutral faces was therefore represented by a positive score.

### 2.2.7 Data Analysis

Data Analysis was performed using IBM SPSS Statistics, Version 22. The main analysis assessing the effect of ABM training (active or control) and tES condition (active tRNS or sham tES) on attention bias and on state anxiety was performed using ANOVAs with ABM and tES as the between participants factors and assessment session as the within participants factor. ANCOVAs were also conducted with ABM and tES as the between participants factors, assessment session as the within participants factor and pre-existing attention bias, pre-existing trait anxiety and pre-existing attentional control as covariates. This allowed examination of the effects of ABM on attention bias and anxiety whilst controlling for each of the 'pre-existing' variables.

Significance

Throughout the present thesis, results are considered significant for $p < .05$. Results are considered marginally significant for $p =/< .058$ and approaching significance for $p > .058$ and $< .07$.

Bonferroni Correction

For all analyses in the present thesis the Bonferroni Correction has been applied to adjust for multiple comparisons. Rather than calculating and reporting an adjusted α level, the p value obtained from each relevant analysis output has been multiplied by the number of comparisons conducted. Therefore, the significance level (α) remains at $p < .05$ throughout. The adjustment applied will be indicated as follows: "significant if number of tests conducted*$p < .05$". For example, if three comparisons have been conducted, reporting of the output will be followed with (Bonferroni adjusted for multiple comparisons; significant if $3*p < .05$).

### 2.2.8 Baseline Characteristics

Table 2.1 shows for each experimental group the mean and standard deviation score at baseline for each self-report measure across groups.

Table: 2.1

*Mean (SD) TAS, ACS, CES-D and FNE score for each ABM/tES group*

| | Active ABM/Active tRNS | | Active ABM/Sham tES | | Control ABM/Active tRNS | | Control ABM/Sham tES | |
|---|---|---|---|---|---|---|---|---|
| | M | SD | M | SD | M | SD | M | SD |
| STAI-trait | 39.48 | 9.69 | 43.10 | 12.92 | 39.65 | 13.12 | 44.19 | 11.67 |
| ACS | 50.76 | 6.50 | 47.57 | 7.88 | 50.90 | 6.84 | 46.52 | 9.48 |
| CES-D | 14.57 | 12.11 | 17.10 | 13.97 | 15.25 | 13.12 | 17.43 | 13.54 |
| FNE | 11.19 | 6.42 | 12.71 | 8.78 | 10.75 | 6.92 | 12.95 | 7.51 |

### 2.2.8.1 State and Trait Anxiety across Experimental Groups by Gender

Table 2. 2 shows the mean and standard deviation state anxiety and trait anxiety scores at baseline (before ABM training on day 1).

Table 2.2:

*Baseline mean (standard deviation) state and trait anxiety scores across experimental groups for females and males*

| | | Active ABM | | Control ABM | |
|---|---|---|---|---|---|
| | | Active tRNS | Sham tES | Active tRNS | Sham tES |
| N | | 15 | 16 | 14 | 17 |
| Females | State Anxiety | 33.40 (10.51) | 32.81 (8.46) | 31.00 (9.85)* | 35.35 (14.31) |
| | Trait Anxiety | 40.53 (10.14) | 42.94 (14.15) | 40.14 (10.98) | 45.24 (12.13) |
| N | | 6 | 5 | 7 | 4 |
| Males | State Anxiety | 33.33 (13.02) | 37.40 (6.66) | 33.14 (8.67) | 26.75 (3.86) |
| | Trait Anxiety | 36.83 (8.73) | 43.60 (9.10) | 40.14 (17.33) | 39.75 (9.54) |

* $p < .05$

State anxiety mean and standard deviation scores reported for a normative sample of undergraduate students are mean = 36.47 (*SD* = 10.02) for males and mean = 38.76 (*SD* = 11.95) for females (Spielberger, 1983). One sample t-tests (results Bonferroni adjusted for multiple comparisons significant if 4*p < .05) revealed that for females who received control ABM with active tRNS, baseline state anxiety score (*M* = 31.00, *SD* = 9.85) was significantly lower than the mean normative score (*M* = 38.76, *SD* = 11.95), $t(13) = 2.95$, $p = .04$. For females who received active ABM with sham tES, baseline state anxiety (*M* = 32.81, *SD* = 8.46)

was marginally significantly lower than the mean normative score (*M* = 38.76, *SD* = 11.95), *t*(15) = 2.81, *p* = .052. For females in the active ABM with active tRNS and control ABM with sham tES groupss baseline state anxiety score did not differ significantly from the normative mean (*t*s < 1.98, *ps* > .27). For males in all groups, baseline state anxiety did not differ significantly from the normative mean state anxiety score for males (*t*s < 5.03, *ps* > .06).

There was no significant difference between baseline trait anxiety across groups. A 2 x 2 ANOVA revealed no effect of ABM or tES group and no significant interaction between these (*Fs* < 2.18, *ps* > .14). The normative mean of trait anxiety reported for a sample of undergraduate students is 40.40 (*SD* = 10.15) for females and 38.30 (*SD* = 9.18) for males (Spielberger, 1983). One sample t-tests (results Bonferroni adjusted for multiple comparisons; significant if 4*p < .05) revealed that for females in all groups, baseline trait anxiety did not differ significantly from the normative mean (*t*s < 1.64, *ps* > .48). For males in all groups, baseline trait anxiety did not differ significantly from the normative mean (*t*s < 1.30, *ps* > 1.05).

#### 2.2.8.2 Correlations Between State Anxiety Scores

Data from each administration of the state anxiety scale of the STAI (i.e. start of day 1, end of day 1, start of day 2, end of day 2, start of day 3, end of day 3, start of day 30, end of day 30) were subject to a Pearson Product Moment Correlation analysis with SAS data from each of the other assessments. All correlations were significant (all *r*s > .40, all *p*s < .001). The normative test-retest reliability r values reported by Spielberger (1983) for college students,

with a test-retest interval of 20 days were .54 for males and .27 for females. Our results suggest strong test-retest reliability and consistency within the state anxiety data.

### 2.2.8.3 Correlations Between State Anxiety and Trait Anxiety

Trait anxiety describes susceptibility to anxiety which is relatively enduring. Differing levels of trait anxiety render individuals more or less likely to respond to perceived threatening situations with elevations in their state anxiety (Spielberger et al., 1983). The correlations between state and trait anxiety reported by Spielberger et al. (1983) in the STAI manual were .65 for males and .59 for females for college students. As demonstrated in table 2.3, baseline trait anxiety in our sample correlated significantly with state anxiety at each assessment.

Table 2.3:

*Bivariate correlations between baseline trait anxiety scale and state anxiety scale (SAS) scores at assessments 1, 2 and 3*

| | SAS Assessment 1 | SAS Assessment 2 | SAS Assessment 3 |
|---|---|---|---|
| Baseline TAS Score | **.598**** | **.602**** | **.532**** |

** < .001

### 2.2.8.4 Correlations Between Self-Report Measures at Baseline

Baseline scores from questionnaires assessing trait characteristics were subject to a Pearson Product Moment correlational analysis (see table 2.4).

Table 2.4:

*Bivariate correlations for trait anxiety scale (TAS), attentional control scale (ACS), Centre for Epidemiological Studies depression questionnaire (CES-D) and fear of negative evaluation scale (FNE) scores at baseline.*

| | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| 1. Trait Anxiety | 1.00 | | | |
| 2. Attentional Control | **-.515**** | 1.00 | | |
| 3. Depression | **.387**** | **-.274*** | 1.00 | . |
| 4. Fear Negative Evaluation | **.679**** | **-.381**** | **.219*** | 1.00 |

** $p < .001$

* $p < 0.05$

Baseline scores across all questionnaires were significantly correlated (all *r*s > .22, *p*s < .046) suggesting that participants reported consistently across measures. As expected, the Attentional Control Scale correlated negatively with the indices of negative emotionality (TAS, CES-D and FNE).

## 2.3 Results

### 2.3.1 Analyses of Variance Across all Participants

#### 2.3.1.1 Attention Bias (All Participants)

A 2 x 2 x 3 mixed ANOVA was conducted on the attention bias data with the 2 between subjects factors of ABM (active ABM, control ABM) and tES (active tRNS, sham tES) and a within subjects factor of assessment (assessment 1, assessment 2, assessment 3).

For attention bias there was a main effect of assessment which approached significance $F(2,160) = 2.75$, $p = .067$, ($\eta_p^2 = .034$; *observed power* = .54). This indicated a change in mean attention bias across assessment sessions. Paired samples t-tests (change in attention bias between assessments 1 and 2, 1 and 3 and assessments 2 and 3) examined this effect. There was no significant change in attentional bias across assessments (all *ts* < 2.26, *ps* > .08; Bonferroni corrected; significant if 3*p < .05). There were no further main effects or interactions (*Fs* < 1.28, *ps* > .26).

Figure 2.3 depicts the change in attention bias over assessments for each experimental group (ABM/active tRNS, ABM/Sham tES, Control ABM/active tRNS, Control ABM, Sham tES) along with the change in mean attention bias for all participants. Positive values represent threat bias and negative values represent neutral bias.

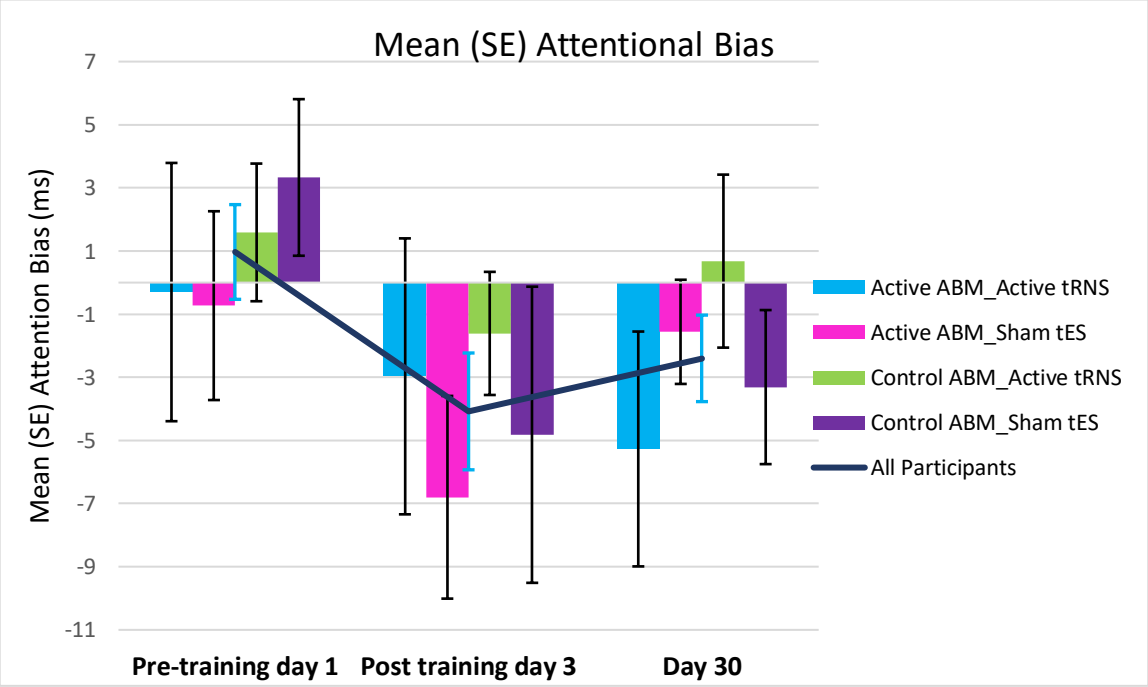


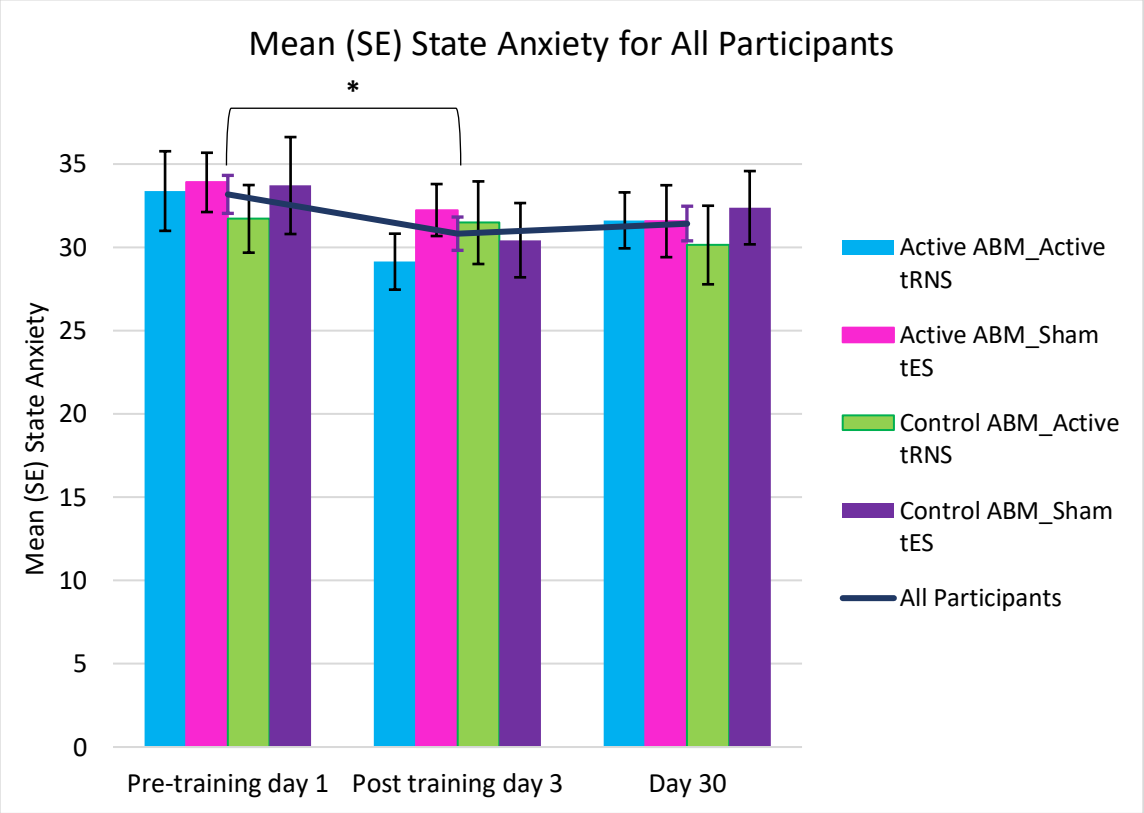

*Figure 2.3*. Mean (SE) attention bias across assessments for each ABM/tES group and for all participants

#### 2.3.1.2 State Anxiety (All Participants)

Replicating the threat bias ANOVA above, a 2 x 2 x 3 mixed ANOVA was conducted on state anxiety data with the two between subjects factors of ABM (active ABM, control ABM) and tES (active tRNS, sham tES) and a within subjects factor of assessment (assessment 1, assessment 2, assessment 3).

This revealed a trend towards a main effect of assessment, $F(1.73,138.04) = 2.99$, $p = .061$, ($\eta_p^2 = .04$; *observed power* = .56; Greenhouse Geisser correction applied). This suggested a change in state anxiety across assessment sessions but the change was independent of ABM or tES group. Paired samples t-tests (change in state anxiety between assessments 1 and 2, 1 and 3 and assessments 2 and 3) examined change in state anxiety across assessments. All results were Bonferroni corrected for multiple comparisons (significant if 3*p < .05). These revealed a difference in state anxiety between assessment 1 and assessment 2, $t(83) = 2.89$, $p = .01$. At assessment 1 participants reported greater state anxiety ($M$ =33.18, $SD$ = 10.46) compared to assessment 2 ($M$ = 30.82, $SD$ = 9.17). The change in state anxiety from assessment 1 to assessment 3 was non-significant ($t$ = 1.53, $p$ = .39) as was the change in state anxiety level from assessment 2 to assessment 3 ($t$ = .61, $p$ = 1.63). There were no other significant main effects or interactions (all $F$s < 1.53, $p$s >.22).

Figure 2.4 shows mean state anxiety levels across assessments by ABM/tES group and for all participants




* $p < .05$

*Figure* 2.4. Mean (SE) state anxiety levels across assessments for each ABM/tES group and for all participants

#### 2.3.1.3 State Anxiety (All Participants) From Start and End of Each Experimental Day

Unlike threat bias and other self-report measures, state anxiety measures were taken for each day of bias modification training at the start of the experimental session and at the end of the experimental session and at the day 30 follow-up at the beginning and end of the session.

To further explore changes in state anxiety across sessions, a 2 x 2 x 2 x 4 mixed ANOVA was conducted on the state anxiety data with the 2 between subjects

factors of ABM (active ABM, control ABM) and tES(active tRNS, sham tES) and 2 within subjects factors of time (start of session, end of session) and day (Day 1, Day 2, Day 3, Day 30). There was a main effect of time, $F(1,80) = 10.03$, $p = .002$, ($\eta_p^2 = .11$; *observed power* = .88). participants reported greater state anxiety at the start of the session ($M$ =32.05, $SD$ = 9.63) compared to at the end of the session ($M$ =30.92, $SD$ = 9.00). No other main or interaction effects were observed (All $Fs < 1.67$ $ps > .18$).

Figure 2.5 gives mean and standard error state anxiety scores for the beginning and end of each experimental session, for each ABM/tES group and across all participants.

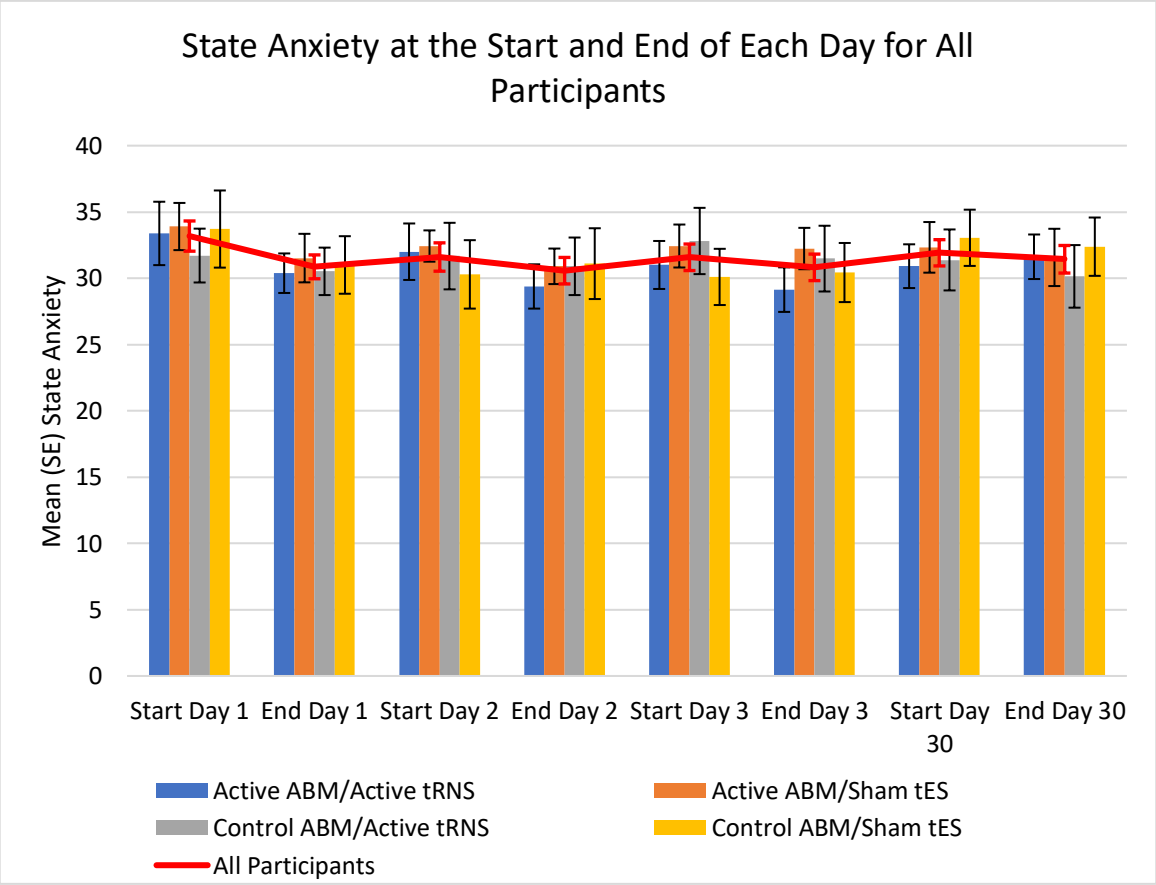



*Figure 2.5*. Mean (SE) state anxiety at the start and end of each experimental day for each ABM/tES group and for all participants

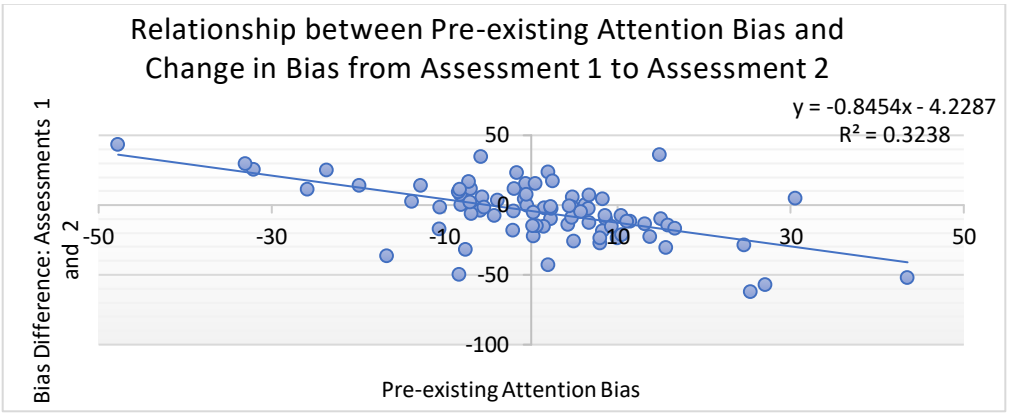
## 2.3.2 Analyses of Covariance with Pre-existing Attention Bias as a covariate

### 2.3.2.1 Attention Bias (Pre-existing Attention Bias as Covariate)

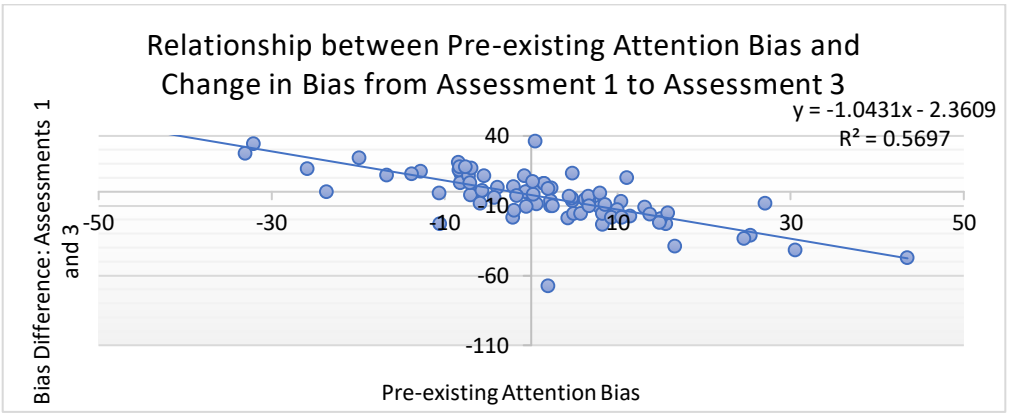
A 2 x 2 x 3 omnibus ANCOVA was conducted on attention bias data with the 2 between subjects factors of ABM (active ABM, control ABM) and tES (active tRNS, sham tES), the within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and pre-existing attention bias as a covariate. The interaction between assessment and pre-existing attention bias was significant, $F(1.62,128.06) = 33.98$, $p < .001$, ($\eta_p^2 = .30$; *observed power* = 1.00). Pearson Product Moment Correlational analyses were conducted to examine the relationship between pre-existing attention bias and: change in attention bias between assessments 1 and 2; change in attention bias between assessments 1 and 3; change in attention bias between assessments 2 and 3. Change in attention bias was calculated by subtracting attention bias score at the earlier assessment from attention bias score at the later assessment e.g. attention bias at assessment 2 – attention bias at assessment 1. A positive score represented an increase in attention bias and a negative score represented a reduction in attention bias. Pre-existing attention bias was moderately to strongly, negatively correlated with change in attention bias between assessment 1 and assessment 2, $r(83) = -.57$, $p < .001$ and was strongly, negatively correlated with the change in attention bias from assessment 1 to assessment 3, $r(83) = -.76$, $p < .001$. There was no significant correlation between pre-existing attention bias and change in attention bias from assessment 2 to assessment 3 ($r = -.14$, $p =$

.21). Figure 2.6 shows the relationship between pre-existing attention bias and difference in attention bias between assessments 1 and 2, assessments 1 and 3 and assessments 1 and 3. This shows that greater attentional bias towards threat at baseline was associated with a greater reduction in threat bias following ABM relative to before ABM training.

a)




b)




c)

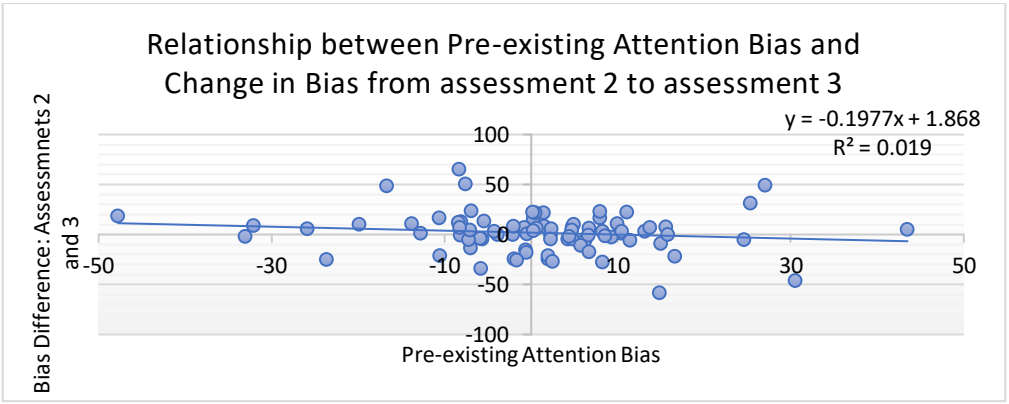



*Figure 2.6*. The relationship between pre-existing attention bias and a) change in attention bias (AB) between assessments 1 and 2, b) change in AB between assessments 1 and 3 and c) change in AB between assessments 2 and 3 across experiment 1. For pre-existing attention bias, positive scores indicate attention bias towards threat and negative scores indicate attention bias towards neutral. For difference scores, positive values represent increase in threat bias and negative scores represent increase in neutral bias (reduction in threat bias).

The main effect of pre-existing attention bias was also significant, $F(1,79) = 37.23$, $p < .001$, ($\eta_p^2 = .32$; *observed power* = 1.00). Pre-existing attention bias was significantly, moderately to strongly and positively correlated with mean attention bias, $r(83) = .57$, $p < .001$ (see figure 2.7).

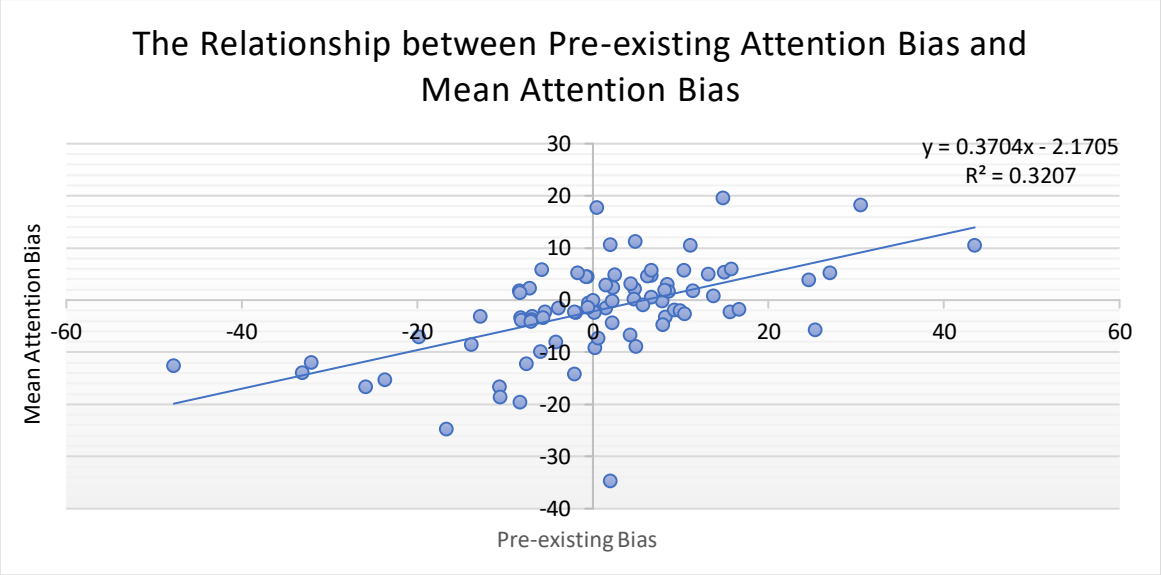



*Figure 2.7*. The relationship between pre-existing attention bias and mean attention bias across experiment 1. Positive values represent attention bias towards threat and negative values represent attention bias towards neutral stimuli.

There were no further significant main or interaction effects ($F$s < 2.65, $p$s > .09).

### 2.3.2.2 State Anxiety (Pre-existing Attention Bias as Covariate)

A 2 x 2 x 3 omnibus ANCOVA was conducted on the state anxiety data with the 2 between subjects factors of ABM (active ABM, control ABM) and tES (active tRNS, sham tES), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and pre-existing attention bias as a covariate. The main effect of

assessment was marginally significant, $F(1.73,136.31) = 2.97$, $p = .062$, ($\eta_p^2 = .04$; *observed power* = 0.57). This effect was investigated in section 2.3.1.2. A reduction in state anxiety at assessment 2 relative to assessment 1 was revealed. There was no change in state anxiety between assessments 1 and 3 and assessments 2 and 3. There were no further significant main or interaction effects ($F$s < 1.51, $p$s > .23).

#### 2.3.2.3 State Anxiety at Start and End of Each Experimental Day (Pre-existing Attention Bias as Covariate)

A 2 x 2 x 4 x 2 omnibus ANCOVA was conducted on the state anxiety data with the 2 between subjects factors of ABM (active ABM, control ABM) and tES (active tRNS, sham tES) and a within subjects factors of day (day 1, day 2, day 3, day 30) and time (start of session, end of session) and pre-existing attention bias as a covariate. This revealed a main effect of time, $F(1,79) = 9.77$, $p = .002$, ($\eta p^2 = .11$; *observed power* = .87; Greenhouse Geisser corrected). This effect was discussed in section 2.3.1.3. There were no further main effects or interaction effects ($F$s < 1.78, $p$s > .16).

### 2.3.3 Analyses of Covariance with Pre-existing Trait Anxiety as a Covariate

#### 2.3.3.1 Attention Bias (Pre-existing Trait Anxiety as Covariate)

A 2 x 2 x 3 ANCOVA was conducted on the attention bias data with the 2 between subjects factors of ABM (active ABM, control ABM) and tES (active tRNS,

sham tES) and a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and pre-existing trait anxiety as a covariate. There were no significant main or interaction effects (*F*s < 1.38, *p*s > .24).

#### 2.3.3.2 State Anxiety (Pre-existing Trait Anxiety as Covariate)

The above ANCOVA was repeated on state anxiety data with pre-existing trait anxiety at a covariate. The main effect of pre-existing trait anxiety was significant, $F(1,79) = 70.29$, $p < .001$, ($\eta_p^2 = .47$; *observed power* = 1.00). Mean state anxiety was highly, positively correlated with pre-existing trait anxiety, $r(84) = .69$, $p < .001$ (see figure 2.8).

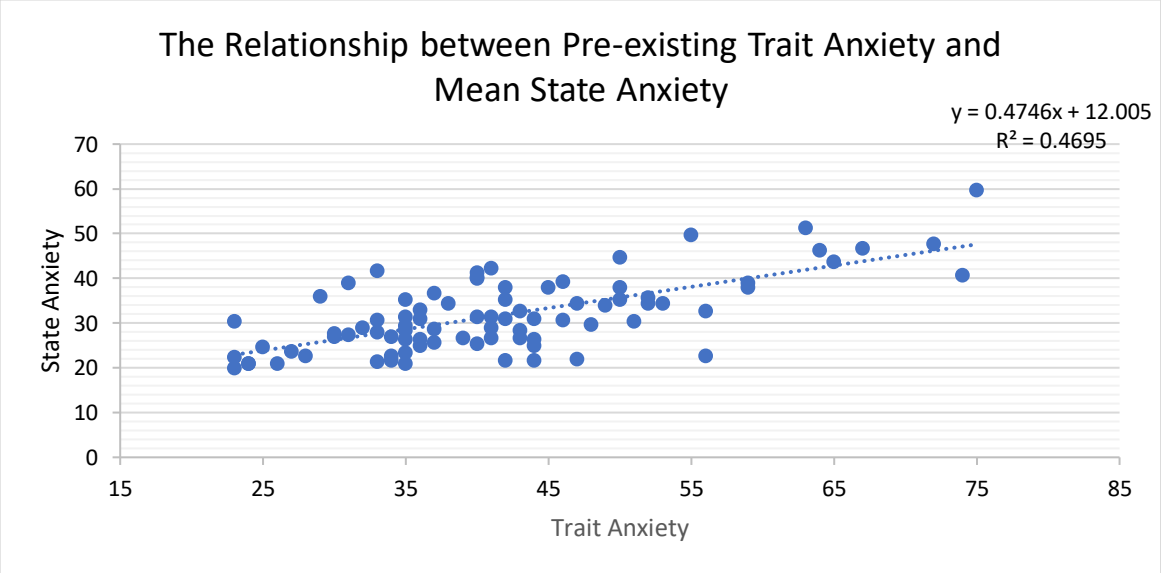



*Figure 2.8*. The relationship between scores on the state anxiety scale of the STAI (Spielberger et al., 1983) across experiment 1 and the trait anxiety scale of the STAI at baseline.

The main effect of assessment was no longer marginally significant ($F = .27$, $p = .76$) suggesting that pre-existing trait anxiety was influential in state anxiety

modulation across assessments. There were no further significant main or interaction effects (*F*s < 1.53, *p*s > .22).

#### 2.3.3.3 State Anxiety at Start and End of each Experimental Day (Pre-existing Trait Anxiety as Covariate)

A 2 x 2 x 4 x 2 omnibus ANCOVA was conducted on the state anxiety data with the 2 between subjects factors of ABM (active ABM, control ABM) and tES (active tRNS, sham tES) and a within subjects factors of day (day 1, day 2, day 3, day 30) and time (start of session, end of session) and pre-existing trait anxiety as a covariate. The main effect of trait anxiety was significant, $F(1,79) = 85.50$, $p < .001$, ($\eta p^2 = .52$; *observed power* = 1.00). Pre-existing trait anxiety was highly, positively correlated with mean state anxiety, $r(84) = .69$, $p < .001$ (see figure 2.20). The main effect of time which was significant in the main analysis (section 2.3.1.3) was no longer significant ($F = .68$, $p = .41$) when controlling for trait anxiety. There were no further significant main or interaction effects ((*F*s < 1.10, *p*s > .35).

### 2.3.4 Analyses of Covariance with Pre-existing Attentional Control as a Covariate

#### 2.3.4.1 Attention Bias (Pre-existing Attentional Control as Covariate)

A 2 x 2 x 3 omnibus ANCOVA was conducted on the attention bias data with the 2 between subjects factors of ABM (active ABM, control ABM) and tES (active tRNS, sham tES) and a within subjects factor of assessment (assessment 1, assessment

2, assessment 3) and pre-existing attentional control as a covariate. No significant main or interaction effects were revealed (*F*s < 1.29, *p*s > .26).

#### 2.3.4.2 State Anxiety (Pre-existing Attentional Control as Covariate)

The same ANCOVA was performed on state anxiety data with pre-existing attentional control as the covariate revealed a significant main effect of pre-existing attentional control, $F(1,79) = 8.30$, $p = .005$, ($\eta_p^2 = .10$; *observed power* = .81). There was a moderate, negative correlation between state anxiety and pre-existing attentional control, $r(84) = -.31$, $p = .004$ (see figure 2.9) suggesting that higher levels of pre-existing attentional control were associated with lower state anxiety over all.

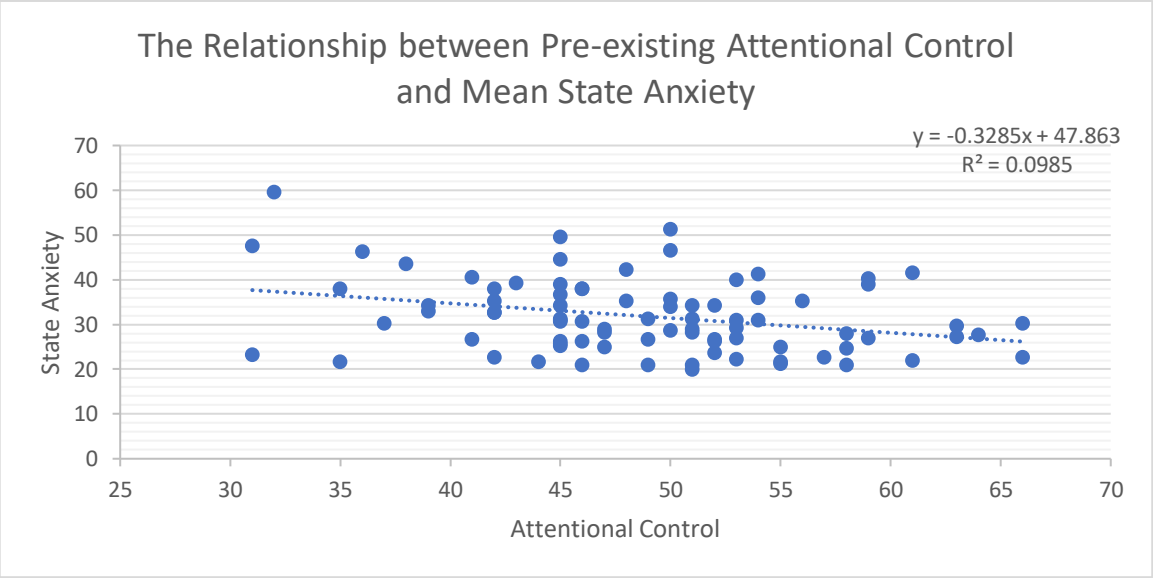



*Figure 2.9*. The relationship between scores on the attention control scale (Derryberry & Reed, 2002) at baseline and mean scores on the state anxiety scale (Spielberger et al., 1983) across experiment 1.

The marginally significant effect of assessment was again abolished, ($F$ = .10, $p$ = .91) when controlling for attentional control. There were no further significant main or interaction effects ($F$s < 1.54, $p$s > .22).

#### 2.3.4.3 State Anxiety from Start and End of each Experimental Day (Pre-existing Attentional Control as Covariate)

A 2 x 2 x 4 x 2 ANCOVA was conducted on the state anxiety data with the 2 between subjects factors of ABM (active ABM, control ABM) and tES (active tRNS, sham tES) and a within subjects factors of day (day 1, day 2, day 3, day 30) and time (start of session, end of session) and pre-existing attentional control as a covariate. The main effect of pre-existing attentional control was significant, $F($1,79) = 9.21, $p$ = .003, ($\eta p^2$ = .10; *observed power* = .85). Pre-existing attentional control was significantly, moderately, negatively correlated with mean state anxiety, $r$(84) = -.31, $p$ = .004 (see figure 2.9). The main effect of time which was significant in the main analysis (section 2.3.1.3) was no longer significant ($F$ = .22, $p$ = .64). There were no further significant main or interaction effects (($F$s < .94, $p$s > .34).

### 2.3.5 tRNS Tolerability

TRNS was well tolerated with no adverse events (see Table 2.5). Participants reported a mild level of 'tiredness' and a mild to moderate level of 'loss of concentration'. It is feasible that these effects were task induced and not attributable to the tES. There was an effect of burning with participants who received sham tES reporting a higher level ($M$ =1.19, $SD$ = .46) than those who

received active tRNS who reported no burning (*M* =1.00, *SD* = .00) *t*(109) = 4.36, *p* < .001. Tiredness was higher for sham tES participants (*M* =2.47, *SD* = 1.13) than active tRNS participants (*M* =2.16, *SD* = 2.20, *t*(214) = 2.06, *p* = .04 and loss of concentration was rated as more severe by sham tES participants (*M* =2.26, *SD* = .95) than by active tRNS participants (*M* =1.92, *SD* = .86, *t*(214) = 2.81, *p* = .005. No contrast survived corrections for multiple comparisons however.

Table 2.5:

*Mean (SD) tES intensity scores for each ABM/tES group*

| | Headache | Neck Pain | Aching Scalp | Tickling | Itching | Burning | Skin Irritation | Tiredness | Loss of Concentration | Mood Swings |
|---|---|---|---|---|---|---|---|---|---|---|
| ABM / active tRNS | 1.5 (.80) | 1.27 (.55) | 1.36 (.79) | 1.68 (.57) | 1.68 (.72) | 1.00 (.00) | 1.05 (.21) | 2.41 (1.05) | 2.27 (1.20) | 1.23 (.87) |
| ABM / Sham tES | 1.23 (.43) | 1.18 (.39) | 1.00 (.00) | 1.14 (.47) | 1.09 (.29) | 1.05 (.21) | 1.00 (.00) | 1.81 (.91) | 1.95 (1.05) | 1.09 (.29) |
| Control ABM / active tRNS | 1.45 (.74) | 1.18 (.50) | 1.32 (.78) | 1.59 (.96) | 1.45 (.86) | 1.23 (.53) | 1.18 (.50) | 2.36 (1.29) | 1.82 (.85) | 1.10 (.30) |
| Control ABM / Sham tES | 1.38 (.59) | 1.14 (.36) | 1.05 (.22) | 1.62 (.67) | 1.33 (.48) | 1.05 (.22) | 1.00 (.00) | 2.52 (1.08) | 2.33 (.80) | 1.29 (.78) |

### 2.3.6 Experimental Condition

Overall, 35.71% of participants guessed both their ABM and tES allocation correctly. The percentage of participants who guessed their ABM group correctly was 63.10%. A one-sample t-test revealed that this percentage did not significantly differ from chance, *t*(83) = 1.138, *p* = .26. The percentage of

participants who guessed their tES group correctly was 54.76%. This level was also not significantly different from chance, $t(83) = .43$, $p = .67$.

## 2.4 Discussion

The aim of the present study was to investigate whether active tRNS, delivered bilaterally to the inferior frontal gyrus, would enhance the effects of ABM. Active or sham tRNS was delivered concurrently with active or control ABM across three consecutive days. It was predicted that active ABM training towards neutral faces (away from threatening faces) would generate greater reductions in attentional bias towards threat and in state anxiety relative to control ABM. It was further hypothesised that active tRNS would enhance the effects of active ABM training in terms of producing greater reductions in threat bias and in state anxiety compared to sham tES. ABM training towards neutral faces did not produce greater threat bias and anxiety reduction than control ABM. There was also no evidence of the modulation of ABM training with active tRNS relative to sham tES.

When data from all participants was analysed, there were no differences in attention bias change across assessments as a factor of ABM or tES group. State anxiety was reduced after training at the end of day three compared to before training on day 1 for all participants, irrespective of ABM or tES group. When pre-existing attention bias was included as a covariate in the analysis, greater reduction in threat bias following ABM training for participants with greater pre-existing attentional bias towards threat was revealed. Participants with a greater pre-existing neutral bias had greater reduction in neutral bias following

training. These patterns emerged across participants irrespective of ABM or tES group. Potential mechanisms are discussed.

These results do not support findings that ABM is more efficacious in reducing attention bias towards threat and anxiety than control ABM training (Amir et al., 2009b; Bar-Haim, 2010; Beard et al., 2012; Li et al., 2008). Previously it was suggested that in active ABM, a contingency between the cue and stimulus trains participants to implicitly attend towards neutral stimuli (Boettcher et al., 2012). Evidence from experiment 1 indicates that this mechanism was ineffective in the present study. The findings are also not consistent with previous studies which have reported enhanced effects for cognitive training with tRNS (e.g. Fertonani et al., 2011; Snowball et al., 2013) or in accord with those which have cited differences in the outcomes of ABM training with concurrent tES compared to ABM with sham tES (Clarke et al., 2014; Heeren et al., 2015b).

### 2.4.1 Anxiety Reduction in the Absence of Threat Bias Reduction

Reduction in threat bias, propagated by contingency based ABM was proposed as the mechanism responsible for anxiety attenuation in past research (Amir et al., 2008; Amir et al., 2009b). In the present study, there was state anxiety reduction across all participants but there was no change in attention bias level across assessments. The anxiety reduction which occurred across all participants following training cannot therefore be explained by a reduction in the involuntary engagement of threatening stimuli. The finding of anxiety reduction in the absence of threat bias reduction is not in isolation. A recent meta-analysis of 34 studies reported that, in many of the studies included in the

analysis, anxiety reduction was reported in the absence of threat bias reduction (Mogg et al., 2017). Amongst these was a study by McNally et al. (2013) in which speech anxious participants were trained to attend happy faces, disgust faces or received control ABM. All groups had reductions in behavioural, self-report and physiological measures of speech anxiety and these reductions were indistinguishable between groups. There were no reductions in threat bias and, in fact, none of the groups had threat bias at any assessment (McNally et al., 2013). Carleton et al. (2015) trained socially anxious participants to attend neutral stimuli or allocated them to receive control ABM twice weekly for four weeks. Social anxiety symptoms declined for all participants and were maintained at eight-week follow-up. Reductions in anxiety did not correlate with threat bias reductions.

In the present study, when pre-existing attention bias was included as a covariate in the analysis of state anxiety data, pre-existing bias did not interact with state anxiety or state anxiety change across assessments. This brings into further question the relationship between change in attentional bias and change in anxiety and the suggestion that the mechanism of anxiety attenuation observed in past studies was a reduction in threat bias (e.g. Amir et al., 2009b; Bar-Haim, 2010; Li, Tan, Qian & Liu, 2008).

### 2.4.2 Equivalent Anxiety Reductions Across Experimental Groups

Anxiety reduction occurred in all participants irrespective of ABM group. Although this result was unexpected, there have been a number of recent studies reporting indistinguishable improvements in anxiety for ABM training and

control ABM training (Carlbring et al., 2012; Carleton et al., 2015; Cristea et al., 2015; Enock et al., 2015; Klumpp & Amir, 2010). In their meta-analysis, Mogg et al. (2017) identified that in 23 of the 34 studies included in the meta-analysis, attend neutral ABM was not more effective than control ABM. Klumpp & Amir (2010) for example, showed that both participants who underwent ABM training towards threat and participants who received training away from threat reported less anxiety in response to an impromptu speech task. Heeren et al. (2013) allocated socially anxious participants to ABM towards threat, ABM away from threat or control (no-contingency) training. There were reductions in anxiety in response to a speech task and in self-report measures of anxiety in all 3 groups which were indistinguishable. In a further study, participants received ABM training towards joy faces, towards disgust faces or control ABM (McNally et al., 2013). After four ABM training sessions, participants in all three groups reported a decline in 'stressor'-elicited anxiety. It is possible, that the improvements from these studies were the result of practice effects. The studies used anxiety response to stressor tasks as a measure of anxiety reduction and, evidently, performing a speech for a second time may not be as stress evoking as the first time around. The present study involved no stressor task and improvements occurred across groups in terms of self-report state anxiety. The study by McNally et al. (2013) also reported reductions in self-report and physiological measures of anxiety. Practice effects can therefore be ruled out as an explanation for anxiety attenuation. If anxiety amelioration also cannot be explained by threat bias reduction there must therefore be alternative modulatory forces at play.

#### 2.4.2.1 Exposure

One candidate mode of action is that ABM training, with or without contingency represents a form of exposure therapy. Repeated presentation of threatening faces may result in habituation to the stimuli thus reducing their salience and anxiety evoking properties (Carleton et al., 2015). Indeed, exposure to threatening stimuli is the foundation of accepted anxiety therapies (McNally et al., 2013). As such, any paradigm which involves the consistent presentation of threat-related stimuli could potentially bring about reduction in anxiety.

#### 2.4.2.2 Non-specific Effects

Another possible explanation for the findings is that they were due to non-specific treatment effects. Enock et al. (2014) proposed that simply taking part in research may bolster the confidence of some participants leading to a reduction in anxiety. In the present project, this may have occurred as a result of attending sessions over 3 consecutive days. Over this time a relationship likely formed between the researcher and the participant who, as a consequence may have felt more at ease by the end of the process (Patterson, 1985). Alternatively, participants may have been responding, consciously or subconsciously, to expectation. If participants perceived that the researcher expected to see a reduction in anxiety level then demand characteristics might be at play (Cristea et al., 2015). Alternatively, a placebo effect may have arisen if participants themselves had positive expectations regarding the outcome from their participation (Carleton et al., 2015; McNally et al., 2013).

### 2.4.2.3 Attentional Control

Perhaps the most widely supported theory for why control ABM produces anxiety reductions matching those achieved with active ABM is the idea that ABM training, regardless of the inclusion of a contingency, increases attentional control and thus the capacity for attention regulation (Enock et al., 2014; Heeren et al., 2013; Klumpp et al., 2010; Taylor, Cross & Amir, 2015). It has previously been suggested that in anxiety, the ability to voluntarily direct attention away from non-threat or to disengage from threat is deficient and that this is responsible for maintaining anxiety (Derryberry & Reed, 2002). Attentional training may boost an individual's attentional control capacity encouraging more efficient allocation of attention to non-threatening stimuli which will subsequently result in reduced anxiety (Heeren et al., 2013). Some researchers have added measures which have tested this concept. In addition to a contingency and no-contingency condition, Enock et al. (2014) added a wait list group in which no training took place but in which anxiety and depression scales were administered at baseline and at a later point. Anxiety and depression were reduced in the active ABM and control ABM groups but not in the waitlist group (Enock et al., 2014). This suggests that the remedial factor within this design was cognitive training. Heeren et al. (2015a) trained socially anxious participants towards threat, away from threat or with no contingency. There were reductions in anxiety response to a speech task and in self-report measures of anxiety in all 3 groups which were indistinguishable. The attention network task was used to assess different dimensions of attention. All 3 groups demonstrated improvements in alerting and executive components of attention after ABM or no-contingency ABM (Heeren et al., 2015a). In another study,

participants underwent dot-probe training with 'non-emotional' stimuli in the form of geometric shapes (Heeren et al., 2016). The researchers included a contingency condition, a no contingency condition and a control condition which involved pressing targets but without any preceding presentation of probes. All three conditions had reduced anxiety in response to a speech task and their performances in the task received higher ratings from independent observers than at the start of the study. Participants in all 3 conditions also demonstrated improvements in a working memory task which were indistinguishable from each other (Heeren et al., 2016). This latter study not only supports the idea that cognitive training regardless of the presence or absence of a contingency can lead to anxiety reduction but also suggests that the presence of emotionally valenced stimuli is an unnecessary component of the training. The concept of reinforcement of attentional regulation via cognitive training as the mechanism for improved inhibition of threat processing appears to be the main line of reasoning and exploration in recent ABM research. Nonetheless, in the present study, although threat bias reduction was observed for participants with pre-existing threat bias and those with high-level anxiety, component analysis did not reveal reductions across all participants. This indicates that reduced threat engagement via enhanced attentional control may not be responsible for anxiety attenuation. However, researchers have suggested alternative mechanisms via which the enhancement of attentional control capacity might attenuate anxiety. Klumpp et al. (2010) suggested that facilitated attentional control may not necessarily reduce engagement to threatening stimuli but may attenuate their *impact* and disrupt threat processing via the increase of self-regulation. Heeren et al. (2016) linked the effects to the upregulation of higher-order activity in the frontal cortices. These structures

are associated with attentional control and are known to down-regulate reactivity in the emotion-centered limbic system. As described above, the authors demonstrated that a dot-probe task with geometric shapes enhanced working memory and led to reduced emotional reactivity to a stressor task. Another explanation submitted by Wallace & Newman (1997) is founded on the notion that maladaptive cognitions contribute to negative affect. Negative affect can be regulated via controlled information processing which requires the availability of attentional resources. When attention is diverted or captured by salient stimuli then attentional resources are depleted and the regulation of negative affect is impaired. By enhancing attentional control capacity, attentional processes are rendered more efficient and attentional resources are available for controlled information processing (Wallace & Newman, 1997).

The explanations above infer that participants with the greatest enhancement in attentional control following ABM training should be those who have the greatest improvement in anxiety. The present study was not able to show that this was the case as no measure was administered which allowed the comparison of pre- and post-training attentional control. Previously Basanovic et al. (2017) reported a positive association between performance in attentional control tasks completed at baseline and degree of attention bias change in the trained direction. The authors proposed that for contingency-based attentional training to be effective, participants should be able to competently inhibit one stimulus and select another (Basanovic et al., 2017). In other words, greater pre-existing attentional control facilitates adherence to the contingency aspect of active ABM and therefore participants with high level attentional control experience a 'deeper' level of training. In the present study however, when pre-existing

attentional control was included as a covariate in the analysis of ABM/tES impact on attention bias and state anxiety, there was no indication of a relationship between baseline attentional control and change in these dimensions across assessments.

### 2.4.3 TRNS

In the present study tES did not appear to have a modulatory effect on attention bias. This was unlike the findings reported by Ironside et al. (2015) in which a reduction in threat bias after bilateral tDCS of the DLPFC (cathode over the right DLPFC) but not after unilateral cortical anodal tDCS (cathode over supra-orbital ridge) or after sham tDCS was observed. It is worth noting that in this previous study tDCS was delivered offline and no ABM took place. Additionally, no baseline measure of attention bias was taken. Participants received tDCS or sham tDCS and subsequently performed attention bias assessment. It is not possible to state with certainty therefore that performance disparities were due to the effect of stimulation and not individual differences. The fact that Ironside et al. (2015) demonstrated that it is possible to attenuate vigilance to threat via tES without ABM training, does raise some interesting questions regarding the mechanisms of this improvement. The present research assumed that high frequency tRNS would serve to boost the intrinsic neural activity associated with learning to engage neutral rather than angry faces. In the model put forward by Ironside et al, (2015) learning is not a necessary part of this process. One possible explanation is that, as previously suggested, there is a neural mechanism which sub-serves avoidance of or disengagement from threatening stimuli (Heeren et al., 2013). This system is in frontal areas of the

brain and is responsible for inhibiting emotionally driven responses via the regulation of a more posterior system which controls attentional allocation and processing (Derryberry & Reed, 2002). With the appropriate form of tES and by targeting the optimal frontal brain area, it is perhaps possible to bolster or even activate this pre-established system without the need for attentional training.

Two previous studies have combined tES with ABM training (Clarke et al, 2014; Heeren et al., 2015b). Clarke et al. (2014) reported a significant reduction in threat bias following ABM training away from threat for participants who received concurrent active tDCS over the left DLPFC but not for participants who received sham tES. The present study did not replicate this finding. The following section discusses potential explanations for why this may have occurred.

### 2.4.4 Measure of Attention Bias

It is, of course, possible that anxiety reduction across participants was attributable to diminished threat engagement but that this effect was obfuscated because the procedure used to assess attention bias was ineffective in detecting this effect. It is also possible that active ABM training evoked reductions in threat bias which were superior to those induced by control ABM but that this was not revealed by the emotional dot-probe used to measure attention bias. Macleod et al. (2016) suggested that a failure to find evidence of reduction in threat bias following ABM procedures might be explained by an ineffectiveness of the attention bias assessment task to accurately measure attention bias (Macleod et al., 2016). If potential outcome differences between

ABM groups were not detected using the attention bias assessment then any enhancement of ABM effects via tRNS would also be concealed. The emotional dot-probe task used to measure attention bias in the present study was the same as that used to modify it, without the contingency. Studies such as Amir et al. (2008; 2009b) which reported greater reduction of threat bias following active ABM compared to control ABM used a different task (the modified Posner or 'spatial cueing task') to assess change in attention bias. In this task attention bias towards threat is indicated by slower reactions times for targets appearing in the opposing location to a previously presented single threatening stimulus relative to targets appearing opposite to a previously presented neutral stimulus (Mogg et al., 2008). This suggests greater difficulty in disengaging from threatening stimuli compared to neutral stimuli. The modified dot probe, on the other hand measures engagement to threatening and neutral stimuli with faster responses to targets replacing threatening stimuli relative to neutral stimuli taken as evidence of threat bias. Perhaps using the task employed by Amir et al. (2008, 2009b) reduced threat bias may have been found. Alternatively (or additionally) a measure of spatial attention with greater temporal specificity may have revealed a different pattern of attention bias change. Heeren et al. (2015b) did not find a reduction in the behavioural measure of threat bias after ABM training with atDCS or sham tES. Instead, eye-tracking data revealed a greater reduction in gaze time for threatening faces after ABM with atDCS than after ABM training with sham tDCS. It has been posited that reaction time data represent a poor psychometric measure of attention bias as the 500ms presentation of faces in a standard emotional dot probe provides ample time for gaze to be averted from the threatening face before the appearance of the target (Kappenman et al., 2014). Eye-tracking data is perhaps a more precise

indication of attentional engagement and shifting within the first few milliseconds of cue presentation (Heeren et al., 2015b). It is possible that a measure with more detailed temporal resolution such as eye-tracking or event related potential (ERP) data may have uncovered changes in attentional bias and differences in these modulations between experimental groups.

### 2.4.5 Ceiling Effects

Many of the types of cognitive functions which have been previously enhanced via the administration of tES during training have been multi-faceted, explicit learning tasks such as arithmetic (Snowball et al., 2013) and novel vocabulary learning (Meinzer et al., 2014). As such, performance on these tasks were not at ceiling, leaving room for tES to boost the impact of training. In the present paradigm, the intended outcome of active ABM (anxiety reduction) was achieved irrespective of ABM training group and tES group. The mechanism of this reduction is not known. If, however, it was the enhancement of attentional control and control ABM could readily achieve the enhancement of attentional control processes then active ABM may not have been able to induce further improvements. Furthermore, there may not have been scope for active tRNS to enhance this outcome. From a mechanistic perspective, if neural populations are active in a way which generates the desired behaviour, there may be no scope for tES to facilitate this activity.

### 2.4.6 State Dependency

Research has drawn attention to the influence of state dependency on the outcome of tES research (Horvath et al., 2015b). Borteletto, Pellicciari, Rodella & Miniussi, (2015) reported that tES improved performance in a motor task when applied during control training but impaired performance when applied during active training. The authors indicated that the effects of tES are dependent upon the task and activation state of the brain during application and that when excitatory tES is applied during another excitability enhancing event, one might negate the facilitatory impact of the other (Bortoletto et al., 2015). Certainly. in the present research, the application of tRNS did not appear to cancel out the effects of active ABM. However, it is credible that excess excitatory inputs might have elicited homeostatic neural mechanisms resulting in a weakening of excitatory signals.

### 2.4.7 TES Stimulation Type

Assuming that the outcomes of ABM were open to modulation, there may be other explanations for why active tRNS was not able to provide their anticipated intensification. One rationale may be that tRNS is not the optimal form of stimulation for the current paradigm. TRNS was selected as recent work had provided robust evidence of the capacity for tRNS to modulate the effects of cognitive training (Fertonani et al., 2012; Snowball et al., 2013). However, previous studies used tDCS with ABM and successfully modulated its impact (Clarke et al., 2014; Heeren et al., 2015b). Although tRNS and tDCS are both said to exert their effects via the modification of spontaneous neural activity, it

could be that the pattern and distribution of the spontaneous activity elicited during ABM are more amenable to fortification via continuous anodal direct current than alternating current at random frequencies and amplitudes. In the present study, active ABM did not produce superior reductions in threat bias and anxiety than control ABM. There was therefore no evidence that the process previously proposed to be responsible for these improvements (implicit training of attention towards neutral stimuli via a contingency between face cues and targets) was active. As such, enhancement of this mechanism with tRNS would not have been apparent. However, there were reductions in anxiety across all participants which are likely to have been the result of a mechanism common to both active and control ABM. There was also no evidence of the enhancement of this mechanism via active tRNS. Without knowing the nature of the mechanism (e.g. augmentation of attentional control, exposure effect, placebo effect etc.) it is difficult to speculate whether it may have been susceptible to enhancement using tES and if so, why this did not occur. Investigating which training paradigms are most susceptible to modulation by which forms of tES is an avenue for future research. Such research could prove critical in identifying the neural hallmarks of specific cognitive processes.

### 2.4.8 Site of Stimulation

TRNS may have had a modulatory impact upon ABM had a different site of stimulation been chosen. In the present study the IFG was selected as the site of stimulation. This was because the IFG has been implicated in attentional and inhibitory control processes (Aron et al., 2014; Rubia et al., 2003) and because anodal tES applied to the right IFG during training previously resulted in more

enhanced response inhibition relative to training with sham stimulation (Ditye et al., 2012). Because ABM is intended to train the inhibition of automatic engagement to threatening faces, the IFG appeared a logical target for tRNS. However, the two studies already discussed which effectively modulated ABM using tES targeted the left DLPFC based on its association with top-down attentional control (Heeren et al., 2015b) and inhibition (Clarke et al., 2014). Additionally, it is reported that in anxious participants, activity of the left DLPFC during attentional control is lower than it is for non-anxious individuals (Heeren et al., 2015b). It is therefore possible that the left DLPFC is a more appropriate target site for tES during ABM.

In the present study, tRNS was administered to both the right and the left IFG simultaneously. Studies which have sought to pinpoint the neural structures which mediate inhibition have tended to implicate either the left DLPFC (e.g. Boggio et al., 2007; Clarke et al., 2014; Grimshaw & Carmel, 2014) or the right IFG (Aron, Robbins & Poldrack, 2004; Aron Robbins & Poldrack, 2014; Jacobson, Javitt & Lavidor, 2011) in this function. Lateralised stimulation may have been more successful in targeting the neural processes involved in ABM. Perhaps, in the case of bilateral stimulation, alteration of neural activity was too widespread and lacking in regional focality to target a specific brain function (Parkin, Ekhtiari & Walsh, 2015).

### 2.4.9 Modulatory Capacity of tES

Finally, it cannot be ruled out that the inefficacy of tRNS to modulate ABM did not stem from any aspect of methodology. In a recent quantitative review,

Horvath et al. (2015b) reported that, across studies assessing the capacity for tDCS to modulate the impact of cognitive training, there was no reliable effect. It is plausible therefore that the potential for tES to facilitate cognitive enhancement has quite simply been overstated in past research. A systematic review of tDCS studies reported that, of 30 neuro-physiological outcome measures including event related potentials (ERPs), electroencephalographic (EEG) spectra, motor evoked potentials (MEPs) and blood oxygenation level dependent (BOLD) signal, tDCS only had a reliable effect on MEP amplitude (Horvath et al., 2015a). A quantitative review by the same authors on the effect of single-session tDCS upon cognitive outcome measures including aspects of executive function, memory and language, reported no reliable effects on any of the measures assessed (Horvath, Forte & Carter, 2015b). However, rather than refuting outright the value of tDCS as a tool in research or therapy, both reviews pointed at methodological variability within the studies reviewed as the potential source of inconsistent findings which, when summated, failed to support the efficacy of tDCS. It was suggested that, to optimise the augmentative impact of tES, methodological factors should be controlled for (Horvath et al., 2015b). This view has been mirrored across tES research with much emphasis placed upon the importance of tES intensity (Bestmann et al., 2015), duration, waveform and electrode shape, size and location (Bikson et al., 2010). The role of Individual differences has also not been overlooked with brain anatomy [including morphology of gyri and sulci, (Bestmann et al., 2015)] the properties and conductance level of grey matter, white matter and CSF (Datta et al., 2012), skin conductance, skull thickness (Bikson et al., 2010; Brunoni et al., 2012), cognitive state e.g. tiredness, alertness (Horvath et al., 2015b) and even

scalp temperature (Gholmi-Bouroujeny, Mekonnen, Batkin, & Bolic, 2015) cited as critical factors for consideration when designing tES protocols.

### 2.4.10 Pre-existing Attention Bias Towards Threat

It has previously been demonstrated that the successful modulation of attention bias away from threatening stimuli is dependent upon there being bias towards threat before training (O'Toole & Dennis, 2012). It may not be possible (or desirable) after all to reverse an attentional bias which is not present. For this reason, ANCOVAs were performed on attention bias data with pre-existing attention bias level as a covariate. Whereas the main analysis revealed no reduction in threat bias across all participants, the analysis clearly showed a decline in threat bias for participants with a pre-existing bias towards threatening stimuli. These findings support the view that ABM is more effective for reducing attentional bias towards threat in participants with a pre-existing threat bias. There were no apparent advantages in terms of anxiety reduction for participants with pre-existing threat bias despite threat bias reductions in this group. This is therefore further evidence that reduction in attentional bias towards threat is not the mechanism via which anxiety reductions were achieved in the present experiment.

### 2.4.11 Pre-existing Neutral Bias

In the present experiment, greater level of pre-existing neutral bias was associated with greater reduction in neutral bias. It is possible that the mechanism behind the reduction in neutral bias might be one already proposed

to explain the reductions in threat bias following active ABM (and control ABM) training. The attentional control model is based on the premise that increased attentional control capacity facilitates engagement to neutral stimuli (Klumpp et al., 2010). This would not therefore account for the changes in attentional bias for participants with pre-existing neutral bias as the engagement to neutral stimuli was reduced following ABM training. Improved attention regulation might, however, facilitate the engagement to threat related stimuli where threat avoidance is a maladaptive behaviour which may reflect attentional *avoidance* of threat related stimuli (Cisler, 2012). A reduction in neutral bias might signify a 'balancing' of attention distribution towards threat and neutral stimuli which is arguably a healthier attentional model. Perhaps more applicable to the present findings is the suggestion that ABM and control ABM are both a form of exposure training. As previously suggested, repeated presentation of threatening faces may result in habituation to the stimuli thus reducing their salience (Carleton et al., 2015). As such, an 'avoidant' individual might be better able to engage threatening faces with reduced negative affect following ABM or control ABM. Identifying the mechanism responsible for the increase in threat bias for participants with pre-existing neutral bias may be as important to understanding the active cognitive processes underlying ABM as elucidating the reason for reductions in threat bias for participants with pre-existing threat bias and warrants further investigation.

### 2.4.12 Pre-existing Anxiety

In the present study, despite reports that ABM is more effective in individuals with high-level anxiety (Bar Haim et al., 2007; Beard et al., 2012; Hakamata et

al., 2010) it was decided to explore tES with ABM in neuro-typical participants. It could therefore be argued that anxiety reduction should not have been expected as anxiety was at a normal, arguably 'healthy' level. In studies which have not pre-selected for high anxiety, a stressor task has been used to induce state anxiety (e.g. Macleod et al., 2002). However, in the present research, a stressor task was not delivered. The decision to neither select for anxious participants nor induce state anxiety via a stress inducing task was a weakness of the present research. Nevertheless, state anxiety reduction did occur following three days of participation. Prior to commencing the research, it was reasoned that the effect of pre-existing anxiety on changes induced by the experimental protocol could still be explored by including this dimension in post hoc analysis. Pre-existing trait anxiety was therefore included as a covariate in the analysis. With trait anxiety held constant, the reduction in state anxiety following ABM training (irrespective of ABM or tES group) which was seen in the analysis of state anxiety without the inclusion of a covariate, was not present. This supports a moderating role for pre-existing trait anxiety in participation induced state anxiety reduction. However, because pre-existing trait anxiety was not shown to interact with ABM condition or assessment, there was no indication participants with high trait anxiety benefitted more in terms of state anxiety reduction or that active ABM was more effective in high anxious participants.

## 2.5 Summary and Future Work

Studies which have used tRNS to enhance training have reported impressive findings (e.g. Snowball et al., 2013). The present study provided an opportunity to build on these promising findings using an exciting new technology. There

was no impact of the stimulation on task performance and measures. TDCS is the most frequently used form of stimulation in the study of cognitive enhancement via tES (Horvath et al., 2015b) with many studies publicising its neuro-modulatory successes (e.g. Ditye et al., 2012; Meinzer et al., 2014; Segrave et al., 2014). Going forward therefore, tDCS may be a more appropriate form of stimulation for the modulation of ABM. With each form of tES possessing its own putative mechanism for the modulation of learning when applied during training, it is feasible that tDCS would be more effective in targeting the neuronal areas and processes specific to ABM. In the current study, high frequency tRNS was targeted towards the bilateral IFG. This cortical area was selected following careful examination of the literature surrounding the neural mechanisms of implicit learning and response inhibition. Equally, the left DLPFC is often the target of stimulation in studies which aim to increase learning (e.g. Javadi & Cheng., 2013; Snowball et al. 2013) and improve mood (Segrave, Arnold, Hoy & Fitzgerald, 2014).

Superior reductions in threat bias for the participants in the active ABM group relative to those in the control ABM group were not revealed in the present study. Neither was diminution of attentional bias towards threat across all participants uncovered despite the fact that anxiety reduction was achieved. This suggests that active ABM is not more effective than control ABM for reducing attentional engagement to threat. It also indicates that anxiety reductions were not mediated by reduced threat engagement. Future work could aim to explain these outcomes which mirror findings from other recent ABM studies (Carlbring et al., 2012; Carleton et al., 2015; Cristea et al., 2015; Enock et al., 2015; Klumpp & Amir, 2010). A previous explanation for these

findings that cognitive training, with or without the presence of a contingency bolster attentional control leading to anxiety reductions (Mogg et al., 2017). Research to date therefore indicates that greater attentional control capacity is associated with greater active ABM and control ABM training effects. However, the mechanism via which attentional control exerts these effects requires clarification. One way to examine whether attentional training outcomes are modulated by changes in task-induced attentional control might be to manipulate the degree to which the training augments attentional control capacity. An ABM group in which little or no attentional control training takes place could be added. Alternatively, a condition in which attentional control is trained to a greater degree than in the present ABM regimen could be included. If smaller or larger relative attention bias and anxiety modifications were obtained in these groups then this would further support the notion that the degree to which attentional control capacity is altered through training is influential in the magnitude of attention bias and anxiety change.

An alternative explanation for why the present experiment did not reveal reductions in threat bias following attend neutral ABM is that the emotional dot-probe task is not a reliable measure of attentional bias (Kappenman et al., 2014; Schmukle, 2005; Sigurjonsdottir et al., 2015). Future studies might use a different or additional measure of attentional bias which provides a more temporally specific measure of attentional control processes such as eye-tracking (e.g. Heeren et al., 2015b) or ERPs (e.g. Kappenman et al., 2014).

# Chapter 3

**Investigating the 'attentional control' theory of ABM. Are reductions in anxiety explained by improved attention regulation?**

**Experiment 2**

## 3.1 Introduction

In Experiment 1 participants received active ABM or control ABM with active tRNS or sham tES over 3 consecutive days. Assessment of attentional bias and anxiety from before and after training revealed reduction in anxiety for all participants irrespective of ABM allocation following training. Recent ABM investigations have generated similar results (Carlbring et al., 2012; Carleton et al., 2015; Cristea et al., 2015; Enock et al., 2015; Heeren et al., 2013; Klumpp & Amir, 2010). Yao et al. (2015) for example, recently found that anxiety rating in response to a speech task was reduced for participants who had received ABM towards mildly smiling faces (away from angry faces), control ABM and ABM training towards geometric shapes. This demonstrates that, not only can anxiety reduction occur independent of contingency in ABM but also exclusive of salient or emotional stimuli, a phenomenon also reported by Heeren et al., (2016). If the contingency element of training is not a factor in anxiety reduction then this suggests that another mechanism is responsible.

Mechanisms discussed in previous chapters include 'non-specific treatment effects' (Enock et al., 2014). Another possibility is that repeated exposure to

threatening faces, words or images render these stimuli less salient and therefore less likely to capture attention and invoke an anxious response (Carleton et al., 2015). However, this exposure effect would not account for the decline in anxiety obtained following dot probe tasks using geometric shapes (e.g. Heeren et al., 2016; Yao et al., 2015). A further explanation is that the dot-probe (ABM) task represents a form of cognitive training which increases attention regulation capacity. Participants who undertake such training are therefore better able to regulate attentional and emotional response towards threatening stimuli (Enock et al., 2014; Heeren et al., 2013; Klumpp et al., 2010; Taylor, Cross & Amir, 2015). Heeren et al. (2016) implicated the frontal cortices in this process proposing that intensification of higher-order activity in the frontal cortex regulates emotional reactivity via projections from this area of the brain to the limbic system (Heeren et al., 2016).

### 3.1.1 Attentional Control and Anxiety

Evidence of a relationship between anxiety and attentional control is pervasive (E.g. Armstrong et al., 2011; Browning et al., 2010; Derryberry & Reed, 2002; Jones, Fazio & Vasey, 2012; Tang & Posner, 2009; Taylor, Cross & Amir, 2016; Weiser et al., 2009). Correlational research has shown that individuals with generalised anxiety disorder (GAD) have lower self-reported attentional control relative to non-anxious controls (Armstrong et al, 2011). Moriya & Tanno (2008) reported a negative relationship between social anxiety and attentional control *(*Moriya & Tanno, 2008). Attentional Control Theory (ACT; Eysenck, Derakshan, Santos & Calvo, 2007) proposes that in

anxiety, bottom-up, salience driven mechanisms such as excessive worry or rumination interfere with attentional control processes reducing efficiency in tasks requiring attentional control (Eysenck et al., 2007). Studies which examined how individuals with high anxiety perform in attentionally demanding tasks have supported this suggestion (e.g. Sadeh & Bredemeier, 2011). Osinsky (2012b) reported that highly trait anxious participants were unable to suppress engagement to task-irrelevant stimuli in a face-word Stroop task. Weiser et al., (2009) demonstrated that participants with high level social anxiety had difficulty inhibiting prosaccades to face images when anti-saccade was required relative to participants with low social anxiety. However, because these studies did not manipulate anxiety levels they did not establish a direct causal relationship between anxiety and attentional control.

Of late, research has begun to investigate whether impaired attentional control is, in fact, causally implicated in anxiety. Sari et al. (2016) delivered attentional control training to high trait anxious individuals for three consecutive weeks. Following training, attentional control was improved (as assessed using a Flanker task) and anxiety was reduced relative to before training (Sari et al., 2016). This finding indicates that interventions targeting attentional control may be effective in reducing anxiety (Taylor et al., 2016). Efficient attentional control involves the ability to focus attention upon task relevant stimuli and to ignore non-relevant information (Eysenck & Derakshan, 2011). These processes are central to ABM training in both its active and control format. Undertaking ABM may therefore facilitate attentional control processes (Heeren et al., 2015a). This potential was demonstrated in an eye-

tracking study which showed that ABM towards neutral stimuli not only reduced attentional bias towards threat but reduced anti-saccade cost in an anti-saccade task (the difference between the main anti-saccade latency and the mean pro-saccade latency; Chen et al., 2015) a reliable measure of attentional control (Ainsworth & Garner, 2013). Given that there is support for the attentional control bolstering effects of ABM, researchers have proposed that the improvements in anxiety which follow active ABM and control ABM training may arise due to the enhancement of attentional control capacity (Enock et al., 2014; Heeren et al., 2013). Some researchers have provided empirical support for this suggestion. Participants in Heeren et al's (2015a) study received ABM training towards neutral faces, ABM towards threat faces or control ABM. All three groups demonstrated reductions in stressor-related anxiety and improvements in the alerting and executive functions of attention following training as evidenced by performance in the attention network task (Heeren et al., 2015a). In a study by Heeren et al., (2015c) participants received contingency dot-probe training or control training with geometric shapes (Heeren et al., 2015c). All participants had reductions in stressor related anxiety and improvements in working memory following training as measured using the backward digit span task. The authors suggested that the diminution in anxiety might be related to enhancement of attentional control, a key function of working memory (Heeren et al., 2015c). Enoch et al. (2014) assigned participants to ABM towards neutral stimuli, control ABM or a waitlist group in which no training was delivered. Anxiety and depression were reduced following the training period in the active ABM and control ABM groups but not in the wait list group. It was therefore suggested that the remedial factor was attentional

training irrespective of contingency (Enoch et al., 2014). Each of these findings supports the view that the active mechanism of ABM is not the contingency associated with stimulus presentation but the attentional training itself which improves aspects of attention control. With enhanced attention regulation, an individual can better control how threatening stimuli are processed and thus the impact of threat related stimuli is attenuated (Klumpp et al., 2010). Training which does not enlist attentional control resources should not augment self-regulation capacity and reduce anxiety.

### 3.1.2 Cognitive Control, Attentional Control and Working Memory

Cognitive control, attentional control and working memory are interrelated cognitive facets. They are each implicated in top-down regulation and associated with shared structures in the pre-frontal cortex (Miller & Cohen, 2001). These functions are involved in facilitating the pursuit of goal-relevant behaviours and inhibiting goal-irrelevant behaviours which may be triggered by external stimuli (Astle & Scerif, 2009).

Cognitive control is defined as the capacity to flexibly modulate cognitive function and behaviour to meet task demands. Where cognitive control has been considered in terms of its capacity to down-regulate emotional response it has been described as an interaction between working memory and the stimulus driven limbic system processes (Brooks et al., 2017). Associated executive processes include attentional shifting, the maintenance and updating of working memory and cognitive or reaction conflict resolution

(Song et al., 2017). Cognitive control there encompasses elements of both attentional control and working memory.

Attentional control capacity is determined by the ability to focus attention upon task relevant stimuli and to ignore non-relevant information (Eysenck & Derakshan, 2011). Some researchers have conceptualised attentional control in terms of its functional components. Derryberry & Reed (2002) for example stated that effective attentional control requires 'shifting' which involves directing attention away from task irrelevant stimuli and on to task relevant stimuli and 'focusing' which requires maintaining attention on task relevant information (Derryberry & Reed, 2002). Others have highlighted the importance of attentional 'inhibition' and 'selection' (e.g. Basanovic et al., 2017).

Working memory refers to the retention of a small amount of information, which is easily accessible in order to facilitate performance in cognitive tasks such as problem solving and learning (Baddeley, 1983). Attentional control is considered a principal function of working memory (Course-Choi, Saville & Derakshan, 2017) as it allows for the focusing of attention on task-relevant information (the information to be retained) and the inhibition of task-irrelevant stimuli (Sari et al., 2015).

Given the inter-dependency between these functions, it might be expected that the manipulation of one would impact upon the efficacy of another. Indeed, evidence exists that the augmentation of cognitive control capacity via working memory training results in attentional control enhancement

(Heeren et al., 2016; Owens et al., 2013). Furthermore, training related improvements have been seen to be related to reduction of emotional vulnerability (Sari et al., 2015; Swainston & Derakshan, 2018). A recent study showed that, adaptive cognitive training in a dual n-back task resulted in greater reduction in anxiety and rumination following training than control training in breast cancer patients (Swainston & Derakshan, 2018). In another study, training-related improvements in the dual n-back task were related with working memory improvement and worry symptom reductions for participants who received active training but not for those who received control training (Hotton, Derakshan & Fox, 2018).

In studies which compare the effects of adaptive working memory training with non-adaptive or control training, it is considered that the extent to which cognitive resources are recruited and trained is determined by characteristics of the task including the task format, task complexity and the time pressures inherent to a task (Paas et al., 2003; Paas et al., 2010). In the studies by Hotton et al. (2017), Owens et al. (2013), Sari et al. (2015) and Swainston et al. (2018) adaptive working memory training took the form of the dual n-back task. In this task, the participant must attend to a sequence of numbers presented in a visual and an auditory format concurrently. The participant must indicate whether a number matches that shown n trials back in either the visual or auditory sequence. This task gets progressively harder as ‘n’ increases as performance improves thus explaining the adaptive nature of the task. In the non-adaptive version of this task, ‘n’ remains at 1.

In summary, tasks designed to enhance cognitive control by enhancing working memory capacity have been seen to improve attentional control. These improvements are also associated with reductions in negative affect (e.g. Swainston & Derakshan, 2018). The degree to which as task recruits and modulates cognitive resources is determined by the task's format, complexity and time pressures (Paas et al., 2003; Paas et al., 2010).

### 3.1.3 Attentional and cognitive control requirements of ABM

A potential explanation for the findings of equivalent reductions in anxiety for participants in the active ABM and participants in the control ABM groups was that both training conditions enhanced attentional control capacity. During active and control ABM the participant responds to a target replacing a stimulus. In doing so they may have to inhibit engagement to an alternative stimulus in order to attend to the location of that which the target replaces. It could be argued therefore that ABM, irrespective of contingency, trains this key facet of attentional control (Basanovic et al., 2017). In addition, participants must select between one of two target identities. This 'forced choice' task therefore also encourages speed and accuracy of decision making (Woodruff et al., 2012) representing an additional layer of cognitive training. If state anxiety reductions are attributable to the enhancement of attentional processing capacity then a version of the task which places less demand on executive attention resources might not be expected to achieve the same degree of anxiety attenuation.

There are a limited number of ways in which it is possible to modify the attentional or cognitive load of the dot-probe ABM task without significantly altering it's design. Unlike the dual n-back task (Hotton et al., 2017; Owen et al., 2013; Sari et al., 2015; Swainston et al., 2018), the ABM paradigm is non-adaptive and therefore it is not possible to simplify the task by eliminating an adaptive element. As mentioned, ABM requires attentional inhibition of task irrelevant stimuli and the shifting of attention to task relevant stimuli (Basanovic et al., 2017), 2 facets of attention control (Derryberry & Reed, 2002). Eliminating the inhibition and shifting facets of ABM might be achievable by presenting a single stimulus on the computer screen followed by a to-be-identified target. However, this would change the design from a dot-probe paradigm. Alternatively, it might be possible for the task to target attentional control mechanisms by modulating demands on cognitive control or working memory (Miller & Cohen, 2001). Studies have previously used a simple reaction time paradigm as a low demand cognitive control task with a choice reaction time paradigm as the more cognitively demanding or active condition (e.g. Cooper et al., 1994; Willison & Tombaugh, 2006). A simple reaction task involves making a response to a single stimulus or a single feature of a stimulus (Deary, Liewald & Nissan, 2011) for example, to respond with a single key press only when the target appears in yellow but to withhold response when the target is not in yellow. This task therefore requires detection of a target as opposed to discrimination between targets. This also describes a simple go-no-go task. When targets are presented for longer latencies (e.g. 2 seconds; Sikström et al., 2016) the go-no-go paradigm demands a relatively low level of attentional resources. In studies which aim

to compare the effects of high cognitive load and low cognitive load, the simple go-no-go has been used as the latter (e.g. Sikström et al., 2016).

#### 3.1.2.1 No-training ABM

Experiment 2 replicated the procedure from experiment 1 except that the training task was simplified to minimise cognitive load. In Experiment 2 participants were required to press a singular key ({enter}) if a target (either p or q) appeared. There was therefore a shifting aspect to the task but, as it was not necessary to identify the target letter, the degree of focus required was notably reduced from the experiment 1 task. There was also no forced choice element to the paradigm as participants responded to either target letter in the same manner. Targets appeared in 80% of trials. Participants were asked to press the {enter} key if a target appeared and to withhold their response if a target did not appear. A time limit of 2000ms was placed on target response (before the target disappeared) and so participants were not subject to significant time pressure. This simple, non-engaging paradigm was designed to maintain equivalence with the ABM training paradigm from experiment 1 as far as possible but to recruit cognitive resources to a lesser degree.

It should be noted that there is no direct evidence that the no-training task designed for the present study involves the elimination of attentional control as no measure of attentional control was administered before and after the task. An assumption is made based on previous evidence that tasks which place fewer demands on cognitive control and working memory resources

produce inferior attentional control and emotional response improvements relative to more cognitively demanding tasks (e.g. Sari et al., 2015; Swainston et al., 2018). If the anxiety reductions observed following active and control ABM in experiment 1 were attributable to attentional control enhancement, then the 'no-training' task should fail to elicit the anxiety reductions seen in experiment 1.

### 3.1.3 Aims

The aim of experiment 2 was to clarify the role of attentional control processes in ABM outcomes. If the reductions in threat bias and anxiety observed in experiment 1 were attributable to enhanced attentional control, then experiment 2 would not produce these beneficial results due to the experiment 2 training task having low cognitive load. If, however anxiety was attenuated following no-training ABM this would suggest that another mechanism was responsible for these reductions e.g. exposure or 'non-specific' effects. It was predicted that there would be no reduction in threat bias or anxiety following 'no-training' ABM.

## 3.2 Method

### 3.2.1 Design

A 2 x 3 mixed methods design was employed. All participants underwent 'no training' ABM. The between-participants factor was tES group (active tRNS and sham tES). As per experiment 1, attentional bias was assessed and self-

report measures were administered at 3 principal time points: before ABM training on day one (assessment 1), following ABM training on day 3 (assessment 2) and at a day 30 follow-up (assessment 3).

### 3.2.2 Participants

Participants were 42 students from the University of Roehampton (32 female), mean age = 21.05 years, *SD* = 5.43, range = 18 to 42). All participants were right-handed and had normal or corrected to normal vision.

A total of 42 participants were recruited. This number was based on the division of participants across two tES groups resulting in group sizes similar to previous studies using tES to modulate cognitive functioning, for example Ditye et al. (2012), Fertonani, Pirulli & Miniussi, (2011) and Snowball et al. (2013).

The recruitment process replicated that from experiment 1

All participants undertook the no-training ABM task and were allocated to one of two tES categories. This resulted in two experimental groups: No-training ABM with tRNS, and no-training ABM with sham tES. Allocation to tES group was randomised and double blinded (see below).

### 3.2.3 Ethics

The study was approved by the University of Roehampton ethics committee

(approval code PSYC 14/ 116). Written consent was provided by all participants before participation. Participants were compensated for their participation with course credits.

### 3.2.4 Materials

#### 3.2.4.1 Measures

The self-report measures used were the same as those used in part 1 of the study. The Experimental Condition Questionnaire included 'no-training condition' as an option where participants indicated which form of training they believed they had received (Appendix 13).

#### 3.2.4.2 Stimuli

The stimuli used were identical to those used in experiment 1.

#### 3.3.4.3 Attention Bias Assessment

Attention bias assessment was the same as in experiment 1.

#### 3.3.4.4 No-training ABM paradigm

The paradigm used for the 'no training' ABM task was the same as the control ABM group in experiment 1 and as that employed during attention bias assessment, except that participants were not required to press a key

corresponding to the identity of the target. Instead participants were instructed to press the {Enter} key if a target (either q or p) appeared and to withhold response if no target was presented. The target letter replaced the neutral face 50% of the time and the angry face 50% of the time. It was considered that the removal of the requirement to identify the target would reduce cognitive load.

In experiment 1 each block of training comprised 96 trials. In the present paradigm 'no-go' trials were added to this total. Training data were not analysed for the present thesis. However, should training data from experiment 2 be subject to analysis in future, reaction time, accuracy and attention bias calculations will be based upon the same number of response trials in experiment 2 as experiment 1. It would be possible to compare data from the two experiments without making adjustments for differently sized data sets. As per previous go/no-go designs (e.g. Redick et al., 2011; Zhang et al., 2016), 'go' trials comprised 80% of trials and 'no-go' trials made up 20% of the total number of trials. Each block therefore consisted of 96 'go' trials and 24 'no-go' trials. No-training ABM consisted of 6 blocks. The addition of trials rendered the training phase of the study longer than training in experiment 1 at approximately 40 minutes compared to 30 minutes.

#### 3.2.4.5 TES

The tES procedure matched that used in experiment 1 of the study. Stimulation lasted for 20 minutes at the beginning of a 40-minute no-training period. As per experiment 1, allocation to stimulation group was randomised

and double blind. The same list of 5-digit codes which generated active tRNS or sham tES in experiment 1 was used. One stimulation code was allocated to each participant and the same code was used for that participant on each of the 3 days of training. The first participant to commence the study was allocated the first code on the list. Each time a new participant attended the study they were allocated the next code on the list. Once all 40 codes had been allocated, the experimenter began again at the beginning of the list.

### 3.2.5 Procedure

The experiment procedure replicated that used in experiment 1 except that all participants performed the no-training ABM task.

### 3.2.6 Data Preparation

Data from inaccurate trials were removed. Mean accuracy across attention bias assessments was 95.30% (*SD* = 2.92). Reaction times below 200ms were omitted from analysis. To remove the effect of outlying data on analysis, reaction times which were more than 2.5 standard deviations from each participant's mean reaction time were excluded (e.g. Brown et al., 2014). These removals led to the rejection of a further 1.85% of the total number of trials.

### 3.2.7 Data Analyses

Data analyses were conducted as per experiment 1.

### 3.2.8 Baseline Characteristics

#### 3.2.8.1 Baseline Scores for Main Variables of Interest

Findings from experiment 2 will be discussed in light of results from experiment 1. Table 3.1 presents baseline attention bias, state anxiety, trait anxiety and attentional control scores across all ABM/tES groups from experiments 1 and 2. Independent t-tests compared baseline scores for all participants from experiment 1 and all participants from experiment 2. For each measure, baseline score did not differ between experiments (see table 3.1)

Table 3.1:

*Baseline mean (SD) scores for major variables of interest*

| | Baseline Mean (SD) Scores | | | |
|---|---|---|---|---|
| | Attention Bias (ms) | State Anxiety | Trait Anxiety | Attentional Control |
| All Participants Experiment 1 | .97 (13.70) | 33.18 (10.46) | 41.73 (11.84) | 48.87 (7.84) |
| All Participants Experiment 2 | -2.25 (14.77) | 34.48 (10.59) | 44.50 (12.19) | 49.48 (7.75) |
| **Between Subjects Effects** | ***t* = 1.21, *p* = .23** | ***t* = .65, *p* = .51** | ***t* = 1.23, *p* = .22** | ***t* = .41, *p* = .68** |
| Active ABM/Active tRNS | -.30 (18.75) | 33.38 (10.94) | 39.48 (9.69) | 50.76 (6.50) |
| Active ABM/Sham tES | -.73 (13.69) | 33.90 (8.15) | 43.10 (12.92) | 47.57 (7.88) |
| Control ABM/Active tRNS | 1.59 (9.77) | 31.71 (9.31) | 40.14 (12.98) | 50.62 (6.79) |
| Control ABM/Sham tES | 3.33 (11.37) | 33.71 (13.34) | 44.19 (11.67) | 46.52 (9.48) |
| No Training ABM/Active tRNS | -4.78 (14.59) | 33.52 (9.78) | 41.24 (10.80) | 50.62 (7.26) |
| No Training ABM/Sham tES | .28 (14.87) | 35.43 (11.51) | 47.76 (12.87) | 48.33 (8.22) |

### 3.2.8.2 Depression and Fear of Negative Evaluation

Table 3.2 shows for each experimental group the mean and standard deviation score at baseline for the CES-D and FNE.

Independent t-tests revealed that baseline scores on self-report measures did not differ significantly between groups (*t*s < .43, *p*s > .67).

Table 3.2:

*Mean (SD) CES-D and FNE score for each self-report measure for each tES group*

| | No-training/active tRNS | | No-training/sham tES | |
|---|---|---|---|---|
| | M | SD | M | SD |
| CES-D | 14.42 | 8.93 | 15.00 | 12.05 |
| FNE | 14.21 | 7.78 | 13.15 | 7.66 |

### 3.2.8.3 State and Trait Anxiety Across Experimental Groups by Gender

Table 3.3 shows the mean and standard deviation state anxiety scores before no-training ABM for males and females.

Table 3.3:

*Baseline mean (standard deviation) state and trait anxiety scores across experimental groups for females and males*

| | | Active ABM | |
|---|---|---|---|
| | | Active tRNS | Sham tES |
| N | | 14 | 18 |
| Females | State Anxiety | 34.57 (9.87) | 36.67 (11.54) |
| | Trait Anxiety | 42.57 (11.19) | 49.67 (12.48)* |
| N | | 7 | 3 |
| Males | State Anxiety | 31.43 (11.00) | 28.00 (5.69) |
| | Trait Anxiety | 38.57 (10.26) | 46.33 (10.21) |

* P< .05

State Anxiety

There was no significant difference in baseline state anxiety between stimulation groups ($t$ = .58, $p$ = .57).

State anxiety mean and standard deviation scores reported for a normative sample of undergraduate students are mean = 36.47 ($SD$ = 10.02) for males and mean = 38.76 ($SD$ = 11.95) for females (Spielberger et al., 1983). One sample t-tests revealed that for females who received active tRNS mean baseline state anxiety score did not differ significantly from the mean normative score, ($t$ = 1.59, $p$ = .14). For females who received sham tES, mean baseline state anxiety score did not differ significantly from the mean normative score, ($t$ = .77, $p$ = .45). For males who received active tRNS mean baseline state anxiety score did not differ significantly from the mean normative score, ($t$ = 1.33, $p$ = .23). For males who received sham tES, mean baseline state anxiety score did not differ significantly from the mean normative score, ($t$ = 1.49, $p$ = .28).

Trait Anxiety

There was no difference in trait anxiety scores between tES groups at baseline ($t$ = 1.78, $p$ = .08).

The normative mean of trait anxiety reported for a sample of undergraduate students is 40.40 ($SD$ = 10.15) for females and 38.30 ($SD$ = 9.18) for males (Spielberger, 1983). One sample t-tests revealed that for females who received active tRNS, baseline trait anxiety did not differ significantly from the normative mean ($t$ = .73, $p$ = .48). Baseline trait anxiety for females who received sham tES ($M$ = 49.67, $SD$ = 12.48) was significantly higher than the normative mean ($M$ = 40.40, $SD$ = 10.15), $t(17)$ = 3.15, $p$ = .012. For males who received tRNS, baseline trait anxiety did not differ significantly from the normative mean ($t$ = .07, $p$ = .95). For males who received sham tES, baseline trait anxiety did not differ significantly from the normative mean ($t$ = .33, $p$ = .77).

### 3.2.8.4 Correlations Between State Anxiety Scores

Data from each administration of the state anxiety scale of the STAI (i.e. start of day 1, end of day 1, start of day 2, end of day 2, start of day 3, end of day 3, start of day 30, end of day 30) were subject to a Pearson Product Moment Correlation analysis. All correlations were significant (*r*s > .57, all *p*s < .001). The normative test-retest reliability r values reported by Spielberger et al. (1983) for college students, with a test-retest interval of 20 days were .54 for males and .27 for females. Our results therefore suggest strong test-retest reliability and consistency within the state anxiety data.

### 3.2.8.5 Correlations Between State Anxiety and Trait Anxiety

As with the data from experiment 1, baseline trait anxiety score was correlated with state anxiety score at each of the principal 3 assessment points. As demonstrated in table 3.4, baseline trait anxiety correlated significantly with state anxiety at each assessment.

Table 3.4:

*Bivariate correlations between baseline trait anxiety scale and state anxiety scale (SAS) at assessments 1, 2 and 3*

| | SAS Assessment 1 | SAS Assessment 2 | SAS Assessment 3 |
|---|---|---|---|
| Baseline Trait Anxiety | **.626**** | **.636*** | **.724**** |

** *p* < .001

#### 3.2.8.6 Correlations Between Self-report Measures at Baseline

Baseline scores from questionnaires assessing trait characteristics were subject to a Pearson Product Moment correlational analysis. Table 3.5 shows the correlation between baseline scores on trait self-report measures.

Table 3.5:

*Bivariate correlations for trait anxiety scale (TAS), attentional control scale (ACS), Centre for Epidemiological Studies depression questionnaire (CES-D) and fear of negative evaluation scale (FNE) at baseline.*

| | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| 1. Trait Anxiety | 1.00 | | | |
| 2. Attentional Control | **-.524**$^{**}$ | 1.00 | | |
| 3. Depression | **.881**$^{**}$ | **-.400**$^{*}$ | 1.00 | . |
| 4. Fear Negative Evaluation | **.694**$^{**}$ | **-.353**$^{**}$ | **.634**$^{*}$ | 1.00 |

* $p < 0.05$

** $p < 0.0$

Baseline scores across all questionnaires were significantly correlated (all *r*s > .35, *p*s < .022 suggesting that participants reported consistently across measures.

## 3.3 Results

### 3.3.1 Analyses of Variance Across all Participants

#### 3.3.1.1 Attention Bias (All Participants)

A 2 x 3 mixed ANOVA was conducted on the attention bias data with a between subjects factor of tES (active tRNS, sham tES) and a within subjects

factor of assessment (assessment 1, assessment 2, assessment 3). There were no significant main or interaction effects *(Fs* < 1.79, *ps* > .17).

Figure 3.1 shows mean attentional bias across assessments for each tES group (active tRNS, sham tES) and for all participants. Positive attention bias scores represent threat bias and negative scores represent neutral bias.

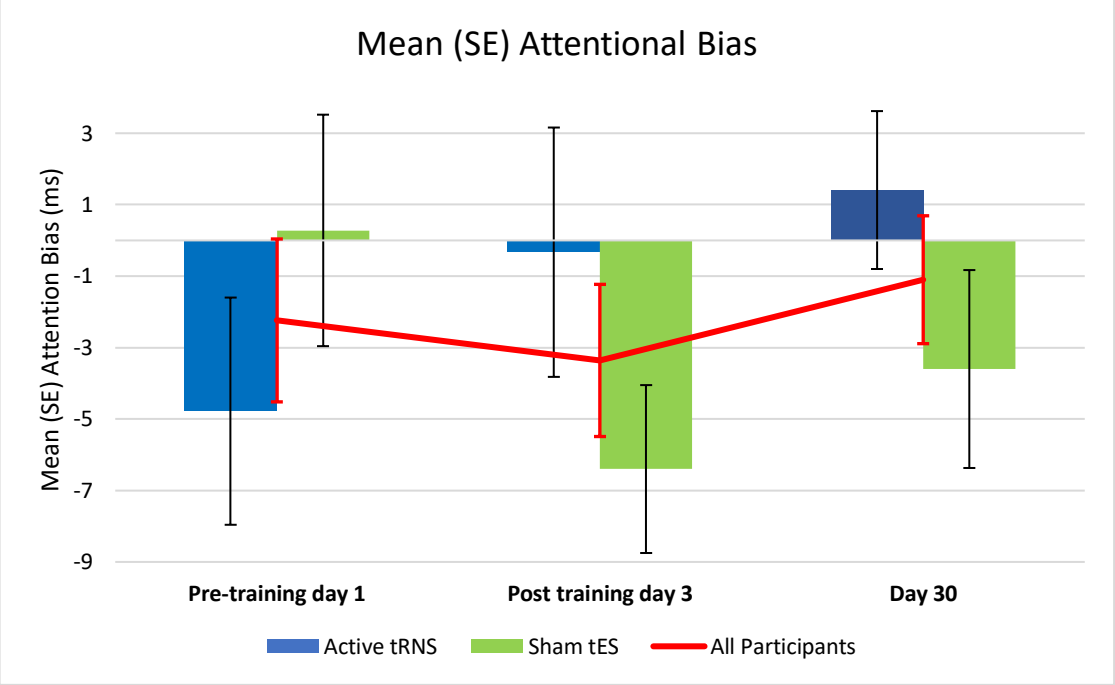



*Figure 3.1.* Mean (SE) attention bias across assessments for each tES group and for all participants

### 3.3.1.2 State Anxiety (All Participants)

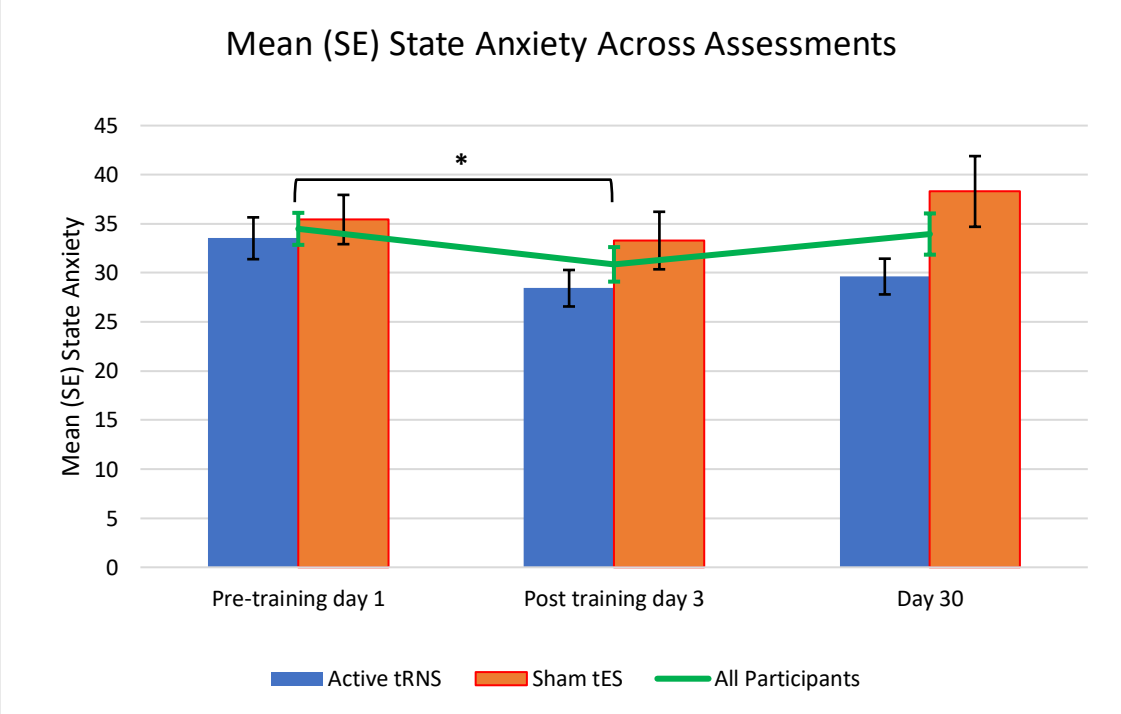
Replicating the threat bias ANOVA above, a 2 x 3 mixed ANOVA was conducted on state anxiety data with between subjects factor of tES (active tRNS, sham tES) and a within subjects factor of assessment (assessment 1, assessment 2, assessment 3). As demonstrated in figure 3.2 there was a significant main effect of assessment, $F(2,80) = 4.12$, $p = .02$, ($\eta_p^2 = .09$; *observed power* =

.71) suggesting a change in state anxiety across assessments for all participants. Paired samples t-tests examined change in state anxiety across assessments. All results were Bonferroni corrected for multiple comparisons (significant if 3*p < .05). At assessment 1 participants reported greater state anxiety *(M* = 34.48, *SD* = 11.38) than at assessment 2 *(M* = 30.86, *SD* = 11.38), *t(*41) = 2.63, *p* = .04. The change in state anxiety from assessment 2 to assessment 3 was marginally significant *t(*41) = 2.48, *p* = .054 with increased state anxiety at assessment 3 *(M* = 33.95, *SD* = 13.46) compared to assessment 2 *(M* = 30.86, *SD* = 11.38). Change in state anxiety level between assessment 1 and assessment 3 was not significant (*t* = .34, *p* = 2.22).

The interaction between assessment and tES was marginally significant *F(*2,80) = 3.10, *p* = .051, ($\eta p^2$ = .07; *observed power* = .58). A component within-participant follow-up analysis for each tES group revealed that there was a significant change in state anxiety across assessments for active tRNS participants, *F(*2,40) = 4.50, *p* = .03, ($\eta p^2$ = .18; *observed power* = .64; Greenhouse Geisser Corrected). For the active tRNS group, paired sample t-tests examined change in state anxiety across assessments. Results were Bonferroni corrected for multiple comparisons (significant if 3*p < .05). These revealed a reduction in state anxiety from assessment 1 *(M* = 33.52, *SD* = 9.78) to assessment 2 *(M* = 28.43, *SD* = 8.51) which approached significance, *t*(20) = 2.53, *p* = .06. There were no further significant changes in state anxiety across assessments, (*t*s < 1.92, *p*s > .21). In the sham tES group there was an effect of assessment which approached significance, *F(*2,40) = 2.95, *p* = .064, ($\eta p^2$ = .13; *observed power* = .54). Follow-up paired samples t-tests did not reveal a significant change in state anxiety across assessment sessions (all *t*s <

2.29, *p*s > .10; Bonferroni corrected for multiple comparisons; significant if 3*p < .05). Independent t-tests examined the impact of tES group on state anxiety at each assessment. After adjusting for multiple comparisons using Bonferroni correction (significant if 3*p < .05), there was no difference in state anxiety between tES groups at any assessment (*t*s < 2.14. *p*s > .12).

The main effect of tES group was non-significant ($F = 2.50$, $p = .12$).




* *p* < .05

*Figure* 3.2. Mean (SE) state anxiety across assessments for each tES group and for all participants

### 3.3.1.3 State Anxiety at Start and End of Each Experimental Day (All Participants)

State anxiety was measured on each day of training at the start and end of each session (see figure 3.3).

A 2 x 2 x 3 mixed ANOVA was conducted on state anxiety data with the between subjects factor of tES (active tRNS, sham tES) and 2 within subjects factors of time (start of session, end of session) and day (Day 1, Day 2, Day 3, Day 30).

This revealed a main effect of day, $F(1.98,79.07) = 3.53$, $p = .03$, ($\eta p^2 = .08$; *observed power* = .64; Greenhouse Geisser corrected). After allowing for multiple corrections (Bonferroni adjustment; significant if 6*p < .05) paired samples t-tests revealed no significant changes in state anxiety across experimental days (*t*s < 2.40, *p*s > 1.26).

The interaction between day and tES approached significance, $F(1.98,79.07) = 2.92$, $p = .06$, ($\eta p^2 = .07$; *observed power* = .55; Greenhouse Geisser corrected). For each tES group, paired samples t-tests were performed to assess change in state anxiety across days. Results were Bonferroni corrected for multiple comparisons (significant if 6*p < .05). These revealed no significant differences in state anxiety across days for active tRNS participants (*t*s < 1.30, *p*s > 1.25) or for sham tES participants (*t*s < 2.53, *p*s > .12). Independent t-tests examined the effect of tES for each day of testing. State anxiety did not differ significantly between tES groups on any

experimental day (*t*s < 2.21, *p*s > 1.40; Bonferroni adjusted for multiple comparisons; significant if 4*p < .05).

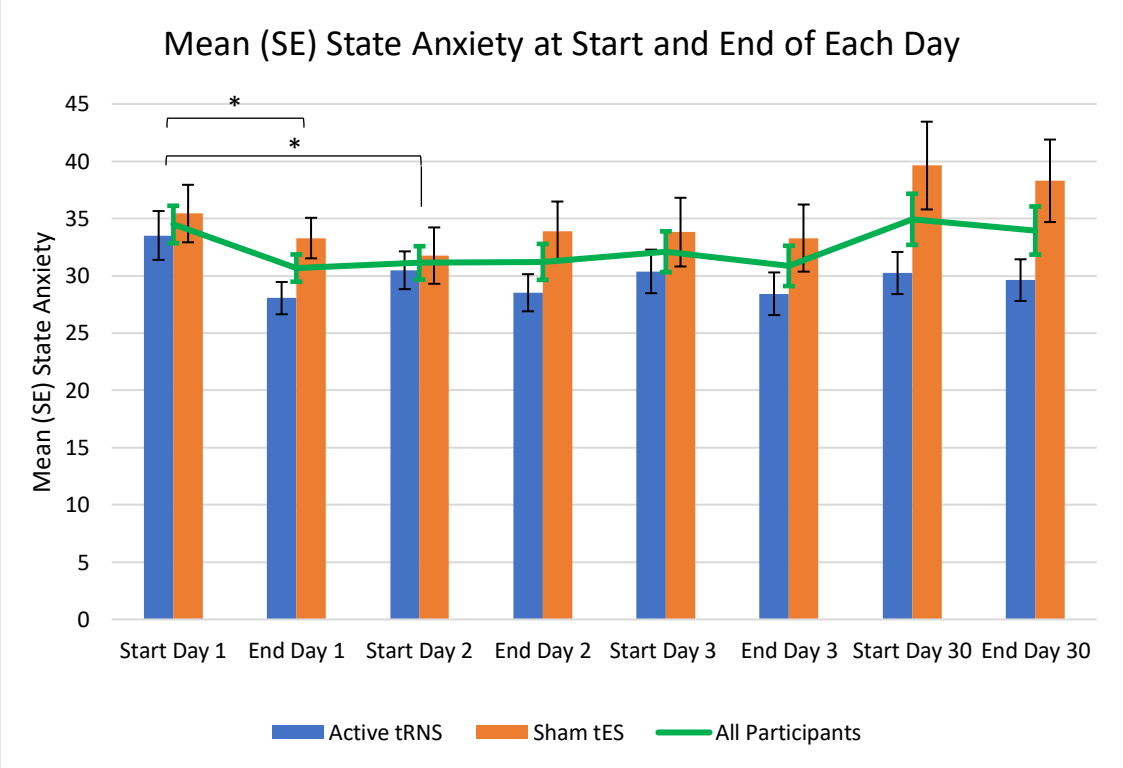
There was a main effect of time, $F(1,40) = 4.37$, $p = .04$, ($\eta p^2 = .10$; *observed power* = .53; Greenhouse Geisser corrected). Participants reported greater state anxiety at the beginning of the session *(M* = 33.15, *SD* = 11.65) compared to the end *(M* = 31.62, *SD* = 10.92).

The interaction between day and time was significant $F(3,120) = 5.48$, $p = .001$, ($\eta p^2 = .12$; *observed power* = .93). A one-way repeated measures ANOVA was carried out on start of session state anxiety to explore changes over days. For start of session state anxiety there was a significant effect of day $F(2.31,94.68) = 3.88$, $p = .02$, ($\eta p^2 = .09$; *observed power* = .73). Paired samples t-tests (Bonferroni adjusted for multiple comparisons; significant if 6*p < .05) revealed a significant reduction in state anxiety from start of day 1 *(M* = 34.38, *SD* = 10.59) to start of day 2 *(M* = 31.12, *SD* = 9.49), $t(41) = 3.51$, $p = .001$. No other change in state anxiety across days for start of session data was significant (all *t*s < 2.65, *p*s > .07).

A one-way repeated measures ANOVA was carried out on end of session data to explore changes over days. There was a significant effect of day $F(1.77,72.50) = 3.46$, $p = .04$, ($\eta p^2 = .08$; *observed power* = .59; Greenhouse Geisser corrected). Paired samples t-tests revealed no significant change in state anxiety across days (all *t*s < 2.48, *p*s > .11; Bonferroni adjusted for multiple comparisons; significant if 6*p < .05). Paired samples t-tests (Bonferroni adjusted for multiple comparisons; significant if 4*p < .05) were

used to assess significant differences between start of session and end of session state anxiety for each experimental day (day 1, day 2, day 3, day 30). There was a significant reduction in state anxiety from start of day 1 *(M* = 34.38, *SD* = 10.59) to end of day 1 *(M* = 30.67, *SD* = 7.71), *t*(41) = 3.21, *p* = .01. The comparison of start to end of day state anxiety was not significant on any other day (*t*s < 1.44, *p*s > .63).

No other main or interaction effects were observed *(F*s < 2.31, *ps* > .08).




* *p* < .05

*Figure 3.3*. Mean (SE) state anxiety scores at the start and end of each experimental day for each tES group and for all participants

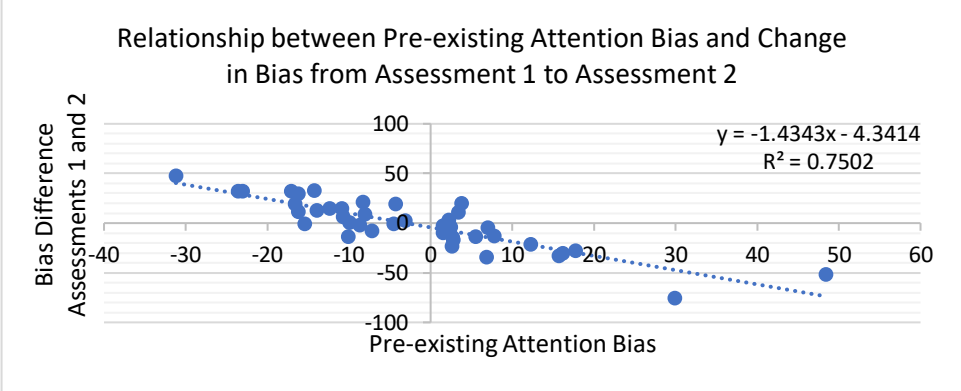
### 3.3.2 Analyses of Covariance with Pre-existing Attention Bias as a Covariate

#### 3.3.2.1 Attention Bias (Pre-existing Attention Bias as Covariate)

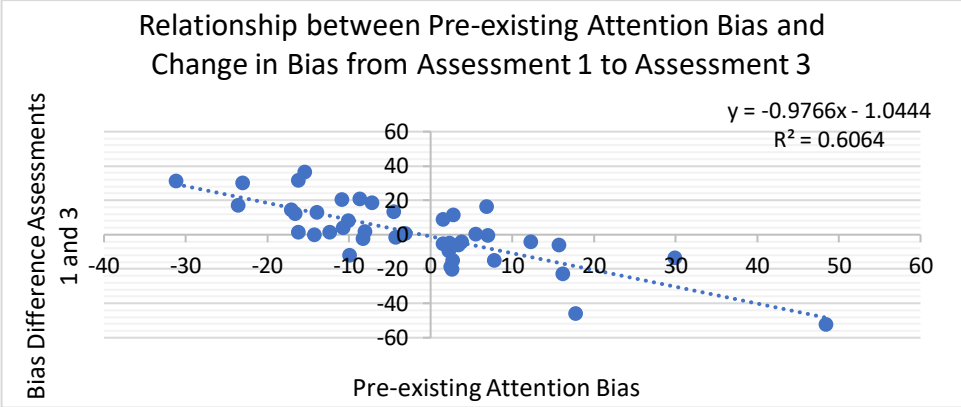
A 2 x 3 ANCOVA was conducted on attention bias data with a between subjects factor of tES (active tRNS, sham tES), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and the covariate of pre-existing attention bias. There was a significant interaction between assessment and pre-existing attention bias, $F(1.31,51.26) = 39.88$, $p < .001$, ($\eta_p^2 = .51$; *observed power* = 1.00; Greenhouse Geisser corrected). In order to explore the relationship between pre-existing attention bias and change in attention bias across assessments, a Pearson Product Moment correlational analysis was conducted with pre-existing attention bias, change in attention bias from assessment 1 to assessment 2, change in attention bias from assessment 1 to assessment 3 and change in attention bias from assessment 2 to assessment 3. Change in attention bias was calculated by subtracting attention bias score at the earlier assessment from attention bias score at the later assessment e.g. attention bias at assessment 2 – attention bias at assessment 1. A positive score represented an increase in attention bias therefore and a negative score represented a reduction in attention bias. Pre-existing attention bias was strongly, negatively correlated with change in attention bias from assessment 1 to assessment 2, $r(42) = -.87$, $p < .001$. Pre-existing attention bias was strongly, negatively correlated with change in attention bias from assessment 1 to assessment 3, $r(42) = -.78$, $p < .001$. Pre-existing attention bias was moderately, positively correlated with change in

attention bias from assessment 2 to assessment 3, $r(42) = .33$, $p = .032$ (see figure 3.10 for regression lines). Figure 3.10 shows that greater attention bias towards threat at baseline was associated with greater reduction in threat bias following ABM training relative to before ABM training at assessment 2 relative to assessment 1 and at assessment 3 relative to assessment 1.

a)




b)




c)

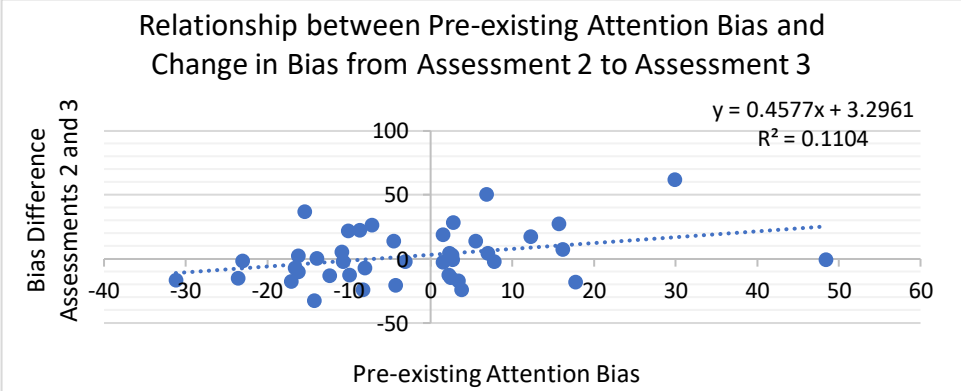



*Figure 3.4*. The relationship between pre-existing attention bias (AB) and a) change in AB between assessments 1 and 2, b) change in AB between assessments 1 and 3 and c) change in AB between assessments 2 and 3 across experiment 2. For pre-existing attention bias, positive scores indicate attention bias towards threat and negative scores indicate attention bias towards neutral. For difference scores, positive values represent increase in threat bias and negative scores represent increase in neutral bias (reduction in threat bias).

There was a significant main effect of pre-existing attention bias, $F(1,39) = 19.11$, $p < .001$, ($\eta_p^2 = .33$; *observed power* = .99). There was a moderate, negative correlation between pre-existing attention bias and attention bias, $r(42) = -.41$, p = .006.

The main effect of tES was also significant, F(1,39) = 4.66, p < .001, ($\eta_p^2 = .11$; *observed power* = .56). An independent t-test revealed no significant difference in attention bias between tES groups ($t = 1.18$. $p = .25$).

There were no further main or interaction effects ($F$s < 1.84, $p$s > .17).

#### 3.3.2.2 State Anxiety (Pre-existing Attention Bias as Covariate)

A 2 x 3 ANCOVA was conducted on the state anxiety data with a between subjects factor of tES (active tRNS, sham tES), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and the covariate of pre-existing attention bias. The main effect of assessment was significant, $F(2,78) = 4.65$, $p = .012$, ($\eta_p^2 = .11$; *observed power* = .77). The assessment x tES interaction was also significant, $F(2,78) = 3.74$, $p = .028$, ($\eta_p^2 = .09$; *observed power* = .67). These effects are discussed in section 3.3.1.2.

#### 3.3.2.3 State Anxiety at Start and End of Each Experimental Day (Pre-existing Attention Bias as Covariate)

With state anxiety as the dependant variable A 2 x 4 x 2 mixed ANCOVA was conducted with a between subjects factor of ABM (active ABM, control ABM),

a within subjects factor of day (day 1, day 2, day 3, day 30) and time (before ABM training, after ABM training) and pre-existing attention bias as the covariate. This revealed a main effect of day, $F(1.95,76.17) = 3.40$, $p = .04$, ($\eta p^2 = .08$; *observed power* = .62; Greenhouse Geisser corrected). The interaction between day and tES was significant, $F(1.95,76.17) = 3.15$, $p = .05$, ($\eta p^2 = .08$; *observed power* = .58; Greenhouse Geisser corrected). There was a main effect of time, $F(1,39) = 4.19$, $p = .047$, ($\eta p^2 = .10$; *observed power* = .52). The interaction between day and time was significant $F(3,117) = 6.38$, $p < .001$, ($\eta p^2 = .14$; *observed power* = .96). Each of these main and interaction effects was explored in section 3.3.1.3.

## 3.3.3 Analyses of Covariance with Pre-existing Trait Anxiety as a Covariate

### 3.3.3.1 Attention Bias (Pre-existing Trait Anxiety as Covariate)

A 2 x 3 ANCOVA was conducted on the attention bias data with a between subjects factor of tES (active tRNS, sham tES), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and the covariate of pre-existing trait anxiety. There were no significant main or interaction effects, ($F$s < 1.24, $p$s > .30).

### 3.3.3.2 State Anxiety (Pre-existing Trait Anxiety as Covariate)

A 2 x 3 ANCOVA was conducted on the attention bias data with a between subjects factor of tES (active tRNS, sham tES), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and the covariate of

pre-existing state anxiety. There was a significant main effect of trait anxiety, $F(1,39) = 41.77$, $p < .001$, ($\eta_p^2 = .52$; *observed power* = 1.00). Pearson's Product Moment correlational analysis revealed that pre-existing trait anxiety was significantly, strongly and positively correlated with mean state anxiety $r(42) = .74$, $p < .001$ (see figure 3.17).

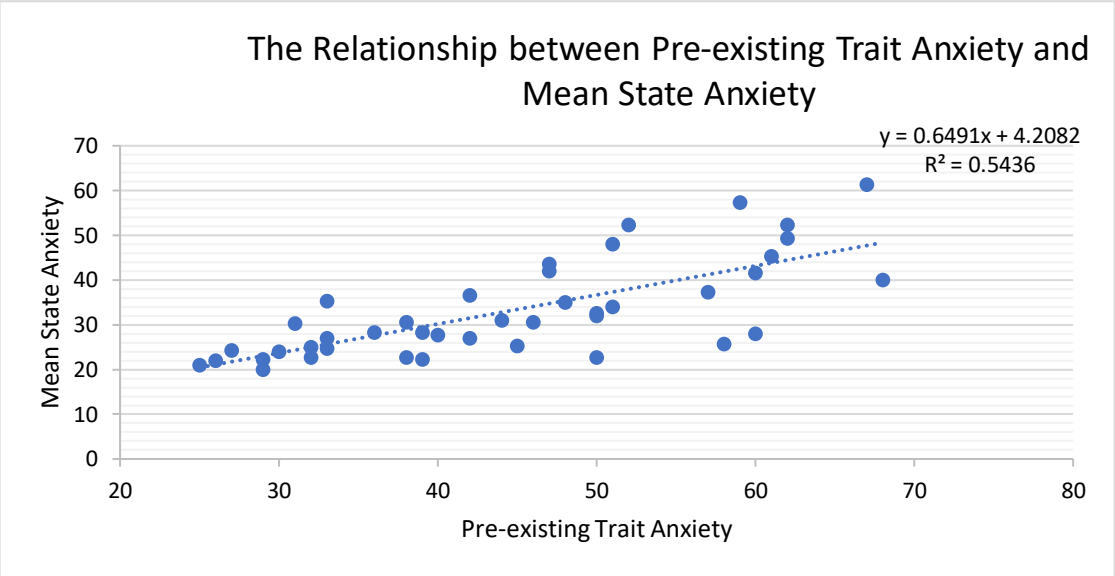



*Figure 3.5*. The relationship between scores on the state anxiety scale of the STAI (Spielberger et al., 1983) across experiment 2 and the trait anxiety scale of the STAI at baseline.

The main effect of assessment seen in the main analysis (section 3.3.1.2) was not observed with trait anxiety held constant ($F = 1.64$, $p = .20$). The tES x Assessment interaction (section 3.3.1.2) was also no longer significant ($F = 1.88$, $p = .16$). There were no further significant main or interaction effects, ($F$s < 1.91, $p$s > .15).

### 3.3.3.3 State Anxiety at Start and End of each Experimental Day (Pre-existing Trait Anxiety as Covariate)

With state anxiety as the dependant variable A 2 x 4 x 2 mixed ANCOVA was conducted with a between subjects factor of ABM (active ABM, control ABM), a within subjects factor of day (day 1, day 2, day 3, day 30) and time (before ABM training, after ABM training) and pre-existing trait anxiety as the covariate. This revealed a main effect of day, $F(2.13,82.97) = 3.94$, $p = .01$, ($\eta p^2 = .09$; *observed power* = .71; Greenhouse Geisser corrected). For a breakdown of this effect see section 3.3.1.3. The main effect of trait anxiety was significant, $F(1,39) = 39.79$, $p < .001$, ($\eta p^2 = .51$; *observed power* = 1.00). See figure 3.5 for the relationship between pre-existing trait anxiety and state anxiety. The day x time x tES interaction was significant, $F(3,117) = 2.85$, $p = .04$, ($\eta p^2 = .07$; *observed power* = .67).

For each day the interaction between time and tES was explored using 2 x 2 ANCOVAs with time (start of session, end of session) as the within participants factor and tES (active tRNS, sham tES) as the between participants factor and trait anxiety as a covariate. Analysis of day 1 data revealed a significant main effect of trait anxiety, $F(1,39) = 27.88$, $p < .001$, ($\eta p^2 = .42$; *observed power* = 1.00). State anxiety on day 1 was significantly, highly, positively correlated with pre-existing trait anxiety, $r(42) = .67$, $p < .001$. The time x trait anxiety interaction was significant for day 1 state anxiety, $F(1,39) = 5.35$, $p = .026$, ($\eta p^2 = .12$; *observed power* = .62). Follow up bivariate correlational analysis revealed that start of day 1 state anxiety was strongly and positively correlated with pre-existing trait anxiety, $r(42) = .63$, $p < .001$) as was end of

day 1 state anxiety, $r(42) = .59$, $p < .001$). For day 1 state anxiety, there was a significant time x tES interaction, $F(1,39) = 4.27$, $p = .045$, ($\eta p^2 = .10$; *observed power* = .52). For each time (start of session, end of session), independent t-tests explored the effect of tES (active tRNS, sham tES) on state anxiety. Results were Bonferroni adjusted for multiple comparisons (significant if 2*p < .05). TES groups did not differ in state anxiety at the start of day 1 ($t = .58$, $p = 1.13$). However, at the end day 1, state anxiety for the active tRNS group ($M = 28.05$, $SD = 6.45$) was lower than for the sham tES group ($M = 33.29$, $SD = 8.12$) at a near significant level, $t(40) = 2.32$, $p = .052$. For each tES condition (active tRNS, sham tES), paired samples t-tests were used to investigate the main effect of time on day 1 state anxiety. Results were Bonferroni adjusted for multiple comparisons (significant if 2*p < .05). For the active tRNS group, state anxiety at the end of day 1, ($M = 28.05$, $SD = 6.45$) was lower than at the start of day 1, ($M = 33.52$, $SD = 9.78$), $t(20) = 3.96$, $p = .002$. The effect of time was not significant for the sham tES group ($t = 1.13$, $p = .52$). For day 1 state anxiety, there were no further significant main effects or interaction effects ($F$s < 1.89, $p$s > .18).

For day 2 state anxiety there was a significant main effect of the covariate trait anxiety, $F(1,39) = 22.33$, $p < .001$, ($\eta p^2 = .36$; *observed power* = 1.00). Pre-existing trait anxiety was highly, positively correlated with day 2 state anxiety, $r(42) = .62$, $p < .001$. The interaction between time and tES conditions was significant for day 2 state anxiety, $F(1,39) = 4.62$, $p = .038$, ($\eta p^2 = .11$; *observed power* = .55). For each time (start of session, end of session) an independent t-test examined the effect of tES condition on day 2 state anxiety. Results were Bonferroni adjusted for multiple comparisons

(significant if 2*p < .05). There were no significant effects (*t*s < 1.76, *p*s < .17). For each tES group (active tRNS, sham tES) a paired samples t-test investigated the effect of time on day 2 state anxiety. Results were Bonferroni adjusted for multiple comparisons (significant if 2*p < .05). For the active tRNS group, a reduction in state anxiety from start of day 2 (*M* = 30.48, *SD* = 7.55) to end of day 2 (*M* = 28.52, *SD* = 7.44) was marginally significant, $t(20) = 2.26$, $p = .07$. For the sham tES group, an increase in state anxiety at the end of day 2 relative to the start of day 2 was not significant ($t = 1.27$, $p = .44$). There were no further main or interaction effects arising from the analysis on day 2 state anxiety data (*F*s < .12, *p*s > .73).

For day 3 state anxiety there was a significant main effect of trait anxiety, $F(1,39) = 28.60$, $p < .001$, ($\eta p^2 = .42$; *observed power* = 1.00). Pre-existing trait anxiety was highly, positively and significantly correlated with state anxiety at day 3, $r(21) = .70$, $p < .001$. There were no further main or interaction effects for day 3 state anxiety data, (*F*s < .35, *p*s > .55).

For day 30 state anxiety there was a significant main effect of trait anxiety, $F(1,39) = 38.72$, $p < .001$, ($\eta p^2 = .50$; *observed power* = 1.00). Pre-existing trait anxiety was highly, positively and significantly correlated with state anxiety at day 30, $r(21) = .62$, $p = .003$. There were no further main or interaction effects for day 30 state anxiety data, (*F*s < 1.63, *p*s > .21).

For each time (start of session, end of session) a 4 x 2 ANCOVA was conducted with day as the within participants factor (day 1, day 2, day 3, day 30) and tES (active tRNS, sham tES) as the between participants factor and with pre-

existing trait anxiety as a covariate. For start of session state anxiety, there was a significant main effect of trait anxiety, $F(1,39) = 40.21$, $p < .001$, ($\eta p^2 = .51$; *observed power* = 1.00). Pre-existing trait anxiety was highly, positively and significantly correlated with start of session state anxiety, $r(42) = .73$, $p < .001$. For start of session state anxiety there was also a significant day x trait anxiety interaction, $F(2.45,95.62) = 3.28$, $p = .033$, ($\eta p^2 = .51$; *observed power* = 1.00; Greenhouse Geisser corrected). Pearson Product moment correlational analysis was used to examine the relationship between start of session state anxiety on each day (day 1, day 2, day 3, day 30) and pre-existing trait anxiety. Pre-existing trait anxiety was highly, positively correlated with state anxiety at the start of day 1, $r(42) = .59$, $p < .001$, at the start of day 2, $r(42) = .59$, $p < .001$, at the start of day 3, $r(42) = .66$, $p < .001$ and at the start of day 30, $r(42) = .72$, $p < .001$. Analysis of start of session data revealed no further main or interaction effects ($F$s < 2.44, $p$s > .08). For end of session state anxiety, the main effect of trait anxiety was significant, $F(1,39) = 31.71$, $p < .001$, ($\eta p^2 = .45$; *observed power* = 1.00). Pre-existing trait anxiety was highly, positively correlated with state anxiety at the end of session, $r(42) = .70$, $p < .001$. The main effect of day was also significant, $F(1.92,74.87) = 5.14$, $p = .009$, ($\eta p^2 = .12$; *observed power* = .80; Greenhouse Geisser corrected). End of day state anxiety was compared across days using paired samples t-tests. Results were Bonferroni adjusted for multiple comparisons (significant if 6*p < .05). No paired comparisons were significant ($t$s < 2.48, $p$s > .11). For end of day state anxiety there was a significant day x pre-existing trait anxiety interaction, $F(1.92,74.87) = 7.73$, $p = .001$, ($\eta p^2 = .17$; *observed power* = .94; Greenhouse Geisser corrected). For each day, Pearson Product moment correlational analysis was used to examine

the relationship between end of session state anxiety (day 1, day 2, day 3, day 30) and pre-existing trait anxiety. Pre-existing trait anxiety was highly, positively correlated with state anxiety at the end of day 1, $r(42) = .59$, $p < .001$, at the end of day 2, $r(42) = .58$, $p < .001$, at the end of day 3, $r(42) = .64$, $p < .001$ and at the end of day 30, $r(42) = .72$, $p < .001$. For end of day state anxiety there were no further significant main or interaction effects ($F$s < 1.22, $p$s > .28).

For each tES group (active tRNS, sham tES) a 4 x 2 ANCOVA was carried out with the within participants factors of day (day 1, day 2, day 3, day 30) and time (start of session, end of session) and with trait anxiety as a covariate. Only the main effect of trait anxiety was significant for the active tRNS group, $F(1,19) = 4.88$, $p < .001$, ($\eta p^2 = .53$; *observed power* = .99). Pre-existing trait anxiety was highly, positively correlated with mean state anxiety for participants in the active tRNS group, $r(21) = .75$, $p < .001$. No further main or interaction effects arose from analysis of data from the active tRNS group ($F$s < 2.61, $p$s > .12). For the sham tES group there was a significant main effect of day, $F(1.96,19.00) = 4.73$, $p = .015$, ($\eta p^2 = .20$; *observed power* = .75; Greenhouse Geisser corrected). Paired samples t-tests examined change in state anxiety across experimental days for participants who received sham tES. Following correction for multiple comparisons (Bonferroni adjustment) change in state anxiety was not significant across any pairs of days ($t$s < 2.53. $p$s > .12). For the sham tES group there was also a significant day x trait anxiety interaction, $F(1.96,19.00) = 7.78$, $p = .002$, ($\eta p^2 = .29$; *observed power* = .93). For each day, the relationship between pre-existing trait anxiety and state anxiety was explored using Pearson Product Moment correlational

analyses. For participants in the sham tES group, pre-existing trait anxiety was highly and positively correlated with state anxiety on day 1, $r(21) = .68$, $p = .001$, on day 2, $r(21) = .65$, $p = .001$, on day 3, $r(21) = .70$, $p < .001$ and on day 30, $r(21) = .62$, $p = .003$. For the sham tES group, there were no further significant main or interaction effects ($F$s < 2.43, $p$s > .14).

There were no further main or interaction effects ($F$s < 2.43, $p$s > .08).

### 3.3.4 Analyses of Covariance with Pre-existing Attentional Control as a Covariate

#### 3.3.4.1 Attention Bias (Pre-existing Attentional Control as Covariate)

A 2 x 3 ANCOVA was conducted on the attention bias data with a between subjects factor of tES (active tRNS, sham tES), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and the covariate of pre-existing attentional control. No main or interaction effects were significant, ($F$s < 1.24, $p$s > .30).

#### 3.3.4.2 State Anxiety (Pre-existing Attentional Control as Covariate)

The ANCOVA above was repeated on state anxiety data with pre-existing attentional control as the covariate. The assessment x tES interaction

approached significance, $F(2,78) = 3.02$, $p = .054$, ($\eta_p^2 = .07$; *observed power* = .57). This effect was explored in section 3.3.1.2.

The main effect of pre-existing attentional control was marginally significant, $F(1,39) = 3.65$, $p = .064$, ($\eta_p^2 = .09$; *observed power* = .46). Pearson Product Moment Correlational analysis revealed a weak to moderate, negative correlation between pre-existing attentional control and mean state anxiety which was significant, $r(42) = -.32$, $p = .04$. This suggested that greater attentional control at baseline was associated with lower level state anxiety. See figure 3.6 for the relationship between pre-existing attentional control and state anxiety.

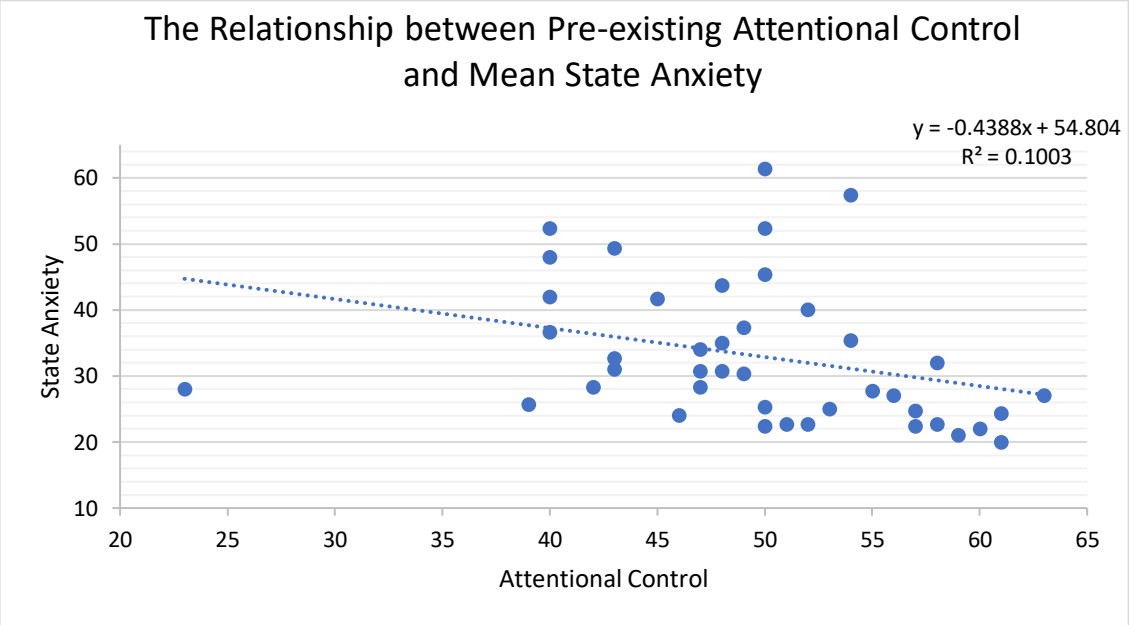



*Figure 3.6*. The relationship between scores on the attention control scale (Derryberry & Reed, 2002) at baseline and mean scores on the state anxiety scale (Spielberger et al., 1983) across experiment 2.

The main effect of assessment seen in the main analysis (section 3.3.1.2) was not observed with pre-existing attentional control as a covariate ($F$ = .70, $p$ = .50)

There were no further significant main or interaction effects, ($F$s < 1.77, $p$s > .19).

#### 3.3.4.3 State Anxiety at Start and End of each Experimental Day (Pre-existing Attentional Control as Covariate)

With state anxiety as the dependent variable 2 x 4 x 2 ANCOVA with tES (active tRNS, sham tES) as the between participants factor and day (day 1, day2, day 3, day 30) and time (start of session, end of session) as within participants factors was conducted with pre-existing attentional control as a covariate. There was a marginally significant interaction between day and time, $F(3,117) = 2.45$, $p$ = .067, ($\eta p^2$ = .06; *observed power* = .60). For state anxiety data from each day (day 1, day 2, day 3, day 30) a paired samples t-test examined the effect of time (start of session, end of session). Results were Bonferroni adjusted for multiple comparisons (significant if 4*p < .05). State anxiety at the end of day 1 ($M$ = 30.67, $SD$ = 7.71) was significantly reduced compared to start of day 1 ($M$ = 34.48, $SD$ = 10.59), $t(41) = 3.21$, $p$ = .009. The difference between start and end of session state anxiety was not significant for any other experimental day ($t$s < 1.44, $p$s > .63). For each time, the effect of day was examined using paired samples t-tests. Results were Bonferroni adjusted for multiple comparisons (significant if 6*p < .05). State anxiety was significantly reduced at the start of day 2 ($M$ = 31.12, $SD$ = 9.49) compared to the start of day 1 ($M$ = 34.48, $SD$ = 10.59), $t(41) = 3.51$, $p$ =

.006. There was a marginally significant increase in state anxiety at the start of day 30 (*M* = 34.93, *SD* = 14.42) compared to the start of day 2 (*M* = 31.12, *SD* = 9.49), *t*(41) = 2.65, *p* = .066. No other change in state anxiety across days was significant for start of session state anxiety data (*t*s < 1.96, *p*s > .34). For end of day state anxiety there was no significant change across experimental days (*t*s < 2.48, *p*s > .11).

The day x time x tES interaction was significant, *F(*3,117) = 2.72, *p* = .048, ($\eta p^2$ = .07; *observed power* = .65).

For each day a 2 x 2 ANCOVA was conducted on state anxiety data with time (start of session, end of session) as the within participants factor and tES (active tRNS, sham tES) as the between participants factor and with attentional control as a covariate. The main effect of pre-existing attentional control was significant for day 1 state anxiety data, *F(*1,39) = 5.68, *p* = .022, ($\eta p^2$ = .13; *observed power* = .64). Pre-existing attentional control was significantly, moderately and negatively correlated with state anxiety on day 1, *r*(42), *p* = .014. There were no further main or interaction effects to emerge from analysis of day 1 data (*F*s < 2.35. *p*s > .13). For day 2 state anxiety, there was a significant time x tES interaction, *F(*1,39) = 4.27, *p* = .045, ($\eta p^2$ = .10; *observed power* = .52). For each time (start of day 2, end of day 2) the effect of tES was examined using an independent t-test. Results were Bonferroni adjusted for multiple comparisons (significant if 2*p < .05). There were no significant effects (*t*s < 1.76, *p*s > .17). For each tES group, the effect of time was explored with a paired samples t-test. Results were Bonferroni adjusted for multiple comparisons (significant if 2*p < .05). For

the active tRNS group, a reduction in state anxiety from start of day 2 (*M* = 30.48, *SD* = 7.55) to end of day 2 (*M* = 28.52, *SD* = 7.44) was marginally significant, $t(20) = 2.26$, $p = .07$. For the sham tES group, an increase in state anxiety at the end of day 2 relative to the start of day 2 was not significant ($t = 1.27$, $p = .44$). Analysis of day 2 state anxiety data revealed no further main or interaction effects ($F$s < 2.07, $p$s > .16). Analysis of day 3 state anxiety data revealed no main or interaction effects ($F$s < 2.01, $p$s > .16). For day 30 state anxiety the 2 x 2 ANCOVA with pre-existing attentional control as a covariate revealed a marginally significant main effect of tES, $F(1,39) = 4.03$, $p = .051$, ($\eta p^2 = .09$; *observed power* = .50). State anxiety for the sham tES group (M = 38.95, *SD* = 16.79) was significantly higher than state anxiety for active tRNS group (M = 29.93, *SD* = 8.29), $t(40) = 2.21$, $p = .033$. There were no further significant main or interaction effects, ($F$s < 2.82, $p$s > .10).

For each time a 4 x 2 ANCOVA was conducted on state anxiety data with day (day 1, day 2, day 3, day 30) as the within participants factor and tES (active tRNS, sham tES) as the between participants factor and with attentional control as a covariate. Analysis of start of session state anxiety data revealed a day x tES interaction, $F(2.42,94.28) = 4.27$, $p = .012$, ($\eta p^2 = .10$; *observed power* = .79; Greenhouse Geisser corrected). For each tES condition (active tRNS, sham tES) paired samples t-tests examined change in start of day state anxiety across days. Results were Bonferroni adjusted for multiple comparisons (significant if 6*p < .05). For participants in the active tRNS group there was no significant change in start of session state anxiety across days ($t$s < 1.82, $p$s > .50), For participants in the sham tES group, state anxiety at the start of day 2 (*M* = 31.76, *SD* = 11.26) was significantly lower

than state anxiety at the start of day 1 (*M* = 35.43, *SD* = 11.51), *t*(20) = 3.76, *p* = .006. State anxiety at the start of day 30 (*M* = 39.62, *SD* = 17.57) was significantly higher than state anxiety at the start of day 3 (*M* = 31.76, *SD* = 11.26), *t*(20) = 3.39, *p* = .018. There were no further differences across days in terms of start of session state anxiety for the sham tES group (*t*s < 2.30, *p*s > .20). For each day, independent t-tests examined the effect of tES on start of session state anxiety. Results were Bonferroni adjusted for multiple comparisons (significant if 4*p < .05). There was no significant difference between tES groups in terms of start of session state anxiety for any experimental day (*t*s < 2.21, *p*s > 1.52). There were no further significant main or interaction effects for start of session data (*F*s < 2.38, *p*s > .13). Analysis of end of session state anxiety revealed no significant main effects or interactions (*F*s < 3.31, *p*s > .08).

For each tES group a 4 x 2 ANCOVA was conducted on state anxiety data with day (day 1, day 2, day 3, day 30) and time (start of session, end of session) as within participants factors and attentional control as a covariate. A main effect of the covariate attentional control was revealed from analysis of the active tRNS group data, *F(*1,19) = 5.40, *p* = .031, ($\eta p^2$ = .22; *observed power* = .60). There was a moderate, negative correlation between pre-existing attentional control and mean state anxiety, *r*(42) = -.32, *p* = .04 suggesting that higher pre-existing attentional control was associated with lower state anxiety. A significant day x time interaction was also revealed, *F(*3.57) = 5.28, *p* = .003, ($\eta p^2$ = .22; *observed power* = .91). For each day, the effect of time on state anxiety from the active tRNS group was examined using a paired samples t-test. Results were Bonferroni adjusted for multiple

comparisons (significant if 4*p < .05). State anxiety at the end of day 1 (*M* = 28.05, *SD* = 6.45) was significantly reduced compared to state anxiety at the start of day 1 (*M* = 33.52, *SD* = 9.78) for active tRNS participants, *t*(20) = 3.96, *p* = .004). The reduction in state anxiety at the end of day 3 (*M* = 28.43, *SD* = 8.51) relative to the start of day 3 (*M* = 30.38, *SD* = 8.72) was marginally significant, *t*(20) = 2.72, *p* = .052). Change in state anxiety from start to end of session for the active tRNS group was not significant for any other day (*t*s < 2.26, *p*s > .14). For each time (start of session, end of session) the effect of day on active tRNS group state anxiety was examined using paired samples t-tests. Results were Bonferroni adjusted for multiple comparisons (significant if 6*p < .05). Change in state anxiety across days was not significant for start of day data (*t*s < 1.82, *p*s > .50) or for end of session data (*t*s < 1.54, *p*s > .84). For the active tRNS group there were no further significant main or interaction effects (*F*s < .59, *p*s > .45). For the sham tES group there were no significant main or interaction effects (*F*s < .81, *p*s > .50).

The main 2 x 4 x 2 ANCOVA with pre-existing attentional control as a covariate revealed no further main or interaction effects (Fs < 2.75. ps > .071).

### 3.3.5 Analyses with Cognitive Load as a Between Participants Factor

Analysis of data from experiment 2 in isolation has been described. However, the aim of experiment 2 was to explore whether training with low cognitive load produced different outcomes in terms of attention bias and state anxiety

change than training with a high cognitive load. In order to directly compare the effects of cognitive load on training outcomes, the present analysis combined attention bias assessment data and state anxiety data from experiment 2 with data from the control ABM group from experiment 1. Data from the control ABM group of experiment 1 were categorised as 'high cognitive load' data and experiment 2 data as 'low cognitive load' data. Following experiment 1 it was hypothesised that both active and control ABM were tasks which were high in cognitive load. These tasks had recruited and enhanced attentional control and this enhancement had mediated training associated effects on state anxiety. In the present analysis, only data from the control ABM were included and data from the active ABM group were omitted. This was so that the high and low cognitive load groups were of equivalent size (n = 42). Whereas the active ABM task differed from the no-training task in terms of contingency (contingency versus no contingency) and response (forced choice versus single response), the control ABM task difference from the no-training task in terms of only response. The control ABM group was therefore a more suitable comparison group for the no-training group than the active ABM group.

For each dependent variable (attention bias, state anxiety) a 3 x 2 x 2 ANOVA was conducted with the within participants factor of assessment (assessment 1, assessment 2, assessment 3), between participants factors of tES (active tRNS, sham tES) and cognitive load (high cognitive load, low cognitive load). Subsequently, three 3 x 2 x 2 mixed ANCOVAs were conducted. Each had a within participants factor of assessment (assessment 1, assessment 2, assessment 3), between participants factors of tES (active tRNS, sham tES)

and cognitive load (high cognitive load, low cognitive load) and a covariate of pre-existing attention bias or pre-existing trait anxiety or pre-existing attentional control.

#### 3.3.5.1 Attention Bias (Cognitive Load as Between Participants Factor)

A 3 x 2 x 2 ANOVA was conducted on attention bias data with assessment (assessment 1, assessment 2, assessment 3) as the within participants factor, between participants factors of tES (active tRNS, sham tES) and cognitive load (high cognitive load, low cognitive load). There were no significant main or interaction effects ($F$s < 2.44, $p$s > .095).

#### 3.3.5.2 State Anxiety (Cognitive Load as Between Participants Factor)

The above analysis was repeated on state anxiety data. There was a significant main effect of assessment, $F(1.81,145.05) = 3.31$, $p = .044$, ($\eta p^2 = .04$; *observed power* = .59; Greenhouse Geisser corrected). Using paired samples t-tests, change in state anxiety across assessments was examined. Results were Bonferroni adjusted for multiple comparisons (significant if 2*p < .05). State anxiety at assessment 2 ($M = 30.91$, $SD = 10.97$) was significantly reduced relative to state anxiety at assessment 1 ($M = 33.60$, $SD = 10.98$), $t(85) = 2.89$, $p = .015$. Change in state anxiety was not significant across further assessments ($t$s < 1.66, $p$s > .30). There were no further significant main or interaction effects ($F$s < 2.09, $p$s > .15).

### 3.3.5.3 State Anxiety at Start and End of Each Experimental Day (Cognitive Load as Between Participants Factor)

A 4 x 2 x 2 x 2 ANOVA was conducted on attention bias data with day(day 1, day 2, day 3, day 30) and time (start of session, end of session) as the within participants factors and between participants factors of tES (active tRNS, sham tES) and cognitive load (high cognitive load, low cognitive load). There was a significant main effect of time, $F(1,80) = 6.49$, $p = .013$, ($\eta p^2 = .08$; *observed power* = .71). State anxiety at the end of session ($M = 31.67$, $SD = 9.89$) was reduced compared to state anxiety at the start of session ($M = 33.15$, $SD = 10.40$). The day x time interaction was also significant, $F(2.50,199.59) = 4.23$, $p = .01$, ($\eta p^2 = .05$; *observed power* = .80; Greenhouse Geisser corrected). For each day (day 1, day 2, day 3, day 30), paired samples t-tests examined the effect of time (start of session, end of session). Results were Bonferroni adjusted for multiple comparisons (significant if $4*p < .05$). State anxiety at the end of day 1 ($M = 30.71$, $SD = 8.33$) was significantly reduced compared to state anxiety at the start of day 1 ($M = 33.60$, $SD = 10.98$), $t(83) = 3.33$, $p = .004$. No further paired comparisons were significant ($ts < 1.92$, $ps > .24$). For each time, paired samples t-tests examined change in state anxiety across days. Results were Bonferroni adjusted for multiple comparisons (significant if $6*p < .05$). State anxiety at the start of day 2 ($M = 31.05$, $SD = 10.51$) was significantly reduced compared to state anxiety at the start of day 1 ($M = 33.60$, $SD = 10.98$), $t(83) = 2.77$, $p = .042$. No further paired comparison was significant for start of session data ($ts < 2.19$, $ps > .18$). For end of session data, change in state anxiety was not

significant across days (*t*s < 1.75, *p*s > .51). There were no further main or interaction effects (*Fs* < 2.50, *p*s > .08).

### 3.3.6 Analyses with Cognitive Load as a Between Participants Factor and Pre-existing Attention Bias as a Covariate

#### 3.3.6.1 Attention Bias (Cognitive Load as Between Participants Factor and Pre-existing Attention Bias as a Covariate)

A 3 x 2 x 2 ANOVA was conducted on attention bias data with assessment (assessment 1, assessment 2, assessment 3) as the within participants factor, between participants factors of tES (active tRNS, sham tES) and cognitive load (high cognitive load, low cognitive load). Pre-existing attention bias was included as a covariate. The main effect of pre-existing attention bias was significant, $F(1,79) = 42.03$, $p < .001$, ($\eta p^2 = .35$; *observed power* = 1.00). Pre-existing attention bias was moderately to highly, positively correlated with mean attention bias, $r(84) = .57$, $p < .001$. There was a significant main effect of tES, $F(1,79) = 5.62$, $p = .02$, ($\eta p^2 = .07$; *observed power* = .65). Mean attention bias did not differ significantly between tES groups ($t = 1.23$, $p = .22$). The interaction between pre-existing attention bias and assessment was significant, $F(1.42,112.00) = 35.14$, $p < .001$, ($\eta p^2 = .31$; *observed power* = 1.00; Greenhouse Geisser corrected). Pre-existing attention bias was strongly, negatively correlated with change in attention bias from assessment 1 to assessment 2, $r(42) = -.87$, $p < .001$ and change in attention bias from assessment 1 to assessment 3, $r(42) = -.78$, $p < .001$. Pre-existing attention bias was significantly, moderately, negatively correlated with change in

attention bias from assessment 2 to assessment 3, $r(42) = -.33$, $p = .032$. Higher pre-exiting threat bias was associated with greater reduction in threat bias following training. Greater pre-existing neutral bias was associated with greater reduction in neutral bias following training relatively to before training. There were no further main or interaction effects ($F$s < 1.77, $p$s > .17).

#### 3.3.6.2 State Anxiety (Cognitive Load as Between Participants Factor and Pre-existing Attention Bias as a Covariate)

The above analysis was repeated on state anxiety data. There was a significant main effect of assessment, $F(1.82,143.53) = 3.28$, $p = .045$, ($\eta p^2 = .04$; *observed power* = .59; Greenhouse Geisser corrected). This effect was explored in section 3.3.5.2. With pre-existing attention bias held constant, there were no further significant main or interaction effects ($F$s < 2.04, $p$s > .14).

#### 3.3.6.3 State Anxiety at Start and End of Each Experimental Day (Cognitive Load as Between Participants Factor and Pre-existing Attention Bias as a Covariate)

A 4 x 2 x 2 x 2 ANOVA was conducted on attention bias data with day (day 1, day 2, day 3, day 30) and time (start of session, end of session) as the within participants factors and between participants factors of tES (active tRNS, sham tES) and cognitive load (high cognitive load, low cognitive load). Pre-existing attention bias was the covariate. There was a significant main effect

of time, $F(1,79) = 6.41$, $p = .013$, ($\eta p^2 = .08$; *observed power* = .71; Greenhouse Geisser corrected) and a significant time x day interaction, $F(2.49,197.06) = 4.18$, $p = .011$, ($\eta p^2 = .05$; *observed power* = .80; Greenhouse Geisser corrected). These effects were explored in section 3.3.8.3. The day x tES interaction approached significance, $F(2.29,180.81) = 2.65$, $p = .066$, ($\eta p^2 = .03$; *observed power* = .56; Greenhouse Geisser corrected). For each day (day 1, day 2, day 3, day 30) an independent t-test explored whether tES groups differed in terms of state anxiety. Results were Bonferroni adjusted for multiple comparisons (significant if $4*p < .05$). There were no significant effects ($t$s < 2.21, $p$s > .13). For each tES group, paired samples t-tests examined whether state anxiety was changed across days. Results were Bonferroni adjusted for multiple comparisons (significant if $6*p < .05$). Change in state anxiety across days was not significant for the active tRNS group ($t$s < 1.30, $p$s > 1.25) or the sham tES group ($t$s < 2.53, $p$s > .12). There were no further significant main or interaction effects ($F$s < 2.05, $p$s > .13).

## 3.3.7 Analyses with Cognitive Load as a Between Participants Factor and Pre-existing Trait Anxiety as a Covariate

### 3.3.7.1 Attention Bias (Cognitive Load as Between Participants Factor and Pre-existing Trait Anxiety as a Covariate)

A 3 x 2 x 2 ANOVA was conducted on attention bias data with assessment (assessment 1, assessment 2, assessment 3) as the within participants factor, between participants factors of tES (active tRNS, sham tES) and cognitive load (high cognitive load, low cognitive load) and pre-existing trait anxiety as the

covariate. Controlling for pre-existing trait anxiety, there were no significant main or interaction effects (*F*s < 1.86, *p*s > .16).

#### 3.3.7.2 State Anxiety (Cognitive Load as Between Participants Factor and Pre-existing Trait Anxiety as a Covariate)

The above analysis was repeated on state anxiety data. There was a significant main effect of trait anxiety, $F(1,79) = 59.07$, $p < .001$, ($\eta p^2 = .43$; *observed power* = 1.00). Pre-existing trait anxiety was highly, positively correlated with mean state anxiety $r(84) = .67$, $p < .001$. There were no further significant main or interaction effects (*F*s < 1.59, *p*s > .21).

#### 3.3.7.3 State Anxiety at Start and End of Each Experimental Day (Cognitive Load as Between Participants Factor and Pre-existing Trait Anxiety as a Covariate)

A 4 x 2 x 2 x 2 ANOVA was conducted on attention bias data with day(day 1, day 2, day 3, day 30) and time (start of session, end of session) as the within participants factors, between participants factors of tES (active tRNS, sham tES) and cognitive load (high cognitive load, low cognitive load) and pre-existing trait anxiety as a covariate. There was a significant main effect of trait anxiety, $F(1,79) = 70.67$, $p < .001$, ($\eta p^2 = .47$; *observed power* = 1.00). This effect was explored in section 3.3.7.2.

### 3.3.8 Analyses with Cognitive Load as a Between Participants Factor and Pre-existing Attentional Control as a Covariate

#### 3.3.8.1 Attention Bias (Cognitive Load as Between Participants Factor and Pre-existing Attentional Control as a Covariate)

A 3 x 2 x 2 ANOVA was conducted on attention bias data with assessment (assessment 1, assessment 2, assessment 3) as the within participants factor, tES (active tRNS, sham tES) and cognitive load (high cognitive load, low cognitive load) as between participants factors and pre-existing attentional control as a covariate. There were no significant main or interaction effects (*F*s < 1.96, *p*s > .15).

#### 3.3.8.2 State Anxiety (Cognitive Load as Between Participants Factor and Pre-existing Attentional Control as a Covariate)

The above analysis was repeated on state anxiety data. There was a significant main effect of pre-existing attentional control, $F(1,79) = 7.76$, $p = .007$, ($\eta p^2 = .09$; *observed power* = .79). Pre-existing attentional control was moderately, negatively correlated with state anxiety, $r(84) = -.31$, $p = .004$ suggesting that higher attentional control at baseline was associated with lower mean state anxiety. There were no further significant main or interaction effects (*F*s < 1.95, *p*s > .15).

#### 3.3.8.3 State Anxiety at Start and End of Each Experimental Day (Cognitive Load as Between Participants Factor and Pre-existing Attentional Control as a Covariate)

A 4 x 2 x 2 x 2 ANOVA was conducted on attention bias data with day (day 1, day 2, day 3, day 30) and time (start of session, end of session) as the within participants factors and between participants factors of tES (active tRNS, sham tES) and cognitive load (high cognitive load, low cognitive load). There was a significant effect of pre-existing attentional control, $F(1,121) = 11.69$, $p = .001$, ($\eta p^2 = .09$; *observed power* = .92). This was explored in section 3.3.8.2. There were no further significant main or interaction effects ($F$s < 2.41, $p$s > .081).

### 3.3.9 TRNS Tolerability

tRNS was well tolerated with no adverse events (see Table 3.6). Participants reported mild to moderate levels of 'Tiredness' and 'Loss of Concentration' in both tES groups. There was a significant effect of burning with participants who received active tRNS reporting a higher level ($M$ =1.24, $SD$ = .44) than those who received sham tES who reported no burning ($M$ =1.00, $SD$ = .00) $t(40) = 2.5$, $p = .021$. The sensation of headache was marginally higher in the sham tES group ($M$ = 1.81, $SD$ = 1.21) than in the active tRNS group ($M$ = 1.24, $SD$ = .44, $t(40) = 2.04$, $p = .052$. The difference in intensity rating between tES groups was not significant for all other events.

Table 3.6:

*Mean (SD) tRNS intensity scores for each tES group*

| | Headache | Neck Pain | Aching Scalp | Tickling | Itching | Burning | Skin Irritation | Tiredness | Loss of Concentration | Mood Swings |
|---|---|---|---|---|---|---|---|---|---|---|
| Active | 1.24 | 1.24 | 1.00 | 1.43 | 1.43 | 1.24 | 1.05 | 2.38 | 2.14 | 1.14 |
| TRNS | (.44) | (.54) | (.00) | (.60) | (.60) | (.44) | (.22) | (1.07) | (1.01) | (.36) |
| Sham | 1.81 | 1.33 | 1.14 | 1.29 | 1.33 | 1.00 | 1.00 | 2.90 | 2.48 | 1.14 |
| tES | (1.21) | (.66) | (.48) | (.64) | (.73) | (.00) | (.00) | (1.37) | (.98) | (.36) |

### 3.3.10 Experimental Condition

Overall, 26.19% of participants guessed both their ABM and tES group correctly. The percentage of participants who guessed their ABM group correctly was 42.86%. A one-sample t-test revealed that this percentage did not significantly differ from chance, $t(41) = .48$, $p = .63$. The percentage of participants who guessed their tES group correctly was 54.76%. This level was also not significantly different from chance, $t(41) = .30$, $p = .76$.

## 3.4 Discussion

In experiment 1 anxiety was reduced following active ABM training towards neutral faces and following control ABM which did not contain contingent trials. Previous literature had suggested that an increase in attentional control induced by both active and control ABM may have enhanced the capacity to disrupt processing of threatening stimuli and reduce its emotional impact (Enock et al., 2014; Heeren et al., 2013; Klumpp et al., 2010; Taylor, Cross & Amir, 2015). The emotional dot-probe task from experiment 1 was altered to minimise the degree to which cognitive control mechanisms were recruited and to reduce the extent of engagement required for participation.

It was hypothesised that, unlike the ABM training delivered in experiment 1, the experiment 2 task would not result in anxiety diminution.

Analysis of data from the no-training group of experiment 2 revealed no reduction in attentional bias towards threat. It can be assumed that the processes of attentional disengagement from threat related stimuli and engagement to neutral stimuli were not facilitated across participants. However, replicating findings from experiment 1, change in attention bias was robustly associated with pre-existing attention bias. Participants demonstrating the greatest threat bias at baseline had the greatest reductions in threat bias following training and participants with the greatest pre-existing neutral bias having the greatest reductions in neutral bias. State anxiety was reduced at assessment 2 compared to assessment 1 and this reduction was marginally maintained at assessment 3. This effect appeared to be driven by tES group as state anxiety reductions were revealed for participants who received active tRNS during no-training ABM but not participants who received sham tES during no-training ABM. The experiment 2 task was intended to minimise the extent to which cognitive control was enhanced. Tasks which enhance cognitive control have been seen to result in greater improvements in attentional control capacity and in emotional vulnerability (e.g. Sari et al., 2015; Swainston et al., 2018). An assumption was made that this low cognitive control task would not bolster attentional control resources and therefore that training would therefore have no impact on anxiety levels. Nevertheless, anxiety reductions occurred. Following on from the main analysis, data from experiment 2 were analysed with data from the control ABM group of experiment 1 and the effect of cognitive load was

explored. The no-training task represented a low cognitive load condition and control ABM represented a high cognitive load condition. Analysis revealed no difference between these groups in terms of attention bias and state anxiety outcomes. State anxiety was reduced, irrespective of cognitive load. This suggests that a mechanism other than enhanced attentional control capacity was responsible for anxiety reduction.

The results from experiment 2 will be discussed in light of findings from experiment 1. For a baseline attention bias, state anxiety, trait anxiety and attention control scores across all experimental groups from experiments 1 and 2 see table 3.1.

### 3.4.1 Attentional Control

Experiment 1 revealed that pre-existing threat bias was associated with reduced threat bias following training relative to before training and that pre-existing neutral bias was associated with reduction in neutral bias (increase in threat bias) irrespective of ABM training group. It was argued in chapter 2, that an increase in attentional control capacity might facilitate engagement to neutral stimuli in participants with pre-existing threat bias and engagement to threat in participants with a neutral bias by enhancing self-regulatory processes. Experiment 2 also resulted in larger reductions in threat bias for participants with a threat bias at baseline and larger reductions in neutral bias for participants with a pre-existing neutral bias despite the delivery of training with low cognitive load which was intended to not improve cognitive

control capacity. This suggests that cognitive and attentional control enhancement does not explain the findings from experiment 1.

### 3.4.2 Non-specific Effects

If an improvement in attentional control is not implicated in the attenuation of anxiety then another mechanism must be responsible for anxiety reduction following attentional training. O'Toole et al. (2013) suggested that the repetitive and predictable nature of ABM training produces general anxiety-attenuating effects. The authors reported a reduction in anxiety across all participants following ABM training and control ABM irrespective of training group. Although experiment 2 did not include active or control ABM training, the task was repetitive and predictable and this facet of the no-training task may have attenuated anxiety. It has also been suggested that simply taking part in research can bolster the confidence of participants (Enock et al. 2014) and that confidence and a sense of ease may arise as the result of an emerging researcher-participant relationship (Patterson, 1985). More investigation is needed to unravel which elements of research participation might explain participants' decline in anxiety. This might include an investigation of whether other repetitive tasks, including those not intended to manipulate attention, generate anxiety reductions. Studies might also examine whether the extent to which researchers engage with participants is influential in anxiety modification by incorporating experimenter communication style as a between participants factor.

### 3.4.3 Exposure

If anxiety following 'no-training' ABM is not attributable to an increase in attentional control then an exposure effect cannot be ruled out. Because no-training ABM, like active and control ABM, involved the presentation of both neutral and angry stimuli then it is possible that participants became habituated to angry faces thus reducing their anxiety inducing effect. In order to elucidate the impact of threatening face images on anxiety more studies are needed in which neutral-neutral face pairs are included for comparison. No reduction in anxiety following ABM training without threatening faces would suggest a role for exposure to threat in anxiety reduction.

### 3.4.4 Placebo Effect

Experiment 2 revealed a reduction in anxiety at the end of a 'no-training' procedure. This could also be consistent with a placebo effect. The effects cannot be attributed to the training task as this was not designed to deliver benefits in terms of reduced attention bias and anxiety reduction. However, it is possible that they arose as a result of participants positive expectations regarding the outcome from their participation (Carleton et al., 2015).

### 3.4.5 TES Effect

There was a reduction in state anxiety at assessment 2 compared to assessment 1 for participants who received active tRNS but not for those who

received sham tES. Furthermore, covariate analysis showed that, even when trait anxiety was held constant, state anxiety at the end of day 1 was reduced relative to state anxiety at the start of day 1 for the active tRNS group but was not changed for the sham tES group. The same pattern was revealed for day 2 state anxiety. State anxiety at the end of day 1 was lower for the active tRNS group than for the sham tES group. It appears therefore that the reduction in state anxiety observed across all participants was driven by reductions in the active tRNS group. Importantly, a component analysis revealed that at day 30, state anxiety for the active tRNS group was significantly lower than it was for the sham tES group. This suggests that tES-induced anxiety reduction may have been lasting. Although Clark et al. (2014) did not measure anxiety before and after ABM, they revealed greater reductions in attention bias following active but not control ABM for participants who received anodal tDCS relative to participants who received sham tDCS and suggested that active tES had enhanced the effects of active ABM training. In the present study, participants did not receive active ABM and therefore improvement in state anxiety for the active tRNS group but not the sham group cannot be explained by the same mechanism. Heeren et al. (2017) delivered anodal tDCS or sham tDCS during attention bias assessment to socially anxious participants. The authors revealed that threat bias was reduced for the atDCS group relative to the sham tDCS group. Because no attention bias training (only assessment) took place, this reduction could not be explained by tDCS-induced modulation of training effects suggesting that anodal tDCS had a direct impact on mechanisms associated with the reduction of threat bias. In a separate study Ironside et al. (2015) revealed a lower level of attention bias towards threat for participants who had received 20

minutes of offline bilateral atDCS of the DLPFC (anode above F3 and cathode above F4) relative to participants who had received atDCS of the left DLPFC with the cathode above the contralateral supraorbital or sham tDCS just prior to assessment.

The studies by Heeren et al. (2017) and Ironside et al. (2015) suggest that for active tES to produce benefits previously associated with tES related enhancement of ABM training (e.g. Clarke et al., 2014), learning is actually not a necessary part of the process. It is possible therefore that active tRNS produced its anxiolytic effects independently of the training paradigm employed in experiment 2. Research has produced few examples of tES induced improvements in anxiety. A single case study of a GAD patient who received cathodal tDCS above the right DLPFC for 15 consecutive days reported a reduction in anxiety symptoms across the study. One month after the start of treatment the patient no longer met the diagnostic criteria for GAD (Shiowaza et al., 2013). As a single case study these results cannot be generalised. There have however, been more investigations into the efficacy of tES for treating depression. Two randomised controlled trials of anodal versus sham tDCS above the left DLPFC for up to 10 days reported reductions in depressive symptoms for active tDCS relative to sham tDCS (Boggio et al., 2008; Fregni et al., 2006). In the study by Fregni et al. (2006) there was a 69% improvement in Hamilton Depression Rating Scale scores after 5 sessions of atDCS and Boggio et al. (2008) reported a 40.5% improvement in scores on the same scale. These improvements persisted at 1 month follow up. (Boggio et al., 2008; Fregni et al., 2006). Also, in a systematic review of 7 randomised control trials (RCTs) of tDCS as a monotherapy or add-on therapy

for major depressive disorder (MDD), response and remission rates were found to be superior for active tDCS than sham tDCS for all outcomes (Shiozawa et al., 2014). However, another systematic review of 6 RCTs of tDCS for MDD, Berlim et al. (2013) reported no difference between atDCS and sham tDCS in terms of response rates and remission rates. Plazier et al. (2012) reported no change in mood score following 20 minutes of active tDCS or sham tDCS to the bilateral DLPFC or to the bilateral occipital cortex (O1 and O2). No change in mood scores was also reported following bilateral tDCS of the DLPFC, sham tDCS or 'unbalanced' tDCS in which the anode was above the DLPFC and the cathode above the contra-lateral supra-orbital (Ironside et al., 2016). There are evidently mixed findings from studies investigating the impact of off-line tES on mood disorders. The majority of these findings are from studies which have used tDCS however and have focused on its impact in depression. There has been one case report of a trial to treat major depressive disorder with tRNS (Chan et al., 2012). There was greater symptom reduction following tRNS across 15 sessions than following 15 sessions of atDCS. The trial was with only one participant who was not blinded as to the type stimulation being delivered or study aim (Chan et al., 2012) but this initial finding shows that tRNS has potential utility in the treatment of mood disorders. In the studies cited above, tES has been used to alleviate mood disorder by applying it to the frontal cortices. Both anxiety and depression are proposed to be characterised by underactivity in this area of the brain (anxiety: Clarke et al., 2014; Ironside et al., 2016; depression: Koenigs & Grafman, 2009). It is proposed that frontal areas of the brain are responsible for inhibiting emotionally driven responses via the regulation of a more posterior emotion-driven system (Derryberry & Reed, 2002). With the appropriate form of tES

and by targeting the optimal frontal brain area, it may be possible to bolster or even activate this pre-established system without the need for attentional training.

Whilst there is support for the effective treatment of negative affect with stand-alone tES, in experiment 2, tRNS was delivered concurrently with a cognitive task. The task may not have recruited the same neural mechanisms as the active and control ABM paradigms of experiment 1 or may not have recruited mechanisms to the same extent. However, it is probable that some level of task-associated activity was present at the time of stimulation.

### 3.4.6 State Dependency

In opposition to the above suggestion that reductions in anxiety were generated by active tRNS and not due to the modulation of training effects by active tRNS, experiment 1 did not reveal superior reductions in anxiety for the active tRNS group relative to participants who received sham tES.

The importance of neural state dependency on tES outcomes was discussed in chapters 1 and 2. A study by Bortoletto et al. (2015) reported that tES improved performance in a motor task when applied during control training but impaired performance when applied during active training. The authors suggested that when excitatory tES is applied during another excitability enhancing event, one might negate the facilitatory impact of the other (Borteletto et al., 2015). Rosenkranzt et al. (2000) suggested that atDCS may have the potential to interfere with the maintenance of cortical excitability

elicited by a training task. In experiment 1, active tRNS was delivered concurrently with active attentional training. There was no evidence of a 'cancelling out' effect but tRNS did not facilitate the impact of ABM. It is possible that the neural mechanisms activated by active ABM and control ABM were implicated in anxiety reduction and that these had reached a maximal level of activation arising from the training in isolation. Additional excitatory input in the form of active tRNS may have been unable to push neurons beyond this ceiling of excitation. However, in experiment 2 the same mechanisms may not have been triggered by the no-training ABM task or were triggered to a lesser extent. Active tRNS was therefore able to enhance activity in these brain regions. This might account for the anxiety alleviating effect of active tRNS but not sham tES in experiment 2. Attention bias towards threatening information and anxiety have been consistently linked with reduced activity in frontal areas of the brain including the DLPFC (Bishop., 2008; Clarke et al., 2014) and IFG (Hu & Dolcos, 2017). It is possible that more anxious participants had a low level of baseline activity in frontal neural regions. Active tRNS to the IFG provided the greatest 'boost' therefore to these participants in terms of facilitating the neural mechanisms associated with anxiety regulation leading to a greater reduction in anxiety for participants who received active tRNS than for participants who received active tRNS. These suggestions are precisely in line with findings from a study by Sikström et al. (2015). This study showed that participants with lower self-report attentiveness benefitted to a larger extent from auditory noise and tDCS stimulation in terms of their performance in a go-no-go task than participants with high level attentiveness (Sikström et al., 2015). This interaction was not present for an n-back test. As an explanation the authors

pointed to the moderate brain arousal (MBA) model (Sikström & Söderlund, 2007). This model suggests that the brain functions at optimal capacity when arousal level is maximised. In certain individuals baseline arousal is lower and this may impair performance in some tasks. However, it is possible to boost arousal level using stochastic resonance (Sikström & Söderlund, 2007). In terms of why an interaction between attentiveness and stimulation was present for the go-no task but not the n-back task, it was suggested that, because the n-back task is more cognitively demanding than the go-no-go task, arousal level was optimised and performance maximised, leaving no room for enhancement via auditory noise or tDCS (Sikström et al., 2015).

When considered together with previous findings (e.g. Bortoletto et al., 2015) these results suggest that tES and cognitive training interact in a system of neural activation marked by homeostatic processes and limitations on facilitatory excitation. However, it is important to highlight that when cognitive load was included as a between participants factor in the analysis of data from the control ABM group of experiment 1 and experiment 2 data, no interaction between tES and cognitive load emerged.

### 3.4.7 Pre-existing Attention Bias

For participants with greater pre-existing threat bias there was greater reduction in attentional bias towards threat at the end of training which was maintained at follow-up. Covariate analysis revealed a relationship between pre-existing attention bias and attention bias change with greater pre-existing threat bias associated with greater reduction in threat bias and greater pre-

existing neutral bias associated with greater reduction in neutral bias. Previously, reduction in threat bias was found across assessments for participants with pre-existing threat bias but not for participants with attentional bias towards neutral faces at baseline (O'Toole, 2012). However, this was reported following active ABM. It was argued that participants with pre-existing threat bias were more susceptible to the mechanisms of ABM (O'Toole, 2012). In experiment 2, participants did not receive active ABM and so this cannot be the explanation. Again, the exposure effect is a putative mechanism (see Carleton et al., 2015) as no-training ABM involved the repeated presentation of angry as well as neutral faces. This might also explain the finding from experiment 2 that for those with a pre-existing bias towards neutral faces there was a reduction in neutral bias following no-training ABM. If a bias towards neutral faces represented attentional avoidance of threat then this might be reduced via persistent exposure to threatening faces.

### 3.4.8 Pre-existing Trait Anxiety

When pre-existing trait anxiety was included in analysis of the effects of no-training ABM (with active or sham tRNS) on state anxiety the main effect of assessment was no longer present. This suggests that pre-existing trait anxiety had a modulating effect on state anxiety change. However, no interaction between pre-existing trait anxiety and assessment was revealed

and so there was no support for a relationship between pre-existing trait anxiety level and change in state anxiety.

### 3.4.9 Limitations

The purpose of experiment 2 was to examine the impact of attentional control modulation on ABM related outcomes and most specifically, anxiety. It was predicted that because the experiment 2 task was less cognitively demanding than the active or control ABM tasks from experiment 1, attentional control capacity would not be enhanced and anxiety reductions would not occur. However, there was no direct indication or test to show that the less demanding nature of this training involved the elimination of attentional control. Previous studies which have compared the effect of high cognitive load and low cognitive load training on attentional control and emotional vulnerability have included measures of attentional control in order to support or refute it's mediating properties (e.g. Course-Choi et al,. 2017; Sari et al., 2015; Swainston et al., 2018). For example, Course-Choi et al. (2017) demonstrated that engagement with working memory training was associated with improvements in attentional control (as measured using an eye-tracking antisaccade task) and with reductions in worry symptoms (Course-Choi et al., 2017). Future attempts to modulate attentional load via the manipulation of cognitive load should include a measure or measures of attentional control such as the antisaccade task or the attention network task in order to demonstrate the effects of task manipulation on attentional control.

## 3.5 Summary

To summarise, experiment 2, like experiment 1, revealed a significant relationship between pre-existing attention bias and attention bias modulation following no-training ABM with active or sham tRNS. There were larger reductions in threat bias for participants with greater pre-existing bias towards threatening faces and larger reductions in neutral bias for participants with greater pre-existing bias towards neutral faces. There was a reduction in state anxiety across all participants. Because no-training ABM was designed to induce little or no improvement in attentional control capacity this suggests that anxiety attenuation was driven by a mechanism independent of the modulation of attentional control. These might include exposure to threatening images, a placebo effect or non-specific effects related to taking part in research.

Experiment 2 provided evidence of anxiety reduction following active but not sham tES. The fact that this result emerged in the absence of an active ABM training condition suggests that the improvements demonstrated could not be explained by the modulation of ABM training effects. It is therefore possible that 1.5mA tRNS of the bilateral IFG in isolation has anxiolytic effects. Alternatively, active tRNS facilitated the neural mechanisms associated with the basic training task. In experiment 1, anxiety reductions did not differ between the active and sham tES groups. It could be that, at a neuronal level no-training ABM was associated with a greater proportion of sub-threshold relative to above-threshold signals than both active or control ABM. In line with the proposed mechanisms of high frequency tRNS (e.g. Cohen Kadosh,

2013), it is possible that the integration of tES and task-induced signals resulted in a greater degree of above-level activation (more action potentials). Thus, the level of neural facilitation produced by the experiment 1 tasks and the experiment 2 task in conjuction with tRNS became comparable. More research is required to substantiate the present interpretation of results. These findings highlight the need to consider the role of neural state at the time of tES application on outcomes. It is possible that when the neural structures associated with anxiety reduction are optimally activated as might be the case during active and control ABM, tES is unable to further enhance this activity. Where a cognitive task only minimally enlists neural processes as per the no-training group, there may be more capacity for tES to augment activation.

Future studies should clarify the role of exposure to threat in anxiety reduction in paradigms where threat and neutral face pairs are used. It would also be useful for studies to investigate how participation in research might influence anxiety levels across participation by exposing participants to varying testing conditions. There is also the requirement to investigate the effects of tRNS and other forms of tES as a stand-alone treatment for anxiety.

# Chapter 4

**Modulation of Attention Bias Modification using Transcranial Direct Current Stimulation Above Left DLPFC**

**Experiment 3**

## 4.1 Introduction

The aim of study 1 was to establish whether tES could modulate the impact of attention bias modification. In experiment 1, high-frequency tRNS or sham tRNS was delivered bilaterally to the IFG during active or control ABM training. TRNS was selected as an appropriate form of stimulation based on evidence that it can produce considerable and lasting augmentations of learning (e.g. Snowball et al., 2013). Researchers had only recently begun to examine the potential for tRNS to enhance cognitive training and the present study provided the opportunity to contribute to this emerging field. When selecting the site of stimulation, both the DLPFC and the IFG were considered (see chapter 2). The IFG was chosen however due to its involvement in attentional inhibition processes (Mohanty et al., 2005; Song et al., 2017).

Results from experiment 1 revealed reductions in anxiety for all participants irrespective of ABM group or tES group. There was no evidence of tES induced modulation of ABM training. It was postulated that both active ABM and control ABM training enhanced cognitive control capacity and that this effect was responsible for anxiety reduction (Enock et al., 2014; Heeren et al., 2015b). In experiment 2, there were anxiety reductions for participants who received

active tRNS during a low cognitive load task but not for participants who receive sham tRNS during the task. The task was designed to be minimise the degree to which attentional control was enhanced and anxiety reduction following its completion was therefore not predicted. Evidence of anxiety reduction for participants in the active tRNS group was indication that active tRNS may have evoked anxiolytic effect independently of the training task. Alternatively, tRNS enhanced task-related neural activity thus facilitating the neural mechanisms associated with anxiety attenuation. In both experiments therefore, there was no evidence that tRNS applied to the bilateral IFG produced modulations in anxiety stemming from the enhancement of ABM training. These results were in contrast to previous studies demonstrating augmentations of ABM effects with tDCS (Clarke et al., 2014; Heeren et al., 2015b). In the study by Clarke et al. (2014) participants were allocated to attend-neutral or attend-threat ABM with anodal or sham tDCS. There was change in attentional bias consistent with the trained direction for participants who received anodal tDCS only (Clarke et al., 2016). In the study by Heeren et al. (2015b) highly trait anxious participants received active ABM with concurrent anodal tDCS, cathodal tDCS or sham tDCS. There was a reduction in gaze time for threatening faces as measured by eye-tracking following ABM training compared to before ABM training. This reduction was not present for the cathodal or sham tDCS group (Heeren et al., 2015b). A more recent study examined the impact on attention bias of anodal tDCS relative to sham tDCS in socially anxious participants (Heeren et al., 2017). TDCS was not applied during ABM training but during attention bias assessment. In one session participants received anodal tDCS during attention bias assessment and in another, participants received sham tDCS during attention

bias assessment. Attention bias towards threat was lower during the anodal tDCS condition compared to during sham tDCS (Heeren et al., 2017).

### 4.1.1 TES Protocol

TES protocol differed between experiment 1 of the present study and the Clarke et al., (2014) and Heeren et al., (2015b) studies. Both of the published studies used tDCS and not tRNS. Both studies also targeted the left DLPFC (F3) and not the IFG. The authors pinpointed the DLPFC as a neural structure which plays key role in the cognitive processes involved ABM training (Clarke et al., 2014). The evidence for the modulation of ABM training using tDCS of the DLPFC and not tRNS of the bilateral IFG suggests that the former tES protocol may have advantages in terms of its capacity to modulate ABM.

### 4.1.2 Mechanisms of tRNS and tDCS

As discussed in chapter 1, tDCS and tRNS differ in terms of their putative mechanisms of action. TDCS is proposed to induce a shift in resting membrane potential. Anodal stimulation brings neurons closer to their point of excitation thus rendering them more receptive to incoming excitatory input (Brunoni et al., 2012). TRNS generates small, consistent bursts of neural excitation which are thought to trigger the repeated polarisation of sodium channels (Paulus, 2011), bringing neurons closer to their threshold of activation (Fertonani et al., 2011). It could be that the neural adaptations generated by tDCS are more appropriate for modulating the brain activity associated with ABM and facilitating its effects. The answer may lie in the fact that tDCS delivers a constant electrical field

(Zaghi, 2009) and may adapt and maintain the potential of stimulated neurons at a constant level. Consequently, all incoming excitatory signals are more likely to push neuronal membranes beyond their threshold of excitation. Proponents of tRNS to enhance the effects of cognitive training have preferred to describe tRNS in terms of noise upon a background of which sub-threshold signals can 'pop-out' (Van der Groen & Wenderoth, 2016). However, due to its alternating nature, tRNS may have provided a weaker platform for enhancing ABM related neural activity. These arguments are speculative and it is necessary to consider that high frequency tRNS has been used to enhance the outcomes of cognitive training with success (e.g. Fertonani et al., 2011; Snowball et al., 2013). Extensive research is needed to establish the precise neural mechanisms of different forms of tES and of the cognitive paradigms during which they are applied. It will then be possible to more effectively match type of tES to cognitive process.

### 4.1.3 Site of Stimulation

The methodologies employed by Clarke et al. (2014) and Heeren et al. (2015b) also differed from those employed in experiments 1 and 2 in terms of site of stimulation. It is possible that the DLPFC is a more appropriate target location for enhancing the learning effects of active ABM or for enhancing the specific cognitive mechanisms involved in ABM. Exciting this area may even serve to activate these mechanisms. Although some studies have treated the IFG and DLPFC as part of the same inhibitory control network (e.g. Berkman et al., 2014; Song et al., 2017) others have suggested they serve separable roles during tasks requiring the attentional inhibition of emotionally salient stimuli. It has been

proposed, for example that the DLPFC subserves goal-directed processes such as focusing on task relevant stimuli and inhibition of task irrelevant stimuli whilst ventral frontal regions including the IFG deal with emotional processing (Corbetta & Schulman, 2002; Dolcos & MacCarthy, 2006). In one fMRI study, participants were required to identify the emotional expression on a target face image whilst ignoring a word overlying the face which was either congruent with the face (e.g. neutral face with the word 'neutral') or incongruent with the face (e.g. neutral face with the word 'fearful'). During a low expectancy condition in which 35% of trials were incongruent, activation of the IFG and the DLPFC was observed but during a high expectancy task in which 65% of trials were incongruent, only sustained activity of the DLPFC was noted (Krug & Carter, 2012). The authors postulated that participants switched from a reactive strategy involving the sudden implementation of inhibition during the relatively infrequent incongruent trials, to a proactive strategy involving continued preparedness for incongruent trials. Hughes et al. (2014) reported that activity in both the IFG and DLPFC was greater for stop trials than go trials in a stop signal task. However, when activity from a passive condition in which participants simply watched the task on the screen was 'partialled out', this effect was only significant for the DLPFC (Hughes et al., 2014). These reports which have directly compared the roles of the IFG and DLPFC in attentional inhibition where emotional stimuli interfere with task performance propose that there is a role for both. They suggest that the IFG is involved in emotional processing and attentional conflict identification and immediate rectification. However, substantial and even sustained activation of the DLPFC is necessary for goal-oriented functioning and the ongoing maintenance and control of attentional processes including continued vigilance and readiness to inhibit. In

light of the theory that ABM exerts improvements of attentional bias and anxiety via the enhancement of attentional control this might explain why studies which have attempted to modulate ABM via tES to the DLPFC have done so successfully (Clarke et al., 2014; Heeren et al., 2015b).

### 4.1.4 Aims

The DLPFC is thought to have a degree of functional specificity for attentional inhibition of threat related stimuli and selective engagement of neutral stimuli (Bar-Haim et al., 2010), mechanisms which are fundamental to the success of active ABM training. Experiment 3 was designed to investigate whether tES applied to the DLPFC might enhance or activate these processes. Although reduction in anxiety was observed across participants following all conditions in experiment 1, it was considered possible that tRNS of the IFG may not have been the most appropriate tES procedure for illuminating differential effects between active ABM and control ABM and between active and sham tES. Experiment 3 therefore provided a further opportunity to explore the outcomes of active versus control ABM and to compare tRNS with anodal tDCS as a means of modulating ABM training.

Anodal tDCS to the left DLPFC was delivered concurrently with ABM training or control ABM training across 3 consecutive days. It was hypothesised that anodal tDCS would enhance the neural and cognitive mechanisms associated with inhibition of threatening stimuli and engagement to neutral stimuli. The prediction was of greater threat bias reduction for active ABM with anodal tDCS relative to control ABM with anodal tDCS. Section 4.3 will analyse data from

experiment 3 in isolation. Therefore, it will not be possible to infer from the results whether anodal tDCS is more effective than sham tES or high frequency tRNS at enhancing the effects of ABM training. However, section 4.3.8 will summarise the results of an ANOVA performed on data from experiments 1 and 3. This will explore the interaction of all ABM (active ABM, control ABM) and tES (active tRNS, sham tES, anodal tDCS) effects. Chapter 5 will analyse data from experiments 1, 2 and 3 in combination.

## 4.2 Method

### 4.2.1 Design

A 2 x 3 mixed methods design was employed. All participants received anodal tDCS and therefore there was one between participants factor of ABM (active ABM, control ABM). The within subjects factor was assessment (assessment 1, assessment 2, assessment 3). The dependent variables were attention bias and state anxiety.

A sham tES group was not included in the current design. A separate post-hoc mixed ANOVA was conducted subsequently to the following analyses on combined data from experiments 1 and 3. This provided a comparison of active versus sham tES (see section 4.3.8 for a summary of results). Data from experiment 3 will be analysed together with those from experiments 1 and 2 in the following chapter allowing comparison of all ABM and tES groups used in study 1.

### 4.2.2 Participants

A total of 42 participants was recruited. Twenty-one participants were allocated to each ABM group but data from two participants from the control ABM group were omitted from analysis as accuracy scores were below 75%. Data from 40 participants were therefore analysed (37 female), mean age = 19.68 years, SD = 3.37, range = 18 to 39. All participants were right-handed and had normal or corrected to normal vision.

Participant recruitment procedure matched that from experiments 1 and 2.

All participants received anodal tDCS but were allocated to either active ABM or control ABM.

### 4.2.3 Ethics

The study was approved by the University of Roehampton ethics committee (approval code PSYC 14/ 116). Written informed consent was provided by all participants before participation. Participants were compensated for their participation with course credits.

### 4.2.4 Materials

#### 4.2.4.1 Measures

The self-report measures used were the same as those used in experiment 1.

#### 4.2.4.2 Stimuli

The stimuli used were identical to those used in experiment 1.

#### 4.2.4.3 Attention Bias Assessment

Attention bias assessment was the same as in experiment 1.

#### 4.2.4.4 ABM task

Attention bias modification and control attention bias modification were the same as part 1 of the experiment

#### 4.2.4.5 TES

Anodal tDCS was applied at an amplitude of 1.5mA. The anode was placed above the left DLPFC (F3 in the 10/20 system of electrode placement) and the cathode above the contralateral orbitofrontal cortex (Appendix 18). Stimulation lasted for 20 minutes at the beginning of a 35-minute training period. The

current was ramped up and down for 20 seconds at the beginning and end of active stimulation. All participants received anodal tDCS.

### 4.2.5 Procedure

The experimental procedure replicated that used in experiment 1 except that all participants received active or control ABM with anodal tDCS (and not active tRNS or sham tRNS).

### 4.2.6 Data Preparation

Data from inaccurate trials were removed. Mean accuracy across attention bias assessments was 96.04% (*SD* = 4.21). Reaction times below 200ms were removed. To remove the effect of outlying data on analysis, reaction times which were more than 2.5 standard deviations from each participant's mean reaction time were excluded (Brown et al., 2014). These further data removals constituted 2.07% of the total number of trials.

### 4.2.7 Data Analyses

Attention bias and state anxiety data were subjected to mixed ANOVAs with ABM (active ABM, control ABM) as the between participants factor and assessment as the within subjects factor. These ANOVAs were performed on data from all participants. Subsequently the ANOVAs were repeated with pre-existing attention bias or pre-existing trait anxiety or pre-existing attentional control as a covariate.

In three omnibus ANOVAs attention bias and state anxiety data from experiments 1 and 3 were analysed. These was to enable comparison of all tES conditions applied across the 2 experiments (active tRNS, sham tES, anodal tDCS) with active or control ABM on state anxiety and attention bias. Assessment (assessment 1, assessment 2 and assessment 3) was included as the within participants factor and tES (active tRNS, sham tES, anodal tDCS) and ABM (active ABM, control ABM) were between participants factors. These were then repeated with pre-existing attention bias, pre-existing trait anxiety and pre-existing attentional control as covariates.

### 4.2.8 Baseline Characteristics

#### 4.2.8.1 Baseline Scores for Main Variables of Interest

Findings from experiment 3 will be discussed in light of results from experiments 1 and 2. Baseline attention bias, state anxiety, trait anxiety and attentional control from all 3 experiments and for all experimental groups are detailed in table 4.1. One-way ANOVAs compared baseline scores for all participants from experiments 1, 2 and 3 and revealed no differences between participants across experiments in terms of their baseline attention bias, state anxiety, trait anxiety and attentional control scores.

Table 4.1:

*Baseline mean (SD) scores for major variables of interest*

| | Baseline Mean (SD) Scores | | | |
|---|---|---|---|---|
| | Attention Bias (ms) | State Anxiety | Trait Anxiety | Attentional Control |
| All Participants Experiment 1 | .97 (13.70) | 33.18 (10.46) | 41.73 (11.84) | 48.87 (7.84) |
| All Participants Experiment 2 | -2.25 (14.77) | 34.48 (10.59) | 44.50 (12.19) | 49.48 (7.75) |
| All Participants Experiment 3 | -4.45 (13.13) | 33.80 (8.96) | 45.74 (13.61) | 47.08 (8.10) |
| **Between Subjects Effects** | ***F* = 1.57, *p* = .21** | ***F* = .25, *p* = .78** | ***F* = 1.58, *p* = .21** | ***F* = .97, *p* = .38** |
| Active ABM/Active tRNS | -.30 (18.75) | 33.38 (10.94) | 39.48 (9.69) | 50.76 (6.50) |
| Active ABM/Sham tRNS | -.73 (13.69) | 33.90 (8.15) | 43.10 (12.92) | 47.57 (7.88) |
| Control ABM/Active tRNS | 1.59 (9.77) | 31.71 (9.31) | 40.14 (12.98) | 50.62 (6.79) |
| Control ABM/Sham tRNS | 3.33 (11.37) | 33.71 (13.34) | 44.19 (11.67) | 46.52 (9.48) |
| No Training ABM/Active tRNS | -4.78 (14.59) | 33.52 (9.78) | 41.24 (10.80) | 50.62 (7.26) |
| No Training ABM/Sham tRNS | .28 (14.87) | 35.43 (11.51) | 47.76 (12.87) | 48.33 (8.22) |
| Active ABM/Anodal tDCS | -2.64 (11.10) | 33.24 (7.92) | 47.75 (14.22) | 47.20 (8.95) |
| Control ABM/Anodal tDCS | -6.44 (15.11) | 34.42 (10.17) | 43.63 (12.97) | 46.95 (7.34) |

#### 4.2.8.2 Depression and Fear of Negative Evaluation

Table 4.2 shows for each experimental group the mean and standard deviation score at baseline for the CES-D and FNE. Baseline scores on the CES-D and FNE scales did not differ significantly between groups (*t*s < 1.21, *p*s > .23).

Table 4.2:

*Mean (SD) score for each self-report measure per tES group*

| | Active ABM /atDCS | | Control ABM /atDCS | |
|---|---|---|---|---|
| | M | SD | M | SD |
| CES-D | 18.35 | 13.76 | 16.58 | 11.21 |
| FNE | 15.35 | 7.57 | 12.37 | 7.82 |

### 4.2.8.3 State and Trait Anxiety Across Experimental Groups by Gender

Table 4.3 shows the mean and standard deviation state anxiety scores at baseline for males and females.

Table 4.3

*Baseline mean (standard deviation) state and trait anxiety scores across experimental groups for females and males*

| | | Anodal tDCS | |
|---|---|---|---|
| | | Active ABM | Control ABM |
| N | | 19 | 18 |
| Females | State Anxiety | 33.58 (8.16)* | 34.06 (10.33) |
| | Trait Anxiety | 48.33 (14.83)* | 41.94 (11.00) |
| N | | 2 | 1 |
| Males | State Anxiety | 30.00 (5.66) | 41.00 |
| | Trait Anxiety | 42.50 (6.36) | 74.00 |

* P< .05

State Anxiety

There was no significant difference in baseline state anxiety between ABM groups ($t$ = .41, $p$ = .68).

As previously reported, state anxiety mean and standard deviation scores reported for a normative sample of undergraduate students are mean = 36.47 (SD = 10.02) for males and mean = 38.76 (SD = 11.95) for females (Spielberger et al., 1983). One sample t-tests revealed that for females who received active ABM/anodal tDCS, mean baseline state anxiety score was significantly lower than

the normative mean $t(18) = 2.77$, $p = .013$. For females who received control ABM/anodal tDCS, mean baseline state anxiety score did not differ significantly from the mean normative score, $t = 1.93$, $p = .07$. For males who received active ABM/anodal tDCS, mean baseline state anxiety score did not differ significantly from the mean normative score, $t = 1.33$, $p = .23$. As there was only one male in the control ABM group it was not possible to perform a one sample t-test to compare mean baseline state anxiety to the normative mean.

Trait Anxiety

There was no difference in trait anxiety scores between ABM groups at baseline ($t = .94$, $p = .35$).

The normative mean of trait anxiety reported for a sample of undergraduate students is 40.40 (SD = 10.15) for females and 38.30 (SD = 9.18) for males (Spielberger, 1983). One sample t-tests revealed that for females who received active ABM, baseline trait anxiety ($M = 48.33$, SD = 14.83), was significantly higher than the normative mean $t(17) = 2.27$, $p = .037$. Baseline trait anxiety for females who received control ABM was not significantly different to the normative mean ($t = .60$, $p = .56$). For males who received active ABM, baseline trait anxiety did not differ significantly from the normative mean ($t = 1.44$, $p = .17$). There was only 1 male in the control ABM group and therefore mean baseline trait anxiety could not be compared to the normative mean for a population of young males.

#### 4.2.8.4 Correlations Between State Anxiety Scores

Data from each administration of the state anxiety scale of the STAI (i.e. start of day 1, end of day 1, start of day 2, end of day 2, start of day 3, end of day 3, start of day 30, end of day 30) were subject to a Pearson Product Moment Correlation analysis with SAS data from each of the other assessments. All correlations were significant (all R's ≥ .54, all *p*s < .001). The normative test-retest reliability r values reported by Spielberger et al. (1983) for college students, with a test-retest interval of 20 days were .54 for males and .27 for females. Our results therefore suggest strong test-retest reliability and consistency within the state anxiety data.

#### 4.2.8.5 Correlations Between State Anxiety and Trait Anxiety

Baseline trait anxiety score was correlated with state anxiety score on days 1 and 3 but not at assessment 3 (day 30; see table 4.4).

Table 4.4:

*Bivariate correlations between baseline trait anxiety scale and state anxiety scale (SAS) scores at assessments 1, 2 and 3*

| | SAS Assessment 1 | SAS Assessment 2 | SAS Assessment 3 |
|---|---|---|---|
| Baseline Trait Anxiety | **.400*** | **.365*** | **.301** |

* $p < .05$

#### 4.2.8.6 Correlations Between Self-Report Measures at Baseline

Baseline scores from questionnaires assessing trait characteristics were subject to a Pearson Product Moment correlational analysis. Table 4.5 shows the correlation between baseline scores on trait self-report measures. Baseline scores across all questionnaires were significantly correlated (all *r*s > .52, *p*s < .005) suggesting that participants reported consistently across measures.

Table 4.5:

*Bivariate correlations for trait anxiety scale (TAS), attentional control scale (ACS), Centre for Epidemiological Studies depression questionnaire (CES-D) and fear of negative evaluation scale (FNE) scores at baseline.*

| | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| 1. Trait Anxiety | 1.00 | | | |
| 2. Attentional Control | **-.714**** | 1.00 | | |
| 3. Depression | **.829**** | **-.719*** | 1.00 | . |
| 4. Fear Negative Evaluation | **.786**** | **-.521**** | **.579*** | 1.00 |

* p < 0.05

** p < 0.001

## 4.3 Results

### 4.3.1 Analyses of Variance Across all Participants

#### 4.3.1.1 Attention Bias (All Participants)

A 2 x 3 mixed ANOVA was conducted on the attention bias data with a between subjects factor of ABM (active ABM, control ABM) and a within subjects factor of assessment (assessment 1, assessment 2, assessment 3). The main effect of

assessment approached significance, $F(2,72) = 2.97$, $p = .058$, ($\eta_p^2 = .08$; *observed power* = .56). Paired samples t-tests revealed no significant changes in attentional bias across assessments (all *t*s < 1.86, *p*s > .21; Bonferroni adjusted for multiple comparisons; significant if p*3 < .05).

There were no further main effects or interactions (*F*s < 1.34, *p*s > .27).

Figure 4.1 shows mean attentional bias across assessments for each ABM group (active ABM, control ABM) and for all participants. Positive values represent threat bias and negative values represent neutral bias

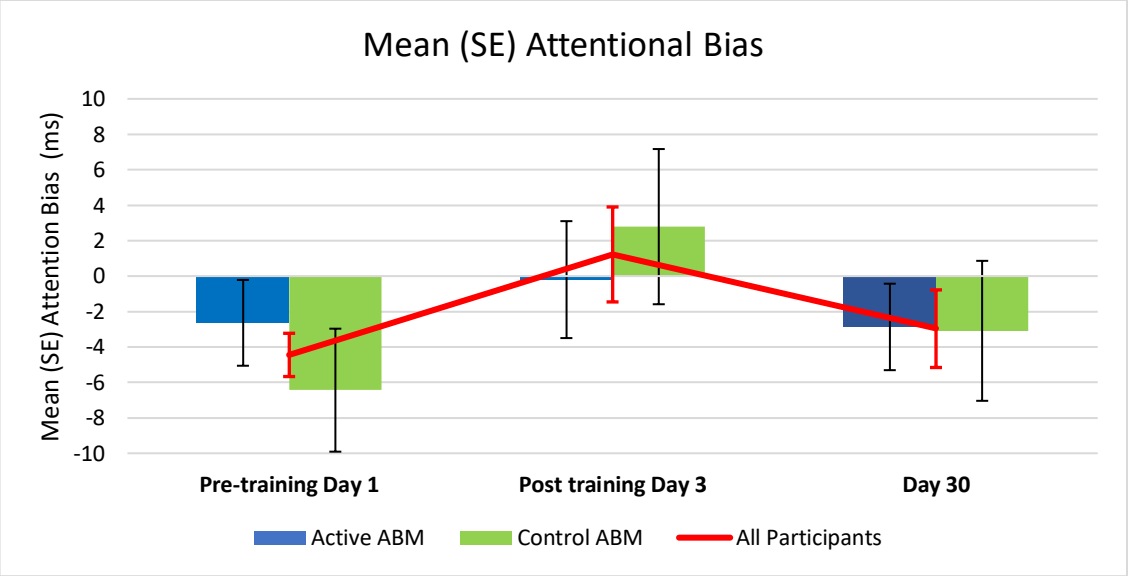



*Figure 4.1*. Mean (SE) attention bias across assessments for each ABM group and for all participants.

#### 4.3.1.2 State Anxiety (All Participants)

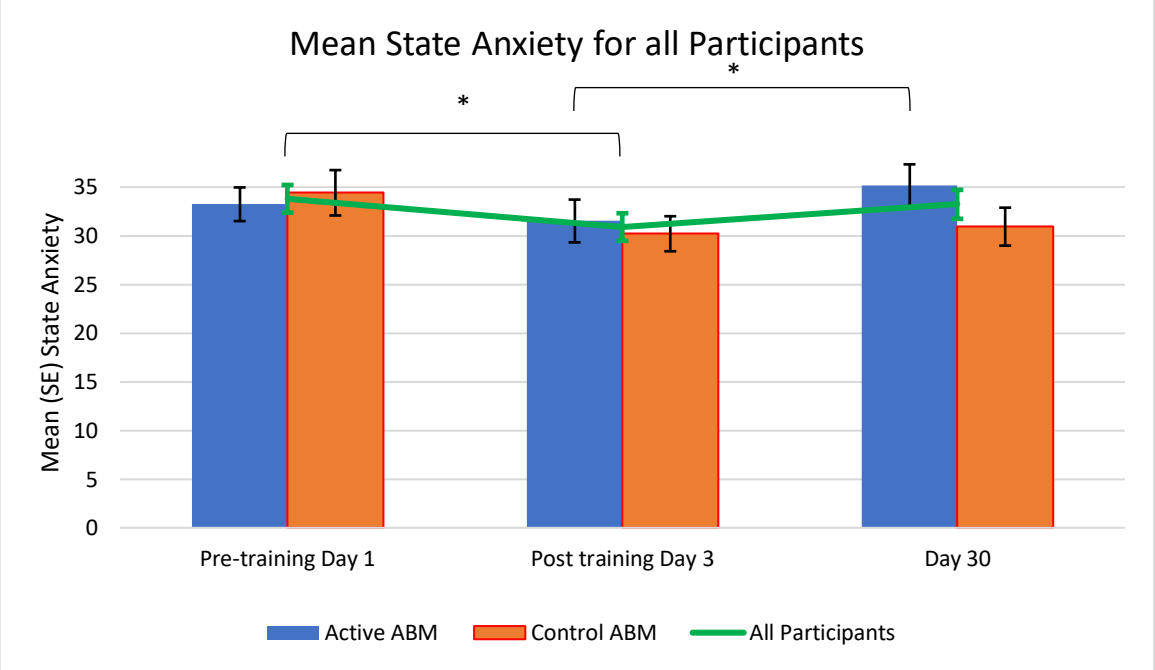
A 2 x 3 mixed ANOVA was conducted on state anxiety data with one between subjects factor of ABM (active ABM, control ABM) and a within subjects factor of assessment (assessment 1, assessment 2, assessment 3). The main effect of assessment was marginally significant, $F(2,74) = 3.10$, $p = .051$, ($\eta_p^2 = .08$; observed power = .58). Paired samples t-tests (Bonferroni corrected for multiple comparisons; significant if 3*p < .05) revealed a difference in state anxiety between assessment 1, and assessment 2, $t(39) = 2.46$, $p = .044$. State anxiety was greater at assessment 1 (M = 33.80, SD = 8.96) compared to assessment 2 (M = 30.90, SD = 9.00). No other change in state anxiety across assessments was significant ($t$s < 1.88, $p$s > .20).

The interaction between assessment and ABM approached significance, $F(2,74) = 2.91$, $p = .061$, ($\eta_p^2 = .07$; observed power = .55). For each ABM group paired samples t-tests examined change in attention bias across assessments. All results were Bonferroni corrected for multiple comparisons (result significant if 3*p < .05). This revealed a significant increase in state anxiety at assessment 3 ($M = 35.19$, $SD = 9.86$) compared to assessment 2 ($M = 31.51$, $SD = 10.09$) for participants in the active ABM group, $t(20) = 3.24$, $p = .012$. No further change in state anxiety across assessments for active ABM participants was significant ($t$s < 1.21, $p$s > .72). No change in state anxiety across assessments was significant for participants in the control ABM group ($t$s < 2.19, $p$s > .13). To further explore the ABM x assessment interaction, state anxiety scores for participants in the active ABM group and participants in the control ABM group were compared for each assessment point using independent t-tests. There was

no significant difference in state anxiety score between the groups at any assessment (*t*s < 1.44, *p*s > .47; Bonferroni adjusted for multiple comparisons; significant if 3*p < .05).

The main effect of ABM was not significant ($F$ = .21, $p$ = .65).

Figure 4.2 shows mean state anxiety levels across assessments by ABM group.




* $p$ < .05

*Figure* 4.2. Mean (SE) state anxiety across assessments for each ABM group and for all participants

Due to the unexpected nature of this finding (increase in state anxiety at assessment 3 relative to assessment 2 for active ABM participants), data related to change in state anxiety from assessment 2 to assessment 3 was examined for outliers. For the active ABM group one participant had an increase in state anxiety score of 20 ($z$ = 3.15). There were no outliers for the control ABM group. When

all state anxiety scores from the outlying participant were removed, there was no longer an ABM x assessment interaction effect ($F$ = 2.47, $p$ = .09). This suggests that the increase in state anxiety at follow-up relative to at the end of training for the active ABM group was driven by change in state anxiety for one participant.

#### 4.3.1.3 State Anxiety (All Participants) From Start and End of Each Experimental Day

As in experiments 1 and 2, state anxiety measures were taken for each day of attention bias modification training before and after the training. Figure 4.3 gives the mean and standard error state anxiety score for the beginning and end of each experimental session, for each experimental group.

A 2 x 2 x 3 mixed ANOVA was conducted on the state anxiety data with the between subjects factor of ABM (Active ABM, control ABM) and 2 within subjects factors of time (start of session, end of session) and day (day 1, day 2, day 3, day 30).

This revealed a main effect of day, $F(3,111) = 3.38$, $p = .02$, ($\eta_p^2 = .08$; observed power = .75). Follow-up paired samples t-tests (results Bonferroni corrected; significant if $6*p < .05$) revealed that state anxiety on day 3 ($M$ = 30.65, $SD$ = 8.53) was significantly reduced compared to state anxiety on day 1 ($M$ = 33.03, $SD$ = 8.68), $t(39) = 3.09$, $p = .024$. State anxiety on day 30 ($M$ = 33.90, $SD$ = 9.22) was increased compared to state anxiety on day 3 ($M$ = 30.65, $SD$ = 8.53), $t(38) = 2.95$, $p = .03$.

There were no further significant main or interaction effects (*F*s < 3.40, *p*s > .11).

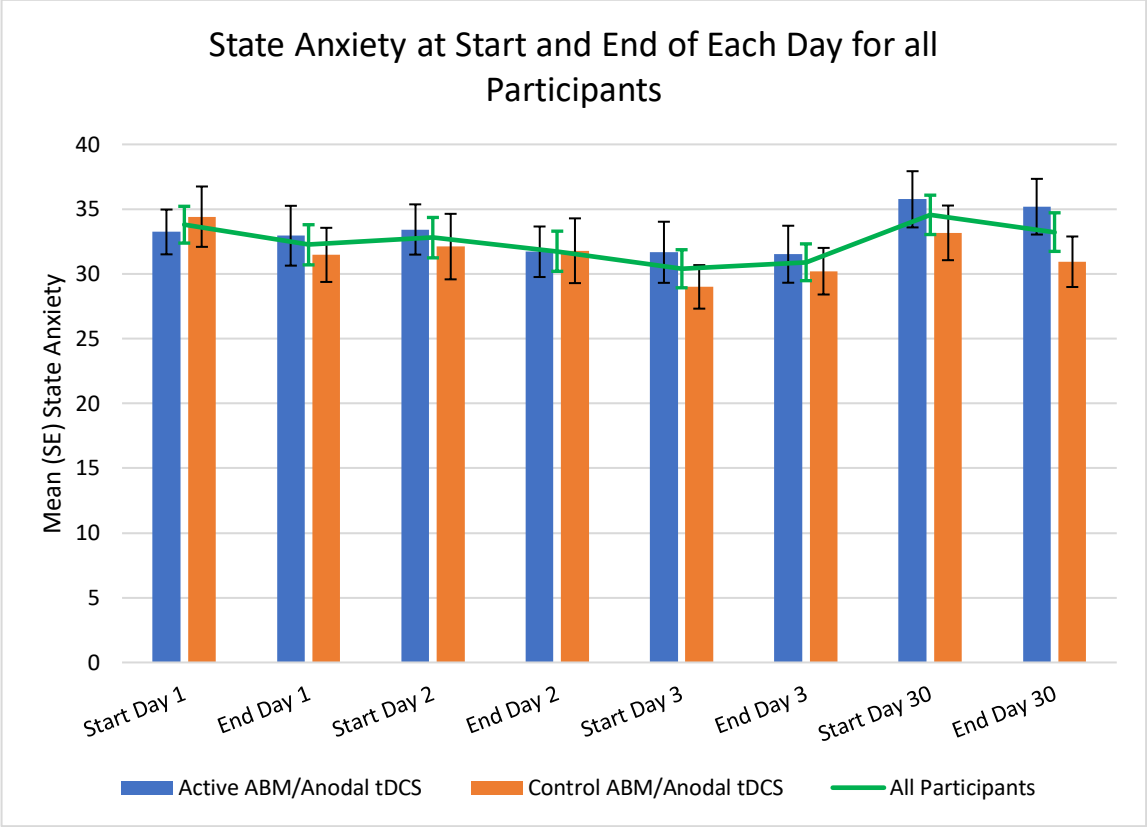



*Figure 4.3*. Mean (SE) state anxiety scores at the start and end of each experimental day for each ABM group and for all participants

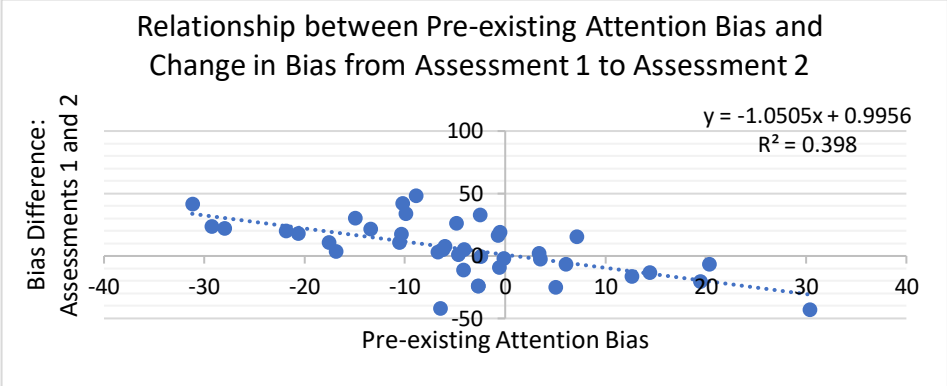
### 4.3.2 Analyses of Covariance with Pre-existing Attention Bias as a Covariate

#### 4.3.2.1 Attention Bias (Pre-existing Attention Bias as Covariate)

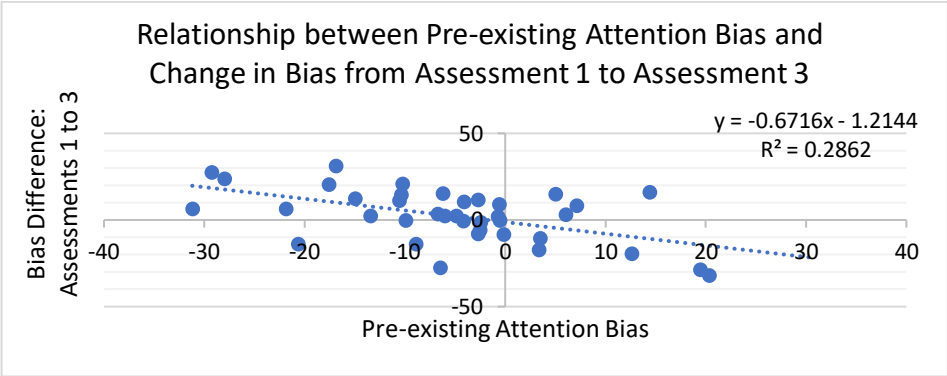
With attention bias as the dependant variable a 2 x 3 mixed ANCOVA was conducted with a between subjects factor of ABM (active ABM, control ABM), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and pre-existing attention bias as the covariate. The main effect of pre-existing attention bias was significant, $F(1,35) = 21.38$, $p < .001$, ($\eta_p^2 = .38$; *observed*

*power* = .99. Pre-existing attention bias and mean attention bias across experiment 3 were highly, positively correlated, $r(40) = .62$, $p < .001$. There was a significant interaction between pre-existing attention bias and assessment, $F(1.54,53.77) = 7.18$, $p = .004$, ($\eta_p^2 = .17$; *observed power* = .86; Greenhouse Geisser corrected). To explore the relationship between pre-existing attention bias and change in attention bias across assessments, a Pearson Product Moment correlational analysis was conducted with pre-existing attention bias, change in attention bias from assessment 1 to assessment 2, change in attention bias between assessment 1 and assessment 3 and change in attention bias between assessments 2 and 3 as the variables. Change in attention bias was calculated by subtracting attention bias score at the earlier assessment from attention bias score at the later assessment e.g. attention bias at assessment 2 – attention bias at assessment 1. A positive score represented an increase in attention bias therefore and a negative score represented a reduction in attention bias. Pre-existing attention bias was significantly, strongly, negatively correlated with change in attention bias from assessment 1 to assessment 2, $r(40) = -.63$, $p < .001$ and moderately, negatively correlated with change in attention bias from assessment 1 to assessment 3, $r(38) = -.54$, $p = .001$. Pre-existing attention bias and change in attention bias between assessments 2 and 3 were not significantly correlated ($r = .17$, $p = .31$). Figure 4.4 shows the relationships between pre-existing attention bias and change in attention bias across assessments.

a)




b)




c)

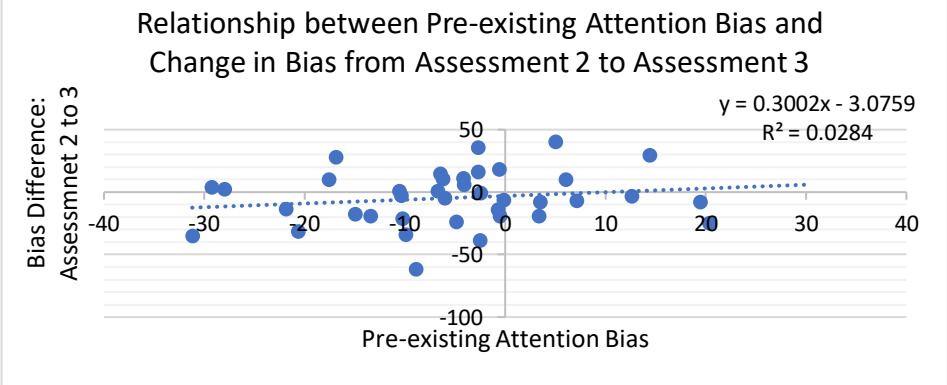



*Figure 4.4*. The relationship between pre-existing attention bias a a) change in attention bias between assessments 1 and 2, b) change in attention bias between assessments 1 and 3 and c) change in attention bias between assessments 2 and 3 across experiment 3. For pre-existing attention bias, positive scores indicate attention bias towards threat and negative scores indicate attention bias towards neutral. For difference scores, positive values represent increase in threat bias and negative scores represent increase in neutral bias (reduction in threat bias).

No further main or interaction effects were significant (*F*s < .79, *p*s > .38).

#### 4.3.2.2 State Anxiety (Pre-existing Attention Bias as Covariate)

With state anxiety as the dependant variable A 2 x 3 mixed ANCOVA was conducted with a between subjects factor of ABM (active ABM, control ABM), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and pre-existing attention bias as the covariate. The main effect of assessment was marginally significant, $F(2,72) = 2.80$, $p = .067$, ($\eta_p^2 = .07$; *observed power* = .54). There was also a significant interaction between assessment and ABM condition, $F(2,72) = 3.29$, $p = .04$, ($\eta_p^2 = .08$; *observed power* = .61; Greenhouse Geisser corrected). These effects were investigated further in section 4.3.1.1. No further main or interaction effects were significant, (*F*s < .86, *p*s > .42).

#### 4.3.2.3 State Anxiety at Start and End of each Experimental Session (Pre-existing Attention Bias as Covariate)

With state anxiety as the dependent variable, a 4 x 2 x 2 mixed ANCOVA was conducted with day (day 1, day 2, day 3, day 30) and time (start of session, end of session) as within participants factors and ABM (active ABM, control ABM) as a between participants factor. Pre-existing attention bias was included as a covariate. There were no significant main or interactions effects (*F*s < 2.39, *p*s > .073).

### 4.3.3 Analyses of Covariance with Pre-existing Trait Anxiety as a Covariate

#### 4.3.3.1 Attention Bias (Pre-existing Trait Anxiety as Covariate)

With attention bias as the dependant variable a 2 x 3 mixed ANCOVA was conducted with a between subjects factor of ABM (active ABM, control ABM), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) with pre-existing trait anxiety as the covariate. There were no significant main or interaction effects (*F*s < 1.58, *p*s > .21).

#### 4.3.3.2 State Anxiety (Pre-existing Trait Anxiety as Covariate)

With state anxiety as the dependant variable A 2 x 3 mixed ANCOVA was conducted with a between subjects factor of ABM (active ABM, control ABM), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and pre-existing trait anxiety as the covariate. The main effect of pre-existing trait anxiety was significant, $F(1,35) = 6.20$, $p = .018$, ($\eta_p^2 = .15$; *observed power* = .68). There was a significant, moderate, positive correlation between pre-existing trait anxiety and state anxiety, $r(39) = .42$, $p = .009$ suggesting that higher pre-existing trait anxiety was associated with higher mean state anxiety (see figure 4.5 for the regression line).

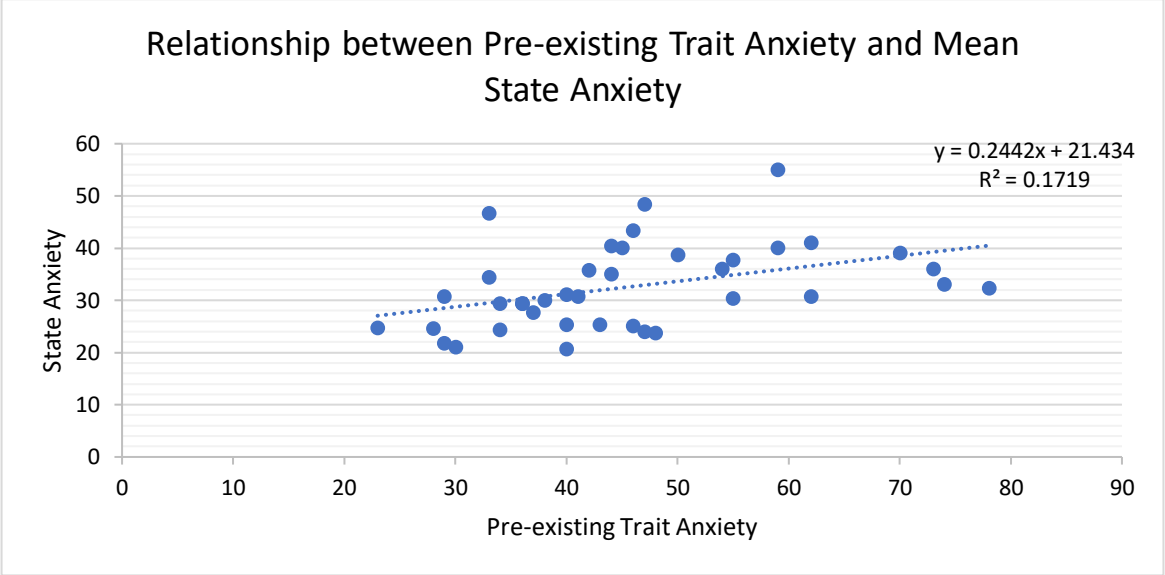



*Figure 4.5*. The relationship between scores on the state anxiety scale of the STAI (Spielberger et al., 1983) across experiment 3 and the trait anxiety scale of the STAI at baseline.

With trait anxiety held constant, the main effect of assessment was no longer present. There were no further significant main or interaction effects (*F*s < 2.48, *p*s > .092).

#### 4.3.3.3 State Anxiety at Start and End of each Experimental Session (Pre-existing Trait Anxiety as Covariate)

A 4 x 2 x 2 mixed ANCOVA was conducted on state anxiety data with day (day 1, day 2, day 3, day 30) and time (start of session, end of session) as within participants factors and ABM (active ABM, control ABM) as a between participants factor. Pre-existing trait anxiety was the covariate. There was a significant main effect of pre-existing trait anxiety, $F(1,35) = 6.85$, $p = .013$, ($\eta_p^2 = .16$; *observed power* = .72). There was a significant, moderate, positive correlation between pre-existing trait anxiety and state anxiety, $r(39) =$

.42, $p$ = .009 (see figure 4.5 for the relationship between pre-existing trait anxiety and mean state anxiety).

### 4.3.4 Analyses of Covariance with Pre-existing Attentional Control as a Covariate

#### 4.3.4.1 Attention Bias (Pre-existing Attentional Control as Covariate)

With attention bias as the dependant variable a 2 x 3 mixed ANCOVA was conducted with a between subjects factor of ABM (active ABM, control ABM), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) with pre-existing attentional control as the covariate. There were no significant main or interaction effects ($F$s < 1.62, $p$s > .21).

#### 4.3.4.2 State Anxiety (Pre-existing Attentional Control as Covariate)

A 2 x 3 mixed ANCOVA was conducted on state anxiety data with a between subjects factor of ABM (active ABM, control ABM), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and pre-existing attentional control as the covariate. There was a significant main effect of pre-existing attentional control, $F(1,35) = 5.82$ $p$ = .021, ($\eta_p^2$ = .14; *observed power* = .65). A Pearson Product Moment correlational analysis revealed a significant, moderate, negative correlation between pre-existing attentional control and state anxiety, $r(39) = -.38$, $p$ = .019 suggesting that higher baseline attentional control was associated with lower state anxiety (see figure 4.6).

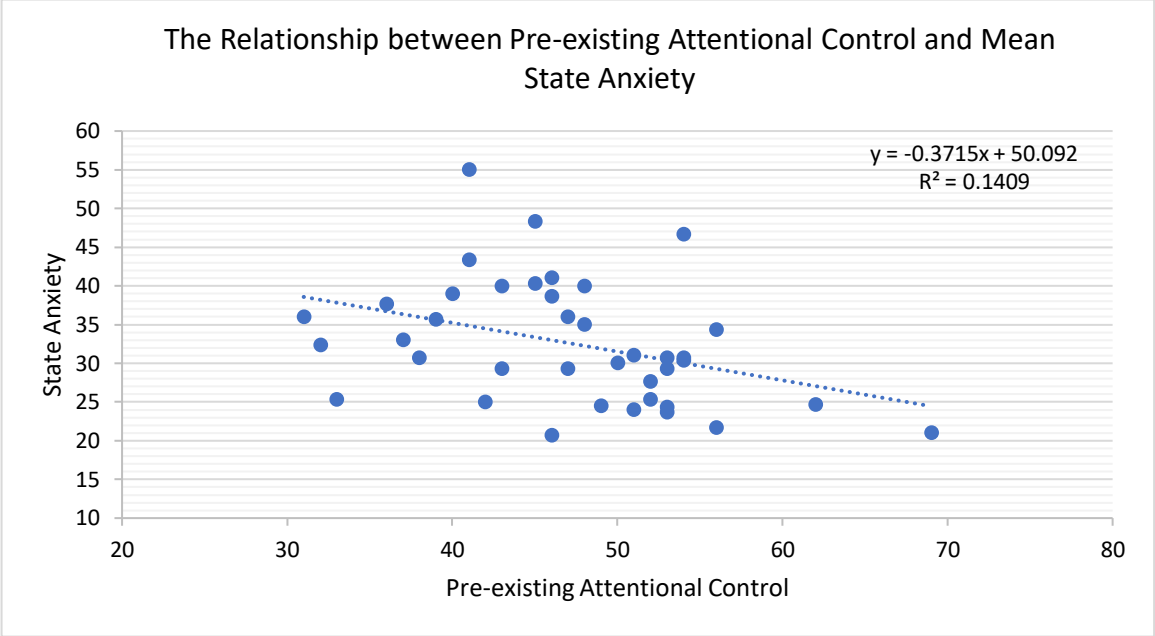



*Figure 4.6*. The relationship between scores on the attention control scale (Derryberry & Reed, 2002) at baseline and mean scores on the state anxiety scale (Spielberger et al., 1983) across experiment 3.

Controlling for pre-existing attentional control the effect of assessment was no longer significant. There were no further significant main or interaction effects (*F*s < 2.27, *p*s > .11).

#### 4.3.4.3 State Anxiety at Start and End of each Experimental Session (Pre-existing Attentional Control as Covariate)

With state anxiety as the dependent variable, a 4 x 2 x 2 mixed ANCOVA was conducted with day (day 1, day 2, day 3, day 30) and time (start of session, end of session) as within participants factors and ABM (active ABM, control ABM) as a between participants factor and pre-existing attentional control as a covariate. There was a significant main effect of pre-existing attentional control, $F(1,35) = 5.66$, $p = .023$, ($\eta_p^2 = .14$; *observed power* = .64). A Pearson Product

Moment correlational analysis revealed a significant, moderate, negative correlation between pre-existing attentional control and state anxiety, $r(39) = -.38$, $p = .019$ (see figure 4.6).

### 4.3.5 Analyses with tES as a Between Participants Factor

In sections 4.3.1 to 4.3.4 analysis of data from experiment 3 in isolation was described. However, the aim of experiment 2 was to explore whether the application of anodal tDCS above the DLPFC might better facilitate the neural mechanisms associated with ABM training than active tRNS of the bilateral IFG or sham tES. This would be reflected in greater attention bias and state anxiety reductions following ABM with anodal tDCS relative to ABM with active tRNS or sham tES. In order to directly compare the effects of stimulation type on training outcomes the present analysis combined experiment 3 and experiment 1. For each dependent variable (attention bias, state anxiety) a 3 x 2 x 3 ANOVA was conducted with the within participants factor of assessment (assessment 1, assessment 2, assessment 3) and between participants factors of ABM (active ABM, control ABM) and tES (active tRNS, sham tES, anodal tDCS). Subsequently, three 3 x 2 x 3 ANOVAs were conducted with the within participants factor of assessment (assessment 1, assessment 2, assessment 3), the between participants factors of ABM (active ABM, control ABM) and tES (active tRNS, sham tES, anodal tDCS) and the covariate of pre-existing attention bias, pre-existing trait anxiety or pre-existing attentional control.

#### 4.3.5.1 Attention Bias (tES Group as Between Participants Factor)

A 3 x 2 x 3 ANOVA was conducted on attention bias data with assessment (assessment 1, assessment 2, assessment 3) as the within participants factor, between participants factors of ABM (active ABM, control ABM) and tES (active tRNS, anodal tDCS, sham tES). The interaction between assessment and tES condition was significant, $F(4,232) = 2.95$, $p = .021$, ($\eta p^2 = .05$; *observed power* = .79). Attention bias data for each assessment was subject to an independent ANOVA to examine the effect of tES group. Attention bias did not differ between tES groups at assessment 1 ($t$s < 2.02, $p$s > .14), assessment 2 ($t$s < 1.81, $p$s > .23) or assessment 3 ($t$s < .21, $p$s > 2.51). For each tES group (active tRNS, anodal tDCS, sham tES) paired samples t-tests examined change in attention bias across assessments. All results were Bonferroni corrected for multiple comparisons (result significant if 3*p < .05). There were no significant changes in attention bias across assessments for the active tRNS ($t$s < .87, $p$s > 1.17) or anodal tDCS ($t$s < 1.64, $p$s > .33) groups. For the sham tES group, the reduction in threat bias between assessments 1 ($M$ = 1.30, $SD$ = 12.60) and assessment 2 ($M$ = -5.81, $SD$ = 18.21) approached significance, $t(41) = 2.40$, $p = .063$. For the sham tES group there were no further significant changes in attention bias across assessments ($t$s < 1.55, $p$s > .39). There were no further significant main or interaction effects ($F$s < .95, $p$s > .43).

#### 4.3.5.2 State Anxiety (tES Group as Between Participants Factor)

The above analysis was repeated on state anxiety data. There was a significant main effect of assessment, $F(1.80,210.14) = 5.38$, $p = .007$, ($\eta p^2 = .04$; *observed*

*power* = .81; Greenhouse Geisser corrected). Paired samples t-tests [Bonferroni corrected for multiple comparisons (result significant if 3*p < .05)] revealed that state anxiety at assessment 2 (*M* = 30.85, *SD* = 9.08) was significantly reduced compared to state anxiety at assessment 1 (*M* = 33.38, *SD* = 9.97), *t*(123) = 3.79, *p* < .001. There was no further significant change in state anxiety across assessments (*t*s < 1.61, *p*s > .11). There were no further significant main or interaction effects (*F*s < 1.78, *p*s > .14).

#### 4.3.5.3 State Anxiety at Start and End of Each Experimental Day (tES Group as Between Participants Factor)

A 4 x 2 x 2 x 3 ANOVA was conducted on attention bias data with day (day 1, day 2, day 3, day 30) and time (start of session, end of session) as the within participants factors and between participants factors of ABM (active ABM, control ABM) and tES (active tRNS, anodal tDCS, sham tES). There was a significant main effect of time, *F(*1,117) = 11.03, *p* = .001, ($\eta p^2$ = .09; *observed power* = .91). State anxiety at the end of session (*M* = 31.26, *SD* = 7.93) was reduced compared to state anxiety at the start of session (*M* = 32.31, *SD* = 7.88). There were no further main or interaction effects (*F*s < 2.06, *p*s > .11).

### 4.3.6 Analyses of Covariance with tES as a Between Participants Factor and Pre-existing Attention Bias as a Covariate

#### 4.3.6.1 Attention Bias (tES group as Between Participants Factor and Pre-existing Attention Bias as a Covariate)

A 3 x 2 x 3 ANOVA was conducted on attention bias data with assessment (assessment 1, assessment 2, assessment 3) as the within participants factor, between participants factors of ABM (active ABM, control ABM) and tES (active tRNS, anodal tDCS, sham tES) and pre-existing attention bias as a covariate. The main effect of pre-existing attention bias was significant, $F(1,115) = 57.84$, $p < .001$, ($\eta p^2 = .34$; *observed power* = 1.00). Pre-existing attention bias was moderately to highly, positively correlated with mean attention bias, $r(124) = .57$, $p < .001$. The interaction between pre-existing attention bias and assessment was significant, $F(1.60,183.800) = 38.40$, $p < .001$, ($\eta p^2 = .25$; *observed power* = 1.00; Greenhouse Geisser corrected). Pre-existing attention bias was strongly, negatively correlated with change in attention bias from assessment 1 to assessment 2, $r(124) = -.61$, $p < .001$ and change in attention bias from assessment 1 to assessment 3, $r(122) = -.71$, $p < .001$ but was not significantly correlated with change in attention bias from assessment 2 to assessment 3 ($r = .011$, $p = .91$). The significant negative correlations indicated that higher pre-exiting threat bias was associated with greater reduction in threat bias following training and greater pre-existing neutral bias was associated with greater reduction in neutral bias following training relatively to before training. There were no further main or interaction effects ($F$s < 1.67, $p$s > .17).

#### 4.3.6.2 State Anxiety (tES group as Between Participants Factor and Pre-existing Attention Bias as a Covariate)

The above analysis was repeated on state anxiety data. There was a significant main effect of assessment, $F(1.80,208.40) = 5.32$, $p = .007$, ($\eta p^2 = .044$; *observed power* = .81; Greenhouse Geisser corrected). This effect was explored in section 4.3.5.2. With pre-existing attention bias held constant, there were no further significant main or interaction effects ($F$s < 1.81, $p$s > .14).

#### 4.3.6.3 State Anxiety at Start and End of Each Experimental Day (tES group as Between Participants Factor and Pre-existing Attention Bias as a Covariate)

A 4 x 2 x 2 x 3 ANOVA was conducted on attention bias data with day(day 1, day 2, day 3, day 30) and time (start of session, end of session) as the within participants factors and between participants factors of ABM (active ABM, control ABM) and tES (active tRNS, anodal tDCS, sham tES). Pre-existing attention bias was the covariate. There was a significant main effect of time, $F(1,116) = 11.06$, $p = .001$, ($\eta p^2 = .09$; *observed power* = .91; Greenhouse Geisser corrected). State anxiety at the end of session ($M = 31.26$, $SD = 7.93$) was reduced compared to state anxiety at the start of session ($M = 32.31$, $SD = 7.88$). The interaction between time, day and pre-existing attention bias was also significant, $F(2.67,309.97) = 3.00$, $p = .036$, ($\eta p^2 = .025$; *observed power* = .67; Greenhouse Geisser corrected). For each day, a repeated measures ANOVA was conducted with the within participants factor of time (start of session, end of

session) and pre-existing attention bias as a covariate. For day 1 state anxiety, there was a significant main effect of time, $F(1,112) = 9.39$, $p = .003$, ($\eta p^2 = .07$; *observed power* = .86). State anxiety at the start of day 1 ($M = 33.38$, $SD = 9.97$) was higher than at the end of day 1 ($M = 33.38$, $SD = 9.97$). For day 1 state anxiety, there were no further significant main or interaction effects ($F$s < 2.32, $p$s > .13). For day 30 state anxiety, there was a significant main effect of time, $F(1,121) = 4.13$, $p = .044$, ($\eta p^2 = .03$; *observed power* = .52). State anxiety at the end of day 30 ($M = 32.00$, $SD = 9.47$) was reduced compared to state anxiety at the start of day 30 ($M = 32.76$, $SD = 9.25$). There were no further main or interaction effects emerging from the analysis of day 30 state anxiety ($F$s < .27, $p$s > .61). There were no significant main or interaction effects for day 2 state anxiety ($F$s < 3.19, $p$s > .08) or for day 3 state anxiety ($F$s < 3.13, $p$s > .08). For each time, a repeated measures ANOVA was conducted with the within participants factor of day (day 1, day 2, day 3, day 30) and pre-existing attention bias as a covariate. For start of session state anxiety there was a significant main effect of day, $F(2.72, 329.38) = 3.51$, $p = .019$, ($\eta p^2 = .03$; *observed power* = .75; Greenhouse Geisser corrected). Paired samples t-tests examined change in start of day state anxiety across days. Results were Bonferroni corrected for multiple comparisons (result significant if 6*p < .05). State anxiety at the start of day 3 ($M = 31.20$, $SD = 9.23$) was significant reduced compared to state anxiety at the start of day 1 ($M = 33.38$, $SD = 9.97$), $t(123) = 2.97$, $p = .024$. Change in start of day state anxiety was not significant across further comparisons ($t$s < 1.94, $p$s > .33). For start of session state anxiety there were no further significant main or interaction effects ($F$s < .59, $p$s > .61). No significant main or interaction effects emerged from the analysis of end of session state anxiety, ($F$s < 1.36, $p$s > .26).

There were no further significant main or interaction effects (*F*s < 1.94, *p*s > .13).

### 4.3.7 Analyses of Covariance with tES as a Between Participants Factor and Pre-existing Trait Anxiety as a Covariate

#### 4.3.7.1 Attention Bias (tES Group as Between Participants Factor and Pre-existing Trait Anxiety as a Covariate)

A 3 x 2 x 3 ANOVA was conducted on attention bias data with assessment (assessment 1, assessment 2, assessment 3) as the within participants factor, between participants factors of ABM (active ABM, control ABM) and tES (active tRNS, anodal tDCS, sham tES) and pre-existing trait anxiety as the covariate. The interaction between assessment and tES condition was significant, $F(4,228) = 2.71$, $p = .031$, ($\eta p^2 = .045$; *observed power* = .75). This effect was explored in section 4.3.5.1. There were no further significant main or interaction effects (*F*s < 1.10, *p*s > .30).

#### 4.3.7.2 State Anxiety (tES group as Between Participants Factor and Pre-existing Trait Anxiety as a Covariate)

The above analysis was repeated on state anxiety data. There was a significant main effect of trait anxiety, $F(1,115) = 59.93$, $p < .001$, ($\eta p^2 = .34$; *observed power* = 1.00). Pre-existing trait anxiety was highly, positively correlated with

mean state anxiety r(124) = .59, $p < .001$. There were no further significant main or interaction effects ($F$s < 1.70, $p$s > .15).

#### 4.3.7.3 State Anxiety at Start and End of Each Experimental Day (tES group as Between Participants Factor and Pre-existing Trait Anxiety as a Covariate

A 4 x 2 x 2 x 4 ANOVA was conducted on attention bias data with day(day 1, day 2, day 3, day 30) and time (start of session, end of session) as the within participants factors, between participants factors of ABM (active ABM, control ABM) and tES (active tRNS, anodal tDCS, sham tES) and pre-existing trait anxiety as a covariate. There was a significant main effect of trait anxiety, $F(1,115) = 67.58$, $p < .001$, ($\eta p^2 = .37$; *observed power* = 1.00). This effect was explored in section 4.3.7.2.

### 4.3.8 Analyses of Covariance with tES as a Between Participants Factor and Pre-existing Attentional Control as a Covariate

#### 4.3.8.1 Attention Bias (tES Group as Between Participants Factor and Pre-existing Attentional Control as a Covariate)

A 3 x 2 x 3 ANOVA was conducted on attention bias data with assessment (assessment 1, assessment 2, assessment 3) as the within participants factor, ABM (active ABM, control ABM) and tES (active tRNS, anodal tDCS, sham tES) as between participants factors and pre-existing attentional control as a covariate. The interaction between assessment and tES condition was significant,

*F(*4,228) = 2.60, *p* = .037, ($\eta p^2$ = .044; *observed power* = .72). This effect was explored in section 4.3.8.1. There were no further significant main or interaction effects (*F*s < 1.09, *p*s > .36).

#### 4.3.8.2 State Anxiety (tES group as Between Participants Factor and Pre-existing Attentional Control as a Covariate)

The above analysis was repeated on state anxiety data. There was a significant main effect of pre-existing attentional control, *F(*1,115) = 14.06, *p* < .001, ($\eta p^2$ = .11; *observed power* = .96). Pre-existing attentional control was moderately, negatively correlated with state anxiety, *r*(124) = -.34, *p* < .001 suggesting that higher attentional control at baseline was associated with lower mean state anxiety. There were no further significant main or interaction effects (*F*s < 1.61, *p*s > .18).

#### 4.3.8.3 State Anxiety at Start and End of Each Experimental Day (tES group as between participants factor and Pre-existing Attentional Control as a Covariate)

A 4 x 2 x 2 x 3 ANOVA was conducted on attention bias data with day (day 1, day 2, day 3, day 30) and time (start of session, end of session) as the within participants factors and between participants factors of ABM (active ABM, control ABM) and tES (active tRNS, anodal tDCS, sham tES). There was a significant main effect of pre-existing attentional control, *F(*1,115) = 15.05, *p* < 001, ($\eta p^2$ = .12; *observed power* = .97). This effect was explored in section

4.3.8.11. There were no further significant main or interaction effects (*F*s < 1.55, *p*s > .21).

### 4.3.9 tRNS Tolerability

TDCS was well tolerated overall (see table 4.6). Participants who received active ABM reported mild to moderate levels of tickling (*M* = 2.10, *SD* = .97), itching (*M* = 2.65, *SD* = 1.14), burning (*M* = 2.40, *SD* = .99), tiredness (*M* = 2.45, *SD* = 1.36) and loss of concentration (*M* = 2.25, *SD* = 1.12). Control ABM participants reported mild to moderate levels of tickling (*M* = 2.47, *SD* = 1.12), itching (*M* = 2.63, *SD* = 1.30), burning (*M* = 2.00, *SD* = 1.41), tiredness (*M* = 2.74, *SD* = 1.19), loss of concentration (*M* = 2.26, *SD* = 1.19). Independent t-tests compared the intensity scores for each ABM group. The effect of ABM group on neck pain approached significance with participants who received control ABM reporting a higher level (*M* =1.53, *SD* = .90) than those who received active ABM (*M* =1.10, *SD* = .31) *t*(37) = 1.99, *p* = .064.

Table 4.6:

*Mean (Std Dev) tDCS intensity scores for each ABM group*

| | Headache | Neck Pain | Aching Scalp | Tickling | Itching | Burning | Skin Irritation | Tiredness | Loss of Concentration | Mood Swings |
|---|---|---|---|---|---|---|---|---|---|---|
| Active ABM | 1.55 (.89) | 1.10 (.31) | 1.35 (.67) | 2.10 (.97) | 2.65 (1.14) | 2.40 (.99) | 1.80 (1.24) | 2.45 (1.36) | 2.25 (1.12) | 1.20 (.62) |
| Control ABM | 1.42 (.69) | 1.53 (.90) | 1.37 (.68) | 2.47 (1.12) | 2.63 (1.30) | 2.00 (1.41) | 1.42 (.69) | 2.74 (1.19) | 2.26 (1.19) | 1.11 (.32) |

### 4.3.10 Experimental Condition

The percentage of participants who guessed their ABM group correctly was 42.50%. A one-sample t-test revealed that this percentage did not significantly differ from chance, ($t$ = .95, $p$ = .35). Of the active ABM participants, 19.05% correctly guessed their ABM group correctly. This was significantly below chance level, $t(20) = 3.53$, $p$ = .002. Of the control ABM participants 68.42% correctly guessed their ABM group. This percentage did not significantly differ from chance, ($t$ = 1.68, $p$ = .11).

The percentage of participants who correctly reported that they had received tDCS was 77.5%. This was significantly above chance level, $t(39) = 4.11$, $p > .01$. A total of 35% of participants correctly guessed both their ABM and tDCS allocation correctly. This was significantly below chance level, $t(39) = 2.33$, $p$ =.025.

## 4.4 Discussion

Experiment 3 was designed to explore the efficacy of anodal tDCS of the left DLPFC for enhancing the effects of ABM. Based on findings from previous studies (Clarke et al., 2014; Heeren et al., 2015b) it was predicted that anodal tDCS with attend-neutral ABM would generate greater reductions in attentional bias towards threat and anxiety than anodal tDCS with control ABM. There was no reduction in threat bias irrespective of condition but there was a reduction in state anxiety at assessment 2 compared to assessment 1 across all participants. The finding of no reduction in threat bias was in opposition to findings from

previous studies in which tES has been used to modulate the effects of ABM training (Clarke et al., 2014; Heeren et al., 2015b). However, the findings were completely consistent with the results from experiments 1 and 2 which also did not find threat bias reduction but noted reduction in state anxiety following training. State anxiety reduction in the absence of reduction in attentional bias towards threat has been demonstrated across participants from all three experiments of study 1. This has occurred irrespective of training paradigm (active ABM, control ABM, no-training ABM) and tES (active tRNS, anodal tDCS, sham tES). As per experiments 1 and 2 of the present study, threat bias reduction was positively associated with threat bias at baseline with greater pre-existing threat bias predicting greater reduction in threat bias across assessments.

A second series of analyses of data from experiment 3 combined with experiment 1 allowed for comparison of effects across tES groups. These analyses also included pre-existing attention bias, trait anxiety and attentional control as covariates. Like the analyses from experiments 1 and 2 these revealed a reduction in state anxiety across participants irrespective of ABM or tES group. There was greater threat bias reduction for participants with greater pre-existing threat bias and greater neutral bias reduction for participants with greater pre-existing neutral bias irrespective of ABM or tES group.

### 4.4.1 Experimental Procedure

In the study by Clarke et al. (2014) participants who received anodal tDCS and attend-neutral ABM training had significant reductions in attentional bias

towards threat but those who received anodal tDCS in the attend threat group did not. In experiment 3 of the present study all participants received anodal tDCS. There was however, no indication of threat bias reductions in participants who received attend-neutral ABM. Heeren et al. (2015b) only delivered active ABM towards neutral stimuli (away from threatening stimuli). In their study participants who received anodal but not cathodal or sham tDCS of the left DLPFC did not demonstrate reductions in threat bias as assessed by reaction time to targets during attention bias assessment but had enhanced disengagement from threat as evidenced by eye-tracking. In the present experiment, eye-tracking data was not taken and it is therefore not possible to claim that results from the experiment did not replicate those reported by Heeren et al. (2015b). Failure to replicate the outcomes of Clarke et al. (2014) might be explained by methodological differences between their study and the present experiment. Clarke et al. (2014) delivered ABM training over one session whereas the present experiment consisted of 3 consecutive days of ABM training. The finding of threat bias reduction for tES with active ABM following one session but not after three sessions is unexpected in light of early meta-analyses of ABM studies which reported larger effect sizes for studies conducted over a number of days (Beard et al., 2012; Hakamata et al., 2010). It was still more surprising given empirical support for the modulation of cognitive training with tES over a number of days (Meinzer et al., 2014; Snowball et al., 2013). However, the finding was consistent with reports from recent meta-analyses of lower effects sizes in terms of symptom reduction with a greater number of training sessions (Cristea et al., 2015) or longer training as calculated by the number of sessions multiplied by length of sessions (Price et al., 2017). As stated by Cohen Kadosh (2012) little is known about the neural mechanisms underlying single-session

versus multi-session training with tES. It is possible that, when combined with tES, single-session ABM is more successful than multi-session ABM. It is also feasible that, had attention bias been assessed at the start and end of each day, there may have been threat bias reductions following ABM training on day 1, with superior reductions for active ABM training compared to control ABM. This may also have revealed greater modulation of active ABM with active tES. However, attention bias assessment was not administered at the end of days 1 and 2 as this may have negated training effects.

State anxiety, in contrast, was measured at the start and end of each experimental session. There was no evidence that active ABM with anodal tDCS produced greater reductions in state anxiety than control ABM with anodal tDCS. Neither the study by Clarke et al. (2014) nor that by Heeren et al. (2015b) included a measure of anxiety and it is therefore not be possible to make a comparison between these and the present study in terms of the impact on anxiety of single session ABM versus multiple session ABM with anodal tDCS.

### 4.4.2 Attention Bias Assessment

Attention bias was calculated by subtracting reaction time for angry faces from reaction time for neutral faces. When calculated in the same way, threat bias was also found not to be reduced across assessment in the study by Heeren et al. (2015b). However, eye tracking data revealed reduced gaze time for angry faces relative to neutral faces following ABM training towards neutral stimuli. Rather than providing a measure of attentional engagement (time taken to visually engage threatening faces relative to neutral faces), the eye tracking data was

used to calculate attentional disengagement (length of time between engaging a stimulus and removing visual attention from it; Heeren et al., 2015b). It is possible that if disengagement latency as opposed to engagement speed had been assessed and calculated as a measure of attentional bias in the present experiment, a reduction in attentional bias towards threat following ABM training may have been observed. It is also viable that eye-tracking or another measure with greater temporal specificity than behavioural reaction time data such as ERP data (e.g. Kappenman et al., 2014), may have revealed a reduction in threat bias as indicated by engagement speed.

### 4.4.3 TES Montage

Unlike in the present experiment and in Heeren et al. (2015b), in the study by Clarke et al. (2014) reaction time data did indicate that attention bias was modulated in the trained direction (towards neutral or towards threat). There were disparities between the studies in terms of tES montage which might have been influential in this finding. Each of the previous studies and experiment 3 administered anodal tDCS to the left DLPFC. The present experiment and that by Heeren and colleagues (for the anodal tDCS group) placed the anode above the left DLPFC (F3) and the cathode above the right, contralateral supra-orbital ridge. In the Clark et al., (2014) study however, the return electrode was positioned in an extra-cephalic position (near the base of the neck on the left-hand side). Researchers have previously emphasised the importance of return electrode positioning in determining current flow (e.g. Datta et al., 2009; Sadleir et al., 2010). Some advocate the use of extra-cephalic placement of the return electrode as a means of ensuring that any effects of tES can be attributed

specifically to the active electrode (Shin, Foerster & Nitche, 2015). When cephalic cathode placement is applied (in the case of anodal tDCS), it is difficult to rule out the possibility of changes in excitability beneath the cathode and cephalic placement may result in unintentional alterations of neural activity between this and the active electrode (Moliadze et al., 2010). Any modulations of cognitive training elicited by active tES might not be solely accorded to changes beneath the "stimulating" electrode. It has also been suggested that extra-cephalic placement of the return electrode might produce greater cortical modulation relative to cephalic placement as more of the current enters the brain rather than being shunted across the scalp (Bikson et al., 2010). The same authors predicted the directionality of current flow using computer modelling. With the anode above the left primary motor cortex and the cathode above the contralateral forehead there was significant electrical field beneath and between the electrodes but particularly in the right frontal lobe. With the anode over the left primary motor cortex and the cathode on the contralateral mastoid, the electrical field distribution was predominantly constrained to the left hemisphere and had a posterior trajectory (Bikson et al., 2010). Based on these predictions, placement of the return electrode on the left trapezius muscle in the Clarke et al. (2014) study may have confined tES effects to the left hemisphere. This pattern of stimulation might better target the neural mechanisms associated with reducing bias towards threat via ABM than one in which electrical field is distributed across the right frontal cortex. Grimshaw and Carmel (2014) posited that emotional processing is characterised by neural frontal lobe asymmetry. Informed by EEG data they concluded that left-lateralised control mechanisms are responsible for inhibiting negative stimuli whereas right-lateralised control inhibits positive stimuli (Grimshaw & Carmel,

2014). If this model is accurate then left-lateralised activation induced by Clarke et al's tES montage may have been more proficient at promoting the inhibitory processes which are central to ABM training. However, there is evidence from a study by D'Alfonso et al. (2000) which would oppose this view. The study reported that a rTMS induced virtual lesion to the left PFC resulted in attentional inhibition of angry faces whereas rTMS of the right PFC was associated with attention bias towards angry faces. More research in the domain of frontal hemispheric specificity is required before attempting to map neural activity changes induced by different tES protocols and montages onto behavioural change. Whilst techniques for computer modelling of tES effects are increasingly sophisticated (Bikson et al., 2010) these models are predictive. There is a need for more 'real-time' measurements of tES effects on neural activity using brain scanning techniques such as fMRI.

### 4.4.4 Analogous Findings

Whilst there is a chance that methodological issues explain discrepancies between findings from studies using tES to modulate ABM, it is also possible that Clarke et al. (2014) and Heeren et al. (2015b) are anomalies in a growing body of research showing no effect of ABM training on attention bias. A recent meta-analysis examining the impact of multisession ABM on attention bias and anxiety in high trait anxious individuals reported three main findings; 1) anxiety reduction consistently occurred without reduction in attention bias towards threat, 2) both active and control ABM often resulted in anxiety reduction, 3) participants often demonstrated no pre-training attentional bias towards threat (Mogg, Waters & Bradley, 2017). Outcomes from the present experiment

perfectly reflect these findings and it is therefore, perhaps, not necessary to rationalise them. The discussion above speculates as to why in the present experiment tES failed to enhance the effects of ABM focusing particularly on methodological differences in tES protocol. If, however, ABM is ineffective in reducing threat bias (possibly because participants had no pre-training bias; see discussion below) then a discussion regarding the enhancement of ABM via tES is redundant.

### 4.4.5 State Anxiety Increase

An unexpected finding from experiment 3 was an increase in state anxiety at assessment 3 compared to assessment 2 for active ABM with anodal tDCS but not control ABM with anodal tDCS. There was no increase in threat bias for the active ABM group at assessment 3 therefore there was no indication that the increase was related to increased engagement to threatening stimuli. Analysis of the data revealed that the increase was driven by one outlier. The participant in question was not outlying in terms of their anxiety score at assessment 3 but in terms of change in state anxiety score from assessment 2 to assessment 3. There was a large increase in their state anxiety score. When the participant's state anxiety scores were omitted from analysis the increase in state anxiety across participants in the anodal tDCS group was no longer present. This finding highlights the need for a discussion regarding the removal of outliers in self-report data. The large increase in state anxiety score may have reflected personal situational factors for the participant in question. Alternatively, it may have been indicative of that participant's experience of the study in which case it may be important for their data to remain in the analysis. In the present

discussion, the most appropriate solution was deemed the reporting of results with and without the outlying data. This illustrates the extent to which the inclusion or omission of one participant's data can change a result and may be relevant to discussions regarding discrepancies in findings from previous ABM studies which have tended to focus on methodological issues (e.g. Hakamata et al., 2010).

### 4.4.6 Pre-existing Attention Bias

As mentioned, in experiments 1 and 2 and as previously reported in an ABM study (O'Toole et al., 2012) participants with greater pre-existing bias towards threat had greater reduction in threat bias following attentional training. This was irrespective of ABM or tES group. Across the experiments of the present study, participants who began the experiment with a bias towards neutral stimuli had reduced neutral bias following attentional training. This suggests that baseline attention bias level is important in the outcome of ABM training. Interestingly, in the aforementioned study by Clarke et al. (2014) participants who received anodal tDCS and attend neutral ABM had a slight pre-existing threat bias and participants allocated to anodal tDCS with attend threat ABM had a neutral bias at baseline. Of those who received sham tDCS, the mean baseline attention bias for participants who performed attend-threat ABM was towards threat stimuli and for those who undertook attend-neutral ABM was towards neutral stimuli. The outcome reported was greater increase in bias in the trained direction for participants who received anodal tDCS relative to participants who received sham tDCS (Clarke et al., 2014). However, it is possible that the post-training

inter-group differences reported were a factor of group differences related to pre-existing attention bias.

### 4.4.7 Attentional Control

There is converging evidence that attentional control capacity has a role in determining the efficacy of ABM training. Previous studies have demonstrated the enhancement of attentional control capacity following ABM training compared to before ABM training (Chen et al., 2015; Heeren et al., 2016). These findings supported the suggestion that the mechanism via which both active ABM and control ABM generated reductions in threat bias (Chen et al., 2015) and stressor related anxiety (Heeren et al., 2016) following training, was the enhancement of attentional control capacity. Furthermore, attentional control level has been seen to predict the magnitude of attention bias change following ABM training relative to pre-training (Basanovic et al., 2017). It is proposed that higher level attentional control facilitates the process of attention bias modification by enhancing goal-directed deployment of attention (Basanovic et al., 2017). This might expedite or increase learning of the 'rules' implicitly imparted by contingency-based ABM training. In the present experiment there was no evidence that pre-existing attentional control level had an impact on ABM-induced attention bias. When pre-existing attentional control was included as a covariate in the analysis on state anxiety data, the main effect of reduction in state anxiety following training relative to before training disappeared. This suggests that pre-existing attentional control influences state anxiety and it's modulation. However, given the lack of interaction effects between pre-existing attentional control and change in attention bias, if pre-existing attentional

control did indeed mediate state anxiety reduction, this was not via the mechanism proposed by Basanovic et al. (2017).

### 4.4.8 Limitations

There were aspects of the experimental sample which were stronger for experiments 1 and 2 than for experiment 3. In the first two experiments of the present study, 21 participants per experimental group were recruited and attended follow-up. For the present experiment, of the 21 participants recruited and allocated to the tDCS with control ABM group, attention bias data from 2 participants were omitted from analysis due to low accuracy. Three of the remaining 19 participants did not attend their follow-up appointment and, consequently follow-up data from only 16 participants was analysed. Another recruitment issue which may have been instrumental in the results was that only 3 of the 42 participants recruited were male. Male representation was low throughout the study. In both experiments 1 and 2 approximately 25% of all participants were male. For the present experiment only 7% of participants were male. Of primary concern therefore is the fact that the results cannot be generalised. Additionally, comparison of results with those from experiments 1 and 2 is compromised. Furthermore, gender differences have been reported for both attention bias and anxiety. Rates of depression and anxiety disorders are known to be higher in women compared to men (McLean, Asnaani, Litza, & Hofmann, 2011; Van de Velde, Bracke, & Levecque, 2010). Women are twice as likely as men to develop GAD (Kinney, Boffa & Amir, 2017). Pintzinger et al. (2016) demonstrated that males had a greater tendency to engage positive stimuli relative to negative stimuli during an emotional dot probe task but this

pattern was not present in women. They also reported that stronger effortful control (as assessed using the automatic thoughts questionnaire) was associated with greater avoidance of negative stimuli for males only (Pintzinger et al., 2016). An ERP study showed faster engagement to threatening stimuli than pleasant stimuli for males as indicated by elevated P100 amplitude for threat (Sass et al., 2010). Women had prolonged P300 latency suggesting that they were prone to more elaborate processing of threat related stimuli (Sass et al., 2010). One study which compared attentional bias assessment using an emotional dot-probe task reported that faster engagement to threat occurred in women and was positively correlated with anxiety (Tran et al., 2013). Men, however, demonstrated a difficulty disengaging from threat and this was unrelated to anxiety level (Tran et al., 2013). It is also possible that gender might influence the impact of ABM on attentional bias and anxiety. There is limited but mixed evidence in this regard. Liu et al. (2017) reported that gender was a moderator in the effectiveness of cognitive bias modification (including ABM) in social anxiety with females benefitting more from participation. Conversely, a meta-analysis of ABM studies did not find gender to be a moderator of ABM success (Hakamata et al., 2012). These mixed but pertinent findings suggest that measures of both anxiety and attentional bias might be influenced by the gender skew in the current experiment.

## 4.5 Summary

Experiment 3 was designed to extend findings from experiment 1 of the present study. In experiment 1, active tRNS or sham tES was applied above the bilateral IFG during ABM training. There was no difference between ABM groups in terms

of attention bias and anxiety level change and there was no evidence of an enhancement of ABM effects with active tRNS. However, two studies produced since the commencement of experiment 1 demonstrated that that the administration of anodal tDCS during active ABM training enhanced the extent to which attention was trained in the intended direction (Clarke et al., 2014; Heeren et al., 2015b). Both of these studies used anodal tDCS above the left DLPFC during ABM training. Experiment 3 sought to explore whether anodal tDCS of the left DLPFC could modulate ABM training where active tRNS of the bilateral IFG did not. Analysis of data from experiment 3 alone revealed no change in attention bias following training but did show a reduction in state anxiety for all participants. As per experiment 1, these results suggested that active ABM was not more successful than control ABM in reducing attentional bias towards threat and anxiety. A secondary analysis conducted on combined data from experiments 1 and 3 also suggested no impact of ABM group on attention bias and state anxiety change. The results suggested that sham tES but not active tRNS or anodal tDCS resulted in attention bias reduction following ABM training (irrespective of ABM group). Potential mechanisms of this finding are discussed in chapter 5.

# Chapter 5

**Combined Analysis of Data from Experiments 1, 2 and 3**

## 5.1 Introduction

This chapter combines in analysis all data from experiments 1, 2 and 3. The analysis compares the effect of 3 forms of ABM training (active ABM, control ABM and no-training ABM) on attention bias and state anxiety. Active ABM and control ABM were delivered concurrently with active tRNS, anodal tDCS or sham tES. No-training ABM was delivered with either active tRNS or sham tES. A limitation of the following analysis is the omission of an anodal tDCS group with no-training ABM. There is less data related to anodal tDCS than for active or sham tRNS and therefore tES group sizes are not comparable. However, inclusion of this condition was not within the scope of the present thesis.

## 5.2 Method

### 5.2.1 Design

The study was a 3 x 3 x 3 mixed design. The between participants factors were tES (active tRNS, anodal tDCS and sham TES) and ABM (active ABM, control ABM, no-training ABM). The within subjects factor was assessment [before training on day 1(Assessment 1), after training on day 3 (Assessment 2), at 30 day follow up (Assessment 3)].

Two forms of active tES (active tRNS, anodal tDCS) were applied across experiments. However, only one sham condition was included. In the sham group, hfTRNS current was ramped up for 20 seconds and then stopped. As the sham condition involved only a very brief application of active tRNS, it will be treated as a sham (comparison) group for both the active tRNS group and the anodal tDCS group throughout the analysis. This approach was also taken by Fertonani et al. (2011).

### 5.2.2 Participants

Participants were 172 students from the University of Roehampton (137 female), mean age = 20.75 years, SD = 4.17, range = 18 to 42). All participants were right-handed and had normal or corrected to normal vision.

The recruitment process was as outlined in the previous chapters.

Table 5.1 gives the number of participants across experimental groups.

Table 5.1:

*The number of study participants in each experimental group*

| ABM group | tES Group | Number of Participants |
|---|---|---|
| Active ABM | Active tRNS | 21 |
| Active ABM | Anodal tDCS | 21 |
| Active ABM | Sham tES | 21 |
| Control ABM | Active tRNS | 20 |
| Control ABM | Anodal tDCS | 19 |
| Control ABM | Sham tES | 21 |
| No-training ABM | Active tRNS | 21 |
| No-training ABM | Sham tES | 21 |

### 5.2.3 Ethics

The study was approved by the University of Roehampton ethics committee (approval code PSYC 14/ 116; see appendix 1). Written informed consent was provided by all participants before participation. Participants were compensated for their participation with course credits. Participants who were not eligible for course credits received a £20 payment.

### 5.2.4 Materials, Stimuli and Procedure

The present chapter will present an analysis of all the data collected in experiments 1, 2 and 3. The materials and stimuli used and procedure followed were as described in the previous chapters.

### 5.2.5 Data Preparation

Data from 165 participants were analysed. Response times below 200ms were removed prior to analysis. To remove the effect of outlying data on analysis, for each participant reaction times which were more than 2.5 standard deviations from that participant's mean reaction time were excluded (Brown et al., 2014). Previous chapters provide the percentage of data retained for each experiment.

### 5.2.6 Data Analyses

As per experiments 1, 2 and 3, attention bias and state anxiety data were subjected to mixed ANOVAs with ABM (active ABM, control ABM, no-training ABM) and tES (active tRNS, sham tES, anodal tDCS) as between participants factors and assessment as the within subjects factor. These ANOVAs were performed on data from all participants. The main ANOVAs were repeated with pre-existing attention bias, pre-existing trait anxiety and pre-existing attentional control as covariates.

### 5.2.7 Baseline Characteristics

#### 5.2.7.1 Baseline Scores for Main Variables of Interest

For baseline attention bias, state anxiety, trait anxiety and attentional control levels across all 3 experiments see table 4.1 (chapter 4).

### 5.2.7.2 State and Trait Anxiety Across Experimental Groups by Gender

Table 5.2 shows baseline mean and standard deviation state anxiety scores with participants as a factor of experimental group and sex.

Table 5.2:

*Baseline mean (standard deviation) state and trait anxiety scores across experimental groups for females and males*

| | | Active ABM | | | Control ABM | | | No-training ABM | |
|---|---|---|---|---|---|---|---|---|---|
| | | Active tRNS | Anodal tDCS | Sham tES | Active tRNS | Anodal tDCS | Sham tES | Active tRNS | Sham tES |
| Females (N) | | 15 | 19 | 16 | 14 | 17 | 17 | 14 | 18 |
| | State Anxiety | 33.40 (10.51) | 33.58 (8.16) | 32.81 (8.46) | 31.00 (9.85) | 34.06 (10.33) | 35.35 (14.31) | 34.57 (9.87) | 36.67 (11.54) |
| | Trait Anxiety | 40.53 (10.14) | 48.33 (14.83) | 42.94 (14.15) | 40.14 (10.98) | 41.94 (11.00) | 45.24 (12.13) | 42.57 (11.19) | 49.67 (12.48) |
| Males (N) | | 6 | 2 | 5 | 7 | 1 | 4 | 7 | 3 |
| | State Anxiety | 33.33 (13.02) | 30.00 (5.66) | 37.40 (6.66) | 33.14 (8.67) | 41.00 | 26.75 (3.86) | 31.43 (11.00) | 28.00 (5.69) |
| | Trait Anxiety | 36.83 (8.73) | 42.50 (6.36) | 43.60 (9.10) | 40.14 (17.33) | 74.00 | 39.75 (9.54) | 38.57 (10.26) | 46.33 (10.21) |

Note: There is no standard deviation for males who received control ABM with anodal tDCS due to there being only one male in this group.

State Anxiety

There was no significant difference in baseline state anxiety between experimental groups ($F$ = .34, $p$ = .94).

Trait Anxiety

A one-way ANOVA revealed that there was no difference in trait anxiety scores between experimental groups at baseline ($F$ = 1.41, $p$ = .21).

### 5.2.7.3 Correlations Between State Anxiety Scores

Data from each administration of the state anxiety scale of the STAI (i.e. start of day 1, end of day 1, start of day 2, end of day 2, start of day 3, end of day 3, start of day 30, end of day 30) were subject to a Pearson Product Moment Correlation analysis. All correlations were significant (all $r$'s > .52, all $p$s < .001). The normative test-retest reliability r values reported by Spielberger (1983) for college students, with a test-retest interval of 20 days were .54 for males and .27 for females. Our results therefore suggest strong test-retest reliability and consistency within the state anxiety data.

### 5.2.7.4 Correlations Between State Anxiety and Trait Anxiety

Baseline trait anxiety score was significantly correlated with state anxiety score at assessments 1, 2 and 3 ($r$s > .54, $p$s < .001; see table 5.3).

Table 5.3:

*Bivariate correlations between baseline trait anxiety scale (TAS) and state anxiety scale (SAS) scores at assessments 1, 2 and 3*

| | SAS Assessment 1 | SAS Assessment 2 | SAS Assessment 3 |
|---|---|---|---|
| Baseline TAS Score | **.556**** | **.545**** | **.537**** |

** < .001

### 5.2.7.5 Correlations Between Self-Report Measures at Baseline

Baseline scores from questionnaires assessing trait characteristics were subject to a Pearson Product Moment correlational analysis. Table 5.4 shows the correlation between baseline scores on trait self-report measures.

Table 5.4:

*Bivariate correlations for trait anxiety scale (TAS), attentional control scale (ACS), Centre for Epidemiological Studies depression questionnaire (CES-D) and fear of negative evaluation scale (FNE) scores at baseline.*

| | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| 1. Trait Anxiety | 1.00 | | | |
| 2. Attentional Control | **-.568**** | 1.00 | | |
| 3. Depression | **.604**** | **-.413**** | 1.00 | . |
| 4. Fear Negative Evaluation | **.716**** | **-.408**** | **.395**** | 1.00 |

** p < 0.001

Baseline scores across all questionnaires were significantly correlated (all *r*s > .41, *p*s < .001) suggesting that participants reported consistently across measures.

## 5.3 Results

### 5.3.1 Analyses of Variance Across all Participants

#### 5.3.1.1 Attention Bias (All Participants)

A 3 x 3 x 3 mixed ANOVA was conducted on the attention bias data with between subjects factors of ABM (active ABM, control ABM, no-training ABM) and tES (active tRNS, anodal tDCS and sham tES) and a within subjects factor of assessment (assessment 1, assessment 2, assessment 3). There was a significant assessment x tES interaction, $F(3.84,297.35) = 3.41$, $p = .011$, ($\eta p^2 = .042$; *observed power* = .84; Greenhouse Geisser corrected). For each tES group a repeated measures ANOVA was conducted with assessment (assessment 1, assessment 2, assessment 3) as the within participants factor. For the sham tES group there was a significant main effect of assessment, $F(2,124) = 4.25$, $p = .016$, ($\eta p^2 = .064$; *observed power* = .74). Paired samples t-tests examined change in attention bias across assessments. All results were Bonferroni corrected for multiple comparisons (significant if 3*p < .05). Participants in the sham tES group were significantly more biased towards neutral faces at assessment 2 ($M = -6.01$, $SD = 16.02$) compared to assessment 1($M = .96$, $SD = 13.28$), $t(62) = 2.91$, $p = .015$. There was no further change in attention bias across assessments for participants who had received sham tES ($ts < 1.76$, $ps > .08$). The effect of assessment was not significant for participants who had received active tRNS or anodal tDCS ($Fs < 2.58$, $ps > .08$).

There were no further significant main effects or interactions (*F*s < .88, *p*s > .51).

Figure 5.1 shows mean attentional bias across assessments for each experimental group and for all participants. Positive values represent threat bias and negative values represent neutral bias.

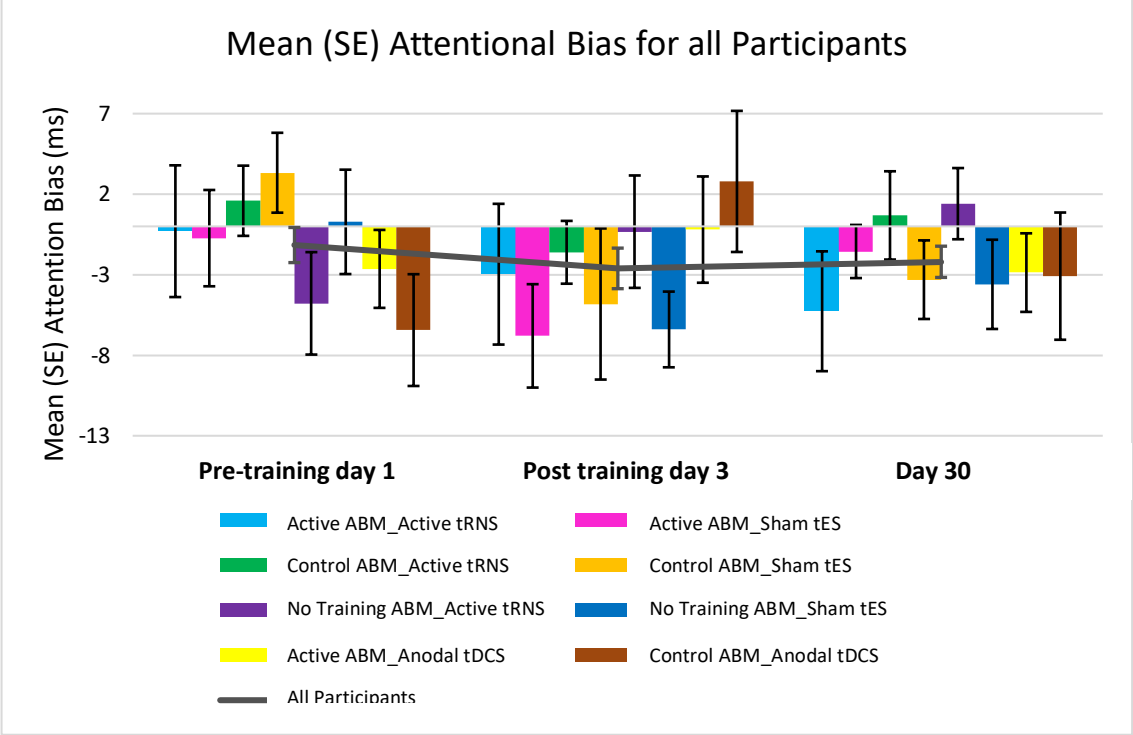


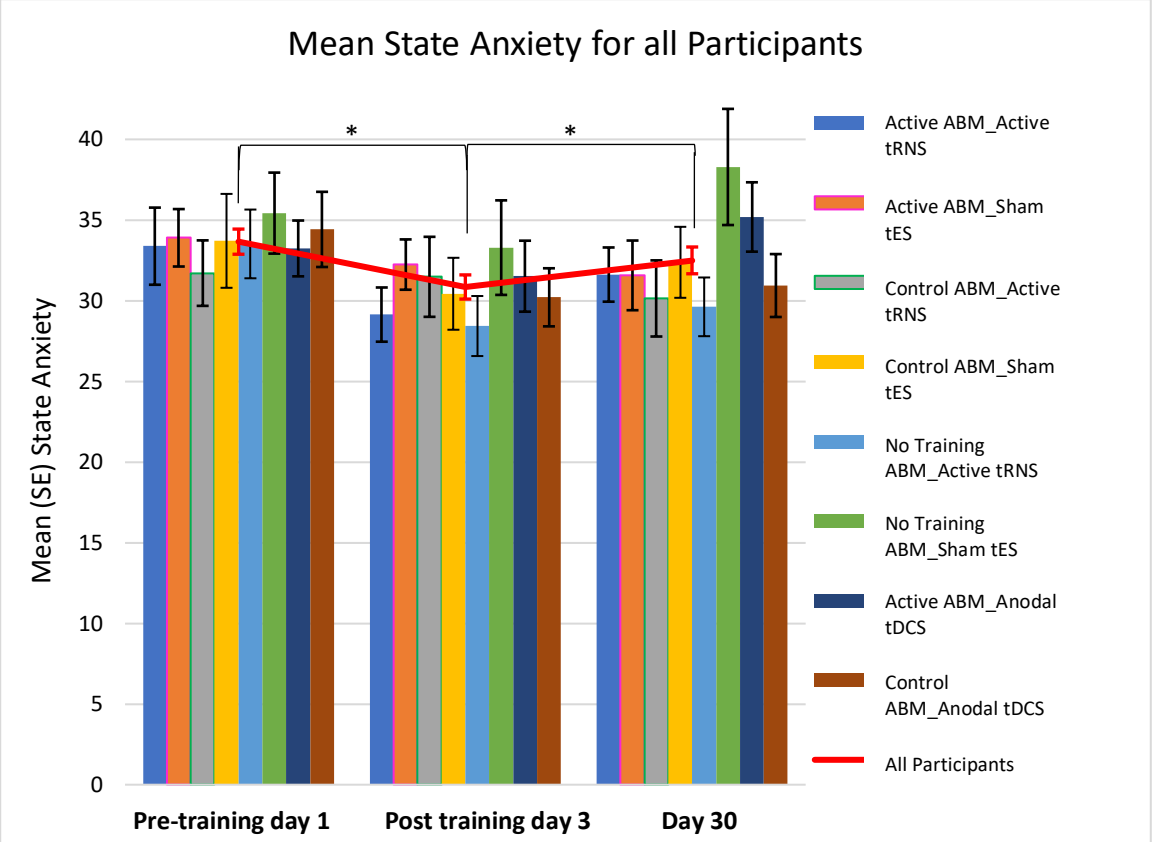

*Figure 5.1.* Mean (SE) attentional bias across assessments for each experimental group and for all participants.

#### 5.3.1.2 State Anxiety (All Participants)

Replicating the threat bias ANOVA above, a 3 x 3 x 3 mixed ANOVA was conducted on the state anxiety data with between subjects factors of ABM (active ABM, control ABM, no-training ABM) and tES (active tRNS, anodal tDCS and sham tES) and a within subjects factor of assessment (assessment 1,

assessment 2, assessment 3). The main effect of assessment was significant, $F(1.85,290.88) = 8.93$, $p < .001$, ($\eta p^2 = .054$; *observed power* = .96; Greenhouse Geisser corrected) suggesting a change in state anxiety across assessments. Paired samples t-tests examined change in state anxiety across assessments. All results were Bonferroni corrected for multiple comparisons (significant if 3*p < .05). At assessment 1, participants reported greater state anxiety ($M = 33.66$, $SD = 10.11$) compared to assessment 2 ($M = 30.85$, $SD = 9.68$), $t(165) = 4.62$, $p < .01$. State anxiety was significantly higher at assessment 3 ($M = 32.50$, $SD = 10.11$) compared to assessment 2 ($M = 30.85$, $SD = 9.68$), $t(164) = 2.44$, $p = .048$. The change in state anxiety between assessments 1 and 3 was not significant ($t = 1.56$, $p$s =.36). There were no further main or interactions effects ($F$s < 1.91, $p$s > .09).

Figure 5.2 shows state anxiety across assessments by experimental group and for all study 1 participants.




*$p < .05$*

*Figure* 5.2. Mean (SE) state anxiety across assessments for each experimental group and for all participants

### 5.3.1.3 State Anxiety (All Participants) From Start and End of Each Experimental Day

State anxiety measures were taken for each day of bias modification training before and after the training and on day 30 at the start and end of the session (see figure 5.3).

A 3 x 3 x 2 x 4 mixed ANOVA was conducted on the state anxiety data with the between subjects factors of ABM (Active ABM, control ABM, no-training ABM) and tES (active tRNS, anodal tDCS, sham tES) and 2 within subjects factors of time (start of session, end of session) and day (day 1, day 2, day 3, day 30). This

revealed a main effect of day, $F(2.42,379.89) = 4.89$, $p = .005$, ($\eta p^2 = .03$; *observed power* = .86; Greenhouse Geisser Corrected). Paired samples t-tests examined change in state anxiety across days. Results were Bonferroni corrected for multiple comparisons (significant if 6*p < .05). State anxiety on day 3 ($M = 31.14$, $SD = 9.37$) was significantly reduced compared to state anxiety on day 1 ($M = 32.40$, $SD = 8.56$), $t(165) = 2.78$, $p = .036$. There were no further significant changes in state anxiety across days ($ts < 2.44$, $ps > .10$). There was also a significant main effect of time, $F(1,157) = 14.62$, $p < .001$, ($\eta p^2 = .09$; *observed power* = .97). State anxiety was reduced at the end of session ($M = 31.36$, $SD = 8.44$) compared to the start of session ($M = 32.52$, $SD = 8.56$), $t(165) = 3.94$, $p < .001$. There was a significant day x time interaction, $F(2.70,242.22) = 4.63$, $p = .005$, ($\eta p^2 = .03$; *observed power* = .87). For each day (day 1, day 2, day 3, day 30) the effect of time was examined using paired samples t-tests. Results were Bonferroni corrected for multiple comparisons (significant if 4*p < .05). On day 1 state anxiety was significantly reduced at the end of session ($M = 31.14$, $SD = 8.51$) compared to at the start of session ($M = 33.66$, $SD = 10.11$), $t(165) = 4.34$, $p < .001$. On day 30 state anxiety was marginally significantly reduced at the end of session ($M = 32.50$, $SD = 10.67$) compared to the start of session ($M = 33.31$, $SD = 10.80$), $t(164) = 2.51$, $p < .052$. The effect of time was not significant for any further day ($ts < 1.38$, $ps > .60$). Paired samples t-tests examined change in state anxiety across days for start of session state anxiety and for end of session state anxiety. Results were Bonferroni corrected for multiple comparisons (significant if 6*p < .05). State anxiety at the start of day 2 ($M = 31.77$, $SD = 9.70$) was significantly reduced compared to at the start of day 1 ($M = 33.66$, $SD = 10.11$), $t(165) = 3.19$, $p < .012$. State anxiety at the start of day 3 ($M = 31.43$, $SD = 9.83$) was

significantly reduced compared to at the start of day 1 ($M$ = 33.66, $SD$ = 10.11), $t(165) = 3.56$, $p < .001$. No further change in state anxiety across days for start of day data was significant ($ts < 2.54$, $ps > .072$). For end of session data, there was no significant change in state anxiety across days ($ts < 2.44$, $ps > .10$).

There were no further significant main effects or interactions ($Fs < 1.45$, $ps > .20$).

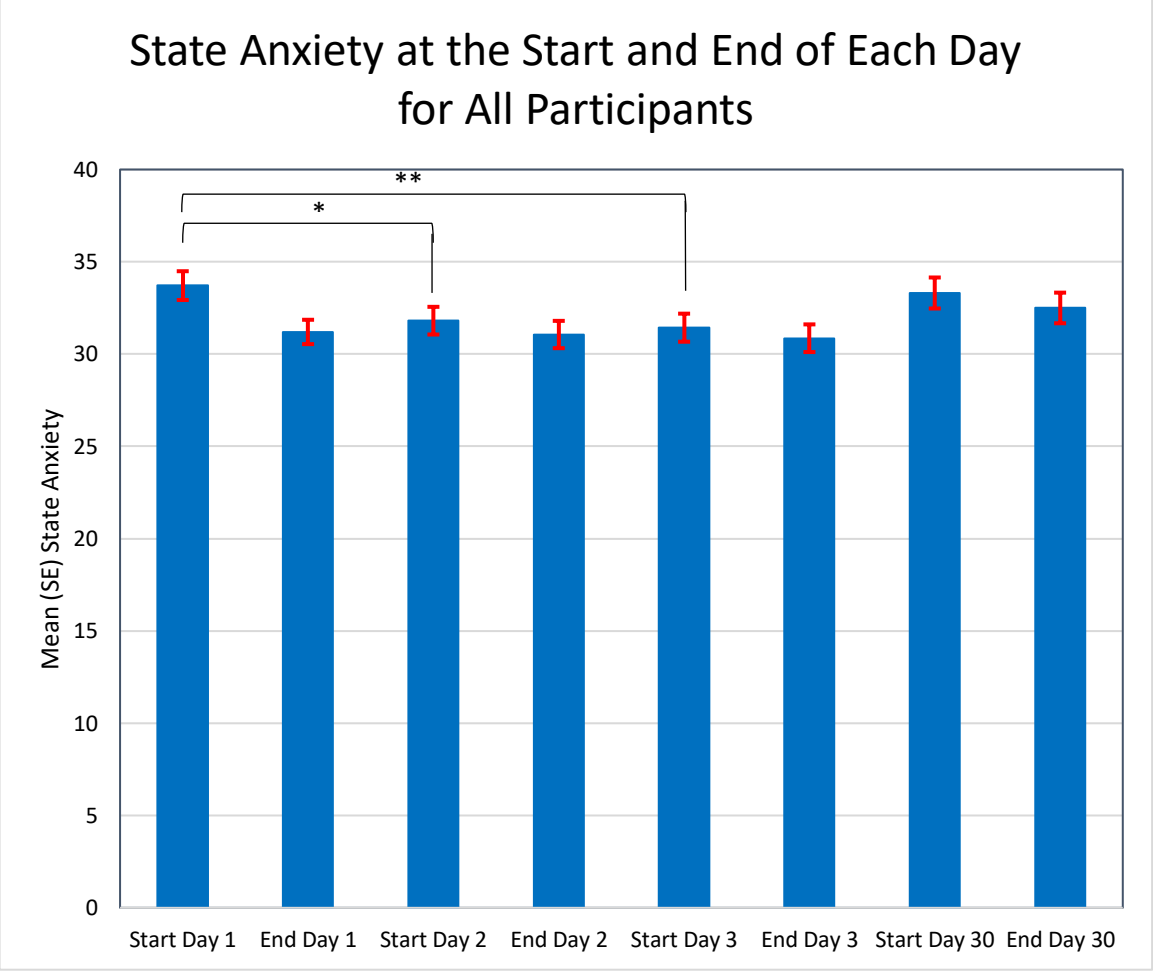



*Figure 5.3*. Mean (SE) state anxiety scores at the start and end of each experimental day for all participants

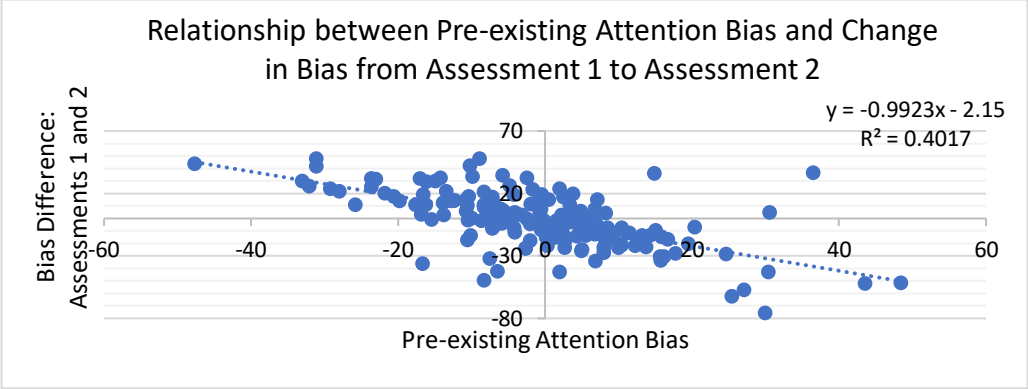
### 5.3.2 Analyses of Covariance with Pre-existing Attention Bias as a Covariate

#### 5.3.2.1 Attention Bias (Pre-existing Attention Bias as Covariate)

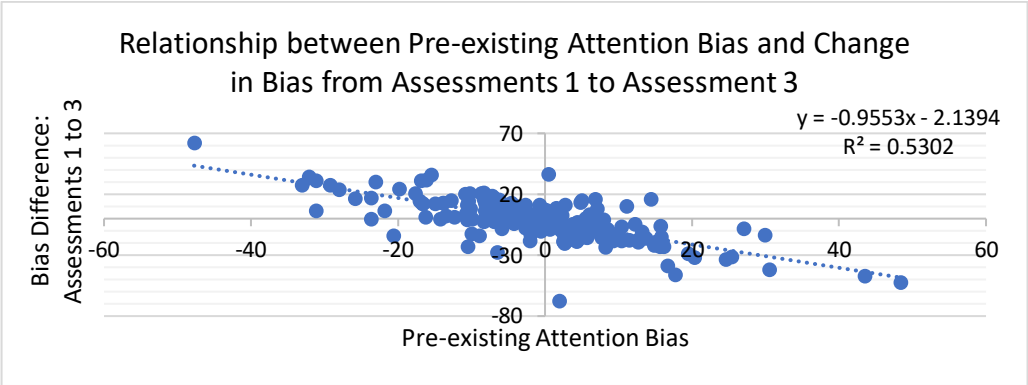
A 3 x 3 x 3 mixed ANCOVA was conducted on the attention bias data with between subjects factors of ABM (active ABM, control ABM, no-training ABM) and tES (active tRNS, anodal tDCS and sham tES), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and pre-existing attention bias as a covariate. There was a significant assessment x pre-existing attention bias interaction, $F(1.54,237.79) = 67.11$, $p < .001$, ($\eta p^2 = .30$; *observed power* = 1.00; Greenhouse Geisser corrected). In order to investigate the relationship between pre-existing attention bias and change in attention bias across assessments, a Pearson Product Moment correlational analysis was conducted with pre-existing attention bias, change in attention bias from assessment 1 to assessment 2, change in attention bias from assessment 1 to assessment 3 and change in attention bias from assessment 2 to assessment 3 as the variables. Change in attention bias was calculated by subtracting attention bias score at the earlier assessment from attention bias score at the later assessment e.g. attention bias at assessment 2 – attention bias at assessment 1. A positive score represented an increase in attention bias therefore and a negative score represented a reduction in attention bias. There was a significant moderate, negative correlation between pre-existing attention bias and change in attention bias from assessment 1 to assessment 2, $r(166) = -.39$, $p < .001$ and between pre-existing attention bias and change in attention bias from assessment 1 to assessment 3, $r(163) = -.53$, $p < .001$. Pre-existing attention

bias was not significantly correlated with change in attention bias between assessments 2 and 3 ($r$ = .024, $p$ = .76). Figure 5.4 shows the relationship between pre-existing attention bias and change in attention bias across assessments. This suggests that higher pre-existing attention bias towards threat was associated with greater reduction in threat bias across assessments.

a)




b)




c)

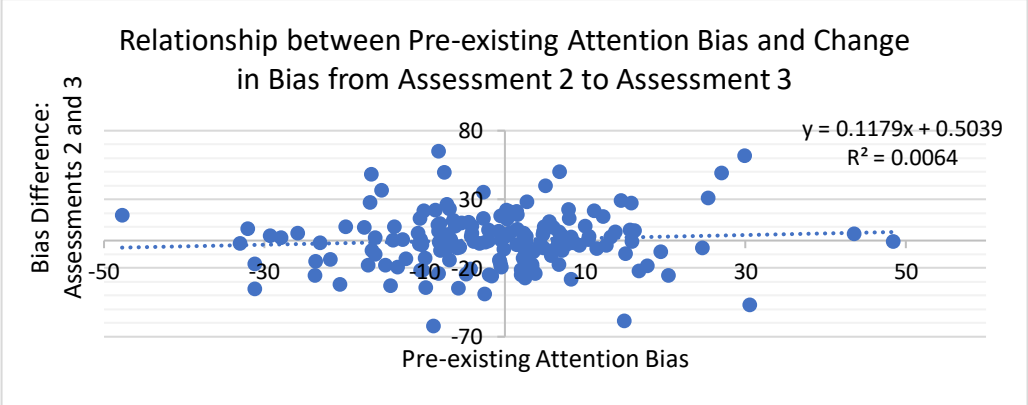



*Figure 5.4*. The relationship between pre-existing attention bias and a) change in attention bias between assessments 1 and 2, b) change in attention bias between assessments 1 and 3 and c) change in attention bias between assessments 2 and 3 across study 1. For pre-existing attention bias, positive scores indicate attention bias towards threat and negative scores indicate attention bias towards neutral. For difference scores, positive values represent increase in threat bias and negative scores represent increase in neutral bias (reduction in threat bias).

The main effect of pre-existing attention bias was significant, $F(1,154) = 70.96$, $p < .001$, ($\eta p^2 = .32$; *observed power* = 1.00). There was a significant, moderate to strong, positive correlation between pre-existing attention bias and mean attention bias, $r(166) = .57$, $p < .001$.

No further main or interaction effects were significant ($F$s < 2.26, $p$s > .11).

#### 5.3.2.2 State Anxiety (Pre-existing Attention Bias as Covariate)

With state anxiety as the dependent variable, a 3 x 3 x 3 mixed ANCOVA was conducted with between subjects factors of ABM (active ABM, control ABM, no-training ABM) and tES (active tRNS, anodal tDCS and sham tES), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and a covariate of pre-existing attention bias. The main effect of assessment was significant, $F(1.84,295.46) = 8.75$, $p < .001$, ($\eta p^2 = .053$; *observed power* = .96; Greenhouse Geisser corrected). Post hoc analysis are described in section 5.3.1.2.

The interaction between assessment, ABM and tES approached significance, $F(5.53,295.46) = 2.16$, $p = .052$, ($\eta p^2 = .04$; *observed power* = .74; Greenhouse Geisser corrected). For state anxiety data at each assessment a 3 x 3 univariate ANOVA was conducted with the between participants factors of ABM (Active ABM, control ABM, no-training ABM) and tES (active tRNS, anodal tDCS, sham tES). Analysis of assessment 1 state anxiety data revealed no significant main or interaction effects ($F$s < .42, $p$s > .66). This was also the case for analysis of assessment 2 state anxiety data ($F$s < .88, $p$s > .42) and assessment 3 state anxiety data ($F$s < 2.18, $p$s > .12).

For each ABM group, a repeated measures ANOVA was carried out with the between participants factor of tES (active tRNS, anodal tDCS, sham tES) and the within participants factor of assessment (assessment 1, assessment 2 and assessment 3). For the active ABM group, there was a significant main effect of assessment, $F(2,120) = 4.03$, $p = .02$, ($\eta p^2 = .06$; *observed power* = .71). Paired samples t-tests examined change in state anxiety across assessments. All results were Bonferroni corrected for multiple comparisons (significant if $3*p < .05$). State anxiety at assessment 2 ($M = 30.97$. $SD = 8.37$) was significantly reduced compared to state anxiety at assessment 1($M = 33.51$. $SD = 8.96$), $t(62) = 3.01$, $p = .012$. No further change in state anxiety across assessments was significant for the active ABM group ($t$s < 2.09, $p$s < .12). There were no further significant main or interaction effects ($F$s < 1.64, $p$s > .17).

For the no-training ABM group, there was a significant main effect of assessment, $F(2,80) = 4.12$, $p = .02$, ($\eta p^2 = .09$; *observed power* = .71). Paired samples t-tests explored change in state anxiety across assessments. All results were Bonferroni corrected for multiple comparisons (significant if $3*p < .05$). State anxiety at assessment 2 ($M = 30.86$. $SD = 11.38$) was significantly reduced compared to state anxiety at assessment 1($M = 34.48$. $SD = 10.59$), $t(41) = 2.63$, $p = .036$. The increase in state anxiety at assessment 3 ($M = 33.95$. $SD = 13.64$) relative to assessment 2 ($M = 30.86$. $SD = 11.38$) approached significance, $t(41) = 2.48$, $p = .054$. State anxiety at assessment 3 ($M = 33.95$. $SD = 13.64$) did not differ significant from state anxiety at assessment 1 ($M = 34.48$. $SD = 10.59$; $t = .34$, $p = 2.21$. For the no-training ABM group, the assessment x tES interaction approached significance, $F(2,80) = 3.10$, $p = .051$, ($\eta p^2 = .07$; *observed power* = .58). For each tES group the main effect of assessment was assessed using

paired samples t-tests. All results were Bonferroni corrected for multiple comparisons (significant if 3*p < .05). For participants who received no-training ABM with active tRNS, state anxiety at assessment 2 (*M* = 33.95. *SD* = 13.64) was marginally significantly reduced compared to state anxiety at assessment 1 (*M* = 33.95. *SD* = 13.64), $t(20) = 2.53$, $p = .06$. There were no further significant changes across assessments for the no-training ABM with active tRNS group (*t*s < 1.92, *p*s > .21). Following application of the Bonferroni correction no change in state anxiety across assessments for the no-training ABM/sham tES group was significant (*t*s < 2.29, *p*s > .099).

State anxiety data from each assessment for participants who received no-training ABM were subject to an independent t-test to examine difference in state anxiety between tES groups (tRNS, sham tES). Results were Bonferroni corrected for multiple comparisons (significant if 3*p < .05). tES groups did not differ significantly in terms of state anxiety at any assessment (*t*s < 2.15. *p*s > .12).

For the no-training group the main effect of tES was not significant ($F = 2.50$, $p = .12$).

No significant main or interaction effects were revealed from the analysis of data from the control ABM group (*F*s < 2.42, *p*s > .09).

For each tES group, a repeated measures ANOVA was carried out with the between participants factor of ABM (active ABM, control ABM, no-training ABM) and the within participants factor of assessment (assessment 1, assessment 2

and assessment 3). For the tRNS group there was a significant main effect of assessment, $F(2,120) = 4.87$, $p = .009$, ($\eta p^2 = .08$; *observed power* = .79). This was assessed using paired samples t-tests. All results were Bonferroni corrected for multiple comparisons (significant if 3*p < .05). State anxiety at assessment 2 (*M* = 29.68. *SD* = 9.26) was marginally significantly reduced compared to state anxiety at assessment 1 (*M* = 32.87. *SD* = 9.90), $t(62) = 3.06$, $p = .009$. For the active tRNS group, there were no further significant changes in state anxiety across assessments (*t*s < 2.09, *p*s > .12). For the active tRNS group there were no further significant main or interaction effects (*F*s < 1.19, *p*s > .32).

For the anodal tDCS group, the main effect of assessment approached significance, $F(2,74) = 3.10$, $p = .051$, ($\eta p^2 = .08$; *observed power* = .58). State anxiety at assessment 2 (*M* = 30.95. *SD* = 8.90) was marginally significantly reduced compared to state anxiety at assessment 1 (*M* = 34.00, *SD* = 8.94), $t(40) = 2.63$, $p = .036$. For the anodal tDCS group, there were no further significant changes in state anxiety across assessments (*t*s < 1.88, *p*s > .20). For the anodal tDCS group, the assessment x ABM interaction was marginally significant, $F(2,74) = 2.91$, $p = .061$, ($\eta p^2 = .07$; *observed power* = .55). State anxiety data for each assessment was subject to a one-way ANOVA to examine the effect of ABM. There was no significant effect of ABM on state anxiety at any assessment for participants who received anodal tDCS (*F*s < 2.08, *p*s > .16). For each ABM condition a repeated measures ANOVA examined the effect of assessment on state anxiety. For participants who received anodal tDCS and active ABM there was a marginally significant effect of assessment, $F(1.59,31.74) = 3.14$, $p = .068$, ($\eta p^2 = .14$; *observed power* = .50). Paired samples t-tests assessed change in state anxiety across assessments for

participants in the anodal tDCS/active ABM group. All results were Bonferroni corrected for multiple comparisons (significant if 3*p < .05). State anxiety at assessment 3 (*M* = 35.19, *SD* = 9.86) was significantly higher than state anxiety at assessment 2 (*M* = 31.52, *SD* = 10.09), *t*(20) = 3.24, *p* = .012. State anxiety did not change significantly across further assessments (*t*s < 1.21, *p*s > .72). For the anodal tDCS group, the main effect of ABM was not significant (*F* = 21. *p* = .65). For the sham tES group, there were no significant main or interaction effects (*F*s < 2.29, *p*s > .11).

There were no further significant main or interaction effects (*F*s < 1.64, *p*s > .20).

#### 5.3.2.3 State Anxiety at Start and End of each Experimental Session (Pre-existing Attention Bias as Covariate)

A 3 x 3 x 2 x 4 mixed ANCOVA was conducted on the state anxiety data with the between subjects factors of ABM (Active ABM, control ABM, no-training ABM) and tES (active tRNS, anodal tDCS, sham tES) and 2 within subjects factors of time (start of session, end of session) and day (day 1, day 2, day 3, day 30) and pre-existing attention bias as a covariate. There was a significant main effect of day, *F*(2.43,377.11) = 4.31, *p* = .009, ($\eta p^2$ = .03; *observed power* = .81; Greenhouse Geisser Corrected). There was a also a significant main effect of time, *F*(1.00,420.65) = 14.11, *p* < .001, ($\eta p^2$ = .08; *observed power* = .96; Greenhouse Geisser Corrected). These effects are explored in section 5.3.1.3.

The day x time interaction was significant, *F*(2.71, 420.65) = 3.86, *p* = .012, ($\eta p^2$ = .024; *observed power* = .79; Greenhouse Geisser Corrected). For each day

(day 1, day 2, day 3, day 30) the effect of time was explored with paired samples t-tests. Results were Bonferroni corrected for multiple comparisons (significant if 4*p < .05). State anxiety at the end of day 1 (*M* = 31.20, *SD* = 8.51) was significantly reduced relative to at the start of day 1 (*M* = 33.71, *SD* = 10.10), *t*(166) = 4.35, *p* < .001). State anxiety at the end of day 30 (*M* = 32.50, *SD* = 10.67) was marginally significantly reduced relative to at the start of day 30 (*M* = 33.30, *SD* = 10.80), *t*(164) = 2.51, *p* = .052). The change in state anxiety from the start to end of session was not significant for any other experimental day (*t*s < 1.47, *p*s > .57). For each time (start of session, end of session) the effect of day was explored using paired samples t-tests. Results were Bonferroni corrected for multiple comparisons (significant if 6*p < .05). State anxiety at the start of day 2 (*M* = 31.81, *SD* = 9.69) was significantly reduced relative to at the start of day 1 (*M* = 33.71, *SD* = 10.10), *t*(166) = 3.21, *p* = .012). State anxiety at the start of day 3 (*M* = 31.43, *SD* = 9.80) was significantly reduced relative to at the start of day 30 (*M* = 33.71, *SD* = 10.10), *t*(164) = 3.64, *p* < .001). Change in start of session state anxiety was not significant across further experimental days (*t*s < 2.54, *p*s > .072). For end of session state anxiety, there was no significant change across days (*t*s < 2.44, *p*s > .10).

There were no further significant main or interaction effects (*F*s < 1.74, *p*s > .13).

### 5.3.3 Analyses of Covariance with Pre-existing Trait Anxiety as a Covariate

#### 5.3.3.1 Attention Bias (Pre-existing Trait Anxiety as Covariate)

A 3 x 3 x 3 mixed ANCOVA was conducted on the attention bias data with between subjects factors of ABM (active ABM, control ABM, no-training ABM) and tES (active tRNS, anodal tDCS and sham tES), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and pre-existing trait anxiety as a covariate. There was a significant assessment x tES interaction, $F(3.84,293.98) = 3.07$, $p = .018$, ($\eta p^2 = .04$; *observed power* = .79; Greenhouse Geisser corrected). Post hoc investigation of this interaction effect is reported in section 5.3.1.1.

There were no further significant main or interaction effects ($F$s < 4.29, $p$s > .26).

#### 5.3.3.2 State Anxiety (Pre-existing Trait Anxiety as Covariate)

With state anxiety as the dependent variable, a 3 x 3 x 3 mixed ANCOVA was conducted with between subjects factors of ABM (active ABM, control ABM, no-training ABM) and tES (active tRNS, anodal tDCS and sham tES), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and a covariate of pre-existing trait anxiety. The main effect of pre-existing trait anxiety was significant, $F(1,155) = 96.54$, $p < .001$, ($\eta p^2 = .38$; *observed power* = 1.00). Pre-existing trait anxiety was significantly, strongly and positively correlated with state anxiety, $r(166) = .63$, $p < .001$ (see figure 5.5).

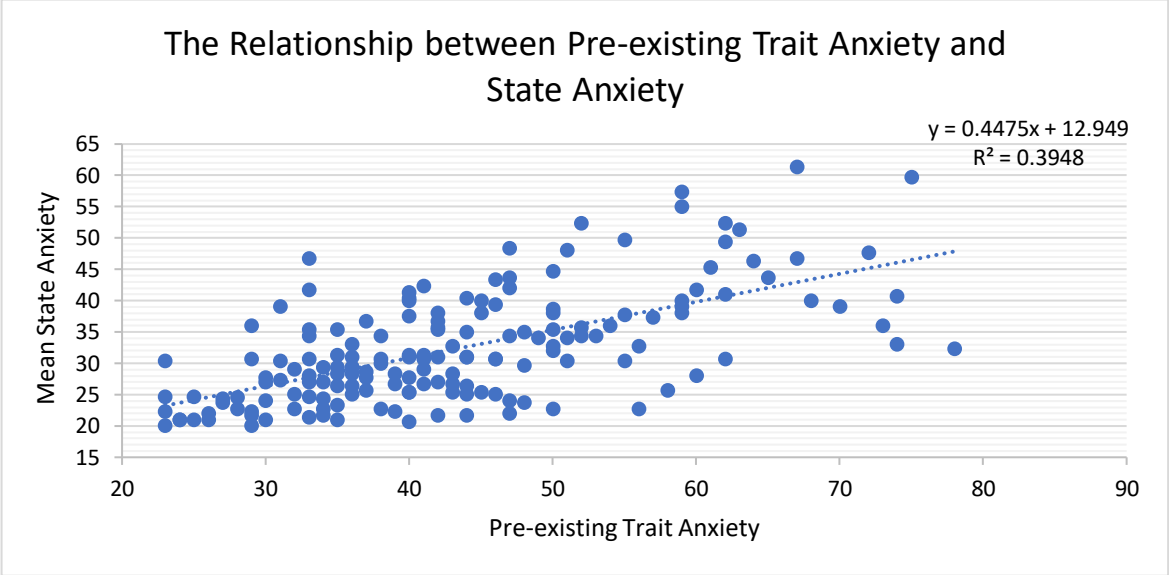



*Figure 5.5*. The relationship between scores on the state anxiety scale of the STAI (Spielberger et al., 1983) across study 1 and the trait anxiety scale of the STAI at baseline.

There were no further significant main effects or interaction effects (*F*s < 1.81, *p*s > .10).

#### 5.3.3.3 State Anxiety at Start and End of each Experimental Session (Pre-existing Trait Anxiety as Covariate)

A 3 x 3 x 2 x 4 mixed ANCOVA was conducted on the state anxiety data with the between subjects factors of ABM (Active ABM, control ABM, no-training ABM) and tES (active tRNS, anodal tDCS, sham tES) and 2 within subjects factors of time (start of session, end of session) and day (day 1, day 2, day 3, day 30) and pre-existing trait anxiety as a covariate. There was a significant main effect of pre-existing trait anxiety, $F(1,155) = 104.03$, $p < .001$, ($\eta p^2 = .40$; *observed power* = 1.00). Pre-existing trait anxiety was significantly, strongly and positively correlated with state anxiety, $r(166) = .63$, $p < .001$.

There were no further significant main effects or interaction effects (*F*s < 1.39, *p*s > .22).

### 5.3.4 Analyses of Covariance with Pre-existing Attentional Control as a Covariate

#### 5.3.4.1 Attention Bias (Pre-existing Attentional Control as Covariate)

A 3 x 3 x 3 mixed ANCOVA was conducted on the attention bias data with between subjects factors of ABM (active ABM, control ABM, no-training ABM) and tES (active tRNS, anodal tDCS and sham tES), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and pre-existing attentional control as a covariate. The assessment x tES interaction from the main analysis remained significant, $F(1.92,3.84) = 3.06$, $p = .019$, ($\eta p^2 = .04$; *observed power* = .79; Greenhouse Geisser corrected) (see section 5.3.1.1 for post hoc analysis of this interaction effect). No further main or interaction effects were significant (*F*s < .95, *p*s > .46).

#### 5.3.4.2 State Anxiety (Pre-existing Attentional Control as Covariate)

A 3 x 3 x 3 mixed ANCOVA was conducted on state anxiety data with between subjects factors of ABM (active ABM, control ABM, no-training ABM) and tES (active tRNS, anodal tDCS and sham tES), a within subjects factor of assessment (assessment 1, assessment 2, assessment 3) and a covariate of pre-existing attentional control. The main effect of pre-existing attentional control was

significant, $F(1,155) = 17.24$, $p < .001$, ($\eta p^2 = .10$; *observed power* = .99). There was a significant, moderate, negative correlation between pre-existing attentional control and state anxiety, $r(166) = -.32$, $p < .001$. This relationship is shown in figure 5.6 and suggests that higher pre-existing attentional control was associated with lower state anxiety.

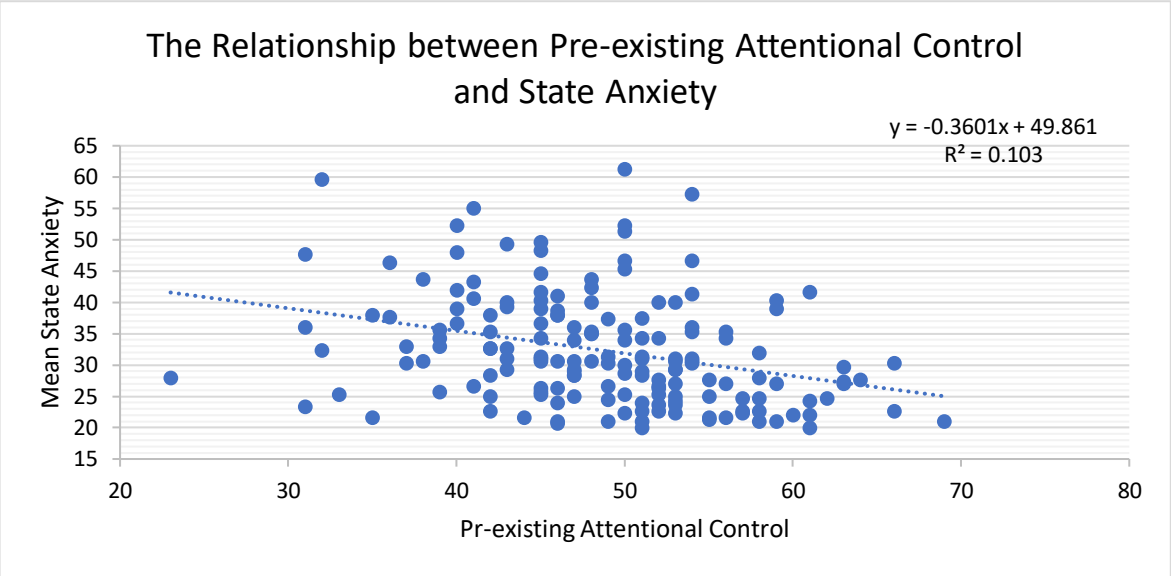



*Figure 5.6*. The relationship between scores on the attention control scale (Derryberry & Reed, 2002) at baseline and mean scores on the state anxiety scale (Spielberger et al., 1983) across study 1.

There were no further significant main effects or interaction effects ($F$s < 1.78, $p$s > .11).

#### 5.3.4.3 State Anxiety at Start and End of each Experimental Session (Pre-existing Attentional Control as Covariate)

A 3 x 3 x 2 x 4 mixed ANCOVA was conducted on the state anxiety data with the between subjects factors of ABM (Active ABM, control ABM, no-training ABM) and tES (active tRNS, anodal tDCS, sham tES) and 2 within subjects factors of time

(start of session, end of session) and day (day 1, day 2, day 3, day 30) and pre-existing attentional control as a covariate. The main effect of pre-existing attentional control was significant, $F(1,155) = 17.16$, $p < .001$, ($\eta p^2 = .10$; *observed power* = .99). There was a significant, moderate, negative correlation between pre-existing attentional control and state anxiety, $r(166) = -.32$, $p < .001$. There were no further significant main effects or interaction effects ($F$s < 1.43, $p$s > .22).

### 5.3.5 tRNS Tolerability

The tES intensity scale was based on that used by Meinzer et al. (2014). As per the Meinzer et al. (2014) study, differences in tES intensity scale ratings between experimental groups was examined. For this analysis each ABM/tES pairing was treated as an experimental group resulting in 8 group (active ABM/active tRNS, active ABM/anodal tDCS, active ABM/sham tES, control ABM/active tRNS, control ABM/anodal tDCS, control ABM/sham tES, no-training ABM/active tRNS, no-training ABM/sham tES). For each item of the tES intensity scale, a one-way ANOVA with the between participants factor of group (active ABM/active tRNS, active ABM/anodal tDCS, active ABM/sham tES, control ABM/active tRNS, control ABM/anodal tDCS, control ABM/sham tES, no-training ABM/active tRNS, no-training ABM/sham tES) was conducted. There was a significant effect of group on ratings of 'tickling' $F(7,155) = 6.38$, $p < .001$. Paired samples t-tests examined differences between experimental groups in terms of tickling intensity. As there were 8 groups, 28 paired comparisons were conducted. Results were Bonferroni corrected for multiple comparisons (significant if $28*p < .05$). Participants who received active ABM with anodal

tDCS reported significantly higher levels of tickling (*M* = 2.10, *SD* = .97) than participants who received active ABM with active tRNS (*M* = 1.19, *SD* = .40), *t*(25.12) = 3.89, *p* = .029. There were higher levels of tickling reported by participants who received control ABM with anodal tDCS (*M* = 2.47, *SD* = 1.12) than participants who received active ABM with active tRNS (*M* = 1.19, *SD* = .40), *t*(22.15) = 4.71, *p* < .001. Participants who received control ABM with anodal tDCS reported a higher level of tickling (*M* = 2.47, *SD* = 1.12) than those who received active ABM with sham tES (*M* = 1.43, *SD* = .60), *t*(26.81) = 3.62, *p* = .029. A higher level of tickling was reported by control ABM with anodal tDCS participants (*M* = 2.63, *SD* = 1.30) than no-training with active tRNS participants (*M* = 1.43, *SD* = .60), *t*(26.81) = 3.62, *p* = .029. The control ABM with anodal tDCS group reported higher levels of tickling (*M* = 2.47, *SD* = 1.12) than the no-training with sham tES group (*M* = 1.00, *SD* = .00), *t*(28.05) = 4.05, *p* <.001. The ANOVA revealed that there was a significant difference in 'itching' ratings between groups, *F*(7,155) = 10.03, *p* < .001. Paired samples t-tests examined differences between experimental groups in terms of itching intensity. Results were Bonferroni corrected for multiple comparisons (significant if 28*p < .05). Itching was reported as being higher by participants who received active ABM with anodal tDCS (*M* = 2.65, *SD* = 1.14) compared to participants who received active ABM with active tRNS (*M* = 1.29, *SD* = .64), *t*(29.74) = 4.70, *p* < .001). Participants who received control ABM with anodal tDCS (*M* = 2.63, *SD* = 1.30) reported higher levels of itching than participants who received active ABM with active tRNS (*M* = 1.29, *SD* = .64), *t*(25.73) = 4.08, *p* < .001. Higher levels of itching were reported by active ABM with anodal tDCS participants (*M* = 2.65, *SD* = 1.14) than active ABM with sham tES participants (*M* = 1.29, *SD* = .56), *t*(27.42) = 4.84, *p* < .001. Control ABM with anodal tDCS participants reported a higher

level of itching (*M* = 2.63, *SD* = 1.30) than active ABM with sham tES participants (*M* = 1.29, *SD* = .56), *t*(23.96) = 4.18, *p* < .001.

There was a marginally significant difference in reported level of itching between the active ABM with anodal tDCS groups (*M* = 2.65, *SD* = 1.14) and the control ABM with active tRNS groups (*M* = 1.63, *SD* = .68), *t*(37) = 3.37, *p* = .058. Higher levels of itching were reported by active ABM with anodal tDCS participants (*M* = 2.65, *SD* = 1.14) than control ABM with sham tES participants (*M* = 1.38, *SD* = .74), *t*(32.42) = 4.21, *p* < .001. The control ABM with anodal tDCS group reported a higher level of itching (*M* = 2.63, *SD* = 1.30) than the control ABM with sham tES group (*M* = 1.38, *SD* = .74), *t*(27.94) = 3.69, *p* = .029. Itching was significantly higher for participants who received active ABM with anodal tDCS (*M* = 2.65, *SD* = 1.14) than for those who received no-training with active tRNS (*M* = 1.43, *SD* = .60), *t*(28.45) = 4.28, *p* < .001. The control ABM with anodal tDCS group reported higher levels of itching (*M* = 2.63, *SD* = 1.30) than the no-training ABM with active tRNS group (*M* = 1.43, *SD* = .60), *t*(28.45) = 4.28, *p* < .001. Active ABM with anodal tDCS participants reported higher levels of itching (*M* = 2.65, *SD* = 1.14) than no-training with sham tES participants (*M* = 1.33, *SD* = .73), *t*(32.15) = 4.39, *p* < .001. There were higher reported higher levels of itching for control ABM with anodal tDCS participants (*M* = 2.63, *SD* = 1.30) than no-training with sham tES participants (*M* = 1.33, *SD* = .73), *t*(27.71) = 3.84, *p* < .001.

There was also a significant difference in ratings of 'burning' between experimental groups, *F*(7,155) = 13.38, *p* < .001. Paired samples t-tests examined differences between experimental groups in terms of burning

intensity. Results were Bonferroni corrected for multiple comparisons (significant if 28*p < .05). Participants who received active ABM with anodal tDCS reported significantly higher levels of burning (*M* = 2.40, *SD* = .99) than participants who received active ABM with active tRNS (*M* = 1.00, *SD* = .00), *t*(19.00) = 6.29, *p* < .001. The active ABM with anodal tDCS group reported significantly higher levels of burning (*M* = 2.40, *SD* = .99) than the active ABM with sham tES group (*M* = 1.05, *SD* = .22), *t*(20.74) = 4.84, *p* < .001. Higher levels of burning were reported by active ABM with anodal tDCS participants (*M* = 2.40, *SD* = .99) than by control ABM with active tRNS participants (*M* = 1.00, *SD* = .00), *t*(19) = 6.29, *p* < .001. The active ABM with anodal tDCS group (*M* = 2.40, *SD* = .99) experienced a greater degree of burning than the control ABM with sham tES group (*M* = 1.29, *SD* = .56), *t*(29.66) = 4.39, *p* < .001. Burning was significantly higher for the active ABM with anodal tDCS group (*M* = 2.40, *SD* = .99) than for the no-training with active tRNS group (*M* = 1.24, *SD* = .44), *t*(25.78) = 4.80, *p* < .001. There was a higher reported level of burning for active ABM with anodal tDCS participants (*M* = 2.40, *SD* = .99) than for no-training with sham tES participants (*M* = 1.00, *SD* = .00), *t*(19) = 6.29, *p* < .001.

Groups also differed significantly in terms of 'skin-irritation' ratings, *F*(7,155) = 5.49, *p* < .001. Paired samples t-tests revealed no significant differences in skin irritation ratings between experimental groups (*t*s < 2.89. *p*s > .26).

There were no further significant differences between experimental groups in terms of items on the tES Intensity Scale (*F*s < 1.31, *p*s > .25).

### 5.3.6 Experimental Condition

The percentage of participants who guessed their ABM group correctly was 53.9%. Chi square test of difference established that this was not significantly different from chance level ($X^2$ = .50, $p$ = .48.). From the active ABM group, 30.2% of participants reported their ABM group correctly. This was significantly lower than chance, $X^2(1)$ = 5.1, $p$ =.02. From the control ABM group, 85% of participants correctly reported their ABM group. This was significantly above chance level, $X^2(1)$ = 16.61, $p$ < .0.001. A total of 45.2% of participants in the no-training ABM group reported their ABM group accurately. This did not differ significantly from chance $X^2(1)$ = .19, $p$ < .0.66.

60% of participants correctly guessed whether they had received active or sham tES. The difference from chance level of this proportion approached significance, $X^2(1)$ = 3.32, $p$ <.07. Of those who received active tRNS, 56.5% correctly guessed their tES group. A Chi square test of difference established that this was not significantly different from chance level ($X^2$ = .52, $p$ = .47). A total of 52.4% of participants who received sham tES correctly reported their tES group. This was not significantly different from chance ($X^2$ = .07, $p$ = .79). Finally, 77.5% of participants who received anodal tDCS correctly reported their tES group. This was significantly above chance level, $X^2(1)$ = 6.46, $p$ =.01.

The percentage of participants who guessed both their ABM and tES group correctly was 33.3%. This proportion was significantly lower than chance $X^2(1)$ = 9.44, $p$ < .0.001.

## 5.4 Discussion

The present analysis included data from experiments 1, 2 and 3 of study 1. These experiments assessed the impact of three forms of ABM training (active ABM towards neutral faces, control ABM and no-training ABM) with concurrent tES on attention bias and anxiety. Active ABM and control ABM were delivered concurrently with active tRNS, anodal tDCS or sham tES. No-training ABM was delivered with either active tRNS or sham tES. The analysis provided no evidence that active ABM confers any advantages in terms of threat bias and anxiety reductions over control and no-training ABM. Threat bias was reduced for participants in the sham tES group but not for participants in either active tES group. State anxiety was reduced for all participants but this was not maintained at 30-day follow up. There was greater threat bias reduction for participants with larger pre-existing threat bias and greater reduction in neutral bias for participants with larger pre-existing neutral bias following training but anxiety was reduced irrespective of pre-existing bias.

### 5.4.1 Threat Bias Reduction for Sham tES Group

There was a reduction in threat bias for participants who had received sham tES but not for those who had received active tRNS or anodal tDCS. This was an unexpected finding which is in contrast with studies which have found tES to enhance the impact of ABM training (Clarke et al., 2014; Heeren et al., 2015b). It is also in opposition to the many studies which have reported the enhancement of cognitive training with active tES (e.g. Ditye et al., 2012; Fertonani et al., 2011; Snowball et al., 2013; see Cohen Kadosh, 2013 for

review). Previous chapters have discussed the need to consider existing neural activation state when applying tES (Horvath et al., 2015b). It has been proposed that the neural systems associated with cognition favour one state (inhibitory or excitatory) at one time (Silvanto, Muggleton & Walsh, 2008). In order to maintain stable function when neural circuits are subject to excess inhibition or excitation, homeostatic plasticity mechanisms are activated which may involve local synaptic and post-synaptic adaptations (Turrigiano, 2012). These mechanisms might involve, for example, synaptic scaling in which calcium-dependent sensors allow neurons to distinguish changes in the rate at which they are firing and increase or decrease the number of synapses available at relevant locations (Turrigiano, 2012). In support of this notion, studies have shown that when anodal tDCS is applied prior to 'facilitatory' 5-Hz repetitive TMS, corticospinal excitability is reduced relative to baseline and that priming of a neural system with cathodal tDCS results in increased cortico-spinal facilitation following 5-Hz repetitive TMS (Lang et al., 2004; Silvanto et al., 2008). It is possible that in the present study, when added to the neural activation concomitant with attentional training (active, control and no-training ABM), excitatory tES triggered homeostatic neural mechanisms resulting in abolition of the facilitatory effects of the training alone. However, with sham tES, neural activity enhancement generated by attentional training was not hampered and threat bias reduction was facilitated. A recent meta-analysis of the impact of single-session tDCS on cognitive training reported that tDCS had no significant effect proposing that null results might be due to state-dependent effects (Horvath et al., 2015). It was suggested that in future these effects could be controlled for (Horvath et al., 2015). More research related to state-

dependency is needed before state dependent effects can be identified, quantified and incorporated into analyses.

### 5.4.2 Pre-existing Attention Bias

There is another, arguably more likely explanation for threat bias reductions which were exclusive to participants who received sham and not active tES. It was evident from findings in the present study that greater threat bias at baseline was associated with greater reduction in threat bias and that greater neutral bias at baseline was related to larger decline in neutral bias. This occurred irrespective of ABM or tES group. Where ABM and tES group were not influential in attention bias change, pre-existing attention bias was. Across the study more participants who received sham tES had a pre-existing threat bias than had a neutral bias and more participants who received active tES had pre-existing neutral bias than had threat bias. In the active tES groups therefore, any reductions in threat bias achieved for participants with pre-existing threat bias may have been 'cancelled out' by increases in threat bias for participants with pre-existing neutral bias who made up a larger proportion of this group. As previously discussed, this highlights the importance of considering baseline attention bias when interpreting change in attention bias following training. It suggests that where attention bias manipulation is the principal focus of an investigation, screening for a particular 'direction' of bias might be advisable. Differences in pre-existing attention bias between experimental groups may play a large part in explaining variability amongst previous ABM studies. When pre-existing bias was included as a covariate in the analysis, the interaction between tES group and change in attention bias across assessments disappeared. The

interaction remained significant when pre-existing trait anxiety and pre-existing attentional control were included as covariates. This further supports the role of pre-existing attention bias in determining ABM-related attention bias modulation.

### 5.4.3 Mechanism of Attention Bias and State Anxiety Change

As discussed, the above findings indicate that a mechanism common to all forms of ABM training is responsible for neutral bias reduction in participants with pre-existing neutral bias and threat bias reduction for participants with a pre-existing threat bias. This could be an enhancement of attentional control capacity. Attentional bias towards neutral stimuli has also been termed attentional avoidance (Koster et al., 2006) a behaviour which has been observed in high trait anxious individuals (Derryberry & Reed, 2002; Koster et al., 2006). Given that some attentional engagement to threat is considered adaptive and necessary to ensure an individual's safety and survival (Koster et al., 2006), attentional avoidance of threat might indicate a maladaptive lack of vigilance. If, as previously argued, ABM training and control ABM training augment attentional control capacity then the likely outcome might be a more 'healthy' pattern of attention distribution. In the case of attentional avoidance therefore, this might be an increase in attentional engagement to threat. In the case of biased attention towards threat, this might be enhanced engagement to neutral stimuli. Derryberry & Reed (2002) suggested that effective coping requires shifting attention between sources of threat and safety. This might be disengaging from threat or disengaging from safety (Derryberry & Reed, 2002). This line of reasoning contradicts the notion that a reduction in threat

engagement is necessary for anxiety reduction to occur. It suggests instead that if a more adaptive attentional strategy can be adopted, anxiety reduction will ensue.

#### 5.4.3.1 Exposure

Habituation to stimuli might also explain the pattern of attention change observed for participants with threat and neutral bias (Carleton et al., 2015). Familiarity with repeatedly presented threatening faces might render the participant less likely to preferentially engage or avoid them. This might also result in a reduced stress response towards emotionally salient stimuli as reflected in reduced anxiety.

#### 5.4.3.2 Exposure and Attentional Control Enhancement

Alternatively, a combination of exposure and attentional control enhancement may explain the 'balancing out' of attentional bias across participants and the accompanying reductions in state anxiety. Macleod & Grafton (2016) recently endorsed making a clear distinction between procedure and process when determining and interpreting the effectiveness of ABM. In their review, the term 'procedure' refers to the methodology employed with the intention of modifying attention bias and 'process' the action of achieving attention bias modification. This is applicable in the present discussion. The ABM dot-probe paradigm involves the repeated presentation of stimuli. Repeated exposure may therefore be the *procedure* via which threatening stimuli become less salient and anxiety inducing. This may occur via a *process* of habituation as stimuli

which have been experienced before no longer present (or need to be treated as) a threat. At this point, attentional control processes may be activated and attention deployed towards or away from stimuli which were previously preferentially selected or avoided.

#### 5.4.3.3 Attentional Control at Baseline

In a study by Basanovic et al. (2017), greater capacity for attentional inhibition and attentional selectivity (2 facets of attentional control) at baseline predicted the magnitude of attention bias change in the trained direction (towards neutral or towards threatening stimuli). In order to further investigate whether attentional control level modulates the success of ABM training, pre-existing high attentional control was included as a covariate in each study 1 analysis. Across these analyses pre-existing attentional control did not predict change in attention bias or state anxiety following attentional training. Study 1 therefore does not provide conclusive support for baseline attentional control level as a mediator of ABM effects. However, the findings do not preclude the possibility that training-induced *enhancement* of attentional control capacity is implicated in state anxiety reduction across the three experiments of study 1. In order to further explore this possibility, future ABM research should incorporate a measure (or measures) of attentional control before and after ABM training.

### 5.4.4 TES Intensity

The physical experience of receiving each form of TES was assessed. There was a greater degree of discomfort for anodal tDCS than for active tRNS and sham

tES. This confirmed previous reports of a higher cutaneous perception threshold for tRNS than for tDCS (Ambrus et al., 2010). There was more tickling, itching and burning for anodal tDCS than active tRNS and sham tES. This will undoubtedly have contributed to the finding that the number of people who guessed their tES group correctly in the anodal tDCS group was above chance. In the present study there was no evidence of the enhancement of ABM with tES but there was some indication of anxiety attenuation with active tRNS. Given the relative undetectability of tRNS and a potential anxiolytic effect, there is scope for examining the efficacy of high frequency tRNS as a treatment for anxiety in future. Although there is no evidence that the negative sensations reported for participants who received anodal tDCS in the present study induced negative affect, a factor for consideration is the impact that the discomfort related to anodal tDCS may have in future research involving its use. This problem might be mitigated by carefully evaluating tDCS montage prior to its use. Studies which have modelled tDCS in the brain have reported that shorter distance between the anode and the cathode (e.g. anode at F3 and cathode at the contralateral supraorbital) is associated with greater risk of current being shunted across the scalp (Bai et al., 2014). Greater distance between electrodes (i.e. with the 'return' electrode in an extracephalic position; e.g. Clarke et al., 2014) results in a larger amount of current entering the brain as the degree of shunting is reduced (Bai et al., 2014). In experiment 3 there was a short distance between electrodes during the application of anodal tDCS. A larger degree of shunting of electrical current across the scalp may have been responsible for the discomfort experienced by participants who received anodal tDCS and prevented more current from entering the brain. As previously postulated (Bestmann et al., 2014), prior to commencing a tES study, computer

modelling of any tES montage and parameters being considered is advisable. This would provide an indication of the effects of an intended tES application in terms of electrical field distribution and intensity across the brain. It would also allow the mapping of electrical field predictions on to behavioural outcomes (Bikson, 2010).

### 5.4.5 Limitations

A key weakness of study 1 was that, despite investigating the role of attentional control in state anxiety reduction, a measure of attentional control was not included. In experiment 2 it was predicted that an adaptation of the traditional dot-probe ABM training with reduced cognitive load would not lead to anxiety reduction. Based on previous studies which have shown that improvement in tasks which enhance cognitive control is related to the augmentation of attentional control and the attenuation of negative effect (e.g. Sari et al., 2015; Swainston et al., 2018) the assumption was that low cognitive load training would fail to elicit attentional control improvements and as such, there would be no effect of the training on anxiety. However, in previous studies, the relationship between training-induced cognitive control enhancement and increase in attentional control capacity was substantiated via the inclusion of measures of attentional control. A study by Sari et al. (2015) demonstrated that improvements in working memory capacity following adaptive working memory training using the dual n-back task, in highly trait anxious participants, was associated with enhanced attentional control. This was indicated via transfer effects on an EEG index of attentional control and on the Flanker task (Sari et al., 2015). Previously, Owens et al. (2013) had shown that, following training

with the same task used by Sari et al. (2015), dysphoric individuals had improvements in working memory performance and increased attentional inhibition as indicated by the contralateral delay activity (CDA) an ERP associated with attentional filtering (Owens et al., 2013). Because study 1 failed to test for transfer effects by including an attentional control measure, any assertions made regarding the impact of attentional control modulation on anxiety based on study 1 results are unsubstantial.

The putative role of attentional control modulation in anxiety reduction was discussed and investigated in light of findings from experiment 1. Prior to experiment 1 attentional control as a modulator or mediator of ABM effects had not been considered and therefore a measure of attentional control was not included in the study 1 design from the outset. As experiments 2 and 3 were designed as extensions to experiment 1, it was deemed important to have consistency across experiments in terms of experimental procedure. To have altered the design may have compromised the opportunity to compare data and findings across the 3 experiments. Adding an extra attentional control measure may have introduced confounding variables to the study. For example, there may have been changes in self-report measure outcomes attributable to differences in session duration. It is for this reason that a measure of attentional control was not introduced part-way through study 1. Instead, experiment 2 attempted to explore the causal role of attentional control modulation in anxiety attenuation by manipulating task-induced attentional control modulation. Going forward, research wishing to investigate the same question would be rendered more robust via the inclusion of attentional control measures.

## 5.5 Summary

The hypotheses from study 1 were not met and some unexpected findings emerged. Active ABM did not induce superior reductions in threat bias and anxiety than control ABM or no-training ABM. The question of whether tES modulates the effects of active ABM training was therefore inapplicable. Anxiety reduction across participants following attention training was a consistent finding in study 1. The attenuation of anxiety was not accompanied by reductions in threat bias raising doubt over the theory that a decline in threat engagement is responsible for anxiety attenuation in ABM paradigms. Alternatively, it is possible that threat bias reduction *is* implicated in anxiety reduction but that the emotional dot-probe task used to assess attention bias failed to capture attention bias change accurately (Kappenman et al., 2014; Schmukle et al., 2005).

Across study 1, threat bias was reduced following training for participants who began their experiment with greater threat bias and neutral bias was reduced for participants with a greater neutral bias at baseline. Study 1 did not pre-select participants for attention bias towards threat and, in parts of study 1, the number of participants with pre-existing neutral bias outweighed the number of participants with pre-existing threat bias. The study was therefore unlikely to reveal a reduction in threat bias across all participants. This repeated outcome suggests that attention bias assessment is in fact measuring attention bias with some accuracy as it has captured a 'phenomenon'. If the emotional dot-probe was unreliable (Kappenman et al., 2014) then such a consistent pattern would be unlikely to emerge. Nonetheless, there is scope for future studies to test other

measures of attentional response towards threatening and non-threatening stimuli which may be more accurate than reaction time data. The question which remains unanswered is whether state anxiety reductions occurred independently of threat bias reductions for participants with pre-existing threat bias and neutral bias reductions for participants with pre-existing neutral bias or whether state anxiety reduction and attention bias reduction were driven by a common mechanism. Whether attentional control enhancement or habituation to the ABM stimuli or, more likely, an integration of the two might account for attention bias adjustments and reductions in state anxiety, has been discussed. This is a worthy avenue for future investigation. Studies might employ additional measures of attentional control to assess the extent to which attentional control change is coupled with anxiety modulation. Also, as previously suggested, future versions of the ABM task could omit threatening stimuli or face stimuli altogether to assess the extent to which exposure to these is linked to anxiety attenuation.

It was revealed that tRNS might elicit or promote anxiolytic effects as in experiment 2 state anxiety was reduced for the active tRNS group but not for the sham tRNS group. It is unclear whether this effect is attributable directly to tRNS stimulation or whether tRNS achieved this benefit by modulating the effects of the training it was delivered with. This warrants investigation in future studies, particularly in light of the physical tolerability of tRNS.

# Chapter 6

**Modulation of Attention Bias Modification using Transcranial Direct Current Stimulation: A Single Session Study using Electrophysiological Measures**

## 6.1 Introduction

ABM studies have reported superior threat bias reduction for participants who received attend-neutral ABM relative to those who received control or attend-threat ABM (Hakamata et al., 2010). Research which has used tES to enhance the effects of ABM training has reported that this effect is enhanced with anodal tDCS relative to sham tDCS (Clarke et al., 2014; Heeren et al., 2015b). Study 1 failed to replicate these findings. It did not reveal greater threat bias reduction for active ABM with active tES than for active ABM with sham tES. In fact, there was no evidence of threat bias reduction following ABM training for participants irrespective of condition. Macleod and Grafton (2016) argued that evidence of the successful modulation of attention bias using active ABM is so pervasive (e.g. Hazen et al., 2009; Najmi & Amir, 2010; See, Macleod & Bridle, 2009) that failure to find this effect might be due to inefficacy of the procedure used to assess attention bias. A study by Schmukle (2005) found the modified dot-probe task to be an unreliable measure of attention allocation. Others have suggested that it is the reaction time data which it produces which represent a poor psychometric measure of attention bias as there is typically enough time during facial cue presentation for gaze to be averted from threatening stimuli before the appearance of the target (Kappenman et al., 2014). The present study aimed to eliminate this potential confound by introducing a measure which more

closely reflected the time-course of neural processes associated with attention allocation.

### 6.1.1 Event Related Potentials (ERPs)

ERPs are recordings of electrical brain processes, time and phase-locked to specific events (Helfinstein et al., 2008). They are measured using electrodes on the scalp during electroencephalography (EEG), a non-invasive imaging technique. Often observed within the first 500ms after the appearance of a stimulus in attention experiments, ERPs are believed to provide specific temporal indices of visual spatial attention allocation and stimulus processing (Holmes, Kragh Nielsen & Green, 2009). As outlined in chapter 1, ERP studies have supported the presence of selective attention to threat related stimuli (Bar-Haim, Lamy & Glickman, 2005; Eldar et al., 2010; Fox, Derakshan & Shoker, 2008; Moser et al., 2008). Threat bias is generally inferred from larger amplitudes or shorter latencies for ERPs associated with attentional selection which are time and phase-locked to the presentation of threatening stimuli, relative to those which are time and phase-locked to the presentation of non-threatening stimuli (e.g. angry-neutral face pairs relative to neutral-neutral faces pairs; Bar Haim et al., 2005).

Some ERP studies have produced findings indicative of greater threat bias in high anxious compared to low anxious individuals (Bechor et al., 2018). High anxious participants presented with individual happy, sad, angry, fearful or neutral faces images followed by a target to be identified elicited greater P2 amplitude for angry faces than low anxious participants who performed the same task (Bar

Haim et al., 2005). Using an emotional dot-probe task with angry-neutral, happy-neutral and neutral-neutral faces pairs, Eldar et al. (2010) reported more enhanced C1 to face pairs containing angry faces for anxious participants relative to non-anxious participants. Also, during an emotional dot-probe task, anxious youths displayed larger P1 amplitude for threatening stimuli than for neutral stimuli whereas non-anxious youths showed the opposite pattern (Bechor et al., 2018). These studies show that high anxious individuals tend to show enhanced early and automatic perceptual processing of threatening stimuli, thought to be a result of preferential attentional allocation. However, investigations which have used ERPs to clarify the neural signatures of attention bias have also demonstrated this tendency in non-anxious cohorts (e.g. elevated C1 for threatening stimuli; Eldar et al., 2010 Pourtois et al., 2014; and enhanced P1 for threatening stimuli; Pourtois et al., 2014; Santesso et al., 2008).

#### 6.1.1.1 The N2pc Component

The N2pc is an ERP component which is typically elicited at posterior electrodes between 180 and 300ms after stimulus onset, contralateral to visual stimuli. It is associated with shifts in visual attention to a specific locus of the right or left visual hemifield (Eimer, 1996). An advantage of this feature of the N2pc is that, if stimuli are presented laterally, it is possible to make an inference regarding attentional selection of a specific visual stimulus based on N2pc calculated from EEG data collected at electrodes contralateral to the stimulus. An example of this type of lateralised presentation would be an angry-neutral face pair, presented in a horizontal alignment with each face image to the left or right of central fixation. Shorter N2pc latency or an enhanced N2pc amplitude at

electrodes contralateral to the angry stimulus than at the neutral stimulus might indicate faster, or preferential attentional engagement to threat. In some of the studies cited above with components of interest such as the P1, N1 or P2, threat bias was inferred by enhanced ERP components to face pairs containing threatening stimuli (e.g. Bechor et al., 2018; Eldar et al., 2010).

Research has shown that the N2pc is elicited earlier (e.g. Holmes et al., 2009) and has greater amplitude (e.g. Weymar et al., 2011; Kappenman et al., 2014) for threatening relative to happy or neutral faces. In a recent study, participants performed a task in which they identified a threatening or friendly face target in an array of neutral faces or a neutral target in an array of threatening or friendly faces. Participants with high social anxiety had higher detection rates for threatening faces and participants with low social anxiety had higher detection rates for friendly stimuli. The high socially anxious group had a higher N2pc amplitude for emotional faces but low anxious participants elicited no reliable N2pc for stimuli of any valence (Wieser et al., 2018). In an emotional dot-probe task with angry-neutral and happy-neutral face pairs, high trait anxious but not low trait anxious participants had an enhanced N2pc amplitude for angry faces (Fox, Derakshan & Shoker, 2008). There was no N2pc for happy faces in either trait anxiety group. Attention bias calculated using reaction time data was, however, not reported and therefore it is not possible to state whether N2pc outcomes may have supported behavioural outcomes. Using the same paradigm but without categorising participants as high or low trait anxious, Holmes et al. (2009) demonstrated faster reaction times for targets replacing emotional faces compared to targets replacing neutral faces. There was enhanced negativity contralateral to the angry face during angry-neutral

face pairs in the early N2pc time bracket (180-250ms post stimulus). This negativity was sustained into the late N2pc time phase (250-320ms post stimulus) and continued until the offset of face pairs at 500ms. N2pc was observed for happy faces in the late N2pc time phase and this also continued until stimulus offset. These results suggest that both angry and happy faces received preferential attentional selection which was maintained throughout stimulus presentation but that angry stimuli were more rapidly attentionally engaged (Holmes et al., 2009). In a later study (Holmes et al., 2014) participants performed an emotional dot-probe task whilst remembering a simple (low memory load) or a more difficult, random (high memory load) digit sequence. The authors reported more enhanced N2pc and SPCN amplitudes for threatening faces compared to neutral faces during high memory load trials relative to low memory load trials. The reaction time measure of attention bias was positively correlated with each ERP measure of attention bias. These results indicated the presence of an attentional bias towards threat which is greater when cognitive control is depleted leaving less attentional resources available to inhibit the engagement to threatening stimuli. In a task delivered by Eimer and Kiss (2007) a fixation cross was flanked to the left and right by an array of face images containing a fearful singleton (a single fearful face amongst an array of neutral faces) or a neutral singleton (a single neutral face amongst an array of fearful faces). Participants were instructed to detect and indicate an infrequent luminance change to the central fixation cross. Response time was not affected by singleton type or location. During trials in which there was no luminance change, there was enhanced negativity in the early N2pc time phase for singleton and non-singleton fearful faces next to fixation. For trials in which there was a luminance change the N2pc was still present for fearful faces

but was attenuated suggesting that attentional capture by task-irrelevant fearful faces was reduced during target processing (Kiss & Eimer, 2007). In a further study, participants were presented with an array of schematic neutral faces with straight (vertical) noses except one face which had a slanted nose (Burra et al., 2016). The participant was required to indicate the direction of the nose slant. In some trials an angry or happy distractor face was included in the array in a position contralateral or ipsilateral to the target. Irrespective of valence, reaction times were slowed by the presence of a distractor. Analysis revealed a significant N2pc for angry distractors but not happy distractors (Burra et al., 2016). In summary, studies have shown that the N2pc, an electrophysiological marker of attentional selection is enhanced for aversive stimuli relative to non-aversive stimuli. Furthermore, it is possible that the N2pc component is more sensitive to attentional selectivity than reaction times (e.g. Kiss & Eimer, 2007). In the present study therefore, measuring N2pc in conjunction with reaction time during attention bias assessment may provide a more detailed and sensitive illustration of attentional engagement to threatening and neutral stimuli.

### 6.1.2 Use of ERPs in ABM Studies

The number of studies which have used ERPs to reflect the impact of ABM on attention bias is limited. In a study by O'Toole et al. (2012), participants received ABM training towards threatening faces or towards neutral faces (away from threatening faces). ABM training led to the modulation of attention bias in the trained direction. However, these changes were exclusive to participants with a pre-existing attention bias towards threat. Across all participants there was a reduction in early ERP (P1 and N170) amplitudes following attend-neutral

ABM training but not attend-threat training. However, there was no evidence that this response was elicited specifically for threatening stimuli (O'Toole et al., 2012). Sass et al. (2017) delivered ABM training towards positive words (away from threat words) or control ABM training to participants who scored high on measures of GAD and panic disorder. Following training, attention was biased towards threat in the control ABM group and biased towards positive stimuli for participants in the active training (attend-positive) condition as indicated by reaction time data. For participants who received attend-positive ABM training, positive bias was significantly enhanced post-training relative to pre-training. Contrary to expectation, the P100 was not enhanced for targets replacing positive stimuli following attend-positive ABM training. However, the P100 amplitude was increased for targets replacing neutral words in threat-neutral word pairs following attend-positive but not control training. The authors suggested that the outcome reflected facilitated early attentional processing of non-threatening stimuli following active training (Sass et al., 2016). Other research has however, failed to reveal modulation of ERPs associated with early attentional processing following ABM training. Eldar and Bar Haim (2010) measured EEG in high and low trait anxious participants during an emotional dot-probe task with threat-neutral and neutral-neutral face pairs before and after ABM training towards neutral faces or control ABM. Reaction time data revealed that, across training trials there was a linear reduction in response time to neutral stimuli in high trait anxious participants in the active ABM group but not for high trait anxious participants who received control ABM training. There was no change in response time to threatening or neutral faces for low trait anxious participants and reaction time to angry stimuli did not change across participants. No differences from pre to post training or between conditions or

anxiety categorisations were apparent for early ERPs (P1 and N1). For anxious participants there was a reduced P2 amplitude and an increased N2 amplitude for the active training group following active ABM and an enhanced P2 and a reduced N2 amplitude following training for the control ABM group. These changes were irrespective of face pair type (angry-neutral, neutral-neutral). The authors concluded, based on training-induced modulation of ERPs associated with attentional processes occurring after initial attention orienting, that active ABM affected top-down mechanisms of attentional control as opposed to early attention orienting processes (Eldar & Bar Haim, 2010). In another study, neurotypical participants received ABM training towards threatening stimuli or control ABM (Suway et al., 2013). Reaction time data from attention bias assessment with threat-neutral faces pairs revealed that in the attend-threat group there was an increase in threat bias following training. The control group showed no change in attentional bias from pre-to post-training. Training groups did not differ in terms of the P1 and N1 components following training but the P2 amplitude was greater following training for participants in the train towards threat condition. The authors highlighted that the P2 is a component previously associated with attention bias towards threat (Bar-Haim, Lamy, & Glickman, 2005; Carretie et al., 2001; Eldar et al., 2010). Furthermore, change in P2 amplitudes from before to after training correlated positively with change in depression vulnerability from pre-to post training with greater increase in P2 amplitudes associated with greater increase in depression vulnerability. Osinsky et al. (2014) examined N2pc response to angry versus neutral facial expressions during attend-neutral or control ABM training. They revealed no change in the N2pc throughout the session.

There is therefore mixed evidence from ERP studies of ABM training with some research outcomes suggesting a modulation of ERPs linked to initial attentional allocation following ABM training (Sass et al., 2016), other research suggesting that ABM training may have an impact on the neuro-electrophysiological correlates of post-selection (attentional control) processes (Eldar et al., 2010; Suway et al., 2013) and research revealing no effect of ABM training on ERP components (Osinsky et al., 2014). It could be argued that the status of ERP-based research on the effects of ABM training reflects that of research which has used only behavioural data. However, the use of ERPs in ABM research is a relatively recent exploratory domain and, as with traditional (reaction time based) ABM research, there is scope for development and improvement. Undoubtedly, ERPs are a useful tool in increasing our understanding of the neural processes involved in attentional selection.

### 6.1.3 Use of ERPs in tES Studies

Few studies have examined the potential modulation of attentional training with tES using ERPs. Tseng et al. (2012) delivered anodal or sham tDCS to the right posterior parietal cortex (PPC) prior to a visual short-term memory task. Participants were required to indicate whether there was a change to an array of coloured rectangles. For naturally low-performing participants, anodal tDCS above the right PPC but not sham tDCS improved change detection. N2pc amplitude was enhanced across participants during change detection relative to change non-detection. For naturally low-performing participants this augmentation of amplitude was greater for participants who had received anodal tDCS compared to participants who had received sham tDCS. For high

performing individuals, N2pc amplitude was elevated during change detection relative to change non-detection but did not differ between tDCS groups (Tseng et al., 2012). The results therefore suggested state-dependent effects with low-performing participants who received anodal tDCS experiencing enhanced change detection capacity which was reflected in an enhanced N2pc. For high-performing participants anodal tDCS did not facilitate change detection, perhaps because neural processes involved in change detection were optimised, leaving no scope for anodal tDCS-induced enhancement. In a study by Lafontaine et al. (2013) participants received 15 minutes of offline, 1.5mA tDCS with the anode above the left DLFPC and the cathode above the right DLPFC (F3 anodal/F4 cathodal), the anode above the right DLPFC and the cathode above the left DLPFC (F4 anodal/F3 cathodal) or as sham tDCS (with a bi-frontal montage). Participants subsequently performed an 'unfamiliar face' encoding exercise during which EEG data were recorded to allow assessment of the N170 and P3 components. P3 was measured to assess tDCS-induced changes in DLPFC function. Recognition of faces was tested 3 days after encoding. TDCS delivered with the F4 anodal/F3 cathodal montage was associated with more reduced N170 and more enhanced P3 during encoding relative to the other tDCS groups. During recognition testing, the F4 anodal/F3 cathodal condition had faster recognition reaction time relative to the other tDCS conditions. Previously, N170 amplitude and latency had been seen to vary as a function of face novelty/familiarity (Heisz, Watter & Shedden, 2006). Specifically, there is evidence of N170 amplitude reduction across repeated presentations of the same unfamiliar face (Caharel et al., 2011). The authors suggested that F4 anodal/F3 cathodal tDCS facilitated N170 reduction and P3 enhancement leading to faster face recognition (Lafontaine et al., 2013).

### 6.1.4 Rationale for Use of ERPs in Study 2

Reaction time data obtained from the emotional dot-probe task has proven to be an unreliable index of attention bias. However, ERP components have demonstrated good internal consistency. Kappenman et al. (2014) recorded both reaction time data and EEG data in order to assess the N2pc component during emotional dot-probe based attention bias assessment. Behavioural data did not reveal a threat bias and reaction time data were not internally reliable. EEG data did however reveal a significant N2pc for threat relative to neutral stimuli and the N2pc was internally reliable. Neither the reaction time based measure of attention bias nor N2pc amplitude or latency correlated with trait anxiety however. Reutter et al. (2017) also compared reaction time measure of attention bias with the N2pc component during attention bias assessment in participants with high levels of self-report social anxiety. In replication of the Kappenman et al. (2014) results, the N2pc component, but not reaction time data indicated an attention bias towards threat reflected in a higher N2pc amplitude at electrodes contralateral to threatening stimuli compared to electrodes contralateral to neutral stimuli. Moreover, in contrast to the reaction time measure of attention bias, the N2pc measure was shown to be of high internal consistency. The later study also showed that greater threat-induced N2pc amplitude and earlier peak latency were associated with greater social anxiety level (Reutter et al., 2017).

There are difficulties with using ERP measurements in conjunction with behavioural measures such as reaction time data. At times, ERP-based findings will conflict slightly with results derived from reaction time data. For example,

in the study by Wieser et al. (2018) participants had higher detection rates for threatening but not happy faces. However, a greater N2pc amplitude was elicited for emotional (both threatening and happy) faces. In light of non-convergent evidence, it is difficult to produce a confident interpretation of findings. At times, ERPs are elicited in the absence of behavioural effects (e.g. Kappenman et al., 2014). It is, perhaps, easy to assume that because ERPs are based on neuro-physiological rather than behavioural measurements that ERPs more accurately represent the cognitive events with which they are associated. However, assumptions regarding the cognitive processes reflected in ERP components are based on repeated observations of a specific ERP component during a specific cognitive process measured behaviourally. For example, P2 is an ERP component previously associated with threat bias (Suway et al., 2013). This is based on evidence of greater P2 amplitude or shorter P2 latency for threatening stimuli relative to non-threatening stimuli (e.g. Bar Haim et al., 2005). Woodman (2010) points out that the presentation of different stimuli may activate different neurons, for example, perception of a white square activates different neurons to the perception of a black square (Woodman, 2010). It may also be the case, that a different set of neurons in the visual system react to the presentation of threatening stimuli to those which respond to neutral stimuli. Therefore, a greater P2 amplitude for threat relative to non-threat may be a factor of the location or characteristics (physical, chemical, electrical etc.) of neurons activated during threatening stimulus presentation relative to those activated during non-threatening stimuli and not of attention bias.

Behavioural responses in cognitive tasks are usually observed at the end of a sequence of ERPs. Therefore, early ERP effects may not have any discernible effect on reaction times. This might also explain conflicting ERP and reaction time based evidence.

Nevertheless, using methodologies such as EEG alongside behavioural tasks to illuminate the impact of attentional training can help to improve our understanding of neural processes linked to attention (Torrence & Troup, 2017). Continued research will assist in the unravelling of associations between cognitive and neural attentional mechanisms.

### 6.1.5 Aims

Study 1 revealed no evidence of threat bias reduction following ABM training towards neutral (away from threatening) stimuli. It has been suggested that failure to find this effect might be due to inefficacy of the procedure used to assess attention bias (Macleod & Grafton, 2016) which in study 1 was an emotional dot-probe paradigm. However, others have argued that it is the data used to calculate attention bias (reaction time data) from this task and not the task per se which lacks reliability (Schmukle, 2005). As an adjunct to the analysis of attention bias across assessments, derived from reaction time data, N2pc was measured from EEG data collected during attention bias assessment. The present study procedure was similar to that of Heeren et al. (2015b). Active ABM was delivered across participants. Anodal tDCS or sham tDCS was delivered concurrently with training. Heeren et al. (2015b) reported that reduction in threat bias following ABM training was not apparent based on analysis of reaction

time data and no differences emerged between tDCS conditions. However, eye-tracking data did reveal a reduction in threat bias following ABM training with anodal tDCS but not following ABM training with sham tDCS. In line with these findings and, based on the results from study 1, it was not expected that reaction time data would reveal superior reduction in threat bias for participants receiving anodal tDCS concurrently with ABM training than for participants receiving sham tDCS with ABM training. However, it was predicted that EEG data might reveal modulation of N2pc from pre-to post-ABM training which differed between tDCS groups. This would be indicative of more reduced attentional selection of threatening stimuli (relative to neutral stimuli) for participants who received anodal tDCS compared to participants who received sham tDCS following ABM training towards neutral faces.

It was posited, following study 1, that reduction in anxiety following training (irrespective of ABM group or tES group) might be attributable to an enhancement of attentional control mechanisms which allowed participants to more effectively regulate the emotional impact of threatening stimuli. In order to examine whether attentional control enhancement was implicated in anxiety reduction, the digit span task was administered before and after ABM training as a behavioural measure of attentional control. Previously, the backward digit-span task was used as a measure of attentional control before and after active and control ABM (Heeren et al., 2016).

## 6.2 Method

### 6.2.1 Design

The present study employed a 2 x 2 mixed methods design with one between subjects factor of tDCS (anodal tDCS and sham tDCS). Attentional bias was assessed with reaction time data and using ERP data before and after active ABM training towards neutral faces. The within subjects measure was assessment (pre ABM, post ABM). Trait self-report measures were administered before ABM training and a state measure of anxiety was taken before and after ABM training. The principal dependent variables were attention bias (measured using reaction time data and N2pc) and state anxiety. Attention bias was measured using reaction time data from the assessment bias (emotional dot-probe) task by subtracting reaction time for targets replacing threatening faces from reaction time for neutral faces. The N2pc was also measured from EEG data recorded during attention bias assessment as an additional indicator of attention bias.

### 6.2.2 Participants

Participants were 39 students from the University of Roehampton (27 female), mean age was 24.77 (*SD* = 6.30), age range was 19 to 44. The number of participants recruited was based on previous studies which have used ERPs in their assessment of tES-induced training effects (e.g. 14 participants per condition: Lafontaine et al., 2013). Sample size was also in line with previous studies in which ERP data have been used as a measure of selective attention (e.g. 12 participants per condition: Kiss, Van Velzen & Eimer, 2008).

Data from 15 participants were omitted from analysis due to excessive artifact in the EEG data. EEG data from 24 participants (18 female), mean age 23.63 (*SD* = 4.98), age range 18 to 35 were subject to analysis. Twelve of these participants received anodal tDCS and twelve received sham tDCS. All participants were right-handed and had normal or corrected to normal vision.

Participants were recruited for the study via posters which included the experimenter's email address and on the university's online booking system for research participation. Participants who expressed an interest in taking part were emailed the tES safety screening form. Participants were asked to reply via email indicating whether they answered 'yes' to any of the questions of the form and whether they were left or right handed. Only participants who did not answer 'yes' to any of the tES screen questions and who indicated that they were right handed were invited to participate in the study.

Participants were allocated to 1 of 2 groups: ABM with anodal tDCS or ABM with sham tDCS. Allocation to tES group was double blinded. The experimenter began stimulation by keying a 5-digit code into the tES machine. Each code used had been programmed by the stimulator manufacturer to trigger anodal tDCS stimulation or sham tDCS and stimulation group relating to the code was unknown to the experimenter. Unlike in experiment 1, all participants underwent active ABM training towards neutral stimuli. The primary aim of the study was to examine the modulating effect of tDCS upon ABM training.

### 6.2.3 Ethics

The study was approved by the University of Roehampton ethics committee (approval code PSYC 14/ 157; see Appendix 2). Written informed consent was provided by all participants before participation (Appendix 4). Participants were compensated for their participation with course credits. Participants who did not require course credits were paid £20 for participation.

### 6.2.4 Materials

#### 6.2.4.1 Measures

Participants completed a tES safety screening form and the Edinburgh Handedness Inventory (Appendix 6). Participants were invited to participate if they met the safety criteria outlined in the safety form and if they were right handed. Participants completed the state scale of the State Trait Anxiety Inventory (STAI: Speilberger, 1983; Appendix 7) at the beginning and end of the session. As in study 1 participants also completed the attentional control scale (ACS: Derryberry & Reed, 2002; Appendix 8), the trait scale of the STAI and the Fear of Negative Evaluation scale (FNE; Watson & Friend, 1969; Appendix 9) at the beginning of the session. The depression inventory employed in study 1, the Centre for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977; Appendix 10) was not used in the present study. This was because a number of participants during study 1 had expressed discomfort answering some the more sensitive questions in the CES-D or indicated that they did not feel that certain questions were an appropriate measure of depression. Instead the Beck

Depression Inventory 2 (BDIii; Beck, Steer & Brown, 1996) was used to assess depression.

Beck Depression Inventory 2 (Appendix 14)

This is a 21-item scale, each item containing 4 statements pertaining to a symptom of depression. For example, for the depression criteria "Sadness" participants are asked to select from the responses 0. I do not feel sad, 1. I feel sad much of the time, 2. I feel sad all the time or 3. I am so sad or unhappy that I can't stand it. For each item, a higher rating indicates a higher level of depression. The maximum possible score for the questionnaire is 63. Internal consistency for the questionnaire has been reported as high (α's = .9; Wang & Gorenstein and .84; Kühner et al., 2007) as has test-retest reliability (r's = .73 to .96 Wang & Gorenstein, 2013 and > .75; Kühner et al., 2007. The BDI-ii has also been shown to be highly correlated with STAI ($r = .69$, $p < .001$; Storch et al., 2004). A total score of 0-13 represents minimal range depression, 14-19 suggests mild depression, 20-28 moderate depression and a score between 28 and 63 denotes severe depression.

Penn State Worry Questionnaire (Appendix 14)

Participants also completed the Penn State Worry Questionnaire (PSWQ; Meyer et al., 1990), not previously used in study 1. The PSWQ is a 16-item inventory which assesses worry on a scale of 1 to 5 with 1 representing 'Not at all typical of me' and 5 'Very typical of me'. Example statements include items 6 "When I am under pressure I worry a lot" and item 12 "I have been a worrier all my life".

Items 1, 3, 8, 10 and 11 are positively worded and therefore reverse scored. The PSWQ has demonstrated strong internal consistency ($a$ =.95) and test-retest reliability ($r$ = .93, $p$ < .001), (Meyer et al., 1990; Stöber, 1998). The authors of the PSWQ reported that it correlated relatively strongly with the STAI-trait ($r$ = .64, $p$ < .001) and moderately with the STAI-state ($r$ = .49, $p$ < .001) and BDI ($r$ = .36, $p$ < .001), (Meyer et al., 1990).

Liebowitz Social Anxiety Scale (Appendix 16)

The Liebowitz social anxiety scale (LSAS; Leibowitz, 1987) was also administered. LSAS assesses individuals on 24 situations likely to elicit social anxiety. For each situation 2 responses are required. The first asks participants to rate on a scale of 0 to 3 how strongly they experience fear or anxiety in the anxiety provoking situation e.g. Telephoning in public with 0 representing None (no fear/anxiety) and 3 representing Severe. For the same situation participants must then indicate how regularly they avoid performing that action or entering that situation on a scale of 0 (Never 0%) to 3 (Usually 67-100%). Studies examining the psychometric properties of the LSAS have yielded alphas of .94 (Fresco et al., 2001) to .96 (Heimberg et al., 1999) demonstrating strong internal consistency. Test-retest reliability has been reported as .81 (Santos et al., 2013). Moderate convergent validity has been reported with correlation with the FNE scale of $r$ = .49, $p$ < .003 (Heimberg et al., 1999) and with the BDI of $r$ = .43, $p$ < .05 (Fresco et al., 2001).

After ABM training participants completed a tES intensity scale (Appendix 11) in which they indicated the intensity with which they experienced physiological

sensations such as headache and aching scalp during tDCS application. They also completed the Experimental Condition (Appendix 12) questionnaire which asked participants to indicate whether they felt they had received anodal tDCS or sham tDCS. These measures were as described in the study 1 report.

#### 6.2.4.2 Stimuli

The stimuli used were identical to those used in experiment 1.

ABM training and attention bias assessment were based on the same task as study 1 except that response targets and response keys were altered as were the positioning and size of the face stimuli (the rationale for these changes is outlined below).

#### 6.2.4.3 Attention Bias Assessment

At the beginning of each trial, a fixation cross appeared in the middle of the screen for 500ms followed by two faces of the same identity, one neutral and one threatening for 500ms. The two photographs of the same individual were presented simultaneously in their neutral-angry pairs and were aligned horizontally. The N2pc component is an EEG measure of cerebral response to visual stimuli contralateral to horizontally positioned posterior electrodes (e.g. P7 P8; Holmes, Bradley, Kragh Nielsen & Mogg, 2009; PO7 and PO8: Kiss, Van Velzen & Eimer, 2008; PO3 and PO4; Hilimire et al., 2011). Electrodes on the right of the scalp measure response to stimuli in the left visual hemifield and electrodes on the left of the scalp measure response to stimuli in the right visual

hemifield (Woodman et al., 2009). It is for this for this reason that stimuli and targets were horizontally positioned for the present study and not vertically positioned as per study 1. Each face image subtended a visual angle of 11.42 º by 15.94º. The photographs were trimmed to remove the white background which might draw excess attention to the images.

After 500ms the faces were replaced by an arrow pointing upwards (↑) or an arrow pointing downwards (↓) appeared in the position previously occupied by either the left or right-hand stimulus. Participants were asked to respond by pressing key 1 on a computer keypad for an upward pointing arrow or key 3 for a downward pointing arrow using the index and ring fingers of the right hand respectively. Targets remained on screen until response or until 2000ms elapsed. This change in response protocol from study 1 (in which participants were required to use the same finger of each hand to press p or q on the computer keyboard) was made to avoid response bias i.e. faster key pressing by the right (dominant) hand than the left. Participants were instructed to respond to the target arrow as quickly and accurately as possible.

During attention bias assessment, the target replaced the neutral cue in 50% of trials. Attention bias assessment comprised 2 blocks of 96 trials which lasted approximately 10 minutes. Figure 6.1 illustrates an example trial.

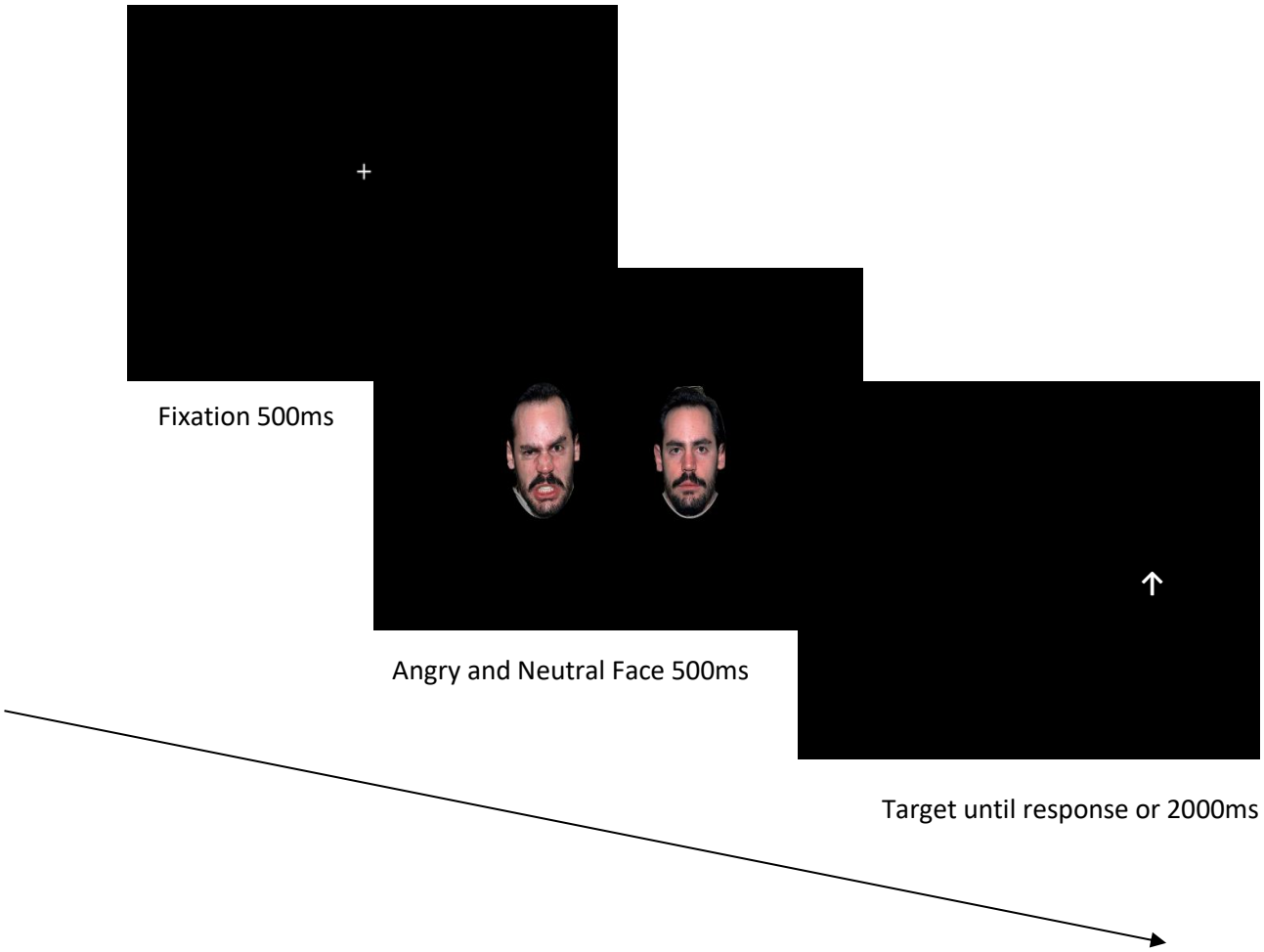



*Figure 6.1*. Paradigm used for attention bias assessment and ABM training. During attention bias assessment the target replaced the neutral cue in 50% of trials. During ABM training, the probe replaced the neutral cue in 95% of trials.

Face identity, target symbol (↑ or ↓) and target location (left or right) were randomised. Each face identity had an equal probability of being presented as did each target symbol. There was an equal chance of a target appearing in the each of the target locations.

#### 6.2.4.4 Attention Bias Modification

In the present study all participants undertook active ABM training. There was no control ABM group. The paradigm used for ABM training was the same as that employed during attention bias assessment with the exception that the target letter appeared in the position of the neutral probe in 95% of trials. ABM training lasted approximately 30 minutes and consisted of 6 blocks of 96 trials with a short break between each block.

#### 6.2.4.5 Digit Span Task

A computerised digit span task was used as a measure of attentional control (see figure 6.2). The task was programmed using E-Prime software (Schneider, Eschman & Zuccolotto, 2002). The task consisted of 6 levels and each level comprised 5 trials. In each trial participants were played a string of numbers through headphones and were required to type the numbers in the order in which they had been played. In level 1 participants were presented with strings of 3 numbers in each of the 5 trials. At each level, the length of the number string increased by 1 until the number string reached a maximum of 8 digits. If, however, the participant answered more than 3 trials in a level incorrectly, the number of digits at the proceeding level was reduced by 1. For example, if, when presented with 7 number digit strings the participant answered 4 out of the 5 trials incorrectly, the following level would contain 6 string digit strings (see figure 6.2). For each level, participants were scored according to the length of the number string and the number of trials performed correctly (in level 1 where 3 number strings were presented, if participants answered all 5

trials correctly they would receive 15 points). If the participant reached the maximum string length possible without errors therefore they would score 165 points (3 x 5) + (4 x 5) + (5 x 5) + (6 x 5) + (7 x 5) + (8 x 5). A higher score would indicate better attentional control.

Example structure of Digit Span Task

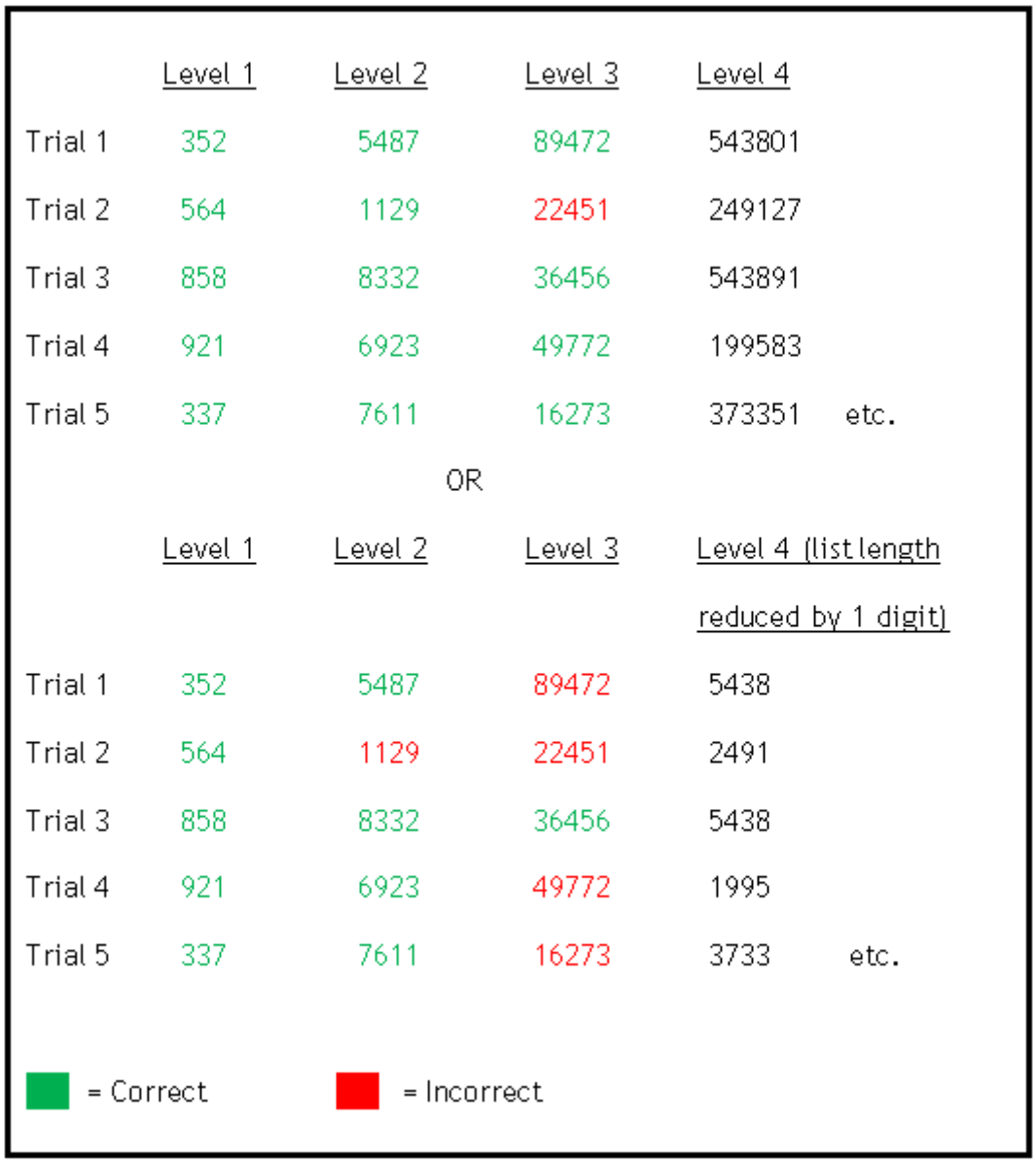



Figure 6.2. Example stimuli from Digit Span task. TOP: No adjustment in level 4 for 1 incorrect response at level 3. BOTTOM : Adjustment in level 4 list length due to > 3 incorrect responses in level 3

### 6.2.5 TDCS

Participants received either anodal tDCS or sham tDCS. TDCS was administered through a DC-Stimulator Plus (neuroConn©). Two electrodes with an area of 5cm x 7cm (35cm$^2$), each placed inside a saline soaked sponge were attached to the scalp and held in place using a rubber headband. The anodal electrode was positioned over the left dorsolateral prefrontal cortex (lDLPFC), F3 based on the 10-20 EEG system (Clarke et al., 2014). The cathode was placed over right supraorbital ridge (above the right eyebrow). Current was applied at an amplitude of 1.5mA. Stimulation lasted for 20 minutes at the beginning of a 30-minute ABM training period. The current was ramped up and down for 20 seconds at the beginning and end of active stimulation. In the sham TES group, the current was ramped up for 20 seconds and then stopped.

### 6.2.6 EEG Data Collection

Continuous EEG data were collected using the Biosemi Active Two EEG recording system (Biosemi B.V., Amsterdam, the Netherlands). Scalp EEG was recorded from 32 electrodes mounted in an elasticated head-cap according to the 10-20 system. The common mode sense (CMS) electrode was positioned at site C1 and the driven right leg (DRL) electrode was placed at site C2. Horizontal and vertical electrooculographs (EOGs) were recorded for the detection of eye blinks and eye movements using four bipolar electrodes. Vertical EOG was measured using electrodes above and below the left eye and horizontal EOG was recorded from electrodes positioned on the outer canthus of each eye. Two additional electrodes were applied (one on each earlobe) for offline referencing. All

electrodes were bandpass filtered online at .01 to 100 Hz. The data were bandpass filtered offline with cut off frequencies of 1-30Hz. DC offsets at critical electrodes (P3, P4, P7, P8, PO3, PO4, O1, O2) were kept within a +/- 10mV range. EEG and EOG were digitised online at 2048Hz and down-sampled following recording to 250Hz to reduce later processing time.

### 6.2.7 Procedure

Upon attending the laboratory, participants were informed of the experimental schedule and then provided with a consent form to read and sign. All participants completed the ACS, FNE, BDIii, PSWQ, LSAS and STAI. Participants were then asked to mount a set of headphones in order to undertake the digit span task. Participants performed the task which lasted approximately 10 minutes.

Participants were then fitted with the EEG headcap, a process which took approximately 20 minutes. Electrode holders were filled with an electrolyte gel (saline based Signa gel) using a syringe. The electrodes were then mounted into the holders. The skin around the eyes and the earlobes were wiped with an abrasive electrolyte gel (Nuprep EEG & ECG Skin Prep Gel) and then cleansed using alcohol to improve contact by the electrodes recording eye movement or acting as offline reference electrodes. Participants were instructed to inform the experimenter if at any point during the procedure they experienced discomfort as a result of the gel or electrodes. The experimenter then began recording EEG data. With the computer monitor at approximately 50cm from

the participant and the keypad within effortless reach, participants commenced the attention bias assessment lasting approximately 10 minutes.

Participants then washed and dried their hair to remove any remaining electrolyte gel which might impact current flow and intensity during the tDCS procedure. Once the hair was dry, participants were fitted with the tDCS montage. Allocation to tDCS group was randomised and double blind. A list was provided to the experimenter which contained 5-digit codes to generate either anodal tDCS or sham tDCS. These were taken from the NeuroConn DC-Stimulator Plus manual. Twenty codes relating to each stimulation group had been selected and randomised within one list by a member of the experimenter's supervisory team. The first participant to commence the study was allocated the first code on the list. Each time a new participant attended the study they were allocated the next code on the list. The experimenter began stimulation by keying the 5-digit code into the tES machine. Participants received anodal tDCS or sham tDCS for 20 minutes at the beginning of a 30-minute ABM training period comprising 6 blocks of 96 trials of ABM training.

After ABM training, participants washed and dried their hair to remove saline solution from the tDCS application. This took approximately 15 minutes. They were fitted with the EEG headcap and completed a second attention bias assessment while EEG recording was taken. Fitting of the headcap and completion of attention bias assessment took around 30 minutes in total. The EEG headcap was removed and participants washed and dried their hair before continuing. Participants once again completed the SAS and filled in the tES intensity questionnaire and experimental procedure questionnaire. They then

completed the digit span task again. Finally, participants were allocated their credits or paid £20 for taking part and debriefed. The complete experimental procedure is outlined in figure 6.3.

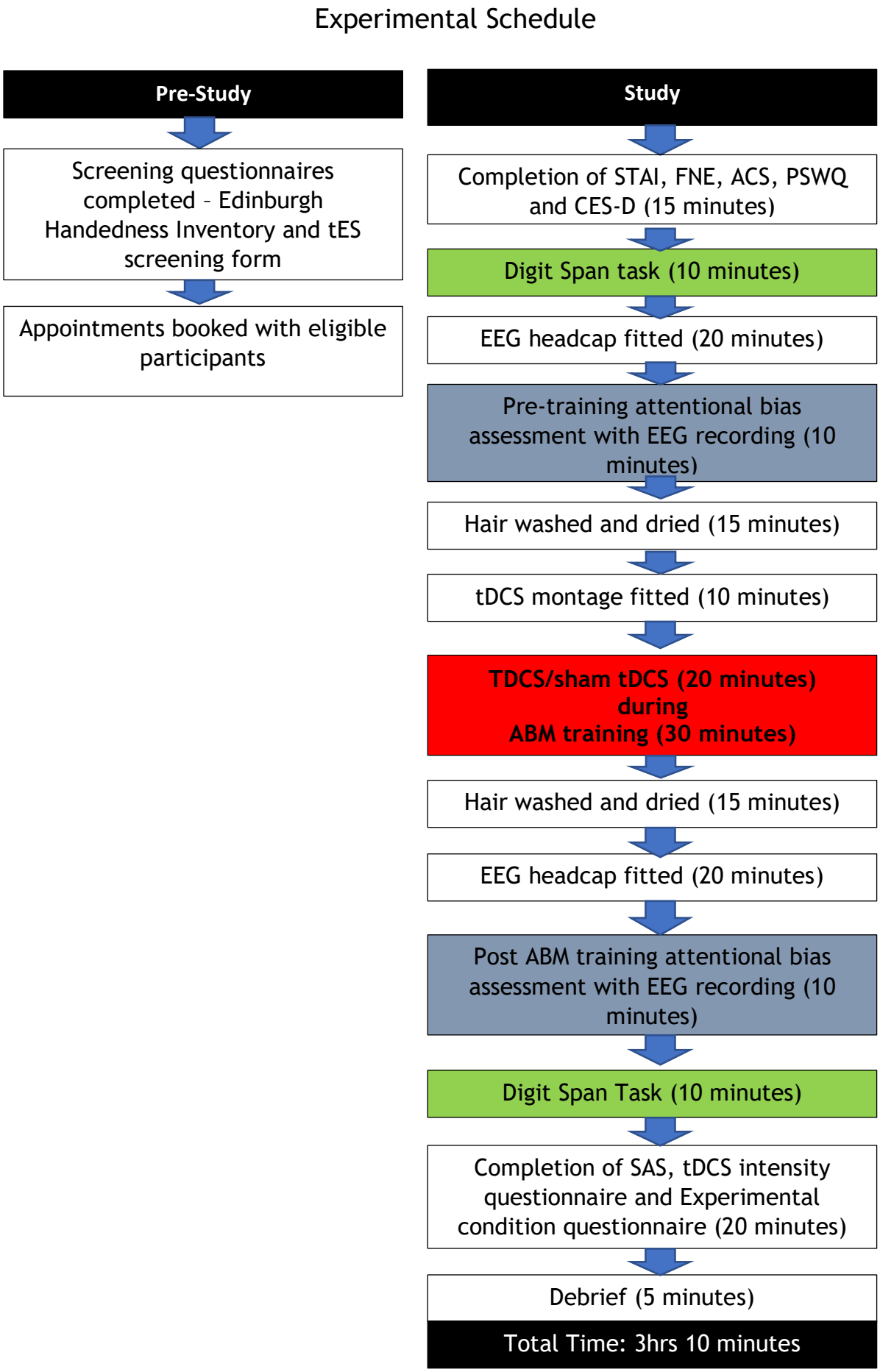



*Figure 6.3.* Experimental procedure: Pre-study and outline of study

### 6.2.8 Data Preparation

#### 6.2.8.1 Behavioural Data

Data from incorrect trials were removed prior to analysis. Mean accuracy across assessments was 96.29% (*SD* = 2.42). Prior to analysis, reaction times below 200ms were also removed. Outlying reaction times from the modified dot-probe task which were more than 2.5 standard deviations from each participant's mean reaction time were excluded as per study 1. This led to the rejection of a further 2.3% of the total number of trials. Attention bias was calculated by subtracting the mean response time to threatening faces from mean response time to neutral faces for each participant. Greater bias towards threatening faces compared to neutral faces was therefore represented by a positive score.

#### 6.2.8.2 EEG Data

EEG and EOG were digitised online at 2048Hz and down-sampled following recording to 250Hz to reduce later processing time. A digital low-pass filter of 30Hz was applied to the data collected and electrodes were referenced to an averaged signal from the left and right earlobe (A1 and A2). Data were segmented offline to 600ms epochs relative to a 100ms pre-stimulus (face cue) baseline extending to 500ms post- stimulus. Post-stimulus data were baseline corrected relative to the 100ms prior to stimulus presentation.

Data from 15 participants were omitted from analysis due to excessive noise. Data from the remaining 24 participants were subject to analysis. To avoid

contamination of data by ocular artifacts, trials containing HEOGs exceeding +/-30μv were rejected as were trials in which VEOGs, blinks or other artifacts exceeding +/-60μv. This resulted in a mean rejection of 16% of trials across the 24 participants whose EEG data were subject to analysis. ERP analysis was focused on the N2pc component elicited in response to the presentation of visual stimuli. Visual inspection of grand average waveforms identified the optimal source of this component as P7 for the left posterior cerebral hemisphere and P8 for the right hemisphere (as per Holmes et al., 2014). Grand average ERPs were calculated for combinations of tDCS (anodal vs sham), laterality of face stimuli relative to position of electrodes (ipsilateral vs contralateral) and assessment (Pre-ABM, Post-ABM). N2pc onset was identified as the time-point at which the lateralised posterior ERPs differed. This was determined using a 'neuron-anti-neuron' analysis (Fuggetta, Bennett & Duke, 2015; Purcell et al., 2013). For every 4 milliseconds post stimulus onset a t-test was carried out to compare ERP amplitude at P7 and P8. Selection time in the present study was defined as the point at which the waveforms were significantly different at a p value of <.001 followed by 10 consecutive t-tests with an outcome of $p < .005$. This represented a period of 168ms to 212ms post stimulus onset.

### 6.2.9 Data Analyses

Data Analysis was performed using IBM SPSS Statistics, Version 22. The main analysis assessing the effect of active ABM with anodal tDCS and control ABM with anodal tDCS on attention bias and on state anxiety was performed using ANOVAs with ABM as the between participants factor and assessment session (pre-ABM training, post-ABM training) as the within participants factor. In order

to investigate the role of pre-existing attention bias, trait anxiety and attentional control on ABM with tES outcomes the ANOVAs were replicated on data from participants with pre-existing threat bias and pre-existing neutral bias, data from participants with pre-existing high trait anxiety and participants with pre-existing low trait anxiety and on data from participants with pre-existing high attentional control and pre-existing low attentional control. Participants were categorised as high or low in trait anxiety/attentional control based on a median split on baseline scores. ANCOVAs were also conducted with ABM as the between participants factor, assessment as the within participants factor and pre-existing attention bias, pre-existing trait anxiety and pre-existing attentional control as covariates.

A second analysis was conducted on data from a subset of participants whose EEG data were suitable for analysis. Mixed ANOVAs were carried out with ABM (active ABM, control ABM) as the between participants factor and assessment (pre-ABM training, post ABM training) as the within participants factor. This analysis was conducted on attention bias and state anxiety data. N2pc was calculated from EEG data and subject to the same analysis.

### 6.2.10 Reporting of Data

Of the 39 participants recruited, EEG data from 15 participants contained excessive ocular artefact or contamination and therefore only EEG data from the remaining 24 participants were subject to analysis (12 participants received anodal tDCS and 12 participants received sham tDCS). It was believed that the excessive artefact arose because of a technical issue (faulty electrodes) rather

than anomalous cortical activity. It was therefore assumed that behavioural and self-report data from all 39 participants would still be suitable for analysis. As it was not possible to confirm the source of the excessive artefact, two separate analyses were conducted. For the first part of the results section, analysis of behavioural and self-report data from all 39 participants will be reported. For the latter part of the section, behavioural and self-report data from only the 24 participants whose EEG data were subject to analyses will be reported and this will be followed by reporting of the EEG analysis.

## 6.2.11 Baseline Characteristics

### 6.2.11.1 Baseline Scores Across Self-Report Measures

Table 6.1 shows for each tDCS group the mean and standard deviation score at baseline for each self-report measure.

Table 6.1:

*Mean (SD) score in each self-report measure per tES group*

| | Active ABM/anodal tDCS | | Active ABM/sham tDCS | |
|---|---|---|---|---|
| | M | SD | M | SD |
| STAI-trait | 40.05 | 11.29 | 44.85 | 10.86 |
| ACS | 52.95 | 8.80 | 49.45 | 10.65 |
| BDI-ii | 9.84 | 7.26 | 9.60 | 8.76 |
| FNE | 12.68 | 8.06 | 14.85 | 8.05 |
| LSAS | 43.11 | 24.58 | 56.25 | 24.15 |
| PSWQ | 59.20 | 15.10 | 59.20 | 15.16 |

### 6.2.11.2 State and Trait Anxiety across Experimental Groups by Gender

Table 6.2 shows the mean and standard deviation self-report scores at baseline (before ABM training) per gender for each tDCS group.

Table 6.2:

*Baseline mean (standard deviation) self-report scores by gender and across experimental groups*

| | | n | SAS | TAS | BDIii | FNE | PSWQ | ACS | LSAS |
|---|---|---|---|---|---|---|---|---|---|
| Females | Anodal tDCS | 10 | 33.20 (9.09) | 43.40 (12.60) | 11.10 (9.05) | 14.90 (8.84) | 56.90 (14.99) | 49.60 (5.76) | 43.30 (26.09) |
| | Sham tDCS | 17 | 30.65 (6.25) | 45.71 (11.38) | 11.12 (8.63) | 15.24 (8.04) | 59.94 (15.62) | 48.41 (10.93) | 56.06 (22.88) |
| Males | Anodal tDCS | 9 | 30.11 (5.99) | 36.33 (8.87) | 8.44 (4.72) | 10.22 (6.74) | 43.11 (12.16) | 56.67 (10.36) | 36.13 (22.31) |
| | Sham tDCS | 3 | 32.00 (3.20) | 40.00 (6.56) | 1.00 (1.73) | 12.67 (9.50) | 55.00 (14.11) | 55.33 (7.77) | 54.00 (35.59) |

State Anxiety

Baseline state anxiety did not differ between tDCS groups (*ts* < .40, *ps* > .69). One sample t-tests revealed that mean baseline state anxiety score for females who received anodal tDCS (*M* = 33.20, *SD* = 9.09) did not differ significantly from mean normative score reported by Spielberger et al. (1983) for female undergraduate students (*M* = 38.76, *SD* = 11.95), *(t = 1.93, p = .09).* However, mean baseline state anxiety score for females who received sham tDCS (*M* = 30.65, *SD* = 6.25) was significantly lower than the normative mean, *t*(16) = 5.35, *p* < .001. Males who received anodal tDCS had significantly lower state anxiety at

baseline (*M* = 30.11, *SD* = 5.99), than the normative mean state anxiety score for males reported by Speilberger et al. (1983; *M* = 36.47, *SD* = 10.02), $t(8) = 3.19$, $p = .013$. For males who received sham tDCS, baseline state anxiety did not differ significantly from the normative mean state anxiety score ($t = 1.49$, $p = .28$).

Trait Anxiety

There was no significant difference in baseline trait anxiety between the anodal tDCS group and the sham tDCS group (*ts* < 1.35, *ps* > .18). One sample t-tests revealed that mean baseline trait anxiety for females who received anodal tDCS (*M* = 43.40, *SD* = 12.60) and females who received sham tDCS (*M* = 45.71, *SD* = 11.38) did not differ significantly from the normative mean for female undergraduate students reported by Spielberger et al. (1983; *M* = 40.40, *SD* = 10.15), (*t*s < 1.92, *ps* > .07). Baseline trait anxiety for males who received anodal tDCS (*M* = 36.33, *SD* = 8.87) and for males who received sham tDCS (*M* = 46.50, *SD* = 28.99) did not differ significantly from the normative mean (*M* = 40.00, *SD* = 6.56), (*ts* < .67, *ps* > .15).

#### 6.2.11.3 Correlations Between State Anxiety Scores

Data from each administration of the state anxiety scale of the STAI (Pre-ABM, Post ABM) were subject to a Pearson Product Moment Correlation analysis. The correlation was significant, $r(39) = .70$, $p < .001$ suggesting strong test-retest reliability.

#### 6.2.11.4 Correlation Between State Anxiety and Trait Anxiety

In previous literature, the correlations reported between state and trait anxiety have been significant and moderately strong (.65 for males and .59 for females for college students; Speilberger et al., 1983). In the present study there was a moderate correlation between trait anxiety and state anxiety before ABM, $r(39) = .32$, $p = .046$ and a slightly stronger but moderate correlation between trait anxiety and state anxiety after ABM, $r(39) = .41$, $p = .01$ (see table 6.3).

Table 6.3:

*Bivariate correlations between baseline trait anxiety scale and state anxiety scale (SAS) scores pre-ABM training and post ABM training*

| | SAS Assessment 1 | SAS Assessment 2 |
|---|---|---|
| Baseline Trait Anxiety | **.322*** | **.406*** |

* $p < .05$

## 6.3 Results

### 6.3.1 Analyses of Variance Across all Participants

The following analyses of behavioural and self-report data is from all 39 participants. Although data from 15 participants were omitted from EEG analysis, this was due to contamination which was isolated to EEG data. Based on accuracy levels (see above) and reactions times across all 39 participants there is no suggestion that the contamination was indicative of (or affected) performance in the attention bias assessment task. Therefore, conclusions

regarding behavioural outcomes of the procedure employed in study 2 (attend-neutral ABM with anodal or sham tDCS) will be based on analysis of data from all 39 participants.

#### 6.3.1.1 Digit Span Score (All Participants)

A 2 x 2 ANOVA with assessment (pre-ABM, post ABM) as the within subjects factor and tDCS (anodal tDCS, sham tDCS) as the between subjects factor was performed on scores from the digit span task. There were no significant main effects or interaction effects (*F*s < 1.35, *p*s > .25) indicating that there was no change in digit span score between assessments and that scores were not significantly modulated by tDCS.

Figure 6.4 shows the mean digit span scores before and after ABM training for each tDCS group and across all participants.

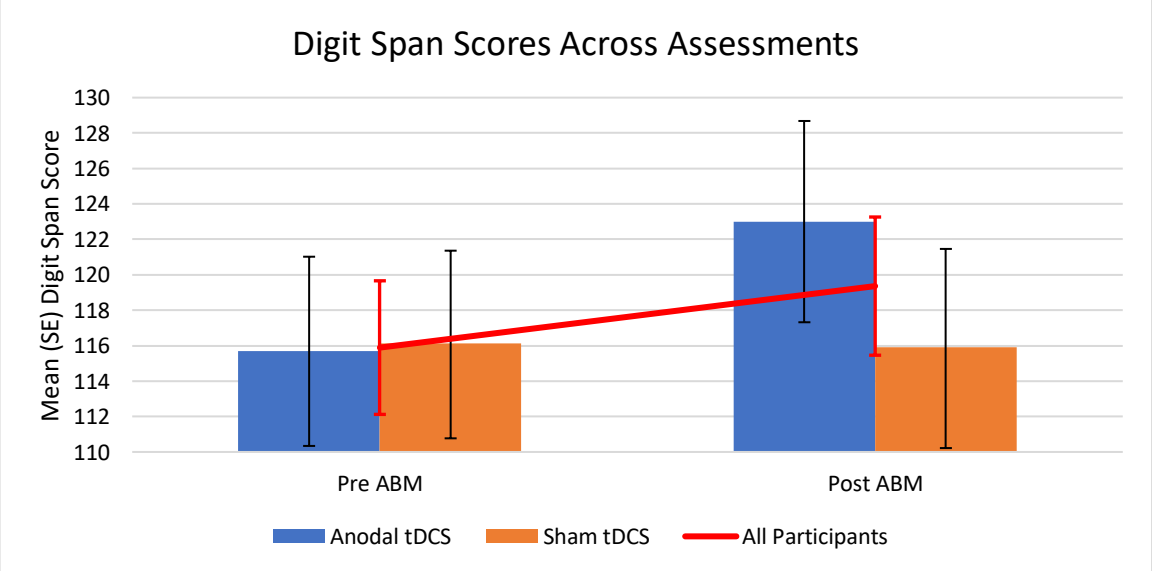



*Figure 6.4*. Mean (SE) digit span score across assessments for each tES group and for all participants

#### 6.3.1.2 Attention Bias (All Participants)

A 2 x 2 mixed ANOVA was conducted on the attention bias data with the between subjects factor of tDCS (anodal tDCS, sham tDCS) and a within subjects factor of assessment (pre ABM, post ABM).

For attention bias there was no main effect of assessment ($F$ = .18, $p$ = .68) indicating that attentional bias did not differ between attention bias assessment before ABM training and attention bias assessment after ABM training. The interaction between assessment and tDCS was also not significant ($F$ = .82, $p$ = .37) and there was no main effect of tDCS ($F$ = .02, $p$ = .89).

Figure 6.5 depicts attention bias across assessments for each experimental group and mean attention bias for all participants. Positive values represent threat bias and negative values represent neutral bias.

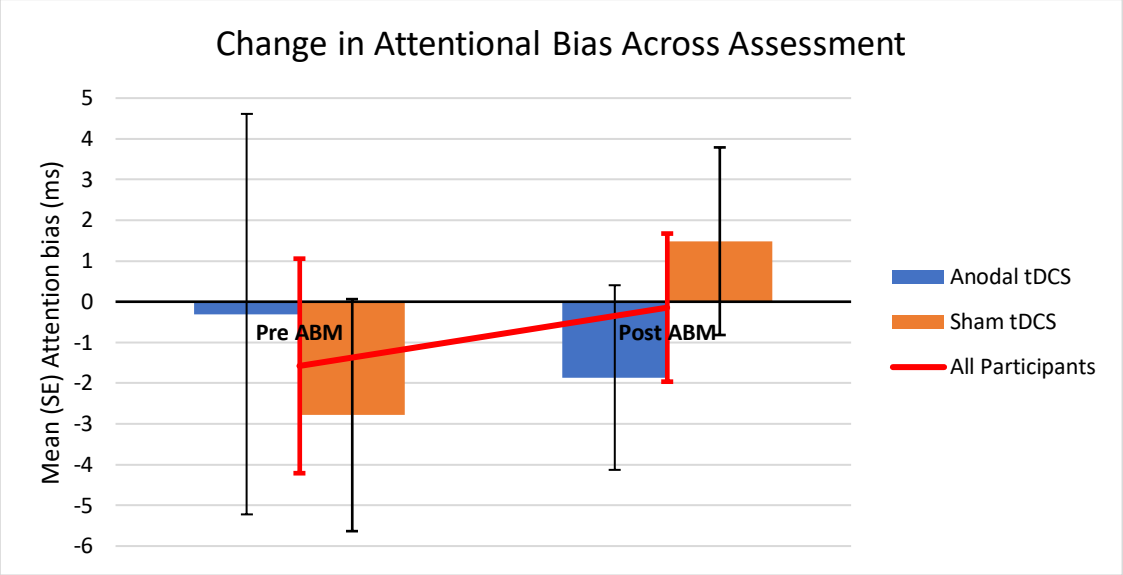



*Figure 6.5*. Mean (SE) attention bias across assessments for each tES group and for all participants. A positive attention bias score represents attentional bias towards threat

#### 6.3.1.3 State Anxiety (All Participants)

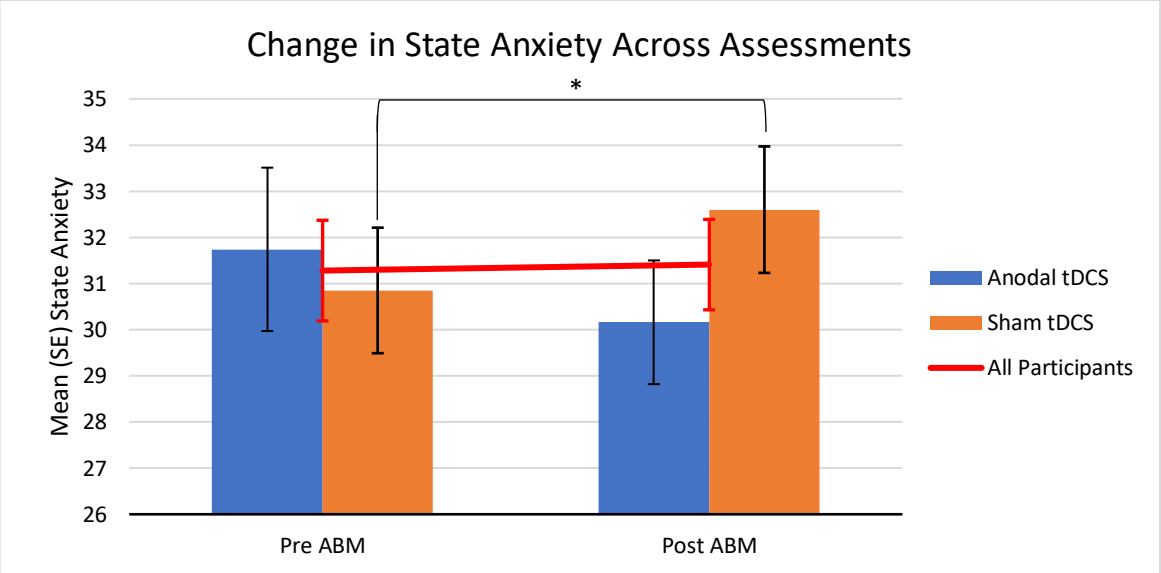
Replicating the threat bias ANOVA above, a 2 x 2 mixed ANOVA was conducted on state anxiety data with the between subjects factor of tDCS (anodal tDCS, sham tDCS) and a within subjects factor of assessment (pre ABM, post ABM).

The interaction between assessment and tDCS group was significant, $F(1,37) = 4.71$, $p = .036$, ($\eta_p^2 = .11$; observed power = .56). For each tDCS group, a follow-up paired samples t-test examined change in state anxiety across assessments. Results were Bonferroni corrected for multiple comparisons (significant if 2*p < .05). State anxiety was significantly increased for the sham tDCS group following ABM training ($M = 32.60$, $SD = 1.37$) compared to before ABM training ($M = 30.85$, $SD = 1.77$), $t(19) = 2.31$, $p = .032$. For the anodal tDCS group, there was no significant change in state anxiety between assessments ($t = 1.16$, $p = .26$). Independent t-tests also examined whether state anxiety

differed significantly between tDCS groups before ABM training and after ABM training. Results were Bonferroni corrected for multiple comparisons (significant if 2*p < .05). There was no significant difference in state anxiety between the two tDCS groups either before ABM training (*t*s = .40, *p*s = 1.38) or after ABM training (*t*s = 1.26, *p*s = .44).

Neither the main effect of assessment (*F* = .012, *p* = .91) nor the main effect of tDCS (*F* = .16, *p* = .69) were significant.

Figure 6.6 depicts state anxiety across assessments for each experimental group (anodal tDCS and sham tDCS) and change in state anxiety for all participants.




* *p* < .05

*Figure* 6.6. Mean (SE) state anxiety across assessments for each tDCS group and for all participants

### 6.3.2 Analyses of Variance for Participants with Pre-existing Threat and Neutral Attention Bias

Analyses of variance were repeated separately for participants with threat bias at baseline and participants with attention bias towards neutral faces at baseline. This was based upon a previous finding that the capacity of ABM for manipulating attention bias in a particular direction has been shown to be restricted to individuals with an existing attention bias in the opposite direction (e.g. O'Toole & Dennis, 2012).

Table 6.4 shows the number of participants in each experimental group with a pre-existing threat bias and the number of participants in each experimental group with a pre-existing neutral bias and mean (SD) attention bias and state anxiety score for each attention bias group.

Table 6.4:

*Number of participants in each experimental group and mean attention bias and state anxiety scores for participants with an attentional bias towards threat at baseline and participants with attentional bias towards neutral at baseline*

| | Baseline Measures: | Threat bias | Neutral bias |
|---|---|---|---|
| Anodal tDCS | N | 9 | 10 |
| | Mean (SD) Digit Span Score | 118.11 (19.98) | 113.50 (26.12) |
| | Mean (SD) Attention Bias (ms) | 18.15 (11.76) | -16.91 (12.19) |
| | Mean (SD) State Anxiety | 33.44 (6.80) | 30.20 (8.54) |
| Sham tDCS | N | 7 | 13 |
| | Mean (SD) Digit Span Score | 115.14 (31.74) | 116.67 (20.30) |
| | Mean (SD) Attention Bias (ms) | 8.76 (6.91) | -9.00 (4.39) |
| | Mean (SD) State Anxiety | 31.57 (6.16) | 30.46 (6.13) |

#### 6.3.2.1 Digit Span Score (Participants with Pre-existing Threat Bias)

A 2 x 2 ANOVA with the between subjects factor of tDCS (anodal tDCS, sham tDCS) and the within participants factor of assessment (pre ABM, post ABM) was conducted on digit span data from participants with pre-existing threat bias. There were no significant main effects or interactions (*F*s < 1.14, *p*s > .30).

Figure 6.7 shows digit span score at each assessment for participants with a pre-existing bias towards threat in each tDCS group and across all participants with pre-existing threat bias.

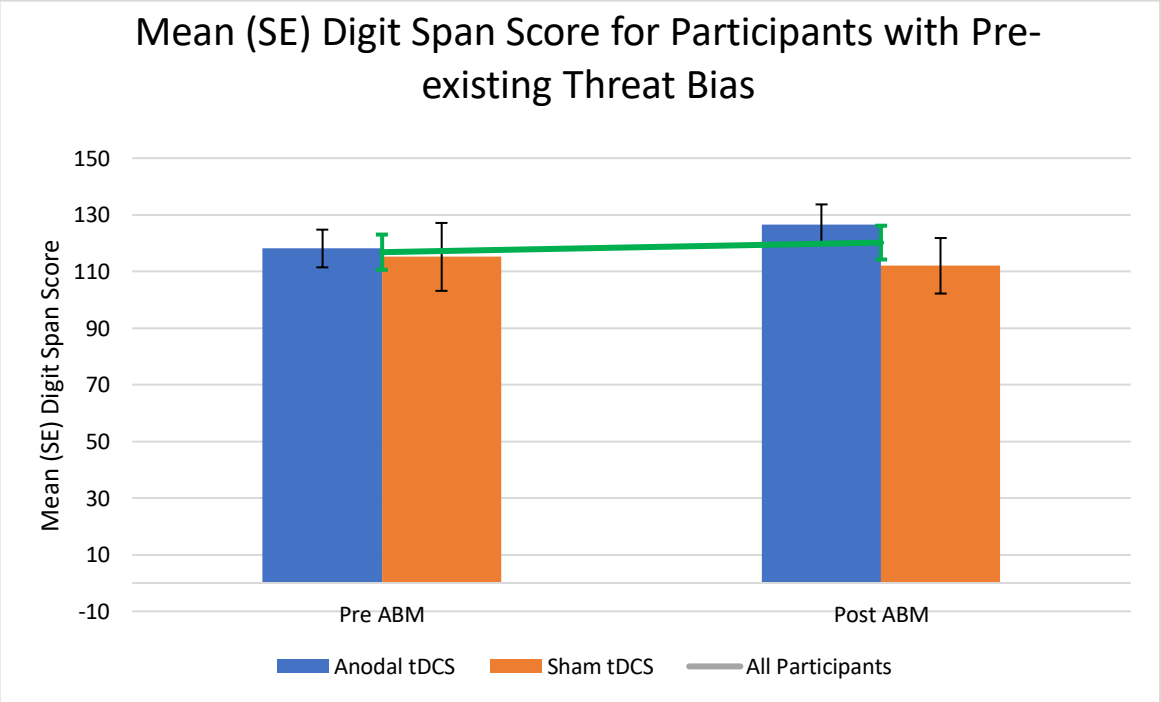



*Figure 6.7*. Mean (SE) digit span score across assessments for participants with pre-existing attention bias towards threat in each tDCS group and all pre-existing threat bias participants

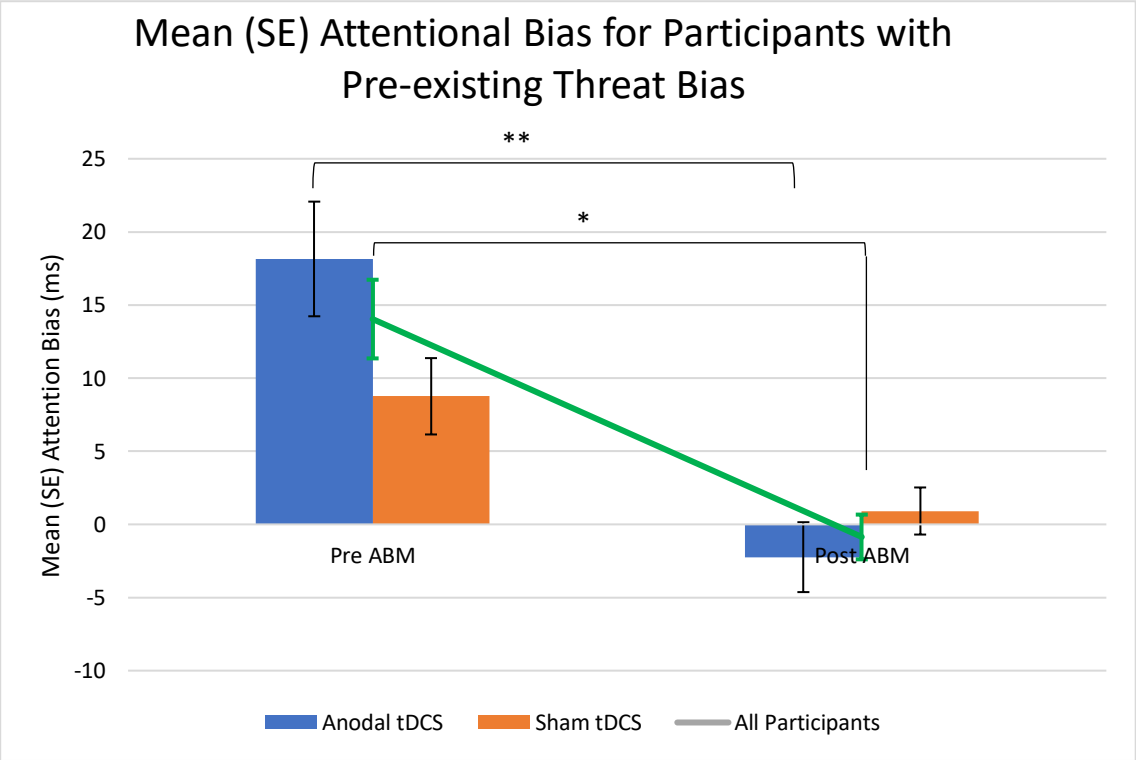
#### 6.3.2.2 Attention Bias (Participants with Pre-existing Threat Bias)

A 2 x 2 ANOVA with assessment (pre ABM, post ABM) as the within subjects factor and tDCS (anodal tDCS, sham tDCS) as the between subjects factor was conducted on data related to participants with pre-existing threat bias. For participants with pre-existing threat bias there was a significant effect of assessment, $F(1,14) = 22.58$, $p < .001$, ($\eta_p^2 = .62$; *observed power* = .99). Attention bias towards threat was significantly reduced following ABM training ($M = -.86$, $SD = 6.10$) compared to before ABM training ($M = 14.04$, $SD = 10.78$). There was also a near significant assessment x tDCS interaction, $F(1,14) = 4.46$, $p = .053$, ($\eta_p^2 = .24$; *observed power* = .50). For each tDCS group, a paired samples t-test examined change in attention bias across assessments. Results were Bonferroni corrected for multiple comparisons (significant if 2*p < .05). Threat bias for participants who received anodal tDCS was significantly reduced following ABM training ($M = -2.24$, $SD = 7.16$) compared to before ABM training ($M = 18.15$, $SD = 11.76$), $t(8) = 4.40$, $p = .004$. For participants who received sham tDCS, change in attention bias was not significant ($t = 2.54$, $p = .088$).

Independent t-tests were conducted to assess the effect of tDCS group on attention bias before ABM training and following ABM training for participants with pre-existing threat bias. Results were Bonferroni corrected for multiple comparisons (significant if 2*p < .05). For participants with a pre-existing threat bias there was no significant difference in attentional bias between tDCS groups (anodal tDCS, sham tDCS) before ABM ($t = 1.87$, $p = .16$) or after ABM ($t = 1.03$, $p = .64$).

The main effect of tDCS was non-significant ($F$ = 1.14, $p$ = .30).

Figure 6.8 shows attention bias before and after ABM for participants with pre-existing threat bias in each tDCS group and across all participants. Positive values represent threat bias and negative values represent neutral bias.




* $p$ < .05

** $p$ < .001

*Figure 6.8*. Mean (SE) attention bias across assessments for participants with pre-existing attention bias towards threat in each tDCS group and for all pre-existing threat bias participants

### 6.3.2.3 State Anxiety (Participants with Pre-existing Threat Bias)

The ANOVA conducted above on attention bias data was replicated on state anxiety data. For participants with baseline threat bias there were no main effects or interaction effects (*F*s < 2.07, *p*s > .17) indicating that state anxiety did not change between assessments or as a factor of tDCS stimulation.

Figure 6.9 shows mean and standard error state anxiety for participants with pre-existing threat bias in both tDCS groups (and for all participants) before and after ABM training.

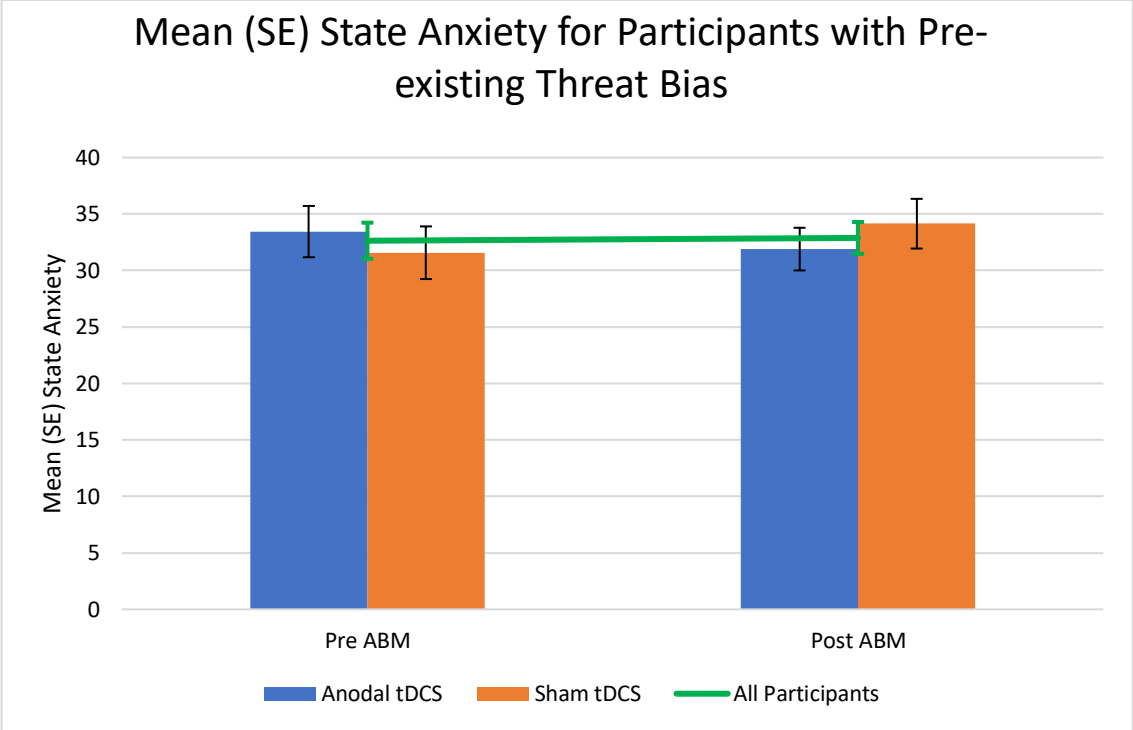



*Figure 6.9*. Mean (SE) state anxiety across assessments for participants with pre-existing attention bias towards threat in each tDCS group and all pre-existing threat bias participants

### 6.3.2.4 Digit Span Score (Participants with Pre-existing Neutral Bias)

A 2 x 2 ANOVA with the between subjects factor of tDCS (anodal tDCS, sham tDCS) and the within participants factor of assessment (pre ABM, post ABM) was conducted on digit span data for participants with a pre-existing attention neutral bias. There were no significant main effects or interactions (*F*s < .61, *p*s > .44).

Figure 6.10 shows digit span score at each assessment for participants in each tDCS group and for all participants with a pre-existing neutral bias.

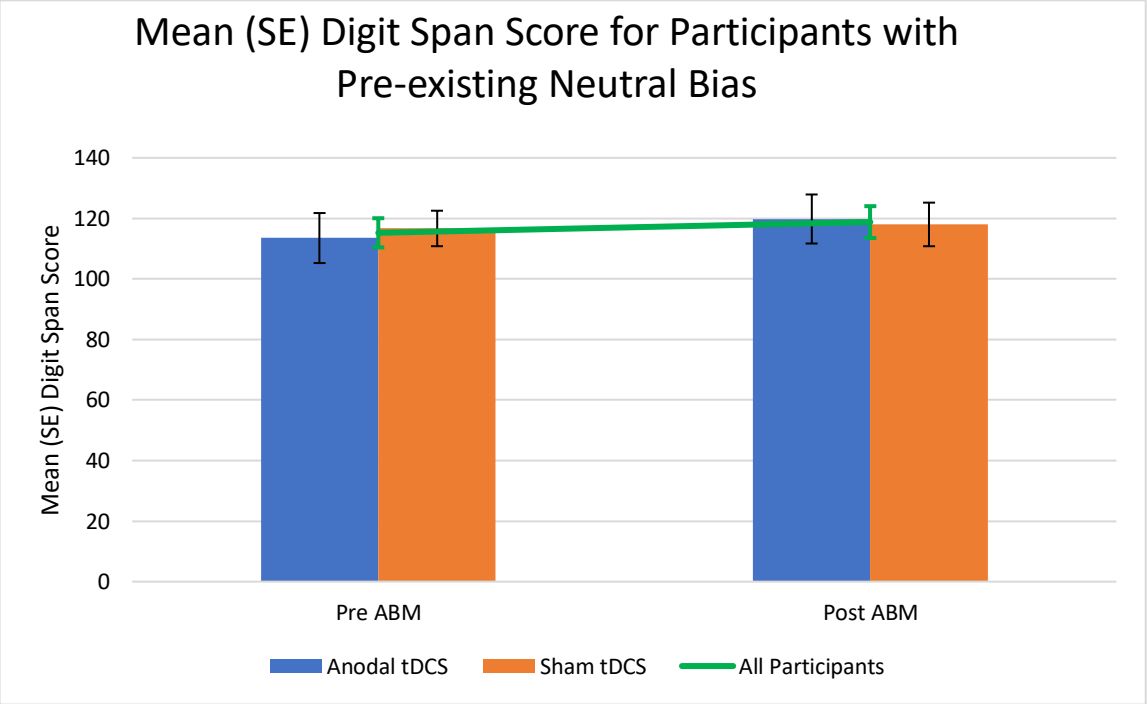


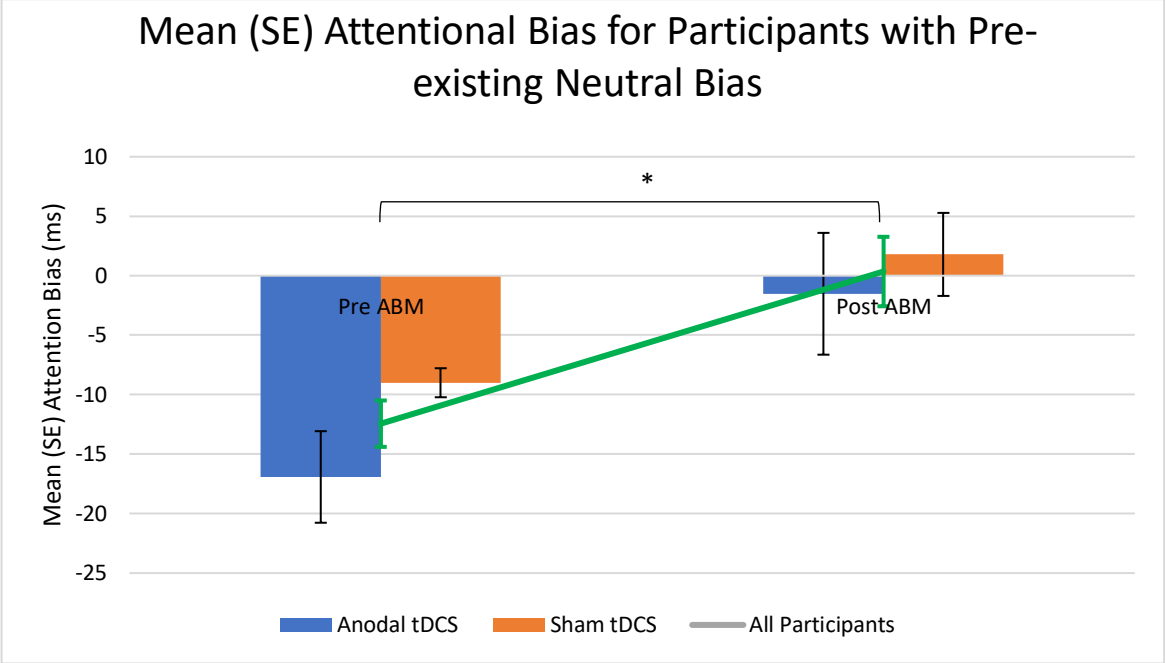

*Figure 6.10*. Mean (SE) digit span score across assessments for participants with pre-existing attention bias towards neutral in each tDCS group and all pre-existing neutral bias participants

#### 6.3.2.5 Attention Bias (Participants with Pre-existing Neutral Bias)

A 2 x 2 ANOVA with assessment (pre ABM, post ABM) as the within subjects factor and tDCS (anodal tDCS, sham tDCS) as the between subjects factor was conducted on data related to participants with pre-existing attentional bias towards neutral faces.

For participants with a pre-existing attention bias towards neutral faces there was a significant effect of assessment, $F(1,21) = 14.99$, $p = .001$, ($\eta_p^2 = .42$; *observed power* = .96). Neutral bias was significantly reduced following ABM ($M = .35$, $SD = 14.03$) compared to before ABM training ($M = -12.44$, $SD = 9.35$). There was no main effect of tDCS ($F = 2.40$, $p = .91$). The interaction between assessment and tDCS was also not significant ($F = .46$, $p = .14$).

Figure 6.11 shows attention bias from before ABM to after ABM training for participants with a pre-existing neutral bias in each tDCS group and for all participants with a pre-existing neutral bias. Positive values represent threat bias and negative values represent neutral bias.




* $p < .05$

*Figure 6.11.* Mean (SE) attention bias across assessments for participants with pre-existing attention bias towards neutral in each tDCS group and all pre-existing neutral bias participants

### 6.3.2.6 State Anxiety (Participants with Pre-existing Neutral Bias)

The ANOVA conducted above on attention bias data was replicated on state anxiety data. For participants with a pre-existing neutral bias there were no significant main effects or interactions ($F$s < 2.59, $p$s > .12).

Figure 6.12 shows mean and standard error state anxiety for participants with pre-existing neutral bias in each tDCS groups and for all participants before and after ABM training.

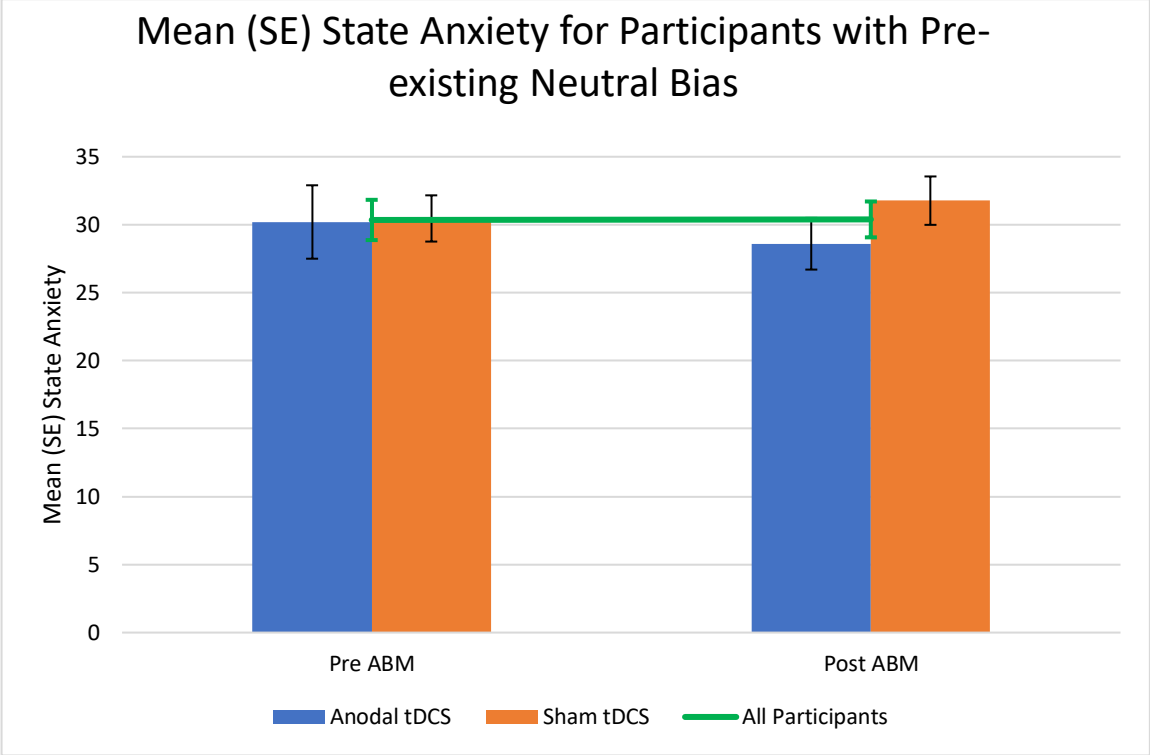



*Figure 6.12*. Mean (SE) state anxiety for participants with pre-existing neutral bias in each tDCS group and for all pre-existing neutral bias participants

### 6.3.3 Analyses of Covariance with Pre-existing Attention Bias as a Covariate

#### 6.3.3.1 Digit Span Score (Pre-existing Attention Bias as Covariate)

With digit span score as the dependent variable a 2 x 2 ANCOVA was conducted with assessment (pre-ABM, post-ABM) as the within participants variable and tDCS (anodal tDCS, sham tDCS) as the between participants and pre-existing attention bias as the covariate. There was a significant assessment x pre-existing attention bias interaction, $F(1,20) = 5.70$, $p = .027$, ($\eta_p^2 = 22$; observed power = .62). For each assessment the relationship between pre-existing attention bias and digit span score was examined using bivariate correlational analysis. Attention bias was not significantly correlated with digit span score at

either assessment (rs < .18, ps > .29). Correlational analysis was also used to examine whether pre-existing attention bias was related to change in digit span score between assessments. There was no significant correlation (r = .1, p = .51). There were no further significant main or interaction effects (Fs < .33, ps > .58).

#### 6.3.3.2 Attention Bias (Pre-existing Attention Bias as Covariate)

With attention bias as the dependent variable, a 2 x 2 ANCOVA was conducted with assessment (pre-ABM, post-ABM) as the within participants variable and tDCS (anodal tDCS, sham tDCS) as the between participants and pre-existing attention bias as the covariate. There was a significant main effect of pre-existing attention bias, $F(1,36) = 76.74$, $p < .001$, ($\eta_p^2 = 68$; observed power = 1.00). Pre-existing attention bias was strongly, positively correlated with mean attention bias ($r = .86$, $p < .001$). There was also a significant assessment x pre-existing attention bias interaction, $F(1,36) = 76.74$, $p < .001$, ($\eta_p^2 = 68$; observed power = 1.00). Pearson Product Moment correlational analysis was used to explore the relationship between pre-existing attention bias and change in attention bias from pre to post-ABM. Change in attention bias was calculated by subtracting attention bias score at the earlier assessment from attention bias score at the later assessment e.g. attention bias at assessment 2 – attention bias at assessment 1. A positive score represented an increase in attention bias therefore and a negative score represented a reduction in attention bias. Pre-existing attention bias was significantly, highly and negatively correlated with change in attention bias score following ABM relatively to before ABM, $r(39) = -.83$, $p < .001$) suggesting that greater attention bias towards threat at baseline

was associated with greater threat bias reduction following ABM. Figure 6.13 shows the relationship between pre-existing attention bias and change in attention bias from pre to post-ABM training.

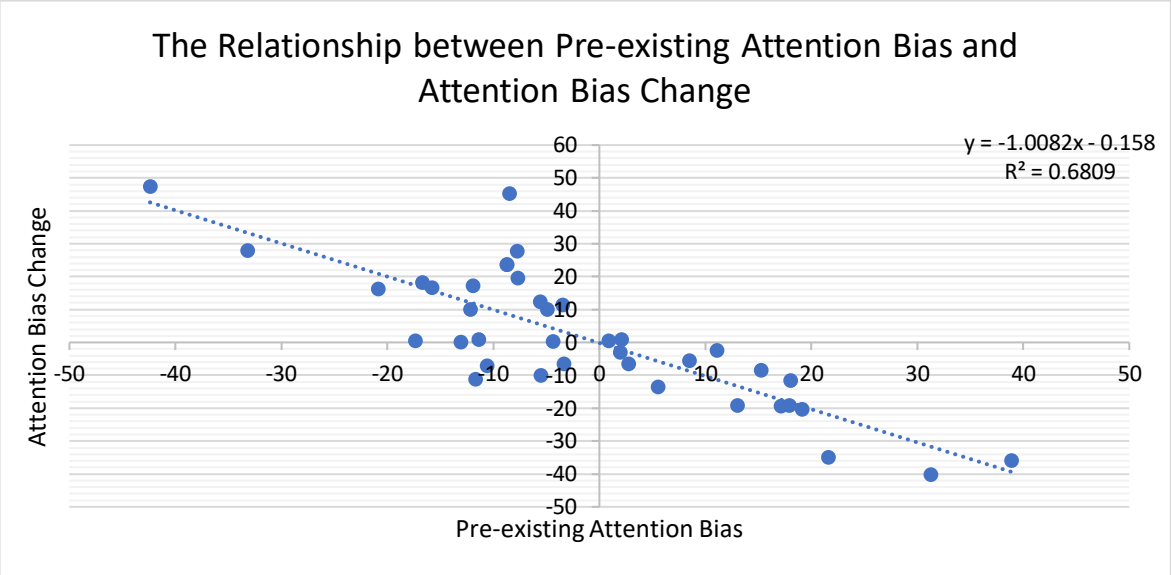



*Figure 6.13*. The correlation between pre-existing attention bias and change in attention bias from pre to post ABM training across study 2. For pre-existing attention bias positive scores represent attention bias towards threat and negative scores represent attention bias towards neutral. For attention bias change, positive scores represent threat bias increase and negative scores represent threat bias reduction.

No further main or interaction effects emerged from the analysis on attention bias data with attention bias as a covariate (*F*s < .82, *p*s > .37).

### 6.3.3.3 State Anxiety (Pre-existing Attention Bias as Covariate)

With state anxiety as the dependent variable, a 2 x 2 ANCOVA was conducted with assessment (pre-ABM, post-ABM) as a within subjects factor and tDCS (anodal tDCS, sham tDCS) as a between participants factor and with pre-existing attention bias as a covariate. There was a significant assessment x tDCS

interaction, $F(1,36) = 5.39$, $p = .026$, ($\eta_p^2 = 13$; observed power = .62). This effect was explored in section 6.3.1.3 revealing an increase in state anxiety for the sham tDCS group but not for the anodal tDCS group following ABM compared to before ABM. There were no further significant main or interaction effects ($F$s < 2.37, $p$s > .13).

### 6.3.4 Analyses of Variance for Participants with Pre-existing High and Low Trait Anxiety

Given the evidence that ABM is more effective in participants with high-level anxiety (Bar Haim et al., 2007; Beard et al., 2012; Hakamata et al., 2010) data were filtered so that separate analyses were conducted on participants with high level trait anxiety at baseline and participants with low level trait anxiety at baseline.

Division of participants into high trait anxiety and low trait anxiety was based upon a median split on baseline trait anxiety scores. The median baseline trait anxiety score was 42. Therefore, participants with a trait anxiety score of 43 or above were categorised as high in trait anxiety and those with a baseline score of 41 or below as low in trait anxiety. Table 6.5 shows the number of participants in each trait anxiety category as a factor of experimental group and baseline attention bias and state anxiety scores across experimental groups/pre-existing trait anxiety categorisation.

Table 6.5:

*Number of participants in each experimental group and mean attention bias and state anxiety for participants with high trait anxiety at baseline and participants with low trait anxiety at baseline*

| | Baseline Measures: | High Trait Anxiety | Low Trait Anxiety |
|---|---|---|---|
| Anodal tDCS | N | 8 | 9 |
| | Mean (SD) Attention Bias (ms) | 2.09 (16.72) | 3.67 (22.89) |
| | Mean (SD) State Anxiety | 33.13 (8.10) | 28.22 (5.36) |
| Sham tDCS | N | 10 | 10 |
| | Mean (SD) Attention Bias (ms) | -2.46 (10.99) | -3.11 (9.80) |
| | Mean (SD) State Anxiety | 34.00 (6.04) | 27.70 (4.19) |

The mean trait anxiety score for high trait anxious participants was 52.50 (*SD* = 7.12) and the mean trait anxiety score for low trait anxious participants was 33.11 (*SD* = 4.83).

#### 6.3.4.1 Digit Span Score (Participants with Pre-existing High Trait Anxiety)

A 2 x 2 ANOVA with assessment (pre ABM, post ABM) as the within subjects factor and tDCS (anodal tDCS, sham tDCS) as the between subjects factor, was conducted on scores from the digit span task for high trait anxious participants.

For participants with pre-existing high anxiety there were no significant main effects or interactions (*F*s < 1.31, *p*s > .27).

Digit span score across assessments for each experimental group and digit span score for all participants with high baseline trait anxiety is shown in Figure 6.14.

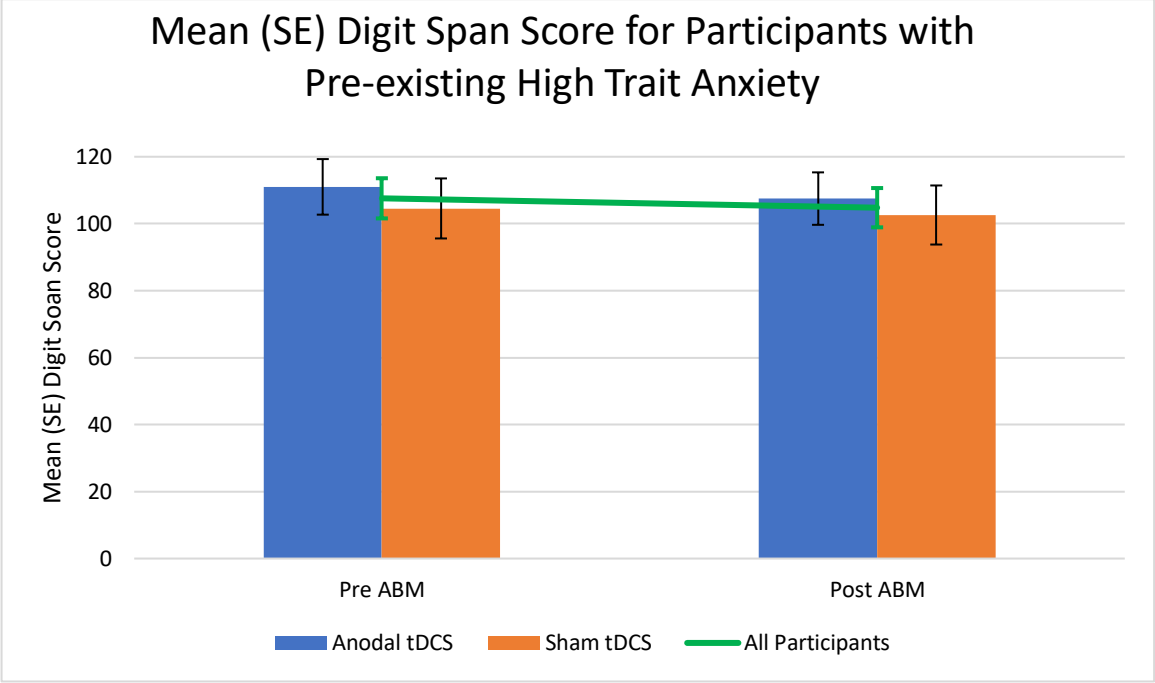



*Figure 6.14*. Mean (SE) digit span score for participants with pre-existing high trait anxiety in each tDCS group and for all high trait anxious participants

### 6.3.4.2 Attention Bias (Participants with Pre-existing High Trait Anxiety)

A 2 x 2 ANOVA with assessment (pre ABM, Post ABM) as the within subjects factor and tDCS (anodal tDCS, sham tDCS) as the between subjects factor was conducted for participants with high baseline anxiety. No main effects or interactions were revealed ($F$s < 1.32, $p$s > .28).

Figure 6.15 shows attention bias before ABM and after ABM training for high trait anxious participants who received anodal tDCS and for high trait anxious participants who received sham tDCS and for all high trait anxious participants. Positive values represent threat bias and negative values represent neutral bias.

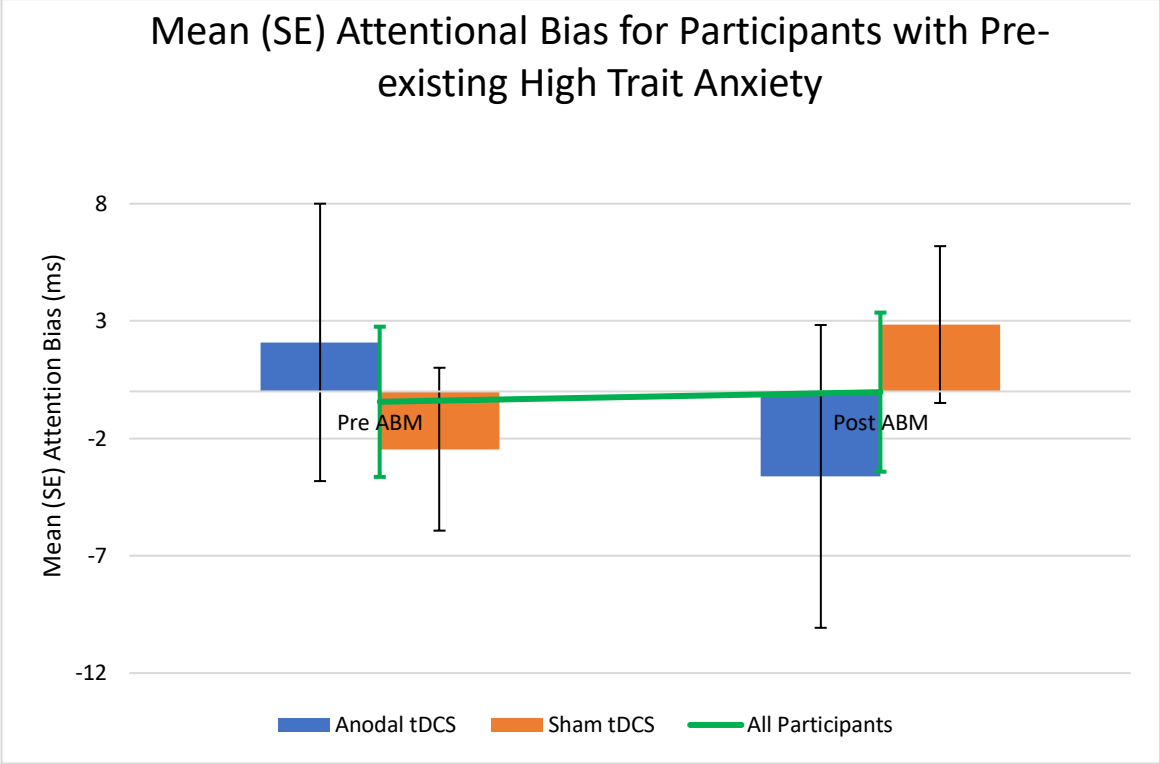



*Figure 6.15*. Mean (SE) attention bias across assessments for participants with pre-existing high trait anxiety in each tDCS group and for all high trait anxious participants

### 6.3.4.3 State Anxiety (Participants with Pre-existing High Trait Anxiety)

A 2 x 2 ANOVA with assessment (pre ABM, post ABM) as the within subjects factor and tDCS (anodal tDCS, sham tDCS) as the between subjects factor was conducted on state anxiety data for high trait anxious participants. This revealed no significant main effects or interactions ($F$s < .88, $p$s > .36).

Figure 6.16 shows mean and standard error state anxiety for participants with baseline high anxiety in each tDCS group and for all high trait anxious participants before and after ABM training.

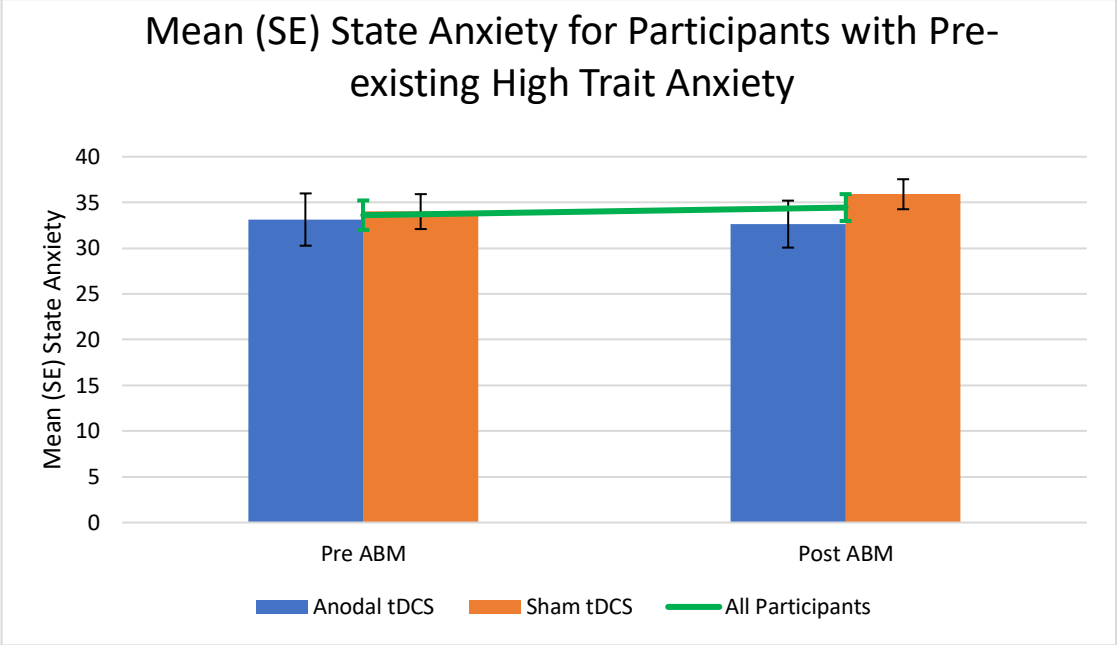



*Figure 6.16*. Mean (SE) state anxiety across assessments for participants with pre-existing high trait anxiety in each tDCS group and for all high trait anxious participants

#### 6.3.4.4 Digit Span Score (Participants with Pre-existing Low Trait Anxiety)

A 2 x 2 ANOVA with assessment (pre ABM, post ABM) as the within subjects factor and tDCS (anodal tDCS, sham tDCS) as the between subjects factor was conducted on scores from the digit span task for participants with low anxiety at baseline.

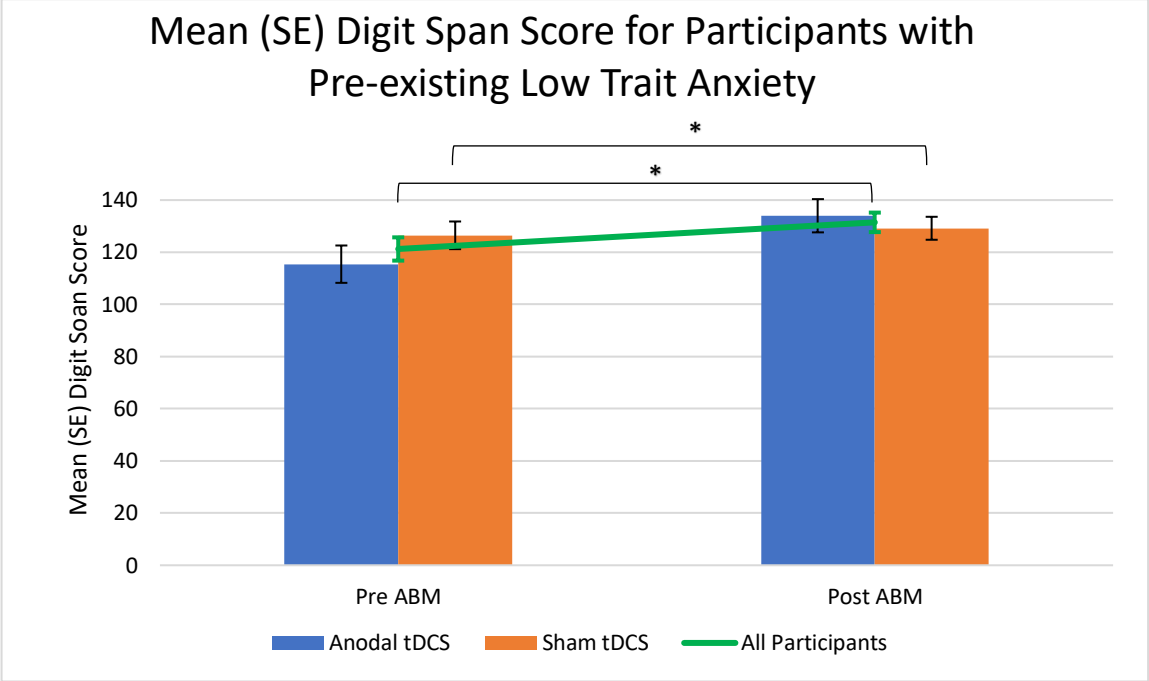
For low trait anxious participants, the main effect of assessment was significant suggesting a change in digit span score following ABM training compared to before ABM training, $F(1,17) = 10.42$, $p = .005$ ($\eta_p^2 = .38$; *observed power* = .86). Digit span score was significantly increased following ABM training ($M = 131.47$, $SD = 16.30$) compared to before ABM training ($M = 121.26$, $SD = 19.45$) suggesting

an improvement in attentional control capacity following ABM training for participants with low trait anxiety.

The interaction between assessment and tDCS was also significant for low trait anxious participants, $F(1,17) = 5.80$, $p = .028$ ($\eta_p^2 = .25$; observed power = .62). For each tDCS group, a paired samples t-test examined change in digit span score across assessments. Results were Bonferroni corrected for multiple comparisons (significant if $2*p < .05$). For participants who received sham tDCS during ABM training, change in digit span score following ABM training was not significant ($t = .89$, $p = .80$). Participants who had received anodal tDCS during ABM training however showed a significant increase in digit span score following ABM ($M = 134.00$, $SD = 19.12$) compared to before ABM training ($M = 115.44$, $SD = 21.49$), $t(8) = 3.05$, $p = .032$. Independent samples t-tests were conducted to explore whether the difference in digit span scores between tDCS groups was significant either before ABM training or after ABM training. Results were Bonferroni corrected for multiple comparisons (significant if $2*p < .05$). TDCS groups did not differ in pre-ABM training digit span score ($t = .42$, $p = .23$) or post ABM training digit span score ($t = .15$, $p = .54$).

For low trait anxious participants, the main effect of tDCS group was not significant ($F = .17$, $p = .68$).

Figure 6.17 gives digit span score at each assessment for participants with low trait anxiety in each tDCS group and for all low trait anxious participants.




* $p < .05$

*Figure 6.17*. Mean (SE) digit span score across assessments for participants with low trait anxiety in each tDCS group and for all low trait anxious participants

### 6.3.4.5 Attention Bias (Participants with Pre-existing Low Trait Anxiety)

A 2 x 2 ANOVA with assessment (pre ABM, post ABM) as the within subjects factor and tDCS (anodal tDCS, sham tDCS) as the between subjects factor was conducted on attention bias data from low trait anxious participants. There were no significant main or interaction effects ($F$s < 1.76, $p$s > .22).

Figure 6.18 shows attention bias before and after ABM training for participants with low pre-existing trait anxiety for each tDCS group and for all low trait anxious participants. Positive values represent threat bias and negative values represent neutral bias.

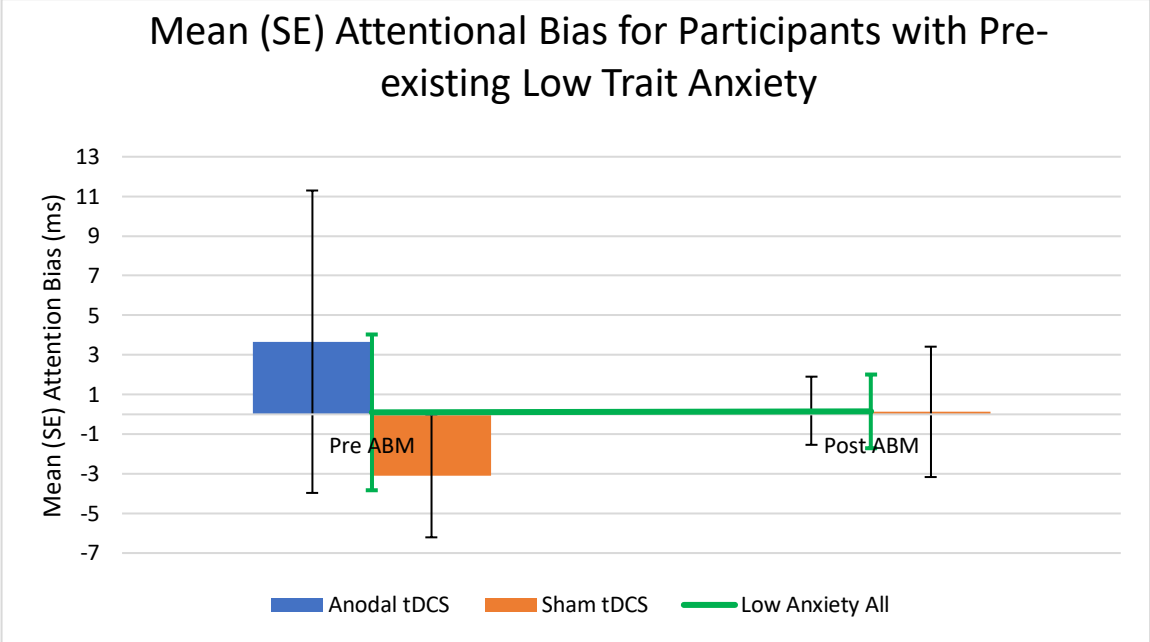



*Figure 6.18*. Mean (SE) attention bias across assessments for participants with low trait anxiety in each tDCS group and for all low trait anxious participants

#### 6.3.4.6 State Anxiety (Participants with Pre-existing Low Trait Anxiety)

The ANOVA conducted above on attention bias data was replicated on state anxiety data. This revealed no significant main effects or interactions for participants with low baseline anxiety ($F$s < 2.92, $p$s > .11).

Figure 6.19 shows mean and standard error state anxiety for participants with baseline low trait anxiety in both tDCS groups and for all low trait anxious participants before and after ABM training.

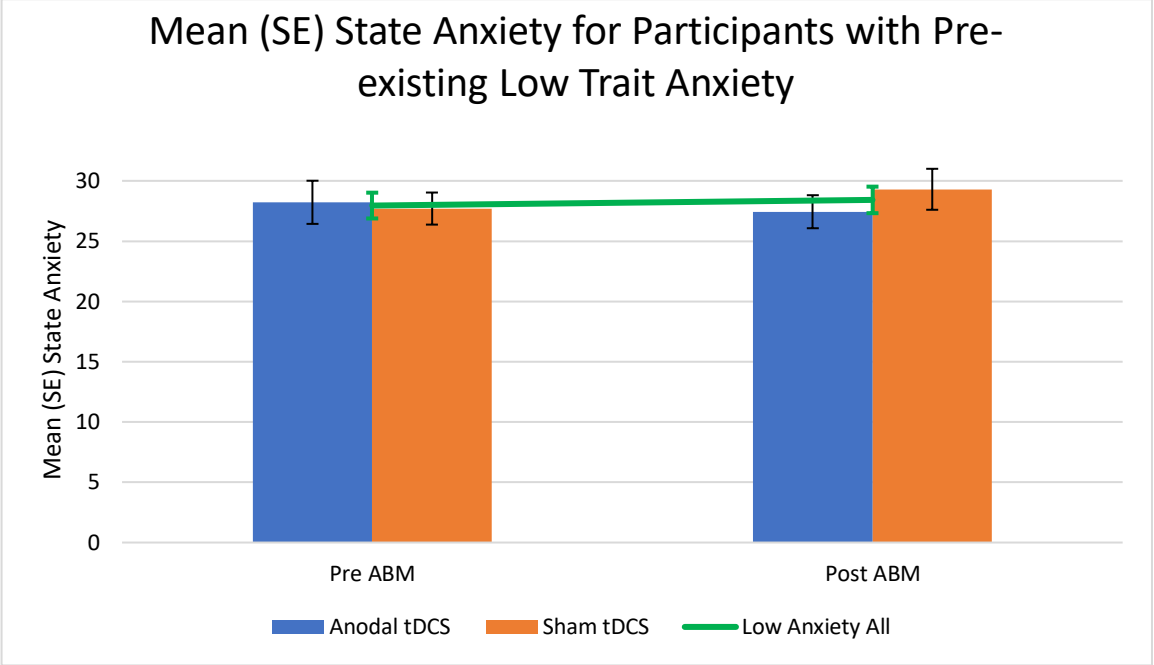



*Figure 6.19*. Mean (SE) state anxiety across assessments for participants with pre-existing low trait anxiety in each tDCS group and for all low trait anxious participants

### 6.3.5 Analyses of Covariance with Pre-existing Trait Anxiety as a Covariate

#### 6.3.5.1 Digit Span Score (Pre-existing Trait Anxiety as Covariate)

A 2 x 2 ANCOVA was conducted on digit span data with assessment (pre-ABM, post-ABM) as the within participants variable and tDCS (anodal tDCS, sham tDCS) as the between participants and pre-existing trait anxiety as the covariate. The main effect of assessment was significant, $F(1,35) = 5.06$, $p = .031$, ($\eta_p^2 = .13$; observed power = .59). However, a paired samples t-test revealed no significant change in digit span score across assessments, ($t = 1.00$, $p = .33$). The interaction between assessment and pre-existing trait anxiety was also significant, $F(1,35) = 4.23$, $p = .047$, ($\eta_p^2 = 11$; observed power = .52). For each assessment, the relationship between pre-existing trait anxiety and digit span score was examined using Pearson's Product Moment correlational analysis. The relationship between pre-existing trait anxiety and change in digit span score across assessments was also examined. Digit span score post-ABM was significantly, moderately, negatively correlated with pre-existing trait anxiety, $r(39) = -.37$, $p = .021$. This suggests that lower trait anxiety at baseline was associated with greater digit span score following ABM training. Change in digit span score was significantly, moderately, negatively correlated with pre-existing trait anxiety, $r(39) = -.35$, $p = .03$ suggesting that lower trait anxiety at baseline was associated with greater increase in digit span score from pre to post-ABM. The relationship between pre-existing trait anxiety and digit span score at assessment 1 was not significant ($r = -.08$, $p = .64$).

Based on results from section 6.3.3.4 which showed an increase in state anxiety for participants with pre-existing low trait anxiety who received anodal tDCS but not for participants with pre-existing low trait anxiety who received sham tDCS, change in digit span score across assessments and pre-existing trait anxiety was subject to correlational analysis for each tDCS group in isolation. In support of the findings reported in section 6.3.3.4, there was a moderate, negative correlation between pre-existing trait anxiety and change in digit span score following ABM relative to before ABM for the anodal tDCS group $r(19) = -.48$, $p = .04$ but not for the sham tDCS group ($r = -.15$, $p = .53$). This suggests that lower trait anxiety at baseline was associated with greater improvement in the digit span score following ABM relative to before ABM for the anodal tDCS group but for participants with low pre-existing trait anxiety who received sham tDCS. There were no further significant main effects of interaction effects arising from the above ANCOVA ($F$s < 2.30, $p$s < .14).

#### 6.3.5.2 Attention Bias (Pre-existing Trait Anxiety as Covariate)

With attention bias as the dependent variable, a 2 x 2 ANCOVA was conducted with assessment (pre-ABM, post-ABM) as the within participants variable and tDCS (anodal tDCS, sham tDCS) as the between participants factor and pre-existing trait anxiety as the covariate. With trait anxiety held constant, there were no significant main or interaction effects ($F$s < .94, $p$s > .34).

### 6.3.5.3 State Anxiety (Pre-existing Trait Anxiety as Covariate)

With state anxiety as the dependent variable, a 2 x 2 ANCOVA was conducted with assessment (pre-ABM, post-ABM) as a within subjects factor and tDCS (anodal tDCS, sham tDCS) as a between participants factor and with pre-existing trait anxiety as a covariate. The main effect of trait anxiety was significant, $F(1,36) = 6.36$, $p = .016$, ($\eta_p^2 = 15$; observed power = .69). Pre-existing trait anxiety and mean state anxiety were significantly, moderately and positively correlated, $r(39) = .39$, $p = .014$. Figure 6.20 shows the relationship between pre-existing trait anxiety and mean state anxiety with higher pre-existing trait anxiety associated with greater mean state anxiety.

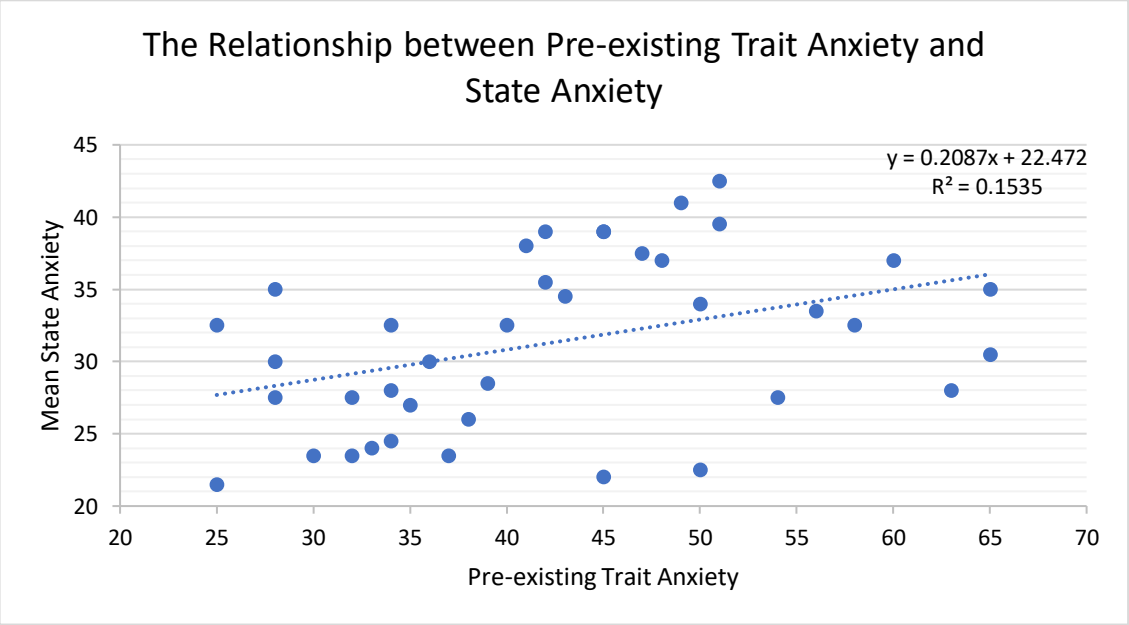



*Figure 6.20*. The relationship between baseline scores on the trait anxiety scale of the STAI (Spielberger et al,. 1983) and mean scores on the state anxiety scale of the STAI across study 2.

The assessment x tDCS interaction was also significant, $F(1,36) = 4.47$, $p = .041$, ($\eta_p^2 = 11$; observed power = .54). This effect was explored in section 6.3.1.3.

No further significant main or interaction effects emerged ($F$s < .019, $p$s > .89).

### 6.3.6 Analyses of Variance for Participants with Pre-existing High and Low Attentional Control

As reported previously, the extent to which it is possible to regulate an individual's attentional bias is dependent upon their level of attentional control (Derryberry & Reed, 2002). In order that this phenomenon could be explored, participants were divided into those with high pre-existing attentional control and those with low pre-existing attentional control. Categorisation of participants as high in attentional control or low in attentional control was based upon a median split (also employed by Derryberry & Reed, 2002). The median attentional control score was 51. Therefore, participants with an attentional control score of 52 or above were categorised as high in attentional control and participants with a score of 50 or below were considered as low in attentional control.

Table 6.6 shows the number of participants with high attentional control and with low attentional control at baseline as a factor of tDCS group and baseline attention bias and state anxiety for each tDCS group/attentional control group.

Table 6.6:

*Number of participants in each experimental group and mean attention bias, state anxiety and trait anxiety for participants with high attention control and participants with low attentional control at baseline*

| | Baseline Measures: | High Attentional Control | Low Attentional Control |
|---|---|---|---|
| Anodal tDCS | N | 10 | 8 |
| | Mean (SD) Attention Bias (ms) | 2.65 (7.06) | -4.15 (8.00) |
| | Mean (SD) State Anxiety | 31.30 (2.45) | 31.75 (3.04) |
| Sham tDCS | N | 9 | 10 |
| | Mean (SD) Attention Bias (ms) | -2.57 (3.97) | -2.82 (3.01) |
| | Mean (SD) State Anxiety | 29.00 (1.74) | 32.70 (2.10) |

The mean attentional control score for participants in the high attentional control group was 58.84 (*SD* = 6.57) and the mean attentional control score for participants in the low attentional control group was 43.06 (*SD* = 5.87).

#### 6.3.6.1 Digit Span Score (Participants with Pre-existing High Attentional Control)

For participants with high attentional control at baseline, a 2 x 2 ANOVA was conducted with the between participants factor of tDCS (anodal tDCS, sham tDCS) and the within participants factor of assessment (pre ABM, post ABM). There were no main effects or interactions ($F$s < 1.63, $p$s > .22).

Figure 6.21 shows mean (SE) digit span score for participants with high attentional control in each tDCS group and for all participants with high attentional control.

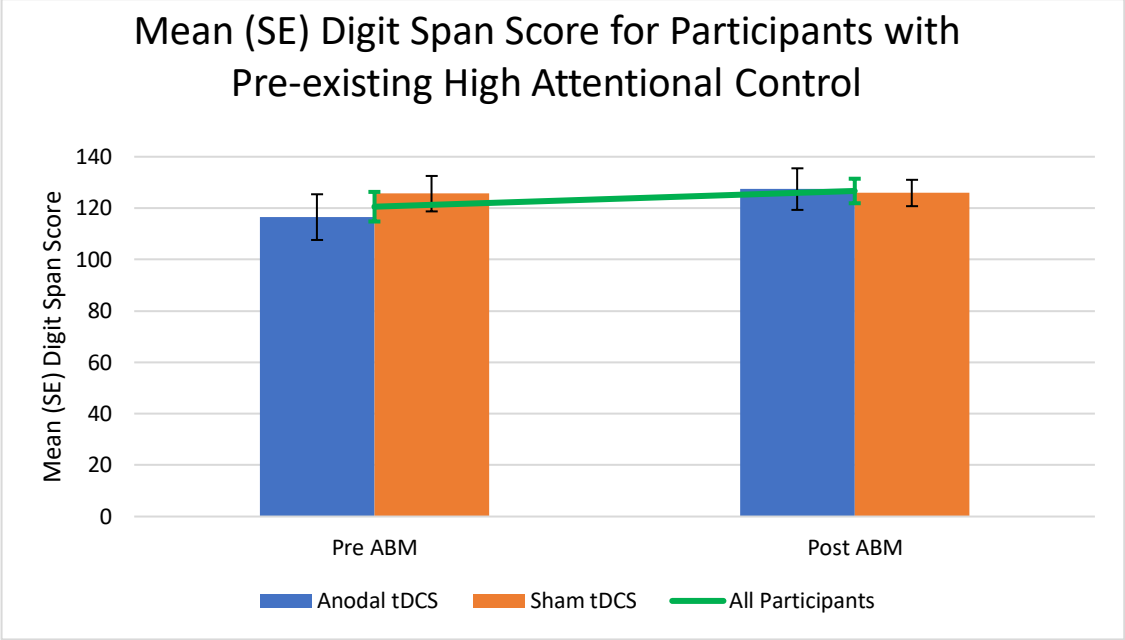



*Figure 6.21.* Mean (SE) digit span score across assessments for participants with pre-existing high attentional control in each tDCS group and for all high attentional control participants

### 6.3.6.2 Attention Bias (Participants with Pre-existing High Attentional Control)

With attention bias as the dependent variable, a 2 x 2 ANOVA was carried out with the between participants factor of tDCS (anodal tDCS, sham tDCS) and one within participants factor of assessment (pre ABM, post ABM) on data from participants with high attentional control at baseline. This revealed no significant main effects or interaction effects ($F$s < .38, $p$s > .55).

Attention bias across assessments for participants with high attentional control in each tDCS group and for all participants with baseline high attentional control is shown in figure 6.22. Positive values represent threat bias and negative values represent neutral bias.

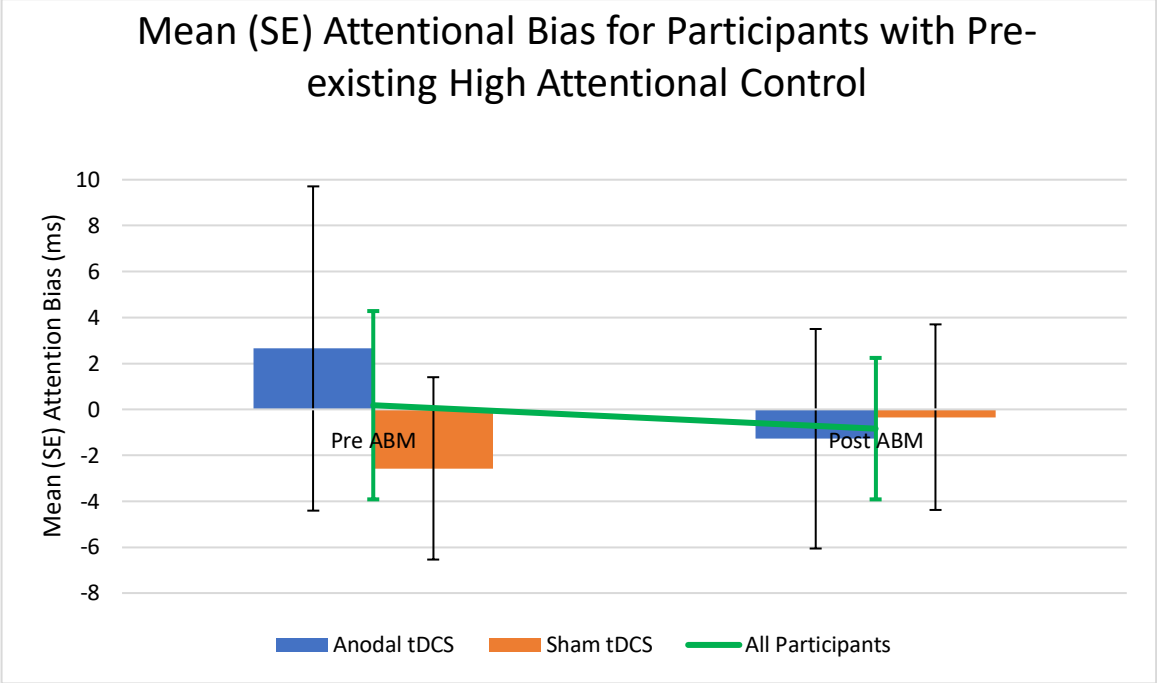



*Figure 6.22*. Mean (SE) attention bias across assessments for participants with pre-existing high attentional control in each tDCS group and for all high attentional control participants

### 6.3.6.3 State Anxiety (Participants with Pre-existing High Attentional Control)

State anxiety data were subject to a 2 x 2 ANOVA with one between subjects factor of tDCS (anodal tDCS, sham tDCS) and one within participants factor of assessment (pre ABM, post ABM). No main effects or interactions emerged from the analysis of data from participants with high level attentional control at baseline (*F*s < 1.49, *p*s > .24).

State anxiety across assessments for participants with pre-existing high attentional control in each tDCS group and for all participants with pre-existing high attentional control is given in figure 6.23.

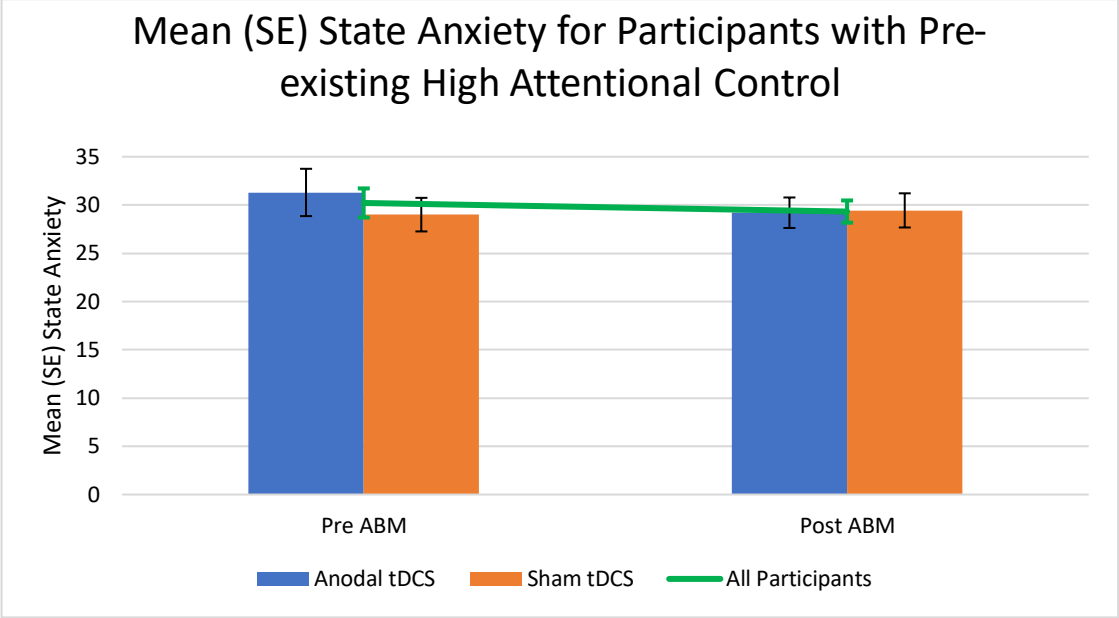



*Figure 6.23*. Mean (SE) state anxiety across assessments for participants with pre-existing high attentional control in each tDCS group and for all high attentional control participants

#### 6.3.6.4 Digit Span Score (Participants with Pre-existing Low Attentional Control)

For participants with low level attentional control at baseline, a 2 x 2 ANOVA was conducted with the between participants factor of tDCS (anodal tDCS, sham tDCS) and the within participants factor of assessment (pre ABM, post ABM). This revealed no significant main effect or interaction effect ($F$s < .93, $p$s > .35).

Digit span score from before ABM training and after ABM training for participants with pre-existing low attentional control in each tDCS group and for all participants with pre-existing low attentional control is shown in figure 6.24.

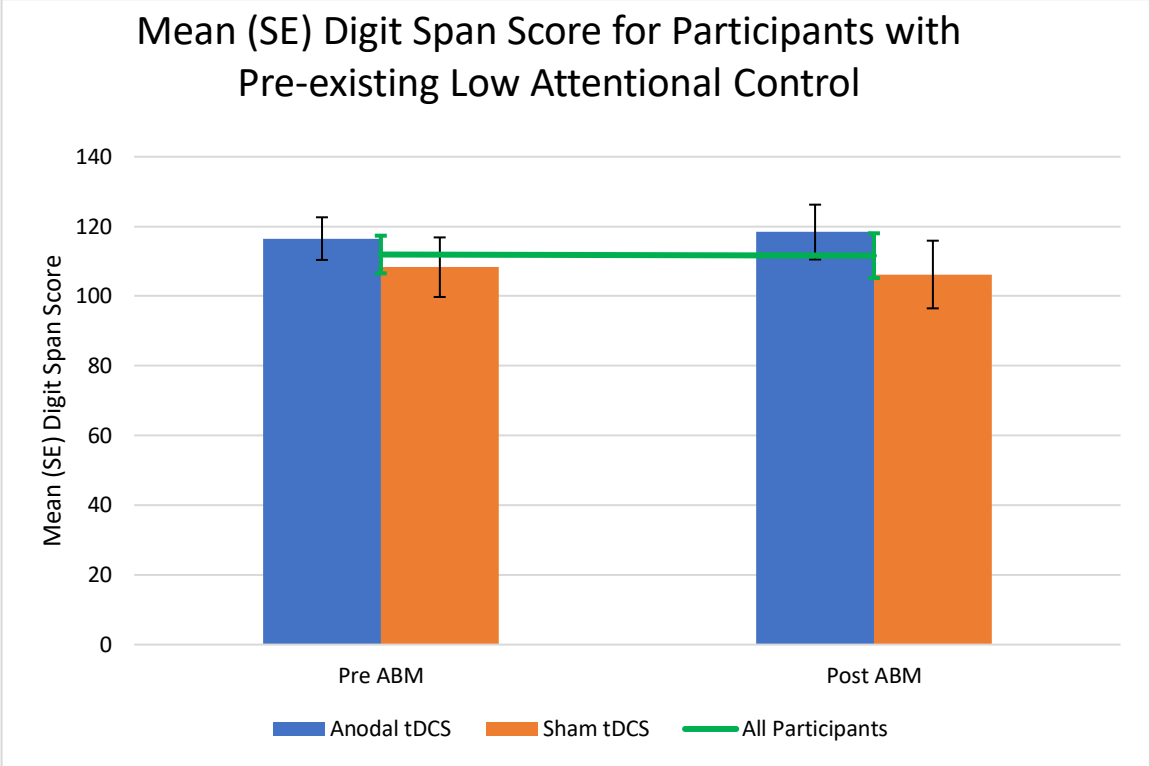



*Figure 6.24*. Mean (SE) digit span score across assessments for participants with pre-existing low attentional control in each tDCS group and for all low attentional control participants

### 6.3.6.5 Attention Bias (Participants with Pre-existing Low Attentional Control)

With attention bias as the dependent variable, a 2 x 2 ANOVA was carried out on data from participants with low pre-existing attentional control with the between participants factor of tDCS (anodal tDCS, sham tDCS) and one within participants factor of assessment (pre ABM, post ABM). No significant main effects or interaction effects were apparent ($F$s < .92, $p$s > .35).

Change in attention bias across assessments for participants with low attentional control in each tDCS group and for all participants with baseline low attentional control is shown in figure 6.25. Positive values represent threat bias and negative values represent neutral bias.

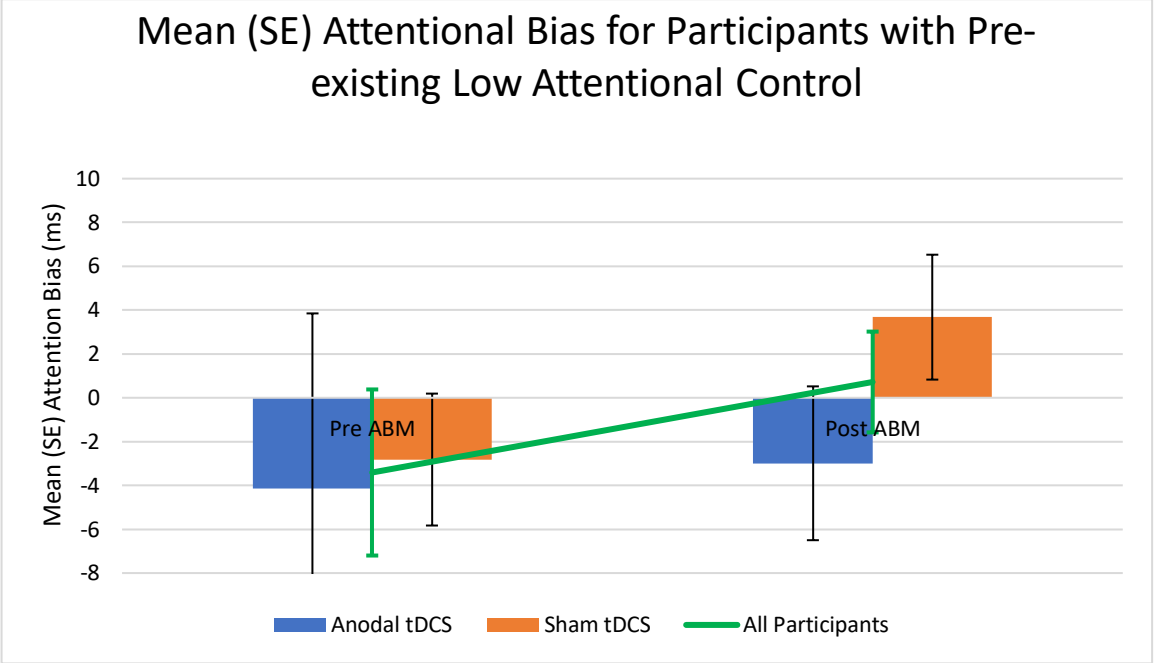



*Figure 6.25*. Mean (SE) attention bias across assessments for participants with pre-existing low attentional control in each tDCS group and for all low attentional control participants

### 6.3.6.6 State Anxiety (Participants with Pre-existing Low Attentional Control)

State anxiety data from participants with low level attentional control at baseline were subject to a 2 x 2 ANOVA with one between subjects factor of tDCS (anodal tDCS, sham tDCS) and one within participants factor of assessment (pre ABM, post ABM). There were no main effects or interaction effects (*F*s < 1.37, *p*s > .26).

Change in state anxiety across assessments for participants with low pre-existing attentional control in each tES group and for all participants with pre-existing low attentional control is given in figure 6.26.

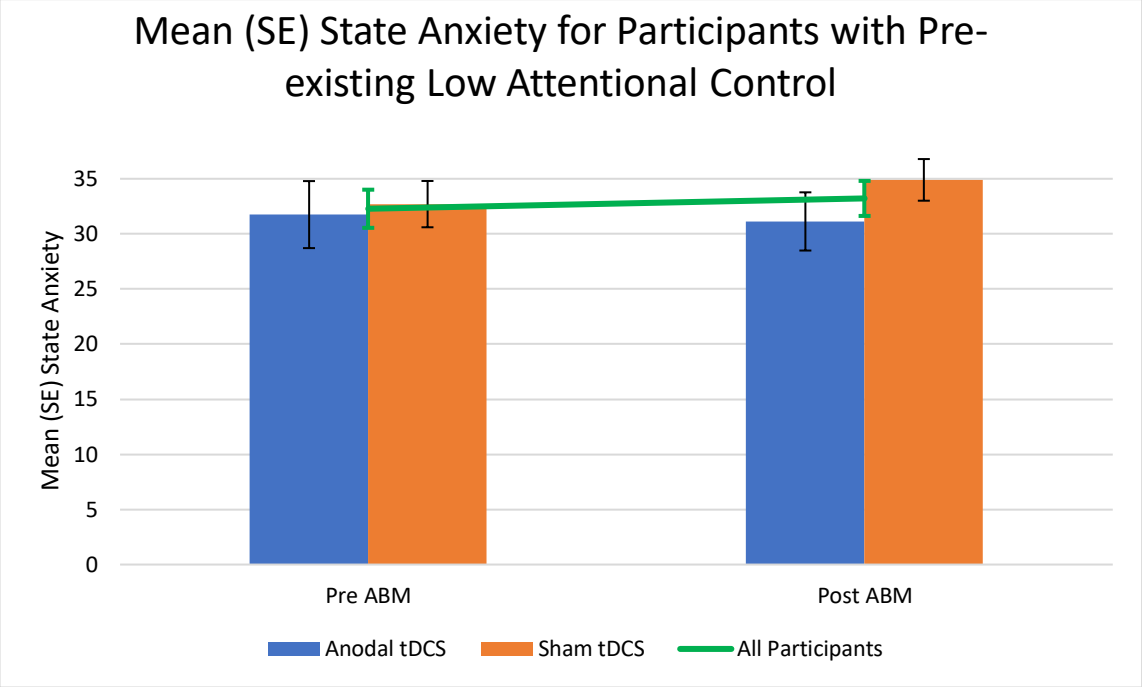



*Figure 6.26*. Mean (SE) state anxiety across assessments for participants with pre-existing low attentional control in each tDCS group and for all low attentional control participants

### 6.3.7 Analyses of Covariance with Pre-existing Attentional Control as a Covariate

#### 6.3.7.1 Digit Span Score (Pre-existing Attentional Control as Covariate)

A 2 x 2 ANCOVA was conducted on digit span data with assessment (pre-ABM, post-ABM) as the within participants variable and tDCS (anodal tDCS, sham tDCS) as the between participants and pre-existing attentional control as the covariate. There were no significant main or interaction effects ($F$s < 2.51, $p$s < .12).

#### 6.3.7.2 Attention Bias (Pre-existing Attentional Control as Covariate)

A 2 x 2 ANCOVA was conducted on attention bias data with assessment (pre-ABM, post-ABM) as the within participants variable and tDCS (anodal tDCS, sham tDCS) as the between participants factor and pre-existing attentional control as the covariate. No main or interaction effects were significant (*F*s < .70, *p*s > .41).

#### 6.3.7.3 State Anxiety (Pre-existing Attentional Control as Covariate)

With state anxiety as the dependent variable, a 2 x 2 ANCOVA was conducted with assessment (pre-ABM, post-ABM) as a within subjects factor and tDCS (anodal tDCS, sham tDCS) as a between participants factor and with pre-existing attentional control as the covariate. As with the previous analyses, the assessment x tDCS interaction was significant, $F(1,36) = 4.24$, $p = .047$, ($\eta_p^2 = 11$; observed power = .52).

There were no further main effects or interaction effects (*F*s < .78, *p*s > .39).

### 6.3.8 tDCS Tolerability

TDCS was well tolerated overall with no adverse events (see Table 6.7). Participants who received anodal tDCS reported mild tickling and itching and participants in both tDCS groups reported mild loss of concentration. Participants who received anodal tDCS reported a higher level of tickling (*M* =2.16, *SD* = .83) than those who received sham tDCS (*M* =1.65, *SD* = .88),

$t(37) = 2.01$, $p = .052$. Participants in the sham tDCS group reported a significantly higher level of tiredness ($M = 2.75$, $SD = 1.16$) than those in the anodal tDCS group ($M = 1.84$, $SD = 1.26$), $t(37) = 2.34$, $p = .025$. Anodal tDCS and sham tDCS groups did not differ significantly on any other measure of tDCS intensity (all $t$s < 1.85, $p$s > .076).

Table 6.7:

*Mean (Std Dev) tDCS intensity scores for each tDCS group*

| | Headache | Neck Pain | Aching Scalp | Tickling | Itching | Burning | Skin Irritation | Tiredness | Loss of Concentration | Mood Swings |
|---|---|---|---|---|---|---|---|---|---|---|
| ABM/Anodal tDCS | 1.00 (.00) | 1.16 (.50) | 1.37 (.50) | 2.16 (.83) | 2.00 (1.11) | 1.68 (.82) | 1.42 (.69) | 1.84 (1.26) | 2.00 (1.29) | 1.11 (.46) |
| ABM/Sham tDCS | 1.13 (.34) | 1.10 (.31) | 1.20 (.52) | 1.65 (.75) | 1.65 (.88) | 1.30 (.57) | 1.10 (.31) | 2.75 (1.16) | 2.60 (1.19) | 1.25 (.55) |

### 6.3.9 Experimental Condition

Overall, 61.54% of participants guessed their tDCS group correctly. A Chi-Squared Goodness of Fit test revealed that this percentage did not differ significantly from chance, $X^2 = 1.32$, $p = .15$.

## 6.4 Analysis of Data from Subset of Participants

As mentioned above, of the 39 participants recruited for study 2, a subset of 24 participants yielded EEG data which were suitable for analysis. The following section includes an analysis of the behavioural and self-report data from just these participants followed by analysis of their EEG data.

### 6.4.1 Baseline Characteristics

#### 6.4.1.1 Baseline Scores Across Self-Report Measures

Table 6.8 shows the mean and standard deviation self-report scores at baseline (before ABM training) for the subset of 24 female and male participants.

Table 6.8:

*Baseline mean (standard deviation) self-report scores by gender and across tDCS groups for study 2 EEG sub-set*

| | | n | SAS | TAS | BDIii | FNE | PSWQ | ACS | LSAS |
|---|---|---|---|---|---|---|---|---|---|
| Females | Anodal tDCS | 6 | 32.83 (11.39) | 40.00 (12.31) | 50.33 (6.89) | 8.50 (7.66) | 54.33 (14.87) | 17.67 (7.63) | 42.67 (20.92) |
| | Sham tDCS | 12 | 30.08 (5.79) | 47.33 (12.24) | 47.83 (11.14) | 11.67 (8.87) | 62.83 (16.31) | 15.00 (8.22) | 59.50 (24.05) |
| Males | Anodal tDCS | 6 | 29.33 (6.95) | 37.33 (9.91) | 52.17 (9.26) | 6.50 (4.23) | 44.67 (13.00) | 12.83 (5.78) | 31.40 (15.24) |
| | Sham tDCS | 0 | | | | | | | |

State Anxiety

An independent t-test examined whether baseline state anxiety differed between the tDCS groups. There was no significant difference between the groups (*ts* = .32, *p* = .75). A one sample t-test revealed that mean baseline state anxiety score for females who received anodal tDCS (*M* = 32.83, *SD* = 11.39) did not differ significantly from mean normative score reported by Spielberger et al.

(1983) for female undergraduate students (*M* = 38.76, *SD* = 11.95), *(t = 1.27, p = .26)*. However, mean baseline state anxiety score for females who received sham tDCS (*M* = 30.08, *SD* = 5.79) was significantly lower than the normative mean, $t(11) = 5.19$, $p < .001$. Baseline state anxiety for males who received anodal tDCS (*M* = 29.33, *SD* = 6.95), was marginally significantly lower than the normative mean state anxiety score for males reported by Speilberger et al. (1983; *M* = 36.47, *SD* = 10.02), $t(5) = 2.52$, $p = .053$.

Trait Anxiety

An independent t-test examined whether baseline trait anxiety differed between the tDCS groups. There was no significant difference between the groups (*ts* = 1.84, *p* = .08). One sample t-tests revealed that baseline trait anxiety for females who received anodal tDCS (*M* = 40.00, *SD* = 12.31) and females who received sham tDCS (*M* = 47.33, *SD* = 12.24) did not differ significantly from the normative mean for female undergraduate students reported by Spielberger et al. (1983; *M* = 40.40, *SD* = 10.15), (*t*s < 1.96, *ps* > .08). Baseline trait anxiety for males who received anodal tDCS (*M* = 37.33, *SD* = 9.91) did not differ significantly from the normative mean (*M* = 40.00, *SD* = 6.56), (*ts* < .66, *ps* > .54).

#### 6.4.1.2 Correlations Between State Anxiety Scores

Data from each administration of the state anxiety scale of the STAI (Pre-ABM, Post ABM) were subject to a Pearson Product Moment Correlation analysis. The correlation was significant $r(24) = .60$, $p = .002$ suggesting strong test-retest

reliability.

#### 6.4.1.3 Correlation Between State Anxiety and Trait Anxiety

In previous literature, the correlations reported between state and trait anxiety have been significant and moderately strong (.65 for males and .59 for females for college students; Speilberger et al., 1983). In the present study trait anxiety was not significantly correlated with state anxiety before ABM, ($r$ = .22, $p$ = .30) or state anxiety after ABM ($r$ = .31, $p$ = .13; see table 6.9).

Table 6.9:

*Bivariate correlations between baseline trait anxiety scale and state anxiety scale (SAS) scores before and after ABM training for study 2 EEG sub-set*

| | SAS Assessment 1 | SAS Assessment 2 |
|---|---|---|
| Baseline Trait Anxiety | **.220** | **.314** |

## 6.5 Results

The following analysis includes just the results from participants whose data were included in ERP analysis.

### 6.5.1 Analyses of Variance Across all Sub-set Participants

#### 6.5.1.1 Digit Span Score

A 2 x 2 ANOVA with assessment (pre ABM, post ABM) as the within subjects factor and tDCS (anodal tDCS, sham tDCS) as the between subjects factor was

performed on scores from the digit span task. Neither the main effect of assessment, the main effect of tDCS nor the assessment x tDCS interaction were significant (*F*s < 1.62, *p*s > .22) indicating that there was no change in digit span score between assessments and that scores were not significantly modulated by tDCS.

Figure 6.27 shows the mean and standard error digit span scores for participants who received anodal tDCS and participants who received sham tDCS before and after ABM training along with mean and standard error digit span scores for all participants whose EEG data were subject to analysis.

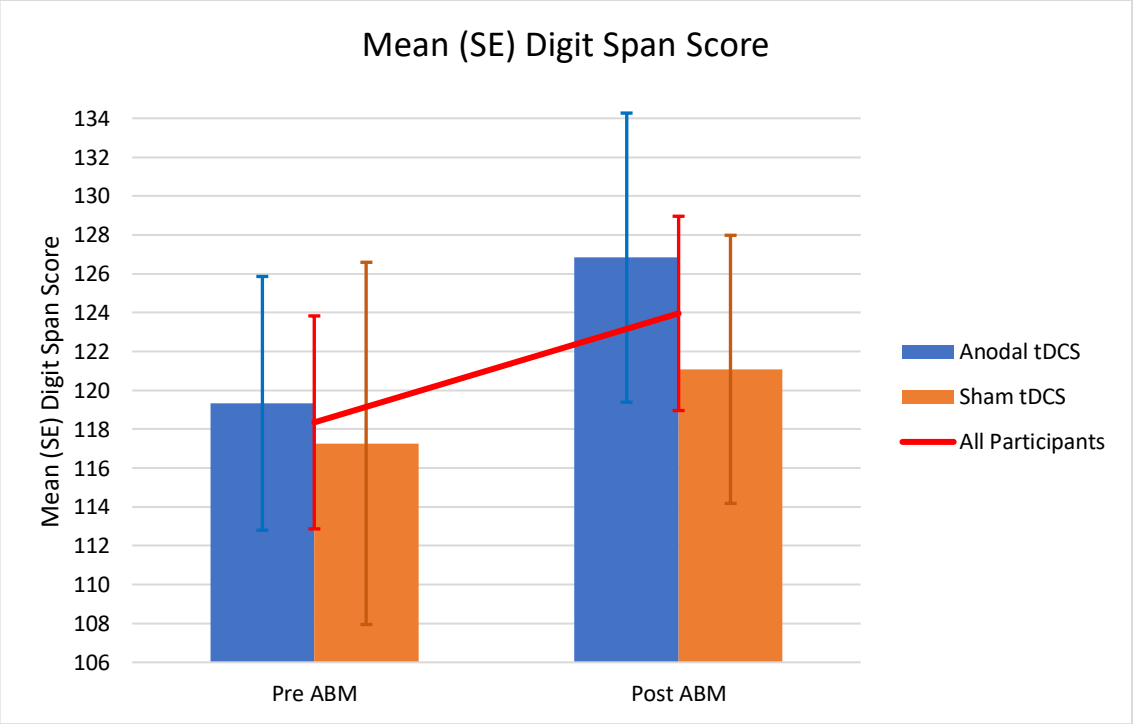



*Figure 6.27.* Mean (SE) digit span scores across assessments for participants in each tDCS group and for all participants in the study 2 EEG subset

### 6.5.1.2 Attention Bias

A 2 x 2 mixed ANOVA was conducted on the attention bias data with the between subjects factor of tDCS (anodal tDCS, sham tDCS) and a within subjects factor of assessment (pre ABM, post ABM). There were no significant main effects or interaction effects (*F*s < 1.49, *p*s > .23).

Figure 6.28 depicts attention bias across assessments for each tDCS group and attention bias for all participants whose EEG data were subject to analysis. Positive values represent threat bias and negative values represent neutral bias.

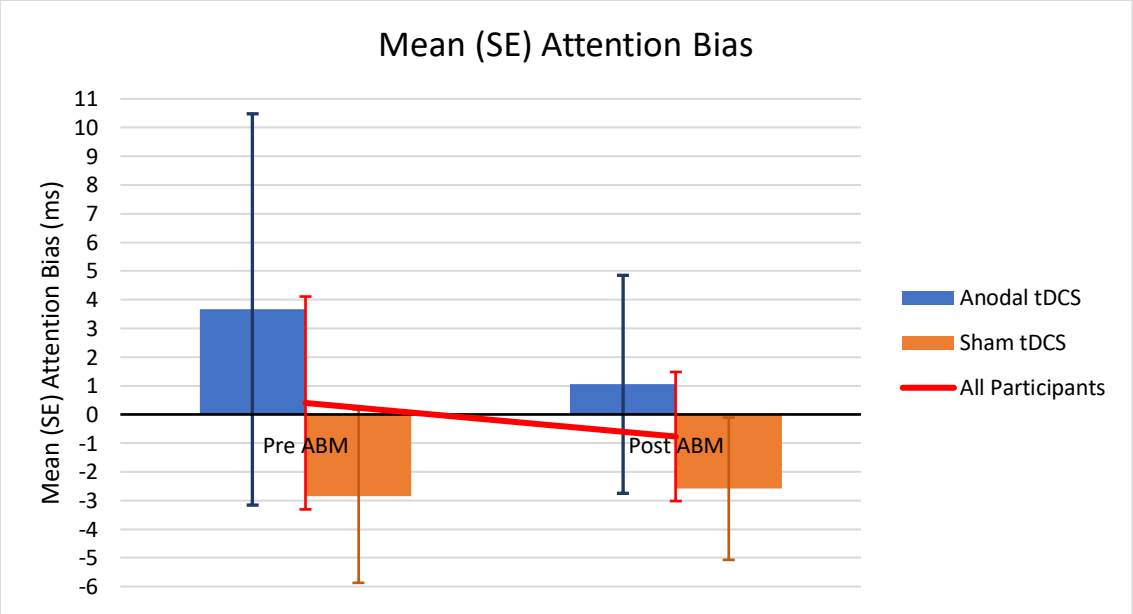



*Figure 6.28.* Mean (SE) attention bias across assessments for each tDCS group and for all participants in the study 2 EEG subset. A positive attention bias score represents attentional bias towards threat.

#### 6.5.1.3 State Anxiety

Replicating the threat bias ANOVA above, a 2 x 2 mixed ANOVA was conducted on state anxiety data with the between subjects factor of tDCS (anodal tDCS, sham tDCS) and a within subjects factor of assessment (pre ABM, post ABM).

The interaction between assessment and tDCS was marginally significant $F(1,22) = 4.19$, $p = .053$, ($\eta_p^2 = .16$; observed power = .50). Following Bonferroni correction for multiple comparisons (significant if 2*p < .05) the difference between pre-ABM and post-ABM state anxiety was not significant for the anodal tDCS group ($t = 1.16$, $p = .54$) or for the sham tDCS group ($t = 2.15$, $p = .11$). Independent t-tests examined whether state anxiety differed significantly between tDCS groups before ABM training and after ABM training. Results were Bonferroni corrected for multiple comparisons (significant if 2*p < .05). There was no significant difference in state anxiety between the 2 groups either before ABM training ($t$s = .32, $p$s = .1.51) or after ABM training ($t$s = 1.62, $p$s = .24).

Neither the main effect of assessment ($F = .00$, $p = 1.00$). nor the main effect of tDCS ($F = .32$, $p = .58$) were significant.

Figure 6.29 depicts state anxiety across assessments for each tDCS group and state anxiety for all participants whose EEG data were subject to analysis.

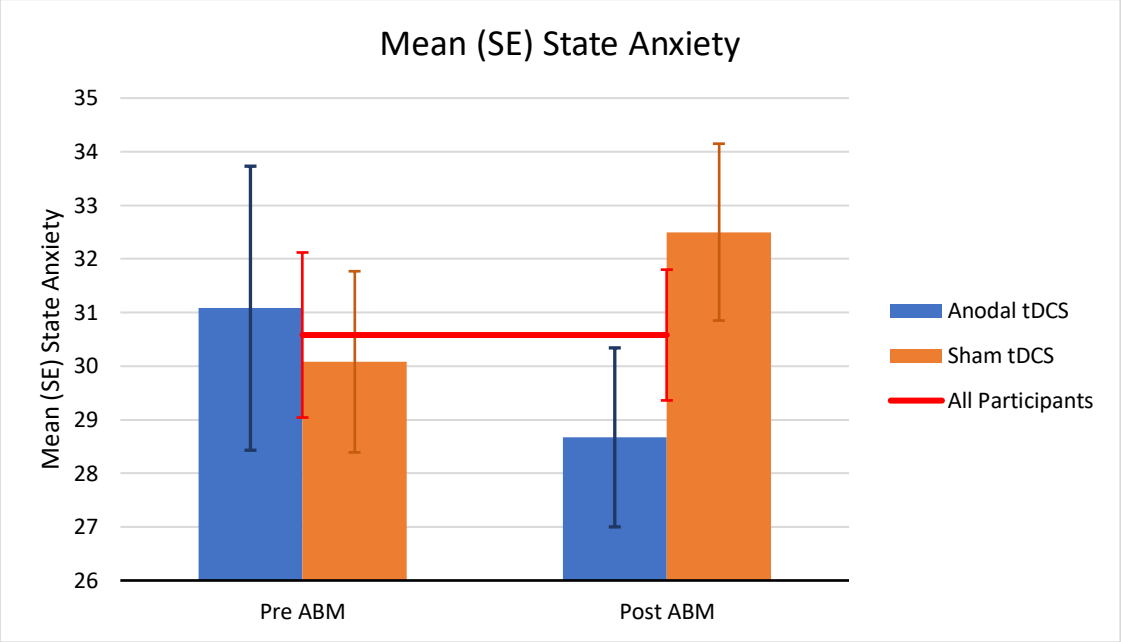



*Figure 6.29*. Mean (SE) state anxiety across assessments for each tDCS group and for all participants in the study 2 EEG subset.

### 6.5.2 Analysis of Filtered data

By analysing a subset of participants, group size was reduced and power compromised. Analyses were not conducted for data relating to pre-existing threat bias/pre-existing neutral bias participants or for data split by high and low scores on the self-report measures as this would have divided the reduced sample into yet smaller groups and compromised the power of the analysis.

### 6.5.3 Analysis of EEG Data

Data from 15 participants were rejected from the following analysis due to contamination. The analysis will therefore encompass data from 24 participants in total (12 who received anodal tDCS and 12 who received sham tDCS).

Grand averaged ERPs to angry-neutral face pairs at electrodes P7 and P8 are shown in figure 6.30. Each chart overlays waveforms at electrodes contralateral to the angry face and ipsilateral to the angry face. The charts illustrate ERP response for the anodal tDCS group and sham tDCS group prior to ABM training and for the anodal tDCS group and sham tDCS group following ABM training. N2pc is defined as the time window between 168ms to 212ms post face stimulus onset. As detailed section 6.2.8.2, this time window was determined using a 'neuron-anti-neuron' analysis (Fuggetta, Bennett & Duke, 2015; Purcell et al., 2013).


Figure 6.30. Grand Averaged ERPs from posterior sites (P7, P8) elicited to angry-neutral face pairs a) before ABM training in the anodal tDCS group, b) after ABM training in the anodal tDCS group, c) before ABM training in the sham tDCS group and c) after training in the sham tDCS group are shown. ERPs are shown at electrodes contralateral and ipsilateral to the angry face. The N2pc is defined as the time window between168ms to 212ms post face stimulus onset.

A 2 x 2 x 2 ANOVA was conducted on ERP amplitudes with the within subjects factors of assessment (pre ABM, post ABM) and laterality (electrodes ipsilateral, contralateral to angry face) and the between subjects factor of tDCS (anodal tDCS, sham tDCS). The dependent variable was mean amplitude between 168 and 212ms for the cue-locked ERP. There was a significant main effect of assessment, $F(1,22) = 12.41$, $p = .002$, ($\eta_p^2 = .36$; *observed power* = .92). Negativity was significantly more enhanced before ABM training ($M = -.26$, $SD = 1.24$) compared to following ABM training ($M = .96$, $SD = 1.50$). The main effect of laterality was also significant, $F(1,22) = 12.93$, $p < .002$, ($\eta_p^2 = .37$; *observed power* = .93) with the contralateral signal ($M = .21$, $SD = 1.10$) significantly more enhanced than ipsilateral signal ($M = .49$, $SD = 1.06$).

No further main effects or interactions were significant ($F$s < 2.81, $p$s > .11).

### 6.5.4 Correlational Analysis

Pre-ABM measures of N2pc for angry faces and attention bias (reaction time based) and pre-existing trait anxiety were subject to correlational analysis ($r$ values are shown in table 6.10).

There were no significant correlations ($r$s < .078, $p$s > .72).

Table 6.10:

*Bivariate correlations between pre-existing trait anxiety scale, pre-ABM attention bias (calculated from reaction time data) and pre-ABM N2pc for angry faces*

| | 1 | 2 | 3 |
|---|---|---|---|
| 1. Pre-existing Trait Anxiety | | | |
| 2. Pre-ABM Attention Bias | **-.078** | | |
| 3. Pre-ABM N2pc | **-.023** | **-.010** | |

Post-ABM measures of N2pc for angry faces and attention bias (reaction time based) and pre-existing trait anxiety were subject to correlational analysis (*r* values are shown in table 6.11). There were no significant correlations (*r*s < .31, *p*s > .14).

Table 6.11:

*Bivariate correlations between pre-existing trait anxiety scale, post-ABM attention bias (calculated from reaction time data) and post-ABM N2pc for angry faces*

| | 1 | 2 | 3 |
|---|---|---|---|
| 1. Pre-existing Trait Anxiety | | | |
| 2. Post-ABM Attention Bias | **-.087** | | |
| 3. Post-ABM N2pc | **.16** | **-.31** | |

## 6.6 Discussion

Study 2 sought to examine the effect of attend-neutral ABM with anodal tDCS and attend-neutral ABM with sham tDCS on attention bias and anxiety.

Following study 1, the reliability of reaction time data from the emotional dot-probe attention bias assessment task was questioned (Schmukle, 2005). Concern stemmed from two major findings. Firstly, there was no evidence of enhanced threat bias reduction following active ABM relative to control or no-training ABM. Secondly, reduced anxiety was revealed in the absence of threat bias reduction. By some reports these findings were not anomalous (Mogg et al., 2017). Based on others, the results might be attributable to inaccuracy of the attention bias assessment procedure (Macleod et al., 2016).

Previous research measured the N2pc ERP component in conjunction with reaction time data (Kappenman et al., 2014). The study reported that reaction time data recorded during an emotional dot-probe attention bias assessment task did not reveal attentional bias towards threat and had poor internal reliability. The N2pc did suggest an initial orienting towards threat and was internally reliable. The results suggested that, in isolation, reaction time data may not present the whole picture in terms of attentional processes and that, to develop a broader knowledge, an understanding of the neural mechanisms of attentional selection is necessary (Kappenman et al., 2014). In the present study, the N2pc was measured to provide information about the underlying cortical processes linked to selective attention. Reaction time data from all participants did not reveal a reduction in threat bias following attention bias modification with active or sham tDCS compared to before training. Despite revealing greater N2pc for angry faces relative to neutral faces overall, suggesting greater attentional capture by angry faces as previously reported (Kappenman et al., 2014), ERP data indicated neither a reduction in threat bias following ABM training nor the facilitation of ABM with anodal tDCS. There was a

reduction in N2pc amplitude following ABM compared to before ABM but this was in response to both angry and neutral faces potentially reflecting reduced attentional capture for both stimuli. Caution must be taken when interpreting ERP outcomes in light of behavioural outcomes from the present study. Behavioural findings were based on analysis of data from the 39 participants recruited to study 2. However, ERP data from only a subset of 24 participants were analysed due to contamination issues. Conclusions should not therefore be formed on the basis of comparison of these two datasets.

In contrast to study 1, there was no reduction in anxiety across participants. Anxiety was increased following ABM training for participants who had received sham tDCS with ABM and there was no change in anxiety level for participants who had received anodal tDCS with ABM. There was a reduction in threat bias for participants with a pre-existing bias towards threat following ABM which was driven by participants in the anodal tDCS group. Neutral bias was reduced for participants with a pre-existing neutral bias following ABM training. Finally, for participants with low pre-existing anxiety, digit span score was significantly increased following ABM training compared to before ABM. Covariate analysis showed that lower trait anxiety at baseline was associated with greater improvement in digit span performance following ABM. Component analysis revealed that this effect was driven by the anodal tDCS group as it was not present for the sham tDCS group.

### 6.6.1 Attention Bias

Attention bias was not altered by ABM training with anodal or sham tDCS as

indexed by reaction time data and ERP data. Early ABM studies produced robust findings in terms of the successful manipulation of attention bias in the intended direction (e.g. Macleod et al., 2002; MacLeod & Bridle, 2009; Van Bockstaele et al., 2012; see Beard et al., 2012, for a review). However, later studies failed to replicate this early success (e.g. Boettcher et al., 2012; Bunnell, Beidel & Mesa, 2013; Julian et al., 2012). Recently, studies have reported a lack of threat bias reduction following ABM training towards neutral faces (see Mogg et al., 2017 for review). The present thesis adds support to this recent evidence.

#### 6.1.1.1 Attention Bias Assessment

Previously, it has been suggested that inconsistency in findings in ABM studies may be due to the unreliability of the dot-probe task for assessing attention bias (Schmukle, 2005). It was proposed that the 500ms presentation of faces provides time for gaze to be averted from threatening stimuli before the appearance of the target (Kappenman et al., 2014). In study 2, the N2pc substantiated findings from reaction time analysis of no alteration in attention bias following ABM. This supported the efficacy of reaction time data for measuring the construct it intended to measure i.e. the visual engagement of threat versus neutral stimuli. However, the possibility remains that speed of attentional engagement is not the most accurate measure of attentional bias (Rudaizky, Basanovic & Macleod, 2014). Attention bias towards threat has been described as enhanced allocation of attention towards threatening stimuli relative to neutral stimuli (Bar-Haim, 2007; Cisler, 2010). This suggests that it is not just the speed at which a stimulus is attended which defines threat bias but all aspects of attention allocation including the amount of time stimuli are

attended. Fox, Russo & Dutton (2002) challenged the view that measures of attentional engagement are optimal for detecting attentional bias. The authors suggested that, due to the relatively long presentation time of the neutral and threatening cue in the dot-probe task, and given that both stimulus positions are task relevant, participants may visually alternate between them before dwelling on one stimulus. Reaction time to the target may therefore not represent the stimulus initially engaged or that to which the participant's attention is biased (Fox et al., 2002). The authors measured attentional disengagement using the modified Posner (spatial cueing) task reporting attentional bias for threatening and happy faces. Using the same task, another study compared attentional distribution to neutral and threatening images in high and low anxious individuals (Koster et al., 2006). The results were enhanced attentional engagement to and delayed disengagement from highly threatening pictures for high anxious participants compared to low anxious participants as well as greater attentional avoidance between 200ms and 500ms for highly anxious participants. Sagliano et al. (2014) also reported facilitated engagement to threatening stimuli for high anxious participants but early avoidance of and later difficulty disengaging from threat for low anxious participants. This demonstrates that attentional bias may be characterised by a complex array of attentional tendencies and yet studies generally only measure and report one facet of attentional bias when assessing the impact of ABM training (e.g. engagement: Clarke et al., 2014: dwell time: Heeren et al., 2015b; disengagement: Amir et al., 2008). In the present study, the choice of emotional dot-probe task to measure initial engagement to stimuli may explain the lack of threat bias reduction following ABM training. However, it is not useful to compare this result to studies which have reported the successful reduction of threat bias

using different indices of attention bias (e.g. Amir et al., 2008;2009b). Moving ahead, ABM research should seek to standardise training and assessment tasks. Ideally, attention bias assessment should gauge all dimensions of attention bias.

#### 6.6.1.2 Pre-existing Attention Bias

As previously suggested (Mogg et al., 2017; O'Toole et al., 2012) it is important to consider pre-existing bias across participants when interpreting results relating to attention bias change. Study 1 revealed a consistent pattern related to baseline attention bias and change in attention bias across assessments. Greater pre-existing threat bias was associated with greater reduction in threat bias following training with tES and greater neutral bias at baseline was associated with great reduction in neutral bias. Study 2 revealed the same pattern. As there was a relatively even split between participants with an attentional bias towards threat at baseline and participants with a bias towards neutral stimuli at baseline any reductions in threat bias for participants with pre-existing threat bias were likely 'cancelled out' by increases in threat bias for participants with pre-existing neutral bias. This is a viable explanation for why no reduction in threat bias across participants was obtained.

#### 6.6.1.3 Efficacy of ABM Training

Explanations have been submitted for why attend-neutral ABM failed to induce a reduction in attentional bias towards threat however, none of these have implicated the ABM training task itself. It is possible that the result directly reflects the inefficacy of attend-neutral ABM for evoking the ABM process.

Heeren et al. (2011) measured indices of attention bias and anxiety following four types of attentional training: disengagement from threat, engagement to non-threatening stimuli, disengagement from threat and engagement of non-threat (dot-probe task) and control. They reported that training in both the disengagement from threat and in the disengagement from threat and engagement of non-threat groups elicited a reduction in threat bias as assessed using the modified Posner task following training but that the other two forms of attentional training did not. This result indicates that ABM training which trains disengagement from threat might be superior for reducing threat bias than training which targets attentional engagement (Heeren et al., 2011). However, it is important to note that the authors used a modified Posner task to assess attention bias which is a measure of attention disengagement. A measure which assessed attentional engagement may have shown superior results for training which facilitated attentional engagement to non-threat. From a mechanistic point-of view it could be argued that identifying the attentional component which underlies attention bias is necessary so that ABM paradigms can target it. However, from a therapeutic perspective if the ultimate aim of ABM training (anxiety reduction) is achieved, even in the absence of threat bias reduction, then perhaps this is not essential. Nevertheless, a failure to target the appropriate attentional processes through ABM training alongside inconsistency of attention bias assessment methods might explain why superior threat bias reductions have not been observed in studies 1 and 2 and in prior research (see Mogg et al., 2017 for review) for participants receiving ABM training towards neutral stimuli relative to participants receiving other forms of ABM training (e.g. control ABM, no-training ABM, attend threat ABM).

### 6.6.2 EEG Data

EEG data from each participant were recorded during attention bias assessment so that the N2pc could be isolated and measured. As reported, EEG data from a number of participants were omitted due to contamination. This compromised the power of the N2pc analysis. Furthermore, the data which were kept were subject to extensive filtering in order to remove the effects of contamination and 16% of trials were rejected. It was suspected that faulty electrodes were responsible for much of the contamination. For this reason, analysis of ERPs was minimised and data are interpreted with caution.

### 6.6.3 tDCS Related Effects

Study 2 revealed findings which suggested the facilitation of ABM effects with anodal tDCS.

#### 6.6.3.1 State Anxiety

Anxiety was increased following ABM training for participants who had received sham tDCS but not for those who had received ABM with anodal tDCS. This result differed from the findings from study 1 of reduced state anxiety across all participants, irrespective of condition. It also contrasted with findings from research showing anxiety reduction, across participants following active or control ABM (e.g. Boettcher et al., 2013; Enock et al., 2014; McNally et al., 2013). Aspects of the experimental procedure may have contributed to the enhancement of anxiety following ABM training. Although the study only

comprised one session, unlike study 1 which was conducted over 3 consecutive days, the session was lengthy. Occasionally, participants attended for over 3 hours. Secondly, each session involved some cumbersome procedures. Set-up of the EEG system and fitting of the head cap took up to 30 minutes. EEG recording was taken during the first attention bias assessment. Following this, participants washed and dried their hair to remove electrolyte gel. The tDCS montage was then fitted to the participant and tDCS was administered for 20 minutes of a 30-minute training period. The EEG headcap was then fitted again for the final attention bias assessment. Participants experienced a relatively high level of physical 'interference' therefore in addition to performing repetitive tasks and may have found the experiment protracted, tiring and stressful. Thirdly, participants performed a digit-span task near the start and end of the experimental session. This was not intended as a 'stressor' task but may have acted as such. State anxiety at the start of the session was measured before the task. State anxiety assessment at the end of the experiment was administered before the second completion of the digit span task. This was to avoid any anxiety arising from performance of the task being reflected in the anxiety measure. However, participants were aware that they were required to complete the task again and this may have induced anxiety.

Compared to study 1 therefore, the study 2 procedure was anxiety-provoking. It appears, however, that this effect may have been mitigated for participants who received anodal tDCS. Areas of the brain which are consistently associated with anxiety response are the pre-frontal cortex and the amygdala (Davidson, 2002). The amygdala is thought to be involved in threat detection and conditioned fear response (Gold et al., 2015). As such, anxiety is associated with hyperactivity of

the amygdala (Etkin & Wager, 2007). It is widely accepted that effective anxiety regulation is driven by top-down processes requiring the recruitment of the DLPFC (Bishop et al., 2007; Bruhl et al., 2014; Clarke et al., 2014; Fitzgerald et al., 2017; Schmid et al., 2015; Tang et al., 2012). Part of the role of the DLPFC is to attenuate performance impairments resulting from threat-induced anxiety by regulating amygdala hyperactivity (Gold et al., 2015). For such regulation to take place, neural connectivity between the PFC and the amygdala must be adequate. The strength of the amygdala-prefrontal pathway is predictive of trait anxiety with a stronger neutral pathway linked to low anxiety (Gold et al., 2015; Kim & Whalen, 2009). Anodal tDCS was applied directly to the DLPFC during ABM training. This suggests that excitatory stimulation of the DLPFC facilitated anxiety attenuating neural mechanisms and may have enhanced signalling in the amygdala-prefrontal pathway. As anodal tDCS was applied during active ABM it can be assumed that the frontal cortices were already engaged. This therefore suggests the enhancement of active ABM with anodal tDCS. As threat bias was not reduced for the ABM with anodal tDCS group as indicated by reaction time and EEG analysis, the mechanism enhanced does not appear to have been that which promotes disengagement from threatening stimuli and the engagement to neutral stimuli. However, it is possible that anodal tDCS bolstered the activation of structures more generally implicated in top-down control which were simultaneously recruited by the ABM task.

#### 6.6.3.2 Attention Bias

For participants with a pre-existing attention bias towards threat, threat bias was reduced following ABM training. There was a tES x assessment interaction

which revealed that this reduction was present for the anodal tDCS group but not for the sham tDCS group. Had study 2 been conducted prior to study 1 then the discussion with relation to this finding may have centered on how anodal tDCS had facilitated active ABM to produce greater threat bias reduction for participants with pre-existing threat bias than that generated by sham tDCS with ABM. However, study 1, consistently showed reduction in threat bias following attentional training, irrespective of ABM or tES group for participants with pre-existing threat bias. The question should perhaps be therefore, how did sham tDCS prevent the diminution of threat bias which has so consistently followed ABM training in this group? Analysis of data across all participants revealed an increase in state anxiety for participants who received sham tDCS but not for participants who received anodal tDCS during ABM training. One possibility is that elevated anxiety prevented the reduction of threat bias. In accordance with theories which propose a positive relationship between anxiety and attentional bias towards threat (Beck et al., 1985; Bower, 1981; Williams et al., 1988, 1997) it could be that persistent or augmented anxiety resulted in continued engagement to threat for participants who received sham tDCS. Attentional control theory (Eysenck et al., 2007) purports that in anxiety there is an imbalance between the top-down attentional control system and the bottom-up stimulus driven system. Typically, the top-down system exerts control over the bottom-up system attenuating the influence of aversive stimuli. In anxiety, it is the bottom-up system which has more influence over attentional processes. However, top-down processes can regain their control over bottom-up processes if they are bolstered via training (Heeren et al., 2013). This might also be possible using tES to enhance activation in the brain areas associated with top-down control. In the present study, increased anxiety may have strengthened

the influence of bottom-up processes. It follows that anodal tDCS provided the facilitation of top-down mechanisms necessary to redress the balance between top-down control and salience driven mechanisms. However, for participants who received sham tDCS, this 'boost' was not provided and attentional processes remained impaired.

#### 6.6.3.3 Digit Span

Separate analyses were conducted on data from participants with higher level trait anxiety at baseline and participants with lower level trait anxiety at baseline. For low trait anxious participants who had received anodal tDCS there was an increase in digit span score following ABM training compared to before training. For low trait anxious participants who had been administered sham tDCS during ABM, there was no change in digit span score. This suggests that anodal tDCS facilitated the attentional control enhancing effects of ABM training in participants with low-level anxiety. Digit span score was not changed for participants with high trait anxiety. This supports the argument made above that higher-level anxiety may have impaired attentional control processes or prevented their enhancement. For low trait anxious participants who received anodal tDCS but not those who received sham tDCS, the frontal-cortex based mechanisms of top-down regulatory control were enhanced redressing the balance between top-down and bottom-up processes resulting in the fortification of attentional control.

### 6.6.4 The Role of Attentional Control

Previous chapters explored the role of attentional control in the outcomes of ABM training. This discussion followed two lines of reasoning. The first was based on findings of indistinguishable improvements in anxiety for ABM training and control ABM training (Carlbring et al., 2012; Carleton et al., 2015; Cristea et al., 2015; Enock et al., 2015; Klumpp & Amir, 2010). It was also motivated by results showing state anxiety reduction across participants, irrespective of condition in study 1. It had been suggested that ABM training, regardless of the inclusion of a contingency, increases attentional control and thus the capacity for attention regulation (Enock et al., 2014; Heeren et al., 2013; Klumpp et al., 2010; Taylor, Cross & Amir, 2015). Klumpp et al., 2010 suggested that facilitated attentional control may not necessarily reduce engagement to threatening stimuli but may attenuate their *impact* and disrupt threat processing via the increase of self-regulation. Heeren et al. (2016) linked the effects to the upregulation of higher-order activity in the frontal cortices. These structures are associated with attentional control and are known to down-regulate reactivity in the emotion-centered limbic system. In order to investigate these ideas further, study 2 included the digit-span task to the battery of pre-and post ABM training measures. Heeren et al. (2016) had previously used the backward digit span task as a measure of working-memory/attentional control. It was reasoned that, if top-down regulatory processes are bolstered by ABM training, irrespective of contingency then an improvement in digit-span performance might be expected following ABM training. Furthermore, if the facilitation of these processes is driven by the upregulation of higher-order frontal lobe activity then this improvement might be greater for participants who received anodal

tDCS during ABM training. Across all participants, there was no change in digit span performance from baseline to after ABM training. There was also no improvement in state anxiety following ABM training as was seen in study 1. On the one hand, this does not support the notion that ABM training, irrespective of condition enhances attentional control capacity. On the other, it could be argued that the failure of the ABM procedure to attenuate state anxiety might be due to its failure to elicit attentional control improvement. As discussed above, there was an augmentation of digit span performance for participants with low trait anxiety and this appeared to be driven by the anodal tDCS group. However, because there was no evidence of state anxiety reduction for this group, there is no support for the theory that attentional control enhancement is implicated in state anxiety improvements.

The second line of reasoning explored in preceding chapters is that pre-existing attentional control level is predictive of ABM training outcomes. In a study by Basanovic et al. (2017), greater capacity for attentional inhibition and attentional selectivity (2 facets of attentional control) at baseline predicted the magnitude of attention bias change in the trained direction (towards neutral or towards threatening stimuli). The authors suggested that greater attentional control facilitated adherence to the training task resulting in enhanced training related outcomes. However, analysis of data across the experiments of study 1 did not reveal this pattern. The present study also looked at the impact of ABM training with anodal or sham tDCS on participants with high level attentional control at baseline and participants with pre-existing low level attentional control. There was no evidence of change in attention bias, state anxiety or

attentional control (digit span score) for either group suggesting that the success of ABM training is not modulated by pre-existing attentional control capacity.

### 6.6.5 Methodological Issues

This chapter has revealed differences between the findings from study 1 and the findings from study 2. In study 2, effects which were present across all participants in study 1, were constrained to participants who had received anodal tDCS. Procedural differences may have been responsible for these discrepancies. Study 2 comprised one experimental session whereas study 1 included four. In study 1, stimuli were small facial images presented vertically on the computer screen. For study 2 stimuli were presented horizontally. This was because the N2pc is a cerebral response to visual stimuli contralateral to horizontally positioned posterior electrodes (Woodman & Luck, 1999). The size of the face images was increased as in previous studies, face stimuli presented horizontally have tended to be larger (e.g. Amir et al., 2011; Heeren et al., 2012). It is possible that it was more difficult to inhibit the processing of larger faces compared the smaller faces from study 1. This might explain why, for participants with an attentional bias towards threat at baseline who did not receive anodal tDCS, threat bias was not reduced. Moreover, if anodal tDCS facilitated better regulation of emotional response to threatening stimuli, participants who did not receive anodal tDCS may have had greater adverse reaction to these more conspicuous threat images as reflected by anxiety increase. Another methodological difference between studies 1 and 2 was that in study 2 participants responded to target identity by pressing one of two response keys on a key pad using two fingers from the same hand rather than one of two

keys on a computer keyboard with the same finger from each hand as per study 1. This was to eliminate the possibility of faster responses for the dominant hand. Although it is unlikely that this impacted upon results related to state anxiety this may have influenced response time measure of attention bias leading to either a slowing or speeding of responses.

### 6.6.6 Limitations

It is evident from figure 6.28 showing grand-averaged ERPs from study 2 that the baseline period (100ms prior to stimulus onset) is noisy showing large deflections. It is likely that this is due to the use of a relatively short inter-stimulus interval (ISI). There was an ISI of 500ms between the offset of the fixation cross and the onset of face stimuli. The baseline activity may therefore have been contaminated by carry-over signal from the presentation of the fixation cross.

A further limitation of the present study was that only active ABM training was delivered with anodal or sham tDCS. A control ABM condition was not included. This prevents analysis of training related effects and assumes that active ABM will have modulatory effects which will may, or may not be enhanced by anodal tDCS.

## 6.7 Summary

In study 2, anodal or sham tDCS of the left DLPFC was delivered concurrently with active ABM training during one experimental session. Attention bias was

measured before and after ABM training using the emotional dot-probe paradigm. EEG data were taken during assessment and the N2pc was isolated as a measure of attentional capture. Neither reaction time data nor the N2pc indicated a reduction in threat bias following ABM training. Behavioural results suggested the facilitation of ABM with anodal but not sham tDCS. Anxiety was increased following ABM training for participants in the sham tDCS group but not for participants who received anodal tDCS during ABM. For participants with a pre-existing threat bias, threat bias was reduced following ABM with anodal tDCS but not following ABM with sham tDCS. Finally, for low anxious participants, attentional control capacity (as indexed by the digit span task) was increased following ABM training with anodal tDCS but not for ABM training with sham tDCS. The most plausible explanation for each of these findings is that anodal tDCS enhanced activity in the pre-frontal cortex which is involved in top-down regulatory control. Where this extra activation was not provided (in the sham tDCS group) anxiety was elevated. This may have impaired attentional processes.

# Chapter 7

**General Discussion**

## 7.1 Introduction

The present research explored the potential of tES for modulating ABM training. Specifically, studies investigated whether tES could enhance the effects of ABM in terms of reducing attention bias towards threatening stimuli and attenuating anxiety. Given the prevalence of anxiety disorders (Craske & Zucker, 2002; MacDonald & Feifel, 2014) and their debilitating effect on social functioning, mental and physical health (Angulo et al., 2017; Bishop, 2007; Hill, Waite & Cresswell, 2016; Kizilcik et al., 2016) the need to investigate potential treatments for anxiety is of great importance. In pursuit of this aim, two studies were conducted. The first study comprised three experiments. Experiment 1 was unique in investigating the effects of active or sham high frequency tRNS on ABM training towards neutral faces or control ABM training. The results supported findings from recent ABM studies showing equivalent reductions in anxiety for attend neutral and control ABM (Carlbring et al., 2012; Enock et al., 2015; Cristea et al., 2015; Carleton et al., 2015; Klumpp & Amir, 2010). There was no reduction in threat bias for any experimental condition and anxiety was reduced across participants irrespective of ABM group and tES group. Experiment 2 sought to explore whether anxiety reduction across all participants was attributable to an enhancement of attentional control induced by both forms of ABM training (active ABM, control ABM). This mechanism was suggested by researchers who had achieved similar results to those revealed following experiment 1 (e.g. Enock et al., 2015; Klumpp & Amir, 2010). A no-training

condition was administered to all participants which was designed to engage and facilitate cognitive control processes to a lesser extent than active or control ABM. This was delivered with active or sham tRNS. The results showed that anxiety reductions occurred even where cognitive control was not intentionally enhanced. However, anxiety reduction was driven by the active tRNS group. This introduced the possibility that anxiety reduction was activation dependent. It was proposed that task-induced activation, enhanced by active tRNS was sufficient to trigger top-down mechanisms associated with anxiety regulation. In contrast, task-relevant activation with sham tRNS was not. Experiment 3 added to a body of work examining the potential of anodal tDCS for enhancing the effects of ABM training (Clarke et al., 2014; Heeren et al., 2015b). These studies, published since the start of the present research had demonstrated greater acquisition of attention bias in the trained direction when ABM training was administered with concurrent anodal tDCS than when it was delivered with sham tDCS. The outcome from experiment 3 was state anxiety reduction without differentiation between experimental groups. No change in attention bias was observed. As might be expected, analysis of data from all three experiments from study 1 confirmed reduction of state anxiety across all participants irrespective of ABM or tES group. Unexpectedly, threat bias was reduced for participants who had received sham tES but not participants who received active tES. It was identified that, at baseline, participants in the sham tES group had had an attentional bias towards threat and participants who had received active tES had a pre-existing neutral bias. As will be discussed, pre-existing attention bias was a key determinant of attention bias outcome following ABM training. Study 2 involved the measurement of attention bias before and after one session of attend-neutral ABM training with anodal or sham

tDCS, using EEG recordings. The N2pc represented an index of attentional selection and by calculating the difference between N2pc response to neutral faces and N2pc response to angry faces an additional measure of attention bias was provided. There was no indication of training-induced threat bias reduction following analysis of reaction time data nor arising from analysis of ERP data. Anxiety increase was limited to participants who had received sham tDCS. Other results from the study suggested the facilitation of ABM training with anodal but not sham tDCS.

Each experiment was analysed and discussed in detail in its respective chapter. This final chapter will therefore review the key themes arising from the present research. These will focus predominantly on findings common to all phases of the research and the most probable mechanistic explanations for the findings. The implications of these issues will be explored. Limitations of the research will be outlined and finally suggestions for future research will be made.

## 7.2 Key Results and Discussion Points from Studies 1 and 2

### 7.2.1 Equivalent Findings across Training Groups

The present research consistently failed to reveal a difference in the outcomes of attentional training between training groups (attend-neutral ABM, control ABM and no-training ABM) replicating findings from other recent ABM studies (Carlbring et al., 2012; Enock et al., 2015; Cristea et al., 2015; Carleton et al., 2015; Klumpp & Amir, 2010). Consistently, anxiety was reduced for all participants following training and attention bias was unchanged.

Early findings from assessments of attention bias in anxiety using the emotional dot probe confirmed faster responses to threatening stimuli relative to neutral stimuli (Bradley et al., 1998, Broadbent & Broadbent, 1988, Mogg, Philipott & Bradley, 2004). ABM training paradigms were founded on the basis that by introducing a contingency to the emotional dot-probe task whereby the target consistently replaced the stimulus of one particular valence, attention bias towards stimuli of that valence could be induced (Macleod et al., 2002). Preliminary studies showed that ABM training towards neutral faces generated greater reduction in threat bias relative to control ABM training and that greater reductions in anxiety were also observed for participants in the active ABM group compared to those in the control ABM group (see Beard et al., 2012 and Bar-Haim et al., 2010 for review). Findings from the present research challenge the efficacy of contingency-based ABM for inducing attentional bias. In line with a number of recent ABM studies (see Mogg et al., 2017 for a review), anxiety reduction was reported in the absence of threat bias reduction at all stages of study 1. The suggestion that attentional threat bias may be causally related to the development and maintenance of anxiety is therefore also challenged (Van Bockstaele et al., 2012) as is the long-held belief that threat bias and anxiety are positively related (e.g. Beck et al., 1983; Bower et al., 1981). Although the present study failed to find a causal or correlational relationship between attention bias and anxiety this does not preclude the possibility of a relationship between these variables. It is feasible that the procedure or measures used in the present research were responsible for the failure to capture an association between attention bias and anxiety accurately. Alternatively, attention bias and

anxiety are related but the nature of their relationship is more complex than previously suggested.

### 7.2.2 The Importance of Pre-existing Attention Bias

When pre-existing attention bias was included as a covariate in analyses of attention bias data, a reduction in the level of pre-existing bias was observed irrespective of tES or ABM group. This lends further dispute to models of ABM which propose that the outcome of attend-neutral ABM is reduction in threat bias (e.g. Bar-Haim et al., 2010). It suggests instead that the result of active ABM training is reduction in *attention* bias (irrespective of the direction of pre-existing attention bias). A singular mechanism may have been responsible for attention bias reduction for participants at each end of the attention bias spectrum. The same process may have been involved in anxiety reduction across participants. A candidate mechanism is attentional control enhancement (Heeren et al., 2013). Another candidate mechanism is habituation to threatening stimuli via exposure (Carleton et al., 2015). It is also possible that during attentional training, attentional control and exposure mechanisms interacted to induce anxiety reduction. An enhancement in attentional control capacity should facilitate effective shifting between sources of threat and safety. This mechanism, it has been suggested, is necessary for successful emotional coping (Derryberry & Reed, 2002). The exposure element of the ABM task may further facilitate this process with repeated presentation of threatening faces rendering these stimuli less potent signals of danger allowing attentional control processes to better regulate their engagement or avoidance. The present study was not able to implicate attentional control or exposure in

anxiety reduction following ABM training with tES and therefore these arguments are speculative. Further research with the aim of disentangling the roles (if any) of attentional control and exposure processes in anxiety attenuation is warranted.

Given the consistency with which attention bias (threat or neutral) was reduced following ABM training, this pattern of attentional change needs to be considered when designing ABM studies. If the aim of the study is to elicit reduction in threat bias then participants should be selected with a pre-existing threat bias as previously suggested (O'Toole et al., 2012). Alternatively, pre-existing bias should be accounted for during analysis of attention bias data. When comparing results to those from previous ABM studies, researchers should take into account pre-existing bias from their own and previous studies as these might explain similarities and differences in attention bias outcomes.

### 7.2.3 Attentional Control

As mentioned above, a proposed mechanism for anxiety attenuation following ABM training (irrespective of condition) is the enhancement of attentional control (Enock et al., 2014; Heeren et al., 2013; Klumpp et al., 2010; Taylor, Cross & Amir, 2015). It has been suggested that facilitated attentional control disrupts threat processing via the increase of self-regulation (Klumpp et al., 2010). Heeren et al. (2016) purported that anxiety reductions following active ABM training and control ABM may be related to ABM-induced upregulation of higher-order activity in the frontal cortices which down-regulates reactivity in the emotion-centered limbic system (Heeren et al., 2016). Following findings

from experiment 1 (study 1) of equivalent reductions in anxiety across training groups, this idea was explored. In experiment 2 of study 1 participants completed a training paradigm which had been designed to minimise the degree to which cognitive control was engaged and enhanced. Previous studies had shown that tasks which place fewer demands on cognitive control and working memory resources produce inferior attentional control and emotional response improvements relative to more cognitively demanding tasks (e.g. Sari et al., 2015; Swainston et al., 2018). An assumption was made that the less cognitively demanding task would fail to bolster attentional control mechanisms. It was hypothesised that without attentional control enhancement, state anxiety attenuation would not be present following training. However, there were, again, reductions in anxiety across participants. This suggested that an alternative mechanism might be responsible for anxiety attenuation following attentional training. It is possible that, perhaps, attentional control mechanisms were unintentionally recruited during the 'no-training' ABM task delivered in experiment 2 and that attentional control enhancement might still be a candidate mechanism in the diminution of anxiety. Study 2 provided the opportunity to explore the potential modulatory impact of attentional control in ABM outcomes further. The study included a task which gauged attentional control before and after ABM training. There was no enhancement in digit span score following active ABM training relative to before active ABM training. This result therefore did not support the theory that ABM training enhances attentional control capacity. However, surprisingly, there was also no reduction in state anxiety revealed by study 2 data. Therefore, it could not be concluded that state anxiety reduction is independent of attention control enhancement. When study 2 participants' data were filtered by pre-existing trait anxiety,

participants with low baseline trait anxiety who received anodal tDCS did demonstrate an increase in digit span score following ABM training but participants with low trait anxiety who received sham tDCS and participants with high trait anxiety did not. Potential mechanisms of this outcome are discussed below (section 7.2.5) but the discussion does not propose a simple model of ABM whereby the effect of ABM training on anxiety is mediated by attentional control. Instead a complex interaction of pre-existing neural and cognitive state, anxiety and activation of top-down regulatory mechanisms is proposed.

In each experiment from the present research, the attentional control scale was completed by participants at baseline allowing for the investigation of baseline attentional control level as a predictor of ABM-related outcomes. Previous research has shown that higher levels of attentional control at baseline are associated with more successful ABM-related outcomes (Basanovic et al., 2017). The authors suggested that efficient attentional control facilitates performance in the ABM training task leading to a deeper level of training. A relationship between baseline attentional control and ABM effects on attention bias and state anxiety was not observed across the studies. On balance therefore, findings from the present research did not support those reported by Basanovic et al. (2017).

The predictive or mediating role of attentional control in ABM training outcomes remains unclear. The present research failed to provide convincing evidence that attentional control is a determinant of ABM success. However, the present research was not wholly focused on the role attentional control in ABM. Instead it explored different aspects of the modulation of ABM training with tES (for

example, the impact of different forms of tES, different training procedures, the reliability of attention bias measures). It is possible that future research which is more intensely oriented towards determining the part played by attentional control in ABM outcomes will be more informative.

### 7.2.4 Activation Dependent Effects

Across studies 1 and 2, a number of tES effects were demonstrated which might be explained via a common mechanism. Experiment 2 of study 1 revealed a reduction in state anxiety for participants who received active tRNS but not for participants who received sham tRNS. In study 2 there was an increase in anxiety for participants who had received attend-neutral ABM with sham tDCS but not for participants who had received attend-neutral ABM with anodal tDCS. Also in study 2, for participants with a pre-existing threat bias, reduction in threat bias was restricted to those who had received anodal tDCS. Finally study 2 revealed an increase in digit span score for participants with low anxiety who had received anodal tDCS but not for participants who had received sham tDCS.

### 7.2.5 Putative Mechanisms

At the outset of the present research it was hypothesised that tES would enhance the impact of ABM by strengthening signals associated with the learning imparted by active ABM. This was based on previous evidence of facilitated learning following cognitive training with tES relative to cognitive training without tES (e.g. Snowball et al., 2013; Meinzer et al., 2014). Previously, researchers suggested that ABM implicitly trains participants to visually engage

neutral stimuli and inhibit engagement to threatening stimuli (Beard et al., 2012). However, there was no evidence of superior threat bias reduction following ABM with tES or indeed, following any combination of ABM group and tES group. It was therefore speculated in previous chapters that the reductions in anxiety obtained across the research following attentional training was attributable to the enhancement of attentional control capacity (Enock et al., 2014; Klumpp & Amir, 2010). However, increased attentional control might also be expected to yield reductions in threat bias as it would facilitate the visual disengagement from threatening stimuli and engagement to neutral stimuli.

The present thesis submits that it was not the enhancement of the learning effects from the ABM procedure nor an increase in attentional control specifically which were responsible for the tES effects summarised above or the reductions in anxiety observed across participants at almost all phases of the research. This idea is discussed in more detail in Chapter 6 and so a summary is presented here. Frontal brain areas are proposed to be responsible for down-regulating anxiety response (Tang et al., 2012). Part of the role of the PFC is to attenuate performance impairments resulting from threat induced anxiety by regulating amygdala hyperactivity (Gold et al., 2015). It is suggested therefore that a general elevation of activity in frontal brain areas associated with top-down regulatory control might explain these results. Via projections to the limbic system (Kim & Whelan, 2009) these neural structures, when optimally activated were able to attenuate emotional response to threatening stimuli. Where the interaction of attentional training with sham tES did not elicit the beneficial effects induced by training with active tES, then frontal activation was insufficient to down-regulate the influence of anxiety evoking stimuli or

circumstances. It was also insufficient to overcome the aversive influence of anxiety on attentional processes.

Future research examining the impact of tES on cognitive training should not assume that tES will modulate the impact of the training but start from the premise that neural activation elicited by the interaction between tES and training determines outcomes. Where task-induced neural activation is sufficient to achieve the desired result (e.g. anxiety reduction) then tES may have no discernible impact (as in experiment 1 of study 1). However, where a task does not in itself evoke the necessary neural activation (as in experiment 2 of study 1) the additive impact of tES may be required to realise the same effect.

### 7.2.6 Putative Neural Mechanisms

Models of cognitive training facilitation using tES (Fertonani et al., 2017) are compatible with an account of anxiety reduction as a factor of the interaction between ABM and tES. TDCS and tRNS are purported to evoke a shift in neuronal resting membrane potential which renders neurons more sensitive to incoming excitatory signals (Cohen Kadosh, 2013). If task-relevant neurons are not sufficiently depolarised for example in the case of sham tES, then sub-threshold training related signals will remain sub-threshold and no facilitation of the 'desired' behaviour would occur. If tES is sufficient to generate resting membrane alteration and provide a platform for raising sub-threshold task-related signals beyond the threshold of excitation (or if task-relevant or tES-relevant signals are sufficient to achieve this), then facilitation is possible.

To gain insight into how (and where) the tES protocols from studies 1 and 2 may have impacted on neural activity in a way which might have influenced behavioural outcomes, computational modelling was conducted using HD Explore 4.0 (Soterix Medical). Field intensity maps are shown in appendix 19. For the stimulation protocol used in the first two experiments of study 1 (1.5mA tRNS of the IFG with electrodes 35cm$^2$ in size) it was not possible to specify tRNS as the form of stimulation using the HD Explore software. A prediction of electrical fields based on tDCS with the anode above the right IFG and the cathode above the left IFG was produced (see appendix 19) but was not informative regarding the present research. For the protocol used in the third experiment of study 1 and in study 2 (1.5mA tDCS with the anode above F3 and the cathode above the contralateral supra-orbital, each electrode 35cm$^2$) electrical field distribution across the frontal cortices was shown with slightly greater field intensity in the right frontal cortex. The results suggest that tES effects are not confined to the area directly beneath the activating electrode (Klooster et al., 2016). However, they are consistent with a model of ABM/tES effects in which the interaction between ABM and tES induced frontal cortex activation facilitates anxiety reduction. TES modelling studies (e.g. Bikson et al., 2010, Bestmann et al., 2015) are beginning to contribute to our understanding of the mechanisms of tES. Nevertheless, tES modelling techniques require development. Furthermore, the findings described here are relatively crude given that tES was modelled on an adult, male head template and did not take into account aspects of inter-individual variability such as anatomical differences which might influence tES-induced electrical field alterations. Major inferences therefore should not be drawn from the results of the tES modelling performed.

## 7.3 Limitations

### 7.3.1 Clarification of Mechanisms of State Anxiety Reduction

Experiment 1 revealed reductions in anxiety across participants, irrespective of ABM or tES group. Experiment 2 sought to discover whether the mechanism responsible for this anxiety reduction was enhanced attentional control. The results neither confirmed nor opposed the 'attentional control' theory of anxiety reduction. It might therefore have been beneficial for experiment 3 to provide further clarity on this matter. For example, a condition designed to extensively train attentional control could have been administered in order to examine whether this produced greater anxiety attenuation than the ABM tasks previously administered. Additionally, a behavioural measure of attention control could have been added to the procedure. An alternative explanation for anxiety attenuation was that repeated exposure to threat faces had rendered them less anxiety evoking. The inclusion of an ABM task presenting neutral-neutral face pairs would have endorsed this or ruled it out as a putative mechanism. A smaller degree of anxiety reduction following ABM with neutral-neutral face pairs compared to ABM training with neutral-angry face pairs would indicate that habituation to threatening faces does occur as a result of their repeated presentation and that this reduces their anxiety inducing effect.

### 7.3.2 Unreliability of Assessment and Training Task

The study may have been limited by the use of the emotional dot-probe task to measure and train attention bias. As discussed in chapter 6, the task is a measure of attentional engagement based on the concept that threat bias is reflected in faster responses to targets replacing threat related stimuli (Macleod et al., 2002). However, a number of studies have demonstrated successful reduction of threat bias using measures of attentional disengagement (e.g. Amir et al., 2008; 2009b) and dwell time recorded by eye-tracking (Heeren et al., 2015b). Study 2 attempted to address this limitation by including an ERP measure, the N2pc component as an indication of the neural processes underlying attentional selection. However, there is scope for more research using measures of attentional engagement, dwell and disengagement to help with an understanding of the cognitive and neural mechanisms involved in ABM.

### 7.3.3 Study 2 Design

A weakness of the study 2 design was that only attend-neutral ABM was delivered with active or sham tDCS. There was no control ABM group. The aim of the study was to examine the modulatory effect of tES on ABM training rather than to compare the outcomes of active ABM with control ABM. The study design was based on that of Heeren et al., (2015b). In study 2 the anodal tDCS group had better outcomes in terms of state anxiety attenuation, threat bias reduction (for those with a pre-existing threat bias) and increase in digit span score (for participants with low anxiety). Without a non-active ABM group, it is not possible to discern whether these effects were attributable to the

interaction between active ABM and anodal tDCS or whether they may have occurred in the absence of attend-neutral ABM. A control group may have shed further light on this matter. Indeed, the inclusion of a 'no-task' condition in which participants were inactive during tDCS would have been even more telling in terms of identifying the extent to which results were uniquely attributable to tDCS and the extent to which they were induced by the ABM/tDCS interaction.

### 7.3.4 Lack of tES Control Site

Previous studies assessing the impact of tES on cognitive training have included a control tES group. Where the enhancement of training effects is induced via tES of the active site and not via tES of the control site this suggests that the active site has functional specificity for the task in which performance is augmented. For example, Barbieri et al. (2016) and Fertonani et al. (2011) applied the same stimulation parameters above Cz as above their active tES site revealing the modulation of training effects only with tES of the chosen active site. In the present research tES effects were deemed attributable to the tES protocol applied if they differed from results arising from a sham tES group. However, without evidence that the same effects would not have been achieved with stimulation of a different neural area, it cannot be concluded with certainty that the sites stimulated had functional specificity for processes modulated.

### 7.3.5 The Adaptive Nature of Threat Bias and the Dangers of Reducing Threat Bias in Non-anxious, Neutral Biased Participants

It could be argued that the attempt to reduce attention bias towards threat in a population without a discernible threat bias, or who were not high in or clinically anxious was flawed both ethically and in terms of its rationale. As discussed in chapter 1 (section 1.1.4) anxiety and vigilance of threatening stimuli possess innate and privileged roles in human cognition (Bar Haim et al., 2007; Gilbert, 2000; LoBue & Rakinson, 2013). These have the aim of promoting mental preparedness and high arousal so that potential threats can be quickly responded to (Gilbert, 1998). However, it is proposed that individuals with anxiety are abnormally sensitive to threat-related stimuli and are thus more likely to perceive benign or ambiguous stimuli as threatening (Barry, 2015). With this in mind, a large proportion of ABM research has been conducted with high or clinically anxious cohorts who are more likely to have a threat bias and who have more to gain from the reduction of threat bias than non-anxious individuals (e.g. Amir et al., 2011; Amir et al., 2009; Amir et al., 2010; Baert et al., 2010; Boettcher et al., 2012; Carlbring et al., 2012; Hayes et al., 2010; Heeren et al., 2012; Li et al., 2008; Neubauer et al., 2010; Schmidt et al., 2010; Wells et al., 2010). Meta-analyses have supported that ABM training away from threat is more effective in anxious individuals than in neuro-typical participants (e.g. Bar Haim et al., 2007; Beard et al., 2012; Hakamata et al., 2010).

In summary, the evolutionary and automatic fear system plays an important part in priming behavioural responses to potential stressors and in relieving negative emotional state (Rosen & Shulkin, 1998). Studies with the aim of reducing anxiety by increasing engagement to non-threatening stimuli have thus focused on individuals with maladaptive levels of anxiety and elevated sensitivity to threat related stimuli. Delivering ABM training to participants without elevated threat bias and anxiety in the present study, risked reducing attention bias towards threat to a level at which it was no longer adaptive. Furthermore, there may have been a danger of reinforcing or inducing attentional avoidance, a form of attention bias which is, like threat bias, considered maladaptive (Koster et al., 2006). It has been proposed that certain individuals overtly orient away from threatening stimuli in order to avoid the emotion of fear or anxiety which might arise from the cognitive evaluation of risk (Aue et al., 2013). However, this attentional (and emotion regulation) strategy may prevent the adoption of active coping skills in reaction to threat (Barlow et al., 2004) as it prevents engagement to stimuli which might oppose the expectation of aversive consequences (Barry et al., 2015). For the avoidant individual therefore, anxiety and fear for stimuli of an ambiguous or threatening valance may persist as there is no disconfirmation that these stimuli are harmful (Helbigland et al., 2010). ABM training away from threat in such individuals may therefore be contraindicative (Evans et al., 2016).

It is important to highlight that in the present research ABM training away from threatening stimuli did not maintain or enhance attentional avoidance in participants with a pre-existing attention bias towards neutral stimuli. In fact, consistently, there was a reduction in neutral bias for these participants

following training (irrespective of ABM or tES condition). There was evidence for state anxiety reduction following training for participants with a pre-existing neutral bias rather than an increased or preserved level of state anxiety. Moreover, in defence of the decision to use ABM with non-clinically anxious participants, study 1 was not exclusively an ABM study. The aim was to explore the modulation of ABM using tES. Although, tES has been safely used with clinically anxious individuals (e.g Heeren et al., 2017; Shiozawa et al., 2013) the interaction effects of applying tES with a task designed to modify anxiety were unknown. The assay of this combined methodology in non-anxious participants was therefore necessary before applying this treatment to high or clinically anxious individuals. Previous studies which have used tES to enhance ABM training effects have also been conducted in non-anxious participants (e.g. Clarke et al., 2014; Heeren et al., 2015b). Nevertheless, it is acknowledged that inducing threat avoidance in already avoidant individuals may have had unfavourable implications.

### 7.3.6 Expectation of State Anxiety Reduction in Non-anxious Participants

Cognitive models of anxiety emphasise the positive relationship between attention bias towards threat and trait or clinical anxiety (Beck et al., 1983; Bower, 1981; Mogg & Bradley, 1998; Williams et al., 1988, 1997). A wealth of evidence supports this relationship (e.g. Amir, Taylor & Donohue, 2011; Bradley, Mogg & Millar, 2000; De Voogd, Wiers, Prins & Salemink, 2014; Fox, Russo & Dutton, 2002; Mathews & Macleod, 1985; Macleod et al., 1986; Mogg, Mathews & Weinman, 1989). In their 2007 meta-analysis, Bar-Haim et al., reported that

threat bias was of equivalent magnitude across clinical and high trait anxiety populations and that the bias was not present in non-anxious participants (Bar-Haim et al., 2007). For this reason, ABM research with the aim of training attention towards non-threatening stimuli and away from non-threatening stimuli has often recruited participants with high level trait anxiety or with clinical anxiety (Amir et al., 2009b; Amir, Taylor & Donohue., 2011; Hazen, Vasey & Schmidt, 2009; Heeren et al.,2015b; Schmidt, Richey, Buckner & Timpano, 2009). Meta-analyses of ABM studies have reported that ABM is more effective at reducing attention bias and anxiety in high or clinically anxious cohorts (e.g. Beard et al., 2012). In low anxious individuals who are not characterised by attention bias towards threat, increasing threat value results in increased attention allocation to potentially threatening stimuli (Mogg & Bradley. 1998). In ABM studies therefore, where trait anxiety has not been selected for, researchers have often employed a stressor task to assess whether increasing the capacity to attend non-threatening stimuli attenuates the reinforcement or elevation of anxious arousal in a stressful situation (e.g. Macleod et al., 2002; Van Bockstaele et al., 2012).

In the present research, participants were not pre-selected for high level trait anxiety. Without selecting for a population likely to demonstrate attention bias towards threat the reduction of threat bias was less likely to be successful. Therefore, anxiety reduction was also less probable. In addition, a stressor task was not included in the experimental design. There was therefore no reason to believe that threat bias and anxiety were elevated and susceptible to manipulation using ABM training. To anticipate state anxiety reduction where state anxiety was not induced or elevated was a weakness of the present

research. Nevertheless, state anxiety was reduced following ABM training, albeit irrespective of tES of ABM condition. It is possible that state anxiety may have been elevated before ABM training, perhaps due to experiment participation. It could be argued that factors other than attentional training were responsible for the observed reduction in state anxiety (e.g. non-specific effects, placebo). This argument could be countered by highlighting that in studies where state anxiety is artificially elevated (for example using a stressor task) factors other than ABM training could explain anxiety attenuation. For example, state anxiety reduction could be the result of practice effects (Heeren et al., 2015c).

The decision to recruit participants who did not demonstrate high trait anxious participants was based on the aim of studying the applicability of ABM with tES in a non-anxious population. It was however, also felt that the modulating effect of trait anxiety could be assessed by including pre-existing trait anxiety as a covariate in follow-up analyses.

### 7.3.7 The Decision to Continue with ABM Without Evidence for a Relationship Between Attention Bias and Anxiety

The present research consistently failed to support a relationship between trait anxiety and attentional bias. Given this, it is reasonable to question why ABM was done. ABM was designed as a cognitive task to attenuate anxiety via the reduction attention bias towards threat (Macleod et al., 2002). Without showing that anxiety and attention bias were related, the assumption that the modulation of one would have an effect on the other was unjustified. This lack

of a relationship was only ascertained upon analysis of data from experiment 1. Had this been established prior to commencing the research, investigations may have taken a different course. For example, participants may have been selected for pre-existing threat bias or high-level trait anxiety. Following experiment 1, the decision could have been taken to abandon ABM as a methodology. However, at this point there were findings such as the reduction state anxiety across participants following training, irrespective of ABM or tES group, which warranted investigation. Additionally, prior to experiment 1, a wealth of studies had demonstrated a relationship between attention bias and anxiety (e.g. Amir, Taylor & Donohue, 2011; Bradley, Mogg & Millar, 2000; De Voogd, Wiers, Prins & Salemink, 2014; Fox, Russo & Dutton, 2002; Mathews & Macleod, 1985; Macleod et al., 1986; Mogg, Mathews & Weinman, 1989). Cognisant that the lack of an effect is not proof that an effect does not exist, it was deemed important to continue with ABM (even if to further investigate the lack of association between anxiety and attention bias). Indeed, the fact that consistently, across experiments a relationship between attention bias and anxiety failed to emerge in the population tested (healthy participants) is a finding which warrants reporting and one which may be of interest to researchers planning to undertake ABM research.

## 7.4 Future Research

Future studies should continue to explore the mechanism or mechanisms responsible for anxiety reduction following attentional training. Moreover, research should focus on whether improved anxiety is related to, or mediated by

reductions in threat bias for participants with pre-existing threat bias and reductions in neutral bias for participants with pre-existing neutral bias.

Research might investigate whether attentional control processes specifically, are augmented via ABM training. This might be done by adding additional measures of attentional control such as the attention network task (ANT: Fan et al., 2002) which assesses the alerting, orienting and executive functions of attention, before and after ABM training. The training task might also be modified to vary the level to which attentional control processes are recruited and trained. Experiment 2 of study 1 attempted to reduce the level of attentional control required for the training task delivered in order to examine whether this eliminated anxiety amelioration following training. However, studies have not increased cognitive load and investigated the impact of this on behavioural and affect measures.

As suggested above, the anxiety inducing effects of ABM training with concurrent tES may have been due to the facilitation of neural structures in the frontal cortices associated with top-down regulatory mechanisms. Once activated these may exert control over hyperactivity of the limbic system leading to anxiety reduction. This interpretation of findings is appealing given the lack evidence (from the present research) that anxiety reduction was mediated by task-induced threat bias reduction. It is further appealing given that the present research provided little evidence that attentional control mediated training effects on anxiety. If, as proposed the anxiety attenuating effects of attentional training in the present study were independent of contingency effects and were attributable to the facilitation of neural mechanisms associated with top-down

processes (which might include but are not confined to attentional control), then any cognitive task which increases activity in frontal cortices might be effective in reducing anxiety. For example, arithmetic learning (Peters & De Smedt, 2018) and lexical processing (Edwards et al., 2005) tasks are known to recruit the DLPFC. Anxiety reduction following participation in such tasks would support the notion that a bolstering of general top-down regulatory capacity is implicated in anxiety reduction. Furthermore, tES has the potential to induce such facilitation without concurrent training. Studies might therefore explore whether excitatory tES delivered offline, during rest has an impact on anxiety. Training which does not use emotional stimuli would also indicate whether repeated exposure to threatening stimuli is implicated in training outcomes.

Finally, to obtain a comprehensive picture of attention bias and attentional processes, studies could use measures which assess all aspects of attention distribution including engagement to, disengagement from and gaze time to stimuli. Eye-tracking, for example might reliably capture each of these proposed attributes or forms of attention bias.

## 7.5 Summary

The aim of this chapter was to outline the key findings and issues arising from the current research and their implications. In doing so, the discussion illuminates how the results contribute to existing research and theory around ABM and the modulation of ABM training using tES. Study 1 revealed equivalent outcomes for all forms of ABM training (attend-neutral, control and no-training). Across all participants anxiety was reduced. Attention bias was modified but

this modification was characterised by reduced threat bias for participants with pre-existing threat bias and reduced neutral bias for participants with pre-existing neutral bias. These findings challenge original models of ABM which purported that anxiety attenuation occurs as a result of reduced engagement of threat. They suggest instead that it may stem from reduced attention bias irrespective of the direction of bias. Study 2 produced several findings which suggested the facilitation of ABM with anodal tDCS. The purported mechanism for these findings was enhanced top-down control of 'bottom up' emotional response produced by the interaction between task-relevant neural activation and anodal tDCS.

The present findings have implications for the future of ABM research. Promising findings from early ABM studies led to speculation that ABM might represent an easily accessible, non-invasive and effective treatment for anxiety. However, if, as indicated by the present study, the mechanism via which ABM achieves the modulation of anxiety level is not that which was originally purported (Amir et al., 2008, Bar-Haim et al., 2010, Hakamata et al., 2011; Macleod et al., 2002) then the study of ABM as a potential treatment for anxiety may not be a worthwhile occupation. Identifying the 'active' element(s) of ABM on the other hand, that which is responsible for anxiety attenuation, is undoubtedly a constructive pursuit and the present thesis has suggested ways in which this could be approached. Nevertheless, the current thesis represents a relatively small body of work amidst a wealth of ABM research, much of which empirically supports the view that contingency-based ABM training induces attention bias modulations which lead to anxiety increase or attenuation, depending on the direction in which attention was trained (towards threatening or towards non-

threatening stimuli). Findings from the present study did not support this previous account of ABM however that is not to say that they disprove it. It is acknowledged that many factors may have been responsible for the disparities in findings across ABM studies including methodological factors. In summary, continued exploration of ABM for the reduction of anxiety would be valuable along with investigation of the mechanisms via which ABM induces anxiety reduction. It is hoped that the present thesis has contributed to a broader understanding of the cognitive processes underlying attention bias modification and the potential for these processes to be modulated using tES.

# APPENDIX 1

## Ethics Approval Statement Study 1

The research for this project was submitted for ethics consideration under the reference PSYC 14/ 116 in the Department of Psychology and was approved under the procedures of the University of Roehampton's Ethics Committee on 22.04.14.

# APPENDIX 2

## Ethics Approval Statement Study 2

The research for this project was submitted for ethics consideration under the reference PSYC 14/ 157 in the Department of Psychology and was approved under the procedures of the University of Roehampton's Ethics Committee on 16.04.15.

# APPENDIX 3

## Participant Consent Form for Study 1


ETHICS COMMITTEE

## PARTICIPANT CONSENT FORM

**Title of Research Project: <u>Brain Stimulation and attention.</u>**

You are invited to take part in a research study in the Department of Psychology at the University of Roehampton. The study aims to further our understanding of how we attend to information and how brain stimulation can affect this. The study will take place in the cognitive laboratory at the University of Roehampton Whitelands campus. You will be asked to take part on three consecutive days; the entire procedure should not take longer than 90 minutes each day.

Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with the researchers or with family, friends, your personal physician or other health professional.

**<u>Description of the Research Project:</u>**

<u>Questionnaires</u>

Before you take part you will need to fill in two screening questionnaires. The first regards which hand you use most often as we are only looking for right-handed participants. The second is a safety screening questionnaire that will allow us to determine whether it is safe for you to take part. You will also be asked to complete a short questionnaire which contains questions relating to how you are feeling. You will also be asked to complete questionnaires which contain questions relating to your attention, to how you feel about other peoples' opinion of you and to how you have been feeling recently. *Please note that the questionnaires are designed simply to look at normal variation in aspects of mood and personality in the population, not as tools to diagnose mental illness.*

Computer task

You will be asked to view some pictures of faces and letters on a computer screen. The faces will have threatening or neutral expressions. One of the faces will be replaced with a letter and your task will be to respond to the location of the letter as quickly and as accurately as possible using a computer keypad. You will be asked to do this task before, after and during the brain stimulation.

Transcranial Direct Current Stimulation (tES)

The next part of the study will involve a technique called transcranial Electical Stimulation (tES) that can change brain processing for a temporary period of time. It works by applying a very small current (1.5 milliamps) to your scalp that passes through your head and brain and changes the electrical properties of the brain cells under the electrode. The amount of current that is discharged from the device across your scalp is very small and poses no physical danger. However, you should tell us if you have a cardiac pacemaker or other implanted medical devices, any metal clips on blood vessels, or pieces of metal inside your body, since the electrical current might have an effect on these. It is important that you realise that transcranial Electrical Stimulation is not the same as procedures used in clinical practice such as ECT (electroconvulsive therapy). You should complete the transcranial Electrical Stimulation Adult Safety Screen (TASS) questionnaire before taking part; this will allow the experimenter to judge if it is safe or not for you to take part.

TES is carried out by applying two soft and wet sponges, one on either side of the front of your scalp, just above your eyebrows. These sponges contain the electrodes and are held in place with a rubber band much like a hair band. A very small current is then passed through the electrodes: exactly 1.5 milliamps. The machine, for the first 20 seconds, slowly ramps up the current from zero to one milliamp so as to accustom you to the sensation of the electricity. During the ramp up period, which lasts 20 seconds, you will likely feel a tingling or an itching sensation under the sponges. The current will be applied to your scalp for a total of 20 minutes. Should you wish to withdraw during this period, or any other time, you can of course do so without any negative consequences.

Possible Side Effects and Hazards of Electrical Stimulation

Transcranial electrical stimulation can be harmful in people who have a pacemaker or other devices in the heart, significant heart disease, an implanted medication pump, a metal plate in the skull, a cochlear (ear) implant, an implanted brain stimulator, increased pressure inside the head, or metal objects inside the eye or skull (for example after brain surgery or a shrapnel wound). Please inform the investigators if you might have any of these. Since the effects of electric current stimulation on the fetus are unknown, we will ask you if there is a chance that you might be pregnant. We will use a screening form to evaluate these and other conditions.

Transcranial electrical stimulation has been used safely in thousands of individuals around

the world. The common side effects of tES are a slight discomfort at the site on your skull where we are applying the stimulation. In healthy human subjects, tES is regarded as a safe and non-invasive method. If you currently suffer from or suffered in the past from any neurological or psychiatric disease, you have to report this to the investigators. If you have any significant adverse event, we will stop the study, even if you are willing to continue.

Benefits of your participation

Information learned from this study will be used to help our understanding of attention, and may eventually lead to advances in the treatment of mental disorders.

Right to withdraw

You are under no obligation to finish the experiment and can withdraw from participation from the whole experiment or any part of it at any point without needing to justify your decision. You can also request for your data to be withdrawn at any time after participation in the study. In order to do this, please contact the investigator with your participant number, which you will find on the Debrief Form. Please be aware, however, that data may already have been published in a collated form at the time of request. Finally, if you are a student who is volunteering for course credits as part of an undergraduate module, please be advised that there will be no adverse consequences in relation to assessment for your degree if you decide to withdraw.

Confidentiality and anonymity

All data relating to your participation in this study will be held and processed in the strictest confidence, in accordance with the Data Protection Act (1998). All data will be held securely in password protected computer files and locked filing cabinets. No one outside of the research team will have access to your individual data. Your identity will not be passed on to anyone who is not involved in this study, and will be protected in the publication of any findings.

Consent

This study will be performed under the supervision of Dr. Margot Crossman and Dr. Jonathan Silas at The Department of Psychology, Roehampton University. This project has been approved under the procedures of the University of Roehampton's Ethics Committee. This study is part of a research protocol, and is not intended to provide a clinical examination of the brain or a clinical evaluation in any respect.

a. I have read and received a copy of this consent form and have been given the opportunity to ask questions. You have given me: (i) an explanation of the procedures to be followed in the project, including an identification of those which

are experimental; and (ii) answers to questions I have made.

b. I understand that there may be no direct benefit to me from my participation in this study as described above.

c. I understand that my participation will not cost me anything other than the time and effort involved.

d. I understand that all personal data relating to volunteers are held and processed in the strictest confidence, in accordance with the Data Protection Act (1998).

e. I understand that by signing this agreement, I do not waive any legal rights or release Roehampton University, its agents, or you from liability for negligence.

f. I understand that I am free to withdraw from the study at any time without needing to justify my decision and without prejudice. Furthermore, I am at liberty to withdraw my data at any time following participation in the study.

g. My identity will not be passed on to anyone who is not involved in this study, and will be protected in the publication of any findings. Researchers involved in the study will be unaware of any links between my identity and the data collected and accordingly no individual feedback will be given.

h. I confirm that I have read and understood the above and freely consent to participating in this study. I have been given adequate time to consider my participation and agree to comply with the instructions and restrictions of the study.

I hereby give my consent to be the subject of your research.

| --- | --- | --- |
| signature | Name | Date |

If you require advice, information or reassurance about a technical or health related matter, or have a concern about any other aspect of your participation, please raise this with the researcher:

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However, if you would like to contact an independent party please contact the Head of Department Dr. Diane Bray [email: d.bray@roehampton.ac.uk; 020-8392 3627; Room 2053, Whitelands College, Holybourne Avenue, Roehampton, London, SW15 4JD].

# APPENDIX 4

## Participant Consent Form for Study 1


ETHICS COMMITTEE

## PARTICIPANT CONSENT FORM

**Title of Research Project: <u>Brain Stimulation and attention</u>**

You are invited to take part in a research study in the Department of Psychology at the University of Roehampton. The study aims to further our understanding of how the brain functions when we attend to information and how brain stimulation can affect this. The study will take place in the cognitive laboratory at the University of Roehampton Whitelands campus and will last approximately three and a half hours.

Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with the researchers or with family, friends, your personal physician or other health professional.

**<u>Description of the Research Project:</u>**

<u>Questionnaires</u>

Before you take part you will need to fill in two screening questionnaires. The first regards which hand you use most often as we are only looking for right-handed participants. The second is a safety screening questionnaire that will allow us to determine whether it is safe for you to take part. You will also be asked to complete a few short questionnaires containing questions relating to how you are feeling, how you have been feeling lately, your attention and to how you feel about other peoples' opinion of you. *Please note that the questionnaires are designed simply to look at normal variation in aspects of mood and personality in the population, not as tools to diagnose mental illness.*

Computer task

You will be asked to view some pictures of faces and letters on a computer screen. One of the faces will be replaced with a letter and your task will be to respond to the location of the letter as quickly and as accurately as possible using a computer keypad. The computer task has been divided into 'blocks'. Between each block you will be given a quick break before you continue with the task.

Electroencephalography (EEG)

Whilst performing the first 2 blocks of the computer task your electroencephalography (EEG) will be recorded. Small electrical signals known as event related potentials or ERPs, will be measured from your scalp. In order to do this, the experimenter will fit you with a head cap which looks like bathing cap with small holes (electrode holders). Electrodes (sensors) with wires attached will be slotted into the electrode holders. These sensors will pick up electrical activity from your brain. In order to ensure good contact between your skin and the sensors, the skin beneath some of the sensors will be cleaned with alcohol, and a conductive gel (a completely harmless saline solution) will be injected into each of the electrode holders before the electrodes are attached. If you find this at all uncomfortable, please inform the experimenter and the procedure will be stopped. Following EEG you will be able to wash any remaining gel out of your hair using the private facilities which are available in the department. The EEG equipment has been fully tested by the manufacturers and is regularly checked by a technician. Please note that EEG only *measures* electrical activity from the brain and does not apply any electricity to you and that the process is entirely safe.

Transcranial Electrical Stimulation (TES)

The next part of the study will involve a technique called transcranial Electrical Stimulation (tES) that can change brain processing. It works by applying a very small current (1.5 milliamps) to your scalp that passes through your head and brain and changes the electrical properties of the brain cells under the electrode. The amount of current that is discharged from the device across your scalp is very small and poses no physical danger. However, you should tell us if you have a cardiac pacemaker or other implanted medical devices, any metal clips on blood vessels, or pieces of metal inside your body, since the electrical current might have an effect on these. It is important that you realise that transcranial electrical stimulation is not the same as procedures used in clinical practice such as ECT (electroconvulsive therapy). You should complete the transcranial Electrical Stimulation Adult Safety Screen (TASS) questionnaire before taking part; this will allow the experimenter to judge if it is safe or not for you to participate.

TES is carried out by applying two soft and wet sponges, on your scalp. These sponges contain the electrodes and are held in place with a rubber band much like a hair band. A very small current is then passed through the electrodes: at 1.5 milliamps. The machine, for the first 20 seconds, slowly ramps up the current from zero to one milliamp so as to accustom you to the sensation of the electricity. During the ramp up period, which lasts 20

seconds, you will likely feel a tingling or an itching sensation under the sponges. The current will be applied to your scalp for 20 minutes. After this time, the tES electrodes will be removed and you will continue with the study. Should you wish to withdraw during this period, or any other time, you can of course do so without any negative consequences.

Towards the end of the computer task (the last 2 blocks), we will once again measure your brain activity. The EEG head cap will be fitted and electrical signals will be recorded

Possible Hazards of EEG

EEG is a safe and non-invasive procedure. The experimenter will however check that you are not susceptible to skin inflammation caused by the application of the cleansing alcohol or conductive gel by applying a small amount to the back of your hand before the procedure begins. If you have any reaction to these substances then the session will not continue.

You may experience discomfort if the alcohol or gel is applied over sensitive skin or breaks in the skin's surface. The positioning of an electrode above such areas might also affect your EEG recordings. It is therefore important that you inform us if you have any moles, scars, pimples or cuts on the face or scalp before taking part in the study.

Possible Side Effects and Hazards of Electrical Stimulation

Transcranial electrical stimulation can be harmful in people who have a pacemaker or other devices in the heart, significant heart disease, an implanted medication pump, a metal plate in the skull, a cochlear (ear) implant, an implanted brain stimulator, increased pressure inside the head, or metal objects inside the eye or skull (for example after brain surgery or a shrapnel wound). Please inform the investigators if you have any of these. Since the effects of electrical stimulation on the fetus are unknown, we will ask you if there is a chance that you might be pregnant. We will use a screening form to evaluate these and other conditions.

Transcranial electrical stimulation has been used safely in thousands of individuals around the world. The common side effects of tES are a slight discomfort at the site on your skull where we are applying the stimulation. In healthy human subjects, tES is regarded as a safe and non-invasive method. If you currently suffer from or suffered in the past from any neurological or psychiatric disease, you have to report this to the investigators. If you have any significant adverse event, we will stop the study, even if you are willing to continue.

Long-lasting effects

The computer task that you will do has been used in large numbers of research projects before and is also available on a number of downloadable apps. It is possible that the

computer task will have a long lasting effect on the way you allocate your attention and that the extent and length of any effect may be increased by tES. It is highly unlikely that you will notice any effect and there is no evidence to suggest that if there is a lasting effect, it would be harmful in any way.

Benefits of your participation

Information learned from this study will be used to help our understanding of attention, and may eventually lead to advances in the treatment of mental disorders.

Right to withdraw

You are under no obligation to finish the experiment and can withdraw from participation from the whole experiment or any part of it at any point without needing to justify your decision. You can also request for your data to be withdrawn at any time after participation in the study. In order to do this, please contact the investigator with your participant number, which you will find on the Debrief Form. Please be aware, however, that data may already have been published in a collated form at the time of request. Finally, if you are a student who is volunteering for course credits as part of an undergraduate module, please be advised that there will be no adverse consequences in relation to assessment for your degree if you decide to withdraw.

Confidentiality and anonymity

All data relating to your participation in this study will be held and processed in the strictest confidence, in accordance with the Data Protection Act (1998). All data will be held securely in password protected computer files and locked filing cabinets. No one outside of the research team will have access to your individual data. Your identity will not be passed on to anyone who is not involved in this study, and will be protected in the publication of any findings.

Consent

This study will be conducted by researcher Sara Pretorius under the supervision of Dr. Margot Crossman and Dr. Jonathan Silas at The Department of Psychology, Roehampton University. This project has been approved under the procedures of the University of Roehampton's Ethics Committee. This study is part of a research protocol, and is not intended to provide a clinical examination of the brain or a clinical evaluation in any respect.

a. I have read and received a copy of this consent form and have been given the opportunity to ask questions. You have given me: (i) an explanation of the procedures to be followed in the project, including an identification of those which

are experimental; and (ii) answers to questions I have made.

b. I understand that my participation will not cost me anything other than the time and effort involved.

c. I understand that all personal data relating to volunteers are held and processed in the strictest confidence, in accordance with the Data Protection Act (1998).

d. I understand that by signing this agreement, I do not waive any legal rights or release Roehampton University, its agents, or you from liability for negligence.

e. I understand that I am free to withdraw from the study at any time without needing to justify my decision and without prejudice. Furthermore, I am at liberty to withdraw my data at any time following participation in the study.

f. My identity will not be passed on to anyone who is not involved in this study, and will be protected in the publication of any findings. Researchers involved in the study will be unaware of any links between my identity and the data collected and accordingly no individual feedback will be given.

g. I confirm that I have read and understood the above and freely consent to participating in this study. I have been given adequate time to consider my participation and agree to comply with the instructions and restrictions of the study.

I hereby give my consent to be the subject of your research.

| --- | --- | --- |
| signature | Name | date |

If you require advice, information or reassurance about a technical or health related matter, or have a concern about any other aspect of your participation, please raise this with the researcher:

Researcher Contact Details:

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However, if you would like to contact an independent party please contact the Head of Department Dr. Diane Bray [email: d.bray@roehampton.ac.uk; 020-8392 3627; Room 2053, Whitelands College, Holybourne Avenue, Roehampton, London, SW15 4JD].

# APPENDIX 5

## Transcranial Electrical Current Stimulation (tES): Safety questionnaire

1. Have you ever:

   a. Had an adverse reaction to tES e.g. transcranial direct current stimulation (tDCS), transcranial random noise stimulation (TRNS), transcranial alternating current stimulation (TACS)? ***Yes /No***

   b. Had a seizure (generalised or partial/focal epileptic seizure)? ***Yes /No***

   c. Had an electroencephalogram (EEG) for clinical purposes? ***Yes /No***

   d. Had a stroke? ***Yes /No***

   e. Had a head injury (including neurosurgery)? ***Yes /No***

2. Do you have any metal in your head (outside of the mouth,) such as shrapnel, surgical clips, or fragments from welding or metalwork? ***Yes /No***

3. Do you have any implanted devices such as cardiac pacemakers, medical pumps, or intracardiac lines? ***Yes /No***

4. Do you suffer from frequent or severe headaches? ***Yes /No***

5. Have you ever had any other brain-related condition? ***Yes /No***

6. Have you ever had any illness that caused brain injury? ***Yes /No***

7. Are you taking any medications? ***Yes /No***

8. Is there any possibility that you might be pregnant? ***Yes /No***

9. Does anyone in your family have epilepsy? ***Yes /No***

10. Do you have an existing skin condition on the scalp? ***Yes /No***

11. Do you need further explanation of tES and its associated risks? ***Yes /No***

# APPENDIX 6

## Edinburgh Handedness Inventory

**Participant no._____**

Please indicate your preferences in the use of hands in the following activities *by putting a check in the appropriate column*. Where the preference is so strong that you would never try to use the other hand, unless absolutely forced to, *put 2 checks*. If in any case you are really indifferent, *put a check in both columns*.

Some of the activities listed below require the use of both hands. In these cases, the part of the task, or object, for which hand preference is wanted is indicated in parentheses.

Please try and answer all of the questions, and only leave a blank if you have no experience at all with the object or task.

| | Left | Right |
|---|---|---|
| 1. Writing | ☐ ☐ | ☐ ☐ |
| 2. Drawing | ☐ ☐ | ☐ ☐ |
| 3. Throwing | ☐ ☐ | ☐ ☐ |
| 4. Scissors | ☐ ☐ | ☐ ☐ |
| 5. Toothbrush | ☐ ☐ | ☐ ☐ |
| 6. Knife (without fork) | ☐ ☐ | ☐ ☐ |
| 7. Spoon | ☐ ☐ | ☐ ☐ |
| 8. Broom (upper hand) | ☐ ☐ | ☐ ☐ |
| 9. Striking Match (match) | ☐ ☐ | ☐ ☐ |
| 10. Opening box (lid) | ☐ ☐ | ☐ ☐ |
| **TOTAL(count checks in both columns)** | | |

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# APPENDIX 7

## State-Trait Anxiety Inventory for Adults

### Trait Anxiety Scale

The following questions are about how you feel. Please read each statement and then mark the appropriate number to indicate how you *generally* feel. There are no right or wrong answers. Please mark like so→ 1 2 (3) 4 5 6 7 using brackets to indicate your choice

| | Almost never | sometimes | often | Almost always |
|---|---|---|---|---|
| I feel pleasant. | 1 | 2 | 3 | 4 |
| I feel nervous and restless. | 1 | 2 | 3 | 4 |
| I feel satisfied with myself. | 1 | 2 | 3 | 4 |
| I wish I could be as happy as others seem to be. | 1 | 2 | 3 | 4 |
| I feel like a failure. | 1 | 2 | 3 | 4 |
| I feel rested. | 1 | 2 | 3 | 4 |
| I feel 'cool, calm and collected'. | 1 | 2 | 3 | 4 |
| I feel that difficulties are piling up so that I cannot overcome them. | 1 | 2 | 3 | 4 |
| I worry too much over something that really doesn't matter. | 1 | 2 | 3 | 4 |
| I am happy. | 1 | 2 | 3 | 4 |
| I have disturbing thoughts. | 1 | 2 | 3 | 4 |
| I lack self-confidence. | 1 | 2 | 3 | 4 |
| I feel secure. | 1 | 2 | 3 | 4 |
| I make decisions easily. | 1 | 2 | 3 | 4 |
| I feel inadequate. | 1 | 2 | 3 | 4 |
| I am content. | 1 | 2 | 3 | 4 |
| Some unimportant things run through my head and bothers me. | 1 | 2 | 3 | 4 |
| I take disappointments so keenly that I can't put them out of my mind. | 1 | 2 | 3 | 4 |
| I am a steady person. | 1 | 2 | 3 | 4 |
| I get in a state of tension or turmoil as I think over my recent concerns and interests. | 1 | 2 | 3 | 4 |

## State Anxiety Scale

Now, please indicate how you feel *right now*, that is, *at this moment.*

| | Not at all | Somewhat | Moderately so | Very much so |
|---|---|---|---|---|
| I feel calm. | 1 | 2 | 3 | 4 |
| I feel secure. | 1 | 2 | 3 | 4 |
| I am tense. | 1 | 2 | 3 | 4 |
| I feel strained. | 1 | 2 | 3 | 4 |
| I feel at ease. | 1 | 2 | 3 | 4 |
| I feel upset. | 1 | 2 | 3 | 4 |
| I am presently worrying over possible misfortunes. | 1 | 2 | 3 | 4 |
| I feel satisfied. | 1 | 2 | 3 | 4 |
| I feel frightened. | 1 | 2 | 3 | 4 |
| I feel comfortable. | 1 | 2 | 3 | 4 |
| I feel self-confident. | 1 | 2 | 3 | 4 |
| I feel nervous. | 1 | 2 | 3 | 4 |
| I am jittery. | 1 | 2 | 3 | 4 |
| I feel indecisive. | 1 | 2 | 3 | 4 |
| I am relaxed. | 1 | 2 | 3 | 4 |
| I feel content. | 1 | 2 | 3 | 4 |
| I am worried. | 1 | 2 | 3 | 4 |
| I feel confused. | 1 | 2 | 3 | 4 |
| I feel steady. | 1 | 2 | 3 | 4 |
| I feel pleasant. | 1 | 2 | 3 | 4 |

# APPENDIX 8

## Attentional Control Scale

*1=almost never; 2=sometimes; 3=often; 4=always*

1. It's very hard for me to concentrate on a difficult task when there are noises around 1 2 3 4
2. When I need to concentrate and solve a problem I have trouble focusing my attention. 1 2 3 4
3. When I am working hard on something, I still get distracted by events around me. 1 2 3 4
4. My concentration is good even if there is music in the room around me. 1 2 3 4
5. When concentrating, I can focus my attention so that I become unaware of What's going on in the room around me. 1 2 3 4
6. When I am reading or studying, I am easily distracted if there are people talking in the same room. 1 2 3 4
7. When trying to focus my attention on something, I have difficulty blocking out distracting thoughts. 1 2 3 4
8. I have a hard time concentrating when I am excited about something. 1 2 3 4
9. When concentrating I ignore feelings of hunger or thirst. 1 2 3 4
10. I can quickly switch from one task to another. 1 2 3 4
11. It takes me a while to get really involved in a new task. 1 2 3 4
12. It is difficult for me to coordinate my attention between the listening and writing required when taking notes during lectures. 1 2 3 4
13. I can become interested in a new topic very quickly if I need to. 1 2 3 4
14. It is easy for me to read or write while I'm also talking on the phone. 1 2 3 4
15. I have trouble carrying on two conversations at once. 1 2 3 4
16. I have a hard time coming up with new ideas quickly. 1 2 3 4
17. After being interrupted or distracted, I can easily shift my attention back to what I was doing before. 1 2 3 4
18. When a distracting thought comes to mind, it is easy for me to shift my attention away from it. 1 2 3 4
19. It is easy for me to alternate between two different tasks. 1 2 3 4
20. It is hard for me to break from one way of thinking about something and look at it from another point of view. 1 2 3 4

# APPENDIX 9

## Fear of Negative Evaluation Scale

Please show your reactions to the following statements by circling either "T" (True) or "F" (False).

Answer the questions quickly without thinking about them too much.

1. I rarely worry about seeming foolish to others. T F
2. I worry about what people will think of me even when I know it doesn't make any difference. T F
3. I become tense and jittery if I know someone is sizing me up. T F
4. I am unconcerned even if I know people are forming an unfavourable impression of me. T F
5. I feel very upset when I commit some social error. T F
6. The opinions that important people have of me cause me little concern. T F
7. I am often afraid that I may look ridiculous or make a fool of myself. T F
8. I react very little when other people disapprove of me. T F
9. I am frequently afraid of other people noticing my shortcomings. T F
10. The disapproval of others would have little effect on me. T F
11. If someone is evaluating me I tend to expect the worst. T F
12. I rarely worry about what kind of impression I am making on someone. T F
13. I am afraid that others will not approve of me. T F
14. I am afraid that people will find fault with me. T F
15. Other people's opinions of me do not bother me. T F
16. I am not necessarily upset if I do not please someone. T F
17. When I am talking to someone, I worry about what they may be thinking of me. T F
18. I feel that you can't help making social errors sometimes so why worry about it. T F
19. I am usually worried about what kind of impression I make. T F
20. I worry a lot about what my superiors think of me. T F
21. If I know someone is judging me, it has little effect on me. T F
22. I worry that others will think I am not worthwhile. T F
23. I worry very little about others may think of me. T F
24. Sometimes I think I am too concerned with what other people think of me. T F

| | | |
|---|---|---|
| 25. I often worry I will say or do the wrong things. | T | F |
| 26. I am often indifferent to the opinions others have of me. | T | F |
| 27. I am usually confident that others will have a favourable impression of me. | T | F |
| 28. I often worry that people who are important to me won't think very much of me. | T | F |
| 29. I brood about the opinions my friends have about me. | T | F |
| 30. I become tense and jittery if I know I am being judged by my superiors. | T | F |

# APPENDIX 10

## Centre for Epidemiological Studies Depression Scale

Below is a list of some ways you may have felt or behaved. Please indicate how often you have felt this way during the last week by ticking the appropriate space.

| | | **Rarely** or none of the time (less than 1 day) | **Some** or a little of the time (1 -2 days) | **Occasionally** or a moderate amount of time (3 – 4 days) | **Most** or all of the time (5 – 7 days) |
|---|---|---|---|---|---|
| 1 | Was bothered by things that usually don't bother me. | | | | |
| 2 | Did not feel like eating; my appetite was poor. | | | | |
| 3 | Felt that I could not shake off the blues even with help from my family and friends. | | | | |
| 4 | Felt that I was just as good as other people. | | | | |
| 5 | Had trouble keeping my mind on what I was doing. | | | | |
| 6 | Felt depressed. | | | | |
| 7 | Felt that everything I did was an effort. | | | | |
| 8 | Felt hopeful about the future. | | | | |
| 9 | Thought that my life has been a failure. | | | | |
| 10 | Felt fearful. | | | | |
| 11 | Had restless sleep. | | | | |
| 12 | Felt happy. | | | | |
| 13 | Talked less than usual. | | | | |
| 14 | Felt lonely. | | | | |
| 15 | Felt that people were unfriendly. | | | | |
| 16 | Enjoyed life. | | | | |
| 17 | Had crying spells. | | | | |
| 18 | Felt sad. | | | | |
| 19 | Felt that people dislike me. | | | | |

| | | | | | |
|---|---|---|---|---|---|
| 20 | Felt that I could not "get going." | | | | |

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# APPENDIX 11

## TES Intensity Scale

Please rate the intensity with which you experienced the following whilst you had the brain stimulation equipment attached:

| | None | Mild | Moderate | Intense | Very intense |
|---|---|---|---|---|---|
| **Headache** | | | | | |
| **Neck pain** | | | | | |
| **Aching scalp** | | | | | |
| **Tickling** | | | | | |
| **Itching** | | | | | |
| **Burning** | | | | | |
| **Skin irritation** | | | | | |
| **Tiredness** | | | | | |
| **Loss of concentration** | | | | | |
| **Mood swings** | | | | | |

Please tick the relevant box

# APPENDIX 12

## Experimental Condition Questionnaire (Experiments 1 and 3 and Study 2)

Training

During the experiment each face pair presented consisted of a face with a neutral expression and a face with an angry expression. One of the faces was replaced by a target letter which you were required to press. In the ***training condition*** the letter replaced the neutral face 95% of the time. In the ***control condition*** the letter replaced the neutral face 50% of the time and the angry face 50% of the time.

Which condition do you think you were allocated to?

Training condition ☐

Control condition ☐

Brain Stimulation

During the experiment some participants received ***active stimulation*** (where stimulation was applied throughout the time that the equipment was attached to the head) or ***control stimulation*** (where the stimulation stopped after 20 seconds and remained switched off).

Which stimulation group do you think you belong to?

Active stimulation ☐

Control stimulation ☐

# APPENDIX 13

## Experimental Condition Questionnaire (Experiment 2)

Training

During the experiment each face pair presented consisted of a face with a neutral expression and a face with an angry expression. One of the faces was replaced by a target letter which you were required to press. In the ***training condition*** the letter replaced the neutral face 95% of the time. In the ***control condition*** the letter replaced the neutral face 50% of the time and the angry face 50% of the time. In the ***no-training*** condition a letter replaced either the angry face or the neutral face 80% of the time and no letter appeared 20% of the time. The instruction was to press {Enter} if a letter appeared and not to press {Enter} if no letter appeared.

Which condition do you think you were allocated to?

Training condition ☐

Control condition ☐

No-training condition ☐

Brain Stimulation

During the experiment some participants received ***active stimulation*** (where stimulation was applied throughout the time that the equipment was attached to the head) or ***control stimulation*** (where the stimulation stopped after 20 seconds and remained switched off).

Which stimulation group do you think you belong to?

Active stimulation ☐

Control stimulation ☐

# APPENDIX 14

## Beck Depression Inventory ii

Instructions: This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the one statement in each group that best describes the way you have been feeling during the past two weeks, including today. Circle the number beside the statement you have picked. If several statements in the group seems to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18 (Changes in Appetite).

1. Sadness

   0 I do not feel sad
   1 I feel sad much of the time
   2 I am sad all the time
   3 I am so sad or unhappy that I can't stand it

2. Pessimism
   0 I am not discouraged about my future
   1 I feel more discouraged about my future than I used to be
   2 I do not expect things to work out for me
   3 I feel my future is hopeless and will only get worse

3. Past Failure
   0 I do not feel like a failure
   1 I have failed more than I should have
   2 As I look back, I see a lot of failures
   3 I feel I am a total failure as a person

4. Loss of Pleasure
   0 I get as much pleasure as I ever did from the things I enjoy
   1 I don't enjoy things as much as I used to
   2 I get very little pleasure from the things I used to enjoy
   3 I can't get any pleasure from the things I used to enjoy

5. Guilty Feelings
   0 I don't feel particularly guilty
   1 I feel guilty over many things I have done or should have done
   2 I feel quite guilty most of the time
   3 I feel guilty all of the time

6. Punishment Feelings
   0 I don't feel I am being punished
   1 I feel I may be punished
   2 I expect to be punished
   3 I feel I am being punished

7. Self-Dislike
   0 I feel the same about myself as ever
   1 I have lost confidence in myself
   2 I am disappointed in myself
   3 I dislike myself

8. Self-Criticalness
   0 I don't criticise or blame myself more than usual
   1 I am more critical of myself than I used to be
   2 I criticize myself for all of my faults
   3 I blame myself for everything bad that happens

9. Suicidal thoughts or wishes
   0 I don't have any thoughts of killing myself
   1 I have thoughts of killing myself, but I would not carry them out
   2 I would like to kill myself
   3 I would kill myself if I had the chance

10. Crying
   0 I don't cry any more than I used to
   1 I cry more than I used to
   2 I cry over every little thing
   3 I feel like crying, but I can't

11. Agitation
   0 I am no more restless or wound up than usual
   1 I feel more restless or wound up than usual
   2 I am so restless or agitated that it's hard to stay still

3 I am so restless or agitated that I have to keep moving or doing something

12. Loss of Interest
    0 I have not lost interest in other people or activities
    1 I am less interested in other people or things than before
    2 I have lost most of my interest in other people or things
    3 It's hard to get interested in anything

13. Indecisiveness
    0 I make decisions about as well as ever
    1 I find it more difficult to make decisions than usual
    2 I have much great difficulty in making decisions than I used to
    3 I have trouble making any decisions

14. Worthlessness
    0 I do not feel I am worthless
    1 I don't consider myself as worthwhile and useful as I used to
    2 I feel more worthless as compared to other people
    3 I feel utterly worthless

15. Loss of Energy
    0 I have as much energy as ever
    1 I have less energy than I used to have
    2 I don't have enough energy to do very much
    3 I don't have enough energy to do anything

16. Changes in Sleeping Pattern
    0 I have not experienced any change in my sleeping pattern

    1a I sleep somewhat more than usual
    1b I sleep somewhat less than usual

    2a I sleep a lot more than usual
    2b I sleep a lot less than usual

    3a I sleep most of the day
    3b I wake up 1-2 hours early and can't get back to sleep

17. Irritability
    0 I am no more irritable than usual
    1 I am more irritable than usual
    2 I am much more irritable than usual
    3 I am irritable all the time

18. Change in Appetite
    0 I have not experienced any change in my appetite

    1a My appetite is somewhat less than usual
    1b My appetite is somewhat greater than usual

    2a My appetite is much less than before
    2b My appetite is much greater than usual

    3a I have no appetite at all
    3b I crave food all the time

19. Concentration Difficulty
    0 I can concentrate as well as ever
    1 I can't concentrate as well as usual
    2 It's hard to keep my mind on anything for very long
    3 I find I can't concentrate on anything

20. Tiredness or Fatigue
    0 I am no more tired or fatigued than usual
    1 I get more tired or fatigued more easily than usual
    2 I am too tired or fatigued to do a lot of the things I used to do
    3 I am too tired or fatigued to do most of the things I used to do

21. Loss of Interest in Sex
    0 I have not noticed any recent change in my interest in sex
    1 I am less interested in sex than I used to be
    2 I am much less interested in sex now
    3 I have lost interest in sex completely

APPENDIX 15

# The Penn State Worry Questionnaire

## The Penn State Worry Questionnaire (PSWQ)

Instructions: Rate each of the following statements on a scale of 1 ("not at all typical of me") to 5 ("very typical of me"). Please do not leave any items blank.

| | Not at all typical of me | | | | Very typical of me |
|---|---|---|---|---|---|
| 1. If I do not have enough time to do everything, I do not worry about it. | 1 | 2 | 3 | 4 | 5 |
| 2. My worries overwhelm me. | 1 | 2 | 3 | 4 | 5 |
| 3. I do not tend to worry about things. | 1 | 2 | 3 | 4 | 5 |
| 4. Many situations make me worry. | 1 | 2 | 3 | 4 | 5 |
| 5. I know I should not worry about things, but I just cannot help it. | 1 | 2 | 3 | 4 | 5 |
| 6. When I am under pressure I worry a lot. | 1 | 2 | 3 | 4 | 5 |
| 7. I am always worrying about something. | 1 | 2 | 3 | 4 | 5 |
| 8. I find it easy to dismiss worrisome thoughts. | 1 | 2 | 3 | 4 | 5 |
| 9. As soon as I finish one task, I start to worry about everything else I have to do. | 1 | 2 | 3 | 4 | 5 |
| 10. I never worry about anything. | 1 | 2 | 3 | 4 | 5 |
| 11. When there is nothing more I can do about a concern, I do not worry about it any more. | 1 | 2 | 3 | 4 | 5 |
| 12. I have been a worrier all my life. | 1 | 2 | 3 | 4 | 5 |
| 13. I notice that I have been worrying about things. | 1 | 2 | 3 | 4 | 5 |
| 14. Once I start worrying, I cannot stop. | 1 | 2 | 3 | 4 | 5 |
| 15. I worry all the time. | 1 | 2 | 3 | 4 | 5 |
| 16. I worry about projects until they are all done. | 1 | 2 | 3 | 4 | 5 |

# APPENDIX 16

## Liebowitz Social Anxiety Scale

This measure assesses the way that social phobia plays a role in your life across a variety of situations. Read each situation carefully and answer two questions about that situation. The first question asks how anxious or fearful you feel in the situation. The second question asks how often you avoid the situation. If you come across a situation that you ordinarily do not experience, imagine "what if you were faced with that situation," and then, rate the degree to which you would fear this hypothetical situation and how often you would tend to avoid it. Please base your ratings on the way that the situations have affected you in the last week. Fill out the following scale with the most suitable answer provided below.

| Fear or Anxiety: | Avoidance |
|---|---|
| 0 = None | 0 = Never (0%) |
| 1 = Mild | 1 = Occasionally (1-33%) |
| 2 = Moderate | 2 = Often (33-67%) |
| 3 = Severe | 3 = Usually (67 – 100%) |

| | | Fear or Anxiety | Avoidance |
|---|---|---|---|
| 1 | Telephoning in public | | |
| 2 | Participating in small groups | | |
| 3 | Eating in public places | | |
| 4 | Drinking with others in public places | | |
| 5 | Talking to people in authority | | |
| 6 | Acting, performing or giving a talk in front of an audience | | |
| 7 | Going to a party | | |
| 8 | Working while being observed | | |
| 9 | Writing while being observed | | |
| 10 | Calling someone you don't know very well | | |
| 11 | Talking with people you don't know very well | | |
| 12 | Meeting strangers | | |
| 13 | Urinating in a public bathroom | | |
| 14 | Entering a room when others are already seated | | |
| 15 | Being the center of attention | | |
| 16 | Speaking up at a meeting | | |
| 17 | Taking a test | | |
| 18 | Expressing a disagreement or disapproval to people you don't know very well | | |
| 19 | Looking at people you don't know very well in the eyes | | |

| | | | |
|---|---|---|---|
| 20 | Giving a report to a group | | |
| 21 | Trying to pick up someone | | |
| 22 | Returning goods to a store | | |
| 23 | Giving a party | | |
| 24 | Resisting a high-pressure salesperson | | |

# APPENDIX 17

## Example Debrief Form


Participant Number: _____

### ETHICS COMMITTEE

### PARTICIPANT DEBRIEF

Title of Research Project: Brain Stimulation and attention.

Thank you very much for taking part in our study, we greatly appreciate your contribution.

This study was interested in finding out how much your attention was automatically captured by threatening faces and whether you could be trained to attend less to threatening faces. We tried to change brain activity in the front part of your brain and then measured whether this affected how much you could be trained to attend to neutral faces and away from threatening ones.

You were in the real tDCS group. This means that electrical stimulation was applied during the twenty minutes when you had the tDCS machine attached to your scalp. 50% of our participants did not actually receive any stimulation. Your allocation to the 'real' group is complete chance.

We would ask you not to discuss the details of the experiment with anyone else who might subsequently agree to participate.

Your data are held securely and anonymously. If you wish to withdraw from the study, contact us with your participant number and your data will be removed from our files.

Please note: if you have a concern or question about any aspect of your participation, please raise this with the research Sara Pretorius in the first instance.

Researcher Contact Details:

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However, if you would like to contact an independent party please contact the Head of Department Dr. Diane Bray [email: d.bray@roehampton.ac.uk; 020-8392 3627; Room 2053, Whitelands College, Holybourne Avenue, Roehampton, London, SW15 4JD].

If you are a student at Roehampton University and are troubled or worried about any aspect of the study or issues it may have raised and you would prefer not to approach members of the Psychology department, you may find it helpful to contact one of the following who will be able to advise you on agencies that can deal with your particular concern:

**Student Welfare Officers:**

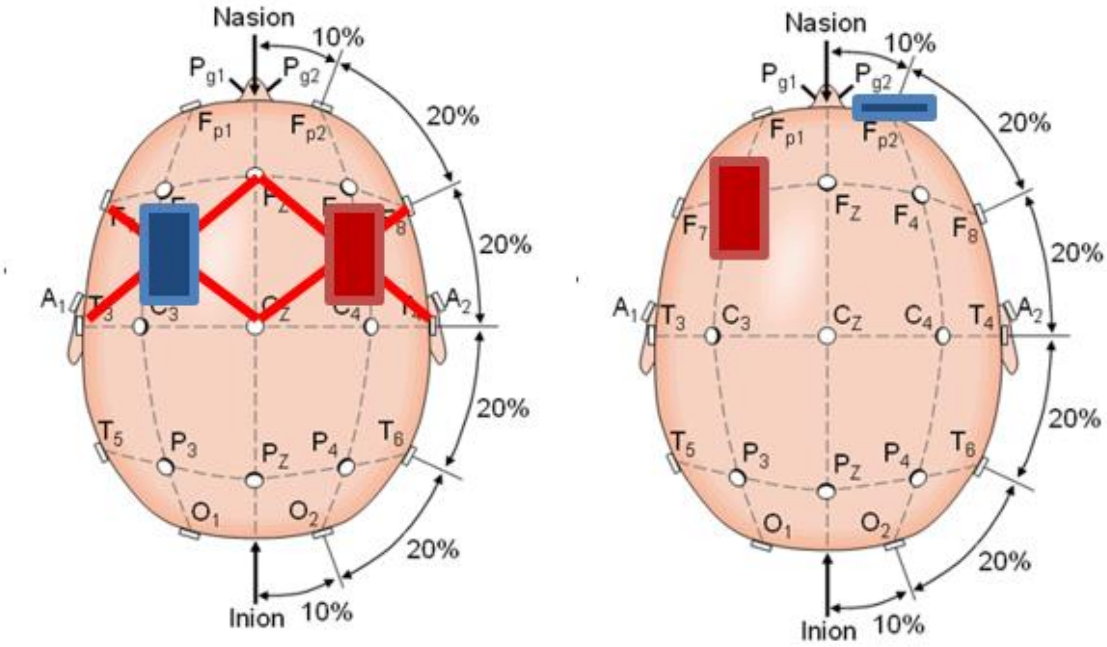
Business School; English & Creative Writing; Humanities; Social Sciences: Will Cooper (tel: 020 8392 3204). Dance; Drama, Theatre & Performance; Education: Anne-Marie Joyes (tel: 020 8392 3304). Life Sciences; Media, Culture & Language; Psychology: Hannah Desmond (tel: 020 8392 3502).

If you feel your concerns are more serious or complex you may wish to contact the **Student Medical Centre** on **Ext 3679.** If you are a non-student your GP should be able to advise you on agencies that can deal with your particular concern.

# APPENDIX18

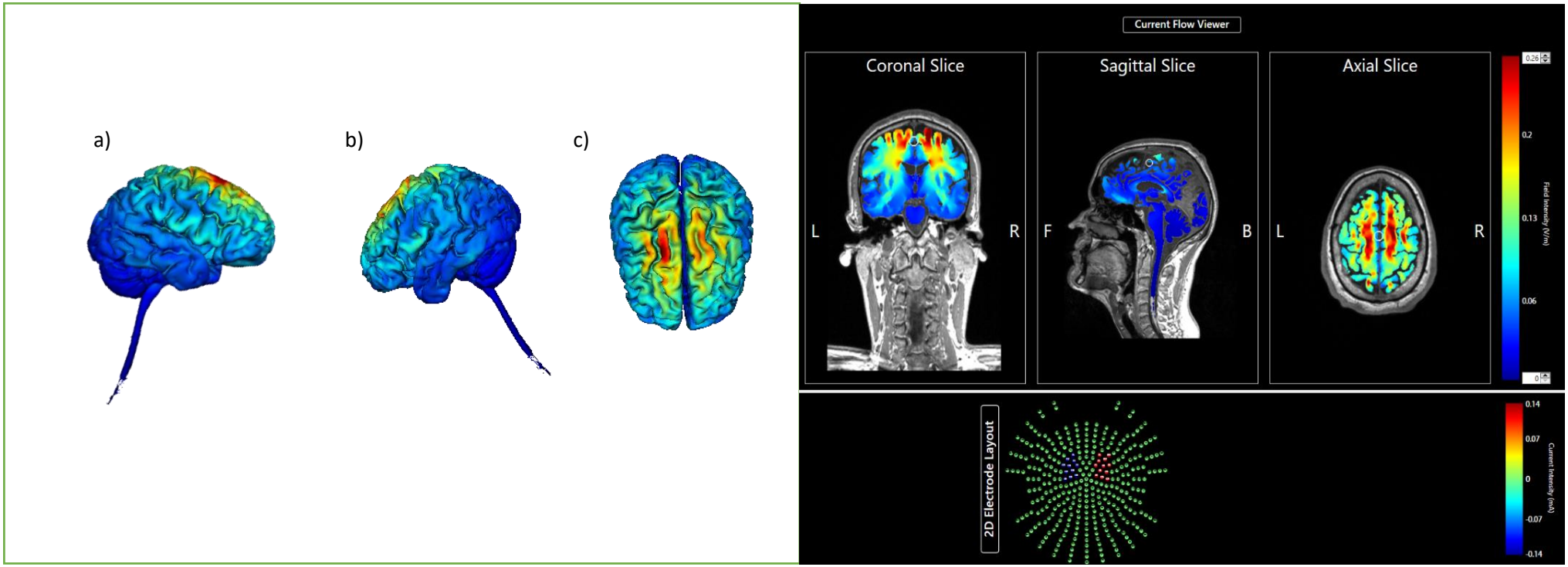
## TES Electrode Placement

A. B.

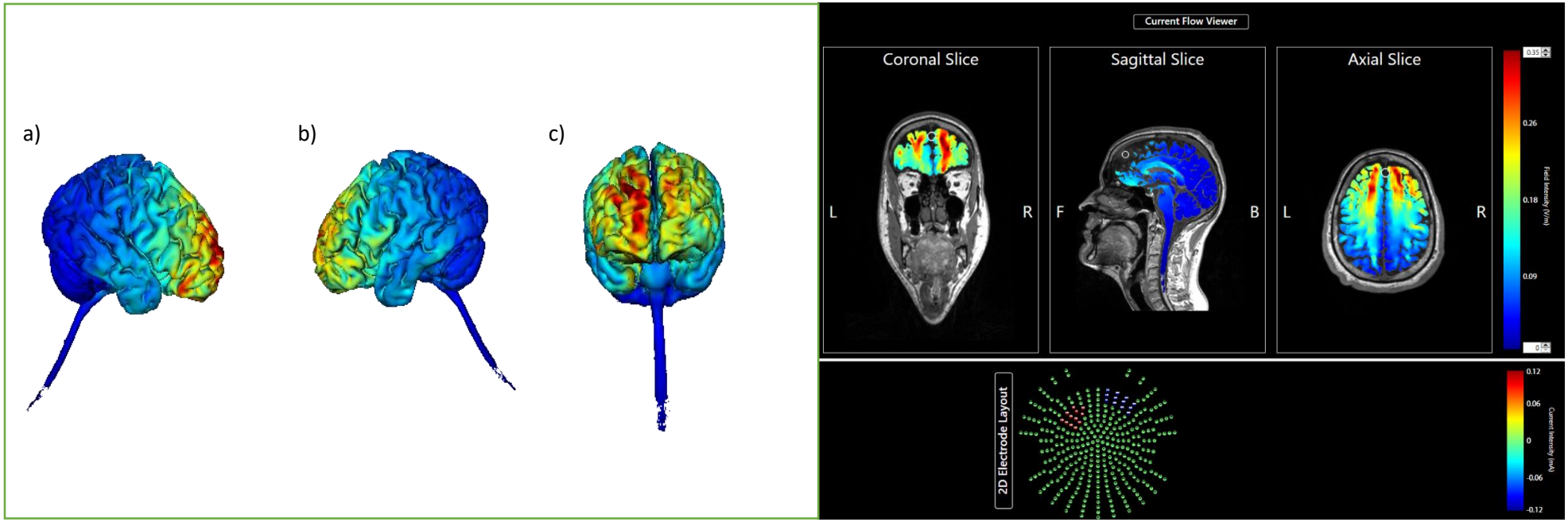



TES electrode placement. A. tRNS protocol – anode above right IFG and cathode above left IFG. Right IFG identified as the intersection between the line joining T4 and Fz and the line joining F8 and Cz based on the 10-20 EEG system (e.g. Ditye et al., 2012). B. tDCS protocol – anode above F3 on the 10-20 EEG system (left DLPFC) and cathode above right supra-orbital ridge.

# APPENDIX 19: Field Intensity Maps




Cortical electric field induced by Montage A: Anode above right IFG (intersection between the line joining T4 and Fz and the line joining F8 and Cz). Cathode at left IFG (intersection between the line joining T3 and Fz and the line joining F7 and Cz). Electrode size: 5cm x 7cm. TES amplitude: 1.5mA. a) left hemisphere, b) right hemisphere, c) top view.




Cortical electric field induced by Montage A: Anode above left DLPFC (F3). Cathode at right contralateral supraorbital. Electrode size: 5cm x 7cm. TES amplitude: 1.5mA. a) left hemisphere, b) right hemisphere, c) frontal cortex.

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