Somatic salience and sensory precision in persistent depression

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Preface

This thesis is the result of my own work and includes nothing which is the outcome of work done in collaboration except as declared in the Preface and specified in the text. It is not substantially the same as any that I have submitted, or, is being concurrently submitted for a degree or diploma or other qualification at the University of Cambridge or any other University or similar institution except as declared in the Preface and specified in the text. I further state that no substantial part of my thesis has already been submitted, or, is being concurrently submitted for any such degree, diploma or other qualification at the University of Cambridge or any other University or similar institution except as declared in the Preface and specified in the text. It does not exceed the prescribed word limit for the relevant Degree Committee.

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Abstract

Persistent depression is a debilitating health condition with a poor prognosis even in the context of current gold-standard pharmacological and psychological interventions. A better understanding of the mechanisms contributing to its maintenance is needed to facilitate the development of more targeted psychological interventions. Bayesian predictive processing models of depression propose that negative emotional and physiological outcomes arise in depressive illness as a result of disturbed interoceptive precision estimation in depressed individuals; however, evidence from the clinical and cognitive neuroscience literatures suggests the hypothesis that sensory precision is attenuated in persistent depression across sensory modalities in general. A series of studies was designed to index sensory precision across somatic and auditory modalities and to identify the level at which any disruption manifested in persistently-depressed participants relative to controls. Study 1 (Chapter 3) measured baseline signal discriminability under conditions of focused attention. Study 2 (Chapter 4) measured the impact of failures of voluntary attention on signal discriminability. Study 3 (Chapter 5) used a simulation approach to model sensory precision in the first two studies and to identify mechanisms which could successfully predict the data. Studies 4 (Chapter 6) and 5 (Chapter 7) measured attentional capture by task-irrelevant and predictive sensory cues respectively. Study 6 (Chapter 8) partially replicated Studies 4 and 5 and used the resulting data to estimate the group-level sensory precision and salience parameters of a predictive processing model of precision optimization. The results suggest that sensory precision is attenuated in persistent depression across sensory modalities, and that this attenuation results from disturbances of voluntary and involuntary attention rather than baseline perceptual sensitivity. Under conditions of voluntary attention, reduced sensory precision may result from efforts at resource conservation; and under conditions of involuntary attentional capture, it may be related to a loss of target discriminability and salience. Conversely, the bottom-up salience of somatic stimuli was uniquely enhanced among depressed participants and was predicted by high anxiety and by low interoceptive sensibility. These findings open up new avenues for investigation of the mechanisms underlying persistent forms of depression, and have direct implications for clinical practice with respect to psychological intervention.

Contents

Chapter 1. Introduction

1.1. Persistent depression

Major depression is a disabling condition characterised by low mood, loss of interest and pleasure in most or all activities, and feelings of worthlessness and guilt (American Psychiatric Association, 2013). Appetite, sleep, concentration and energy levels can all be disturbed, and behaviour may become markedly reduced or avoidant, with presentations typically including a subjective loss of motivation, a narrowing of behavioural repertoires, social withdrawal and sickness behaviours (see Table 1.1 for a full list of diagnostic criteria for a Major Depressive Episode in adults). Depressive disorders have a lifetime prevalence rate of 20-28%, with a median age-of-onset in the early to mid-twenties (Kessler & Bromet, 2013); and they are associated with substantial levels of disability and burden worldwide (Vos et al., 2017).

Table 1.1. Diagnostic criteria for a Major Depressive Episode in adults according to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition: DSM-V (American Psychiatric Association, 2013).

A	**Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.**
1	Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful).
2	Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
3	Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day.
4	Insomnia or hypersomnia nearly every day.
5	Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6	Fatigue or loss of energy nearly every day.

7	Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8	Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9	Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.
B	**The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.**
C	**The episode is not attributable to the physiological effects of a substance or to another medical condition.**

Depression tends to emerge after a period of chronic stress, illness, deprivation or loss (Hammen, 2005; Kendler, Kessler, Neale, Heath, & Eaves, 1993) and is characterised by physiological changes in crucial allostatic systems including the stress system and the immune system (e.g., Dantzer, O'Connor, Freund, Johnson, & Kelley, 2008; Pariante & Lightman, 2008; Wohleb, Franklin, Iwata, & Duman, 2016). An evolutionary perspective suggests that its phenomenology may comprise an adaptive set of responses to a hostile environment during times of hardship (Allen & Badcock, 2006; Beck & Bredemeier, 2016; Keedwell, 2008). Clearly, an ability to assess a context as dangerous or unrewarding, to disengage from current goals, to desist from potentially dangerous exploration and to conserve energy under conditions of high risk or cost is a very adaptive one. Additionally, behavioural avoidance may be an effective means of allostatic regulation of the internal context in such circumstances: for example, withdrawal from challenging situations may help to reduce chronically elevated arousal following a period of unrelenting stress (Hegerl & Hensch, 2014); while increased rest may be restorative following high energy expenditure during an episode of anxiety or illness (Stephan et al., 2016). Depressive episodes are frequently self-limiting (e.g., Posternak et al., 2006), consistent with an interpretation of depression as a time-limited adaptive strategy for loss-limitation and resource conservation during periods of hardship. However, a certain proportion of individuals will not recover from depression despite respite from stress, opportunities for rest, or improved circumstances; and others will quickly relapse even in the absence of further stressors.

Although the majority of episodes of major depression remit within a year (Keller & Shapiro, 1981), a substantial minority become chronic, often following a fluctuating course which may include episodes of major depression interspersed with periods of dysthymia or residual symptomatology (Judd et al., 1998b; Keller, Shapiro, Lavori, & Wolfe, 1982; Wells, Burnam, Rogers, Hays, & Camp, 1992). The presence of primary dysthymia is predictive of a chronic course of lifetime major depression (Kessler et al., 1996) but even in the absence of a history of dysthymia as many as 20% of treated episodes of major depression may persist for 2 years or more (Keller et al., 1984). Recurrent episodes are common (Judd, 1997), and with repeated episodes, progressively lower levels of environmental stress may be sufficient to trigger a new episode (Kendler, Thornton, & Gardner, 2000). Each new episode increases the risk of future recurrence (Solomon et al., 2000), and residual symptomatology following remission constitutes a well-established risk factor for relapse (e.g., Judd et al., 1998a). Therefore, for a substantial proportion of individuals, depression is a lifelong disorder with mounting personal and social costs in terms of health, wellbeing, and opportunity across the lifespan.

Evidence-based interventions (NICE, 2009) for persistent forms of depression include antidepressant medication (ADM) and psychological interventions, of which Cognitive Behaviour Therapy (CBT: Beck, Rush, Shaw, & Emery, 1979) is at present the most well-established. In terms of prophylaxis, both CBT and maintenance ADM reduce the risk of relapse and may therefore contribute to a reduced risk of developing a persistent depressive illness following a first episode (Evans et al., 1992; Hollon et al., 2005). However, once depression persistence is established, treatment response to both ADM and CBT in this population is relatively poor (Fennell & Teasdale, 1982; Sotsky et al., 2006; Thase, Reynolds, Frank, & Simons, 1994; Trivedi et al., 2006). CBT may achieve remission rates of just 20-30% amongst persistently depressed individuals (Paykel et al., 1999; Thase et al., 1994), while nevertheless demonstrating a significant advantage over medication and clinical management in terms of both remission post-treatment and relapse prevention (Paykel et al., 1999, 2005). A related psychological intervention, Mindfulness-Based Cognitive Therapy (MBCT: Segal, Williams, & Teasdale, 2002) was developed in an effort to reduce the risk of relapse following remission from depression, and in contrast to CBT, MBCT appears to offer unique benefits to individuals with more persistent forms of depression. Following MBCT, rates of relapse are significantly reduced in individuals with relatively extensive histories of recurrent depression, earlier age of depression onset, or vulnerability resulting from childhood adversity, while outcomes for those with briefer depression histories fail to improve (Kuyken et al., 2015; Ma & Teasdale, 2004; Teasdale et al., 2000; Williams et al., 2014). Given these differential responses to intervention, it may be the case that distinct neural and cognitive

mechanisms underlie lifelong depression persistence, and that to develop more targeted and effective psychological therapies it will be necessary to develop specific models of these mechanisms.

1.2. Mechanisms of change within clinical models

Cognitive-behavioural interventions for depression are underpinned by the cognitive model (Beck, 2008; Beck & Rush, 1978; Dozois & Beck, 2008; Padesky, 1994), which posits that depression arises from biases within a hierarchically-organised set of beliefs and expectations which construct perceptual and emotional experience, direct attention and drive behaviour. At the top of the hierarchy are core beliefs, typically thought to be learnt in childhood, and representing (in psychopathology) unduly rigid, extreme, absolute and overgeneral expectations about the world, the self and the future. Intermediate beliefs are thought to represent predictions and associated rules for behaviour generalising across many situations; automatic thoughts are situational and represent interpretations of immediate events which are informed by higher-level expectations in the manner of empirical priors. Therapy proceeds by identifying relevant beliefs or predictions, noting their precision (through "belief ratings") and using available evidence (often of a detailed sensory nature) to test and update them. Where existing evidence is unavailable, inadequate or imprecise, individuals are assisted to collect relevant sensory data through the setting up of "behavioural experiments" (Bennett-Levy et al., 2004). The precision of the resulting sensory data can be amplified through the use of attention-training techniques including data logs with detailed prompts (Padesky, 1994), mindfulness exercises (Fennell, 2004), and explicit attention training practices (Papageorgiou & Wells, 2000). In addition to the explicit verbal updating of high-level beliefs and interpretations about self and context, many skills-training and imagery-related practices employed within CBT can be viewed as updating prior expectations at a lower level of the hierarchy: for example, regular practice in progressive muscle relaxation may have the function of updating an implicit expectation that safety depends on a constant physiological preparedness for threat. Along similar lines, MBCT (Segal et al., 2002) requires participants to engage in extensive daily meditation practices which involve sustained selective attention to sensory signals arising in all modalities, both interoceptive and exteroceptive, whilst maintaining an attitude of "non-judgement" (Kabat-Zinn, 2013). In essence this could be theorised as a training in the amplification of sensory precision while attenuating prior expectations about the resulting sensory experience.

1.3. Predictive processing models of persistent depression

Clinical observation and outcome data, then, indicate that depression persistence can be interrupted through the collection of new sensory data from the current (internal and external) context, through strategies for amplifying the precision of such data, and through its explicit use to update ill-fitting or

obsolete models of the environment and the embodied self. This observation is broadly consistent with a number of existing predictive processing theories of depression, which posit that disruptions to precision estimation within allostatic and interoceptive systems lead to a reduced influence of interoceptive prediction error and related failures of model updating in depressed individuals, with negative consequences for both interoceptive experience and allostasis (Barrett, Quigley, & Hamilton, 2016; Paulus, Feinstein, & Khalsa, 2019; Paulus & Stein, 2010; Stephan et al., 2016). Such models are predicated on the proposal that the brain maintains an online predictive model of its internal and external environment, within which perception proceeds through the updating of prior expectations with incoming sensory data or prediction error (those aspects of the data that remain unexplained by the prior). This inferential process is assumed to be a Bayesian one in which the influence of the data on the prior is determined by their relative precision. Action, conversely, is thought to fulfil prior expectations by changing the external or internal milieu in such a way as to systematically reduce prediction error (Brown, Friston, & Bestmann, 2011). The role of attention in this kind of formulation is to optimize the precision of sensory channels relative to each other and to the prior in order to allow the most informative data to update expectations or determine action (Feldman & Friston, 2010; Parr & Friston, 2019). Predictive processing models of depression have in common an assumption that the disorder is specifically characterised by disruptions to precision optimization within the domain of interoception.

1.4. Interoception and bodily precision in depression

Interoception – the moment-by-moment neural representation of internal bodily signals – is emerging as an important topic of research (e.g., Craig, 2009; Khalsa et al., 2018), and has been hypothesised to provide the basis for allostatic behaviour (Barrett et al., 2016), emotion experience (James, 1894; Schachter & Singer, 1962), effective decision-making (Damasio, 2006; Dunn, Galton, et al., 2010), social cognition (Adolfi et al., 2017), conscious awareness (Craig, 2009), and the sense of self (Seth, 2013); all domains which are arguably disturbed in major depression.

It is clear that altered somatic experience is a hallmark of major depression, although it can take a variety of forms. Sensations of exhaustion, heaviness, weakness, illness, tension, aches and pains and a general loss of vitality are commonly reported and may be intrusive and disabling (e.g., Ratcliffe, 2014; Vaccarino, Sills, Evans, & Kalali, 2008). Appetitive sensation (hunger, desire, enjoyment, curiosity, interest and motivation) may, on the other hand, be attenuated or lost. Furthermore, it has been suggested that a dampening or numbing of all forms of emotional experience may be typical of depression (Bylsma, Morris, & Rottenberg, 2008), and perhaps predictive of depression chronicity (Rottenberg, Joormann, Brozovich, & Gotlib, 2005). More severe manifestations of attenuation of

emotional or somatic experience are apparent in the overlap between depression, alexithymia (Leweke, Leichsenring, Kruse, & Hermes, 2012) and depersonalization (Hunter, Sierra, & David, 2004), and again there is evidence that depersonalization (an altered state of consciousness involving a sense of detachment from the body, emotional experience, willed action or the sense of self) may be associated with chronicity and treatment resistance in depression (Mula, Pini, & Cassano, 2007). To complicate the picture further, positive relationships may exist in depressed populations between amplified and attenuated forms of somatic sensation, which are in need of explication (e.g., Sayar, Kirmayer, & Taillefer, 2003).

As described above, leading theories of interoception in depression have typically posited a loss of precision in interoceptive processing as a causal factor in the emotional, physiological and allostatic disturbances which characterise depressive symptomatology. Interoceptive precision is difficult to measure directly, but it has been suggested that the individual differences in the ability to optimize it effectively can be indexed by interoceptive accuracy, as measured, for example, by the heartbeat perception test (Schandry, 1981) which quantifies individual differences in terms of the difference between actual and counted heart beats over brief periods of time. High accuracy (Garfinkel, Seth, Barrett, Suzuki, & Critchley, 2015) in this task is assumed to reflect a trait-like tendency to high interoceptive precision (Ainley, Apps, Fotopoulou, & Tsakiris, 2016) and in healthy subjects has been related to theoretically relevant constructs such as emotion regulation (Fustos, Gramann, Herbert, & Pollatos, 2013) and decision-making acumen (Dunn, Galton, et al., 2010). In support of the suggestion that depression may be characterised by low interoceptive precision, a number of studies (Dunn, Dalgleish, Ogilvie, & Lawrence, 2007; Furman, Waugh, Bhattacharjee, Thompson, & Gotlib, 2013; Terhaar, Viola, Bar, & Debener, 2012) have found evidence for reduced interoceptive accuracy in some depressed populations. These findings are encouraging, but the insights that they offer into the specific mechanisms driving such outcomes are limited, because endogenously-occurring stimuli such as heartbeats cannot be (non-invasively) experimentally manipulated with precision, and because they are difficult to match with control stimuli to account for supra-modal attentional and executive processes. Here we attempt to break down the concept of interoceptive or bodily precision into possible contributing mechanisms, and to consider means of studying them experimentally.

Signal detectability in general depends on the baseline intensity of the signal relative to system noise, and on the precision with which it is attended. Interoceptive precision, therefore, depends both on the baseline intensity of interoceptive signals arising on a moment-by moment basis, and on the tendency of an individual to attend to those signals. Deficits in interoceptive accuracy could arise as a result of reduced signal/noise ratios (whether due to an attenuated signal or to a noisy context)

rendering interoceptive signals hard to differentiate, or because of difficulties in directing and maintaining attention to interoceptive signals in order to increase their precision. A further relevant distinction is between voluntary (top-down) and involuntary (stimulus-driven) forms of attention, which may be distinct processes relying on partially segregated brain networks (Chica, Bartolomeo, & Lupiáñez, 2013; Corbetta & Shulman, 2002). In the heartbeat perception test, voluntary attention to interoceptive sensation is recruited via experimenter instruction. But day-to-day interoceptive precision must surely depend to a much greater extent upon the stimulus-driven likelihood of reorienting attention to interoceptive signals which have only an incidental relation to ongoing task-related priorities.

In order to understand whether and how bodily precision is altered in depression, three mechanisms must therefore be dissociated: baseline bodily signal intensity or discriminability; the ability to direct top-down attention to bodily signals; and the extent of stimulus-driven attentional capture by such signals in the absence of voluntary attention. Given the pace at which the field of interoceptive research is moving and the methodological innovations which are being developed (e.g., Garfinkel et al., 2016; Khalsa et al., 2018; Petzschner et al., 2019), direct means of studying such distinct mechanisms in interoception may soon be available. In the meantime, we have addressed these questions using an analogue approach employing exteroceptive somatic stimuli. The extent to which somatic and interoceptive processing overlap and the implications of any such overlap for the understanding of key processes in depression remain open questions, yet recent advances in our understanding of the relationship between interoceptive and exteroceptive somatic processing at a cortical level (discussed below) support the suggestion that cutaneous somatic stimuli can provide a relevant interoceptive analogue.

Interoceptive and exteroceptive somatic signals are conveyed from peripheral receptors to the cortex via anatomically distinct afferent pathways. Exteroceptive signals include fine and discriminative cutaneous touch, vibration and proprioception, and are conveyed from receptors in the skin and joints via the dorsal column medial lemniscus pathway, which terminates in primary and secondary somatosensory cortices. Interoceptive signals include cutaneous sensations of heat, pain, itch, and crude touch in addition to muscular and visceral sensations, and are conveyed via a phylogenetically recent lamina I spinothalamic pathway terminating in posterior insular cortex (Craig, 2002). Despite the lack of a direct connection between the medial lemniscal pathway and insular cortex, there is mounting evidence, both structural (Cerliani et al., 2012; Cloutman, Binney, Drakesmith, Parker, & Lambon Ralph, 2012; Ghaziri et al., 2015; Jakab, Molnar, Bogner, Beres, & Berenyi, 2012) and functional (Cauda et al., 2011; Deen, Pitskel, & Pelphrey, 2011; Wiech, Jbabdi, Lin, Andersson, &

Tracey, 2014) suggesting that exteroceptive somatic signals are also forwarded from somatosensory cortices to the posterior insula via a ventral somatosensory pathway (Dijkerman & de Haan, 2007; Preusser et al., 2015). Craig (2010) reviews evidence that the posterior insula may support an array of modality specific, topographically organised primary interoceptive representations; while evidence from functional imaging studies demonstrates that exteroceptive forms of somatic stimulation including touch (Davis, Kwan, Crawley, & Mikulis, 1998; Hu et al., 2015; Mazzola, Faillenot, Barral, Mauguiere, & Peyron, 2012) and vibration (Burton, Videen, & Raichle, 1993; Coghill et al., 1994; Francis et al., 2000; Golaszewski et al., 2006; Siedentopf et al., 2008) are similarly associated with posterior insula activity. Studies directly comparing insula activity in response to exteroceptive and interoceptive stimulation have identified areas of overlap (Eickhoff et al., 2006; Ostrowsky et al., 2002; zu Eulenburg, Baumgartner, Treede, & Dieterich, 2013), and such findings, in addition to neuropsychological evidence (Ibanez, Gleichgerrcht, & Manes, 2010)), have led commentators to propose that mid-posterior insular cortex mediates the integration of exteroceptive, interoceptive and vestibular somatic information to form a multimodal body representation (Craig, 2010; Eickhoff et al., 2006; zu Eulenburg et al., 2013). Craig (2010) further suggests that this integrated body representation is subsequently re-represented in anterior insula to form a consciously accessible subjective feeling state. The likelihood, therefore, that exteroceptive and interoceptive somatic representations are integrated at a cortical level at an early stage relative to conscious bodily awareness provides a rationale for the use of exteroceptive somatic stimuli as an alternative to visceral stimuli in the study of somatic awareness in depression.

Use of a somatic stimulus in the measurement of bodily awareness and precision can allow us to differentiate signal detectability, voluntary attention to somatic signals, and involuntary attentional capture by such signals; providing a detailed account of any influence of depression on these processes. In addition, such a stimulus can be relatively easily matched with a control stimulus of a different sensory modality, allowing us to ascertain whether any disturbance in sensory awareness or precision in depression is genuinely specific to signals arising from the body. This is a question of interest, because there are reasons to suspect that altered or dampened sensory experience in depression may in fact generalise more broadly across sensory modalities.

1.5. Perceptual sensitivity in depression

Investigations of perceptual sensitivity in depression have suggested that perceptual experience may be attenuated or suppressed in depressive disorders across the range of sensory modalities. In the visual modality, Bubl et al. (Bubl, Ebert, Kern, van Elst, & Bach, 2012; Bubl, Kern, Ebert, Bach, & Van Elst, 2010; Bubl et al., 2015; Bubl, Tebartz Van Elst, Gondan, Ebert, & Greenlee, 2009) have reported

in a series of studies that depression is associated with acute impairments in visual contrast perception. In the auditory modality, Malone and Hemsley (1977) found reduced sensitivity in auditory stimulus detection during acute depression relative to remission, and Yovell et al. (1995) found similarly affected auditory detection thresholds, particularly on the left side of space, in acutely depressed inpatients relative to healthy controls. A more recent study found evidence of impaired pitch identification in depressed women relative to a control group (Schwenzer, Zattarin, Grözinger, & Mathiak, 2012), although it should be noted that the task loaded relatively heavily on memory and the same study found no support for group differences on other indices of auditory perception. In the olfactory and gustatory modalities, several studies suggest that sensory thresholds for detection and discrimination are acutely impaired in depression (Croy et al., 2014; Khil et al., 2016; Pause, Miranda, Göder, Aldenhoff, & Ferstl, 2001; Steiner, Lidar-Lifschitz, & Perl, 1993) although others have found no support for group differences (e.g., Dichter, Smoski, Kampov-Polevoy, Gallop, & Garbutt, 2010; Swiecicki et al., 2009).

The impact of depression on (exteroceptive) somatic sensitivity has also been studied, specifically in the context of investigations into pain. Studies examining relative pain thresholds in depression have often included a brief test of perceptual threshold for non-nociceptive somatic stimulation. The results of these tests are conflicting, with some investigators finding reduced sensitivity (Adler & Gattaz, 1993; Marazziti et al., 1998), others finding no differences (Bär et al., 2011; Ben-Tovim & Schwartz, 1981; Klauenberg et al., 2008; Marsala et al., 2015; Terhaar et al., 2010) and one finding increased sensitivity (Moroz, Nuller, Ustimova, & Andreev, 1990). However, to our knowledge there are no studies which constitute a robust investigation of somatic thresholds in clinical depression in a non-stressful context; that is, in which participants are not expecting the imminent infliction of pain.

Therefore, although the evidence is inconclusive, studies exist which suggest that depression may attenuate sensory precision in every sensory modality. These outcomes may represent a series of modality-specific and independent influences of depression on the respective sensory systems, or alternatively may be more parsimoniously explained as the result of some supra-modal process which contributes to all perceptual domains. An obvious candidate for such a process is attention.

1.6. Attention in depression

From a phenomenological perspective, there are a number of reasons to suspect that specific aspects of attention towards external sensory stimuli may be affected in persistent depression. Characteristically, the disorder gives rise to a sense that the external world has lost interest and meaning, with sensory details appearing both muted and devoid of their usual value or behavioural

relevance. Attention may become internally-focused, often on lengthy, stimulus-independent ruminations (Nolen-Hoeksema, 2004), while disruptions to the ability to concentrate on basic external tasks (such as reading or following a conversation) are a hallmark of depressive illness (American Psychiatric Association, 2013). A robust neuropsychological literature demonstrating slowed or less efficient performance on attention tasks in general, with increased disadvantage for tasks involving higher levels of effort, has led commentators to suggest that attentional dysfunction may be a central feature of depression (Cohen, Lohr, Paul, & Boland, 2001; Mialet, Pope, & Yurgelun-Todd, 1996); however, surprisingly little is known about the specific mechanisms of attentional dysfunction in persistent depression.

Evidence from visuospatial and dichotic listening tasks (Bruder et al., 1989; Liotti & Mayberg, 2001; Liotti, Sava, Rizzolatti, & Caffarra, 1991) suggests that depression may be characterised by subtle left-sided hemineglect, which could possibly be an indication of disruption of a right-lateralised ventral attention network in the brain (VAN: Corbetta, 2014; He et al., 2007). The VAN is associated with vigilance, with attentional reorienting towards behaviourally relevant exogenous stimuli (Corbetta, Kincade, & Shulman, 2002; Corbetta, Patel, & Shulman, 2008), and with context updating (Geng & Vossel, 2013; Mengotti, Dombert, Fink, & Vossel, 2017). Further support for the tentative hypothesis that depression may be associated with VAN dysfunction is provided by evidence of vigilance deficits in depression (Rock, Roiser, Riedel, & Blackwell, 2014), and by a study which demonstrated disproportionately large validity effects in depressed participants in a classic Posner covert orienting task (Pardo, Pardo, Humes, & Posner, 2006). In this task (Posner, 1980), a target can appear on either the left or the right side of space, and is preceded in each trial by a cue which predicts its location with a probability that remains constant throughout the task. 'Valid' cues (those that accurately predict the target location) are associated with facilitated response latencies, while 'invalid' cues (those that predict the incorrect location) are associated with slowed responses. This latency difference between responses to valid and invalid cues is sometimes known as a 'validity effect', and is robustly elicited regardless of the sensory modality of the cue or target (Spence, 2010). Attentional reorientation following an invalid cue is associated with VAN activity (Corbetta et al., 2002), and therefore disruption to VAN function in depression may be indexed by altered validity effects in this population.

An interesting interpretation of the Posner task has been proposed by Yu and Dayan (2003), who suggest that this task offers insight into individual differences in precision optimization within Bayesian perceptual inference. Yu and Dayan (2003) propose that a small validity effect in the Posner task reflects a relative potentiation of bottom-up sensory information (high sensory precision), while a large validity effect conversely indexes a relative reliance on prior expectancies arising from the cue

(high precision of the prior). According to this interpretation, relatively large validity effects in a depressed population may indicate reduced precision of sensory prediction error relative to prior expectancies.

1.7. Summary

In summary, amplification of sensory precision with respect to both internal and external sensory signals appears to play a key role in effective interventions for persistent depression. Evidence from psychophysics tasks suggests that perception may be dampened across a range of sensory modalities in depression, while increased validity effects have been found in this population in a visuospatial attentional orienting task, perhaps reflecting reduced precision of bottom-up visual information relative to the precision of prior expectation. In the light of this evidence, it is plausible that reduced sensory precision in persistent depression may in fact generalise across sensory modalities, although it appears likely that interoceptive or bodily signals may nevertheless constitute a special or extreme case within this broader framework. A series of studies was designed to investigate these issues.

1.8. Rationale

1.8.1. Research questions

A series of studies was designed with the aim of addressing the following questions:

1. Is there a loss of sensory precision in persistent depression?
2. Is any such loss specific to bodily information or more general?
3. Does it manifest at the level of baseline signal discriminability, or is it a function of voluntary or involuntary attention?

1.8.2. Study design

Two novel paradigms were designed to address these questions. Both employed exteroceptive somatic stimuli as a test condition and comparable auditory stimuli as a control condition. In the first paradigm (Studies 1-3), stimuli were presented in the context of an adaptive procedure for assessing perceptual sensitivity, borrowed from the psychophysics literature. In the second paradigm (Studies 4-6), similar stimuli were employed as cues and targets in a cross-modal Posner task. The tasks are described in detail in Chapter 2.

Study 1 (Chapter 3) used the perceptual sensitivity task to compare perceptual thresholds for somatic and auditory targets across depressed and control participants while minimising group-specific influences of attention on performance. This study aimed to compare baseline signal discriminability in the somatic and auditory modalities across groups. Study 2 (Chapter 4) employed a similar task but aimed to maximise group-specific influences of attention during the task to assess their impact on perceptual sensitivity. This study aimed to measure the influence of voluntary attention on somatic and auditory signal detection in depressed participants relative to controls. Study 3 (Chapter 5) used a computational approach employing a series of Bayesian agents to investigate possible data-generating processes underlying the Study 1 and 2 results. This study aimed to provide a proof-of-principle with respect to hypothesised mechanisms potentially accounting for group differences in performance in the two studies.

Study 4 (Chapter 6) employed the cross-modal Posner task to investigate the extent of attentional capture by task-irrelevant somatic cues, relative to auditory cues, in depressed participants compared to controls. This study aimed to provide an index of the tendency to become involuntarily aware of somatic signals in the absence of top-down attention towards them. Study 5 (Chapter 7) used a similar task, in which cues were predictive rather than irrelevant, to further address the question of the relative salience of somatic versus auditory cues to depressed versus control participants. Finally, Study 6 (Chapter 8) used a third version of the cross-modal Posner task to generate empirical data which was then used to optimize a Bayesian model of predictive processing within the context of a

covert orienting task. The aim of this study was to estimate underlying salience and sensory precision parameters for depressed participants in comparison to controls.

Each of these studies is described in turn in the six experimental chapters which follow the Methods chapter (Chapter 2). In the final Discussion (Chapter 9), the results of all studies are discussed in terms of their theoretical and clinical implications.

1.8.3. Population of interest

Depression is a complex and heterogenous disorder which can present in many different ways. Regardless of presentation, the symptomatology of depression throws specific obstacles in the way of individuals wishing to participate in studies at a time when they are, by definition, feeling unwell and struggling to cope with day-to-day functioning. Importantly, these obstacles are particularly overwhelming for individuals with more severe and complex depressive illnesses. Investigators must make a conscious choice regarding whether to cast the net wide and to include individuals with a range of forms of depression, including mild, dysthymic or transitory presentations; or whether to restrict study inclusion to a small but more tightly characterised group who are likely to be substantially more difficult to recruit. The difficulties associated with the latter approach have contributed to a lack of research specifically investigating more severe and persistent forms of depression. However, it is vital to characterise the mechanisms driving these treatment-refractory presentations in particular if more effective treatments are to be developed. The experimental cost of such a recruitment strategy may be a reduction in power due to small sample sizes; however, it is also possible that larger effect sizes and reduced measurement error due to a more precisely characterised sample will mitigate against this problem.

Our own research questions focused explicitly on maintaining factors contributing to complex and persistent forms of depression; essentially presentations associated with severity, chronicity and recurrence. Inclusion criteria for depressed participants were therefore strict: all participants in all studies were in a Major Depressive Episode (American Psychiatric Association, 2013), assessed by a clinical psychologist, at the time of their participation; and all participants self-reported their symptoms at the time of study participation to be moderate or severe. In addition, all participants' index depressive episodes occurred in the context of chronic or recurrent depressive illness. Control participants were not only healthy at the time of participation but had never met criteria for either depression or anxiety during their lifetime according to an assessment interview conducted by a clinical psychologist.

We mitigated against the risks of both Type 1 and Type 2 error associated with small samples as best we could in the following ways. First, we collected a substantial number of observations (>20,000 per study) to facilitate robust estimation. The single exception to this was Study 1, in which a crucial aspect of the design was the brevity of the task, designed to minimise wandering attention. Secondly, we designed the studies in such a way that outcomes from any one study were tested further in a second or third study. All our key outcomes, therefore, have support from more than one source. Thirdly, we used computational approaches to evaluate precise predictions about data-generating processes in the empirical studies, tested, where possible, against competing explanations. Finally, this thesis reports all studies undertaken with respect to these questions, with the exception of early pilot studies recruiting only healthy participants.

Details of the recruitment procedure are found in the description of the Method in Chapter 2.

Chapter 2. Methods: participants and paradigms

2.1. Participants

2.1.1. Depressed samples

For each of the six studies, a sample of moderately-severely depressed individuals with histories of chronic, treatment-resistant or recurrent depressive illness was recruited from an established panel of potential research volunteers. Major Depressive Disorder (MDD; APA, 2013) was diagnosed via clinical screening assessments including a Structured Clinical Interview for DSM-V Axis I disorders (SCID-I: First, Spitzer, Gibbon, & Williams, 2002) administered by a trained research assistant, and a SCID mood module administered on the day of testing by a registered clinical psychologist. Depression and anxiety severity were estimated using the Beck Depression Inventory (BDI-II: Beck, Steer, Ball, & Ranieri, 1996) and the Beck Anxiety Inventory (BAI: Beck, Epstein, Brown, & Steer, 1988), respectively. Inclusion criteria for the depressed groups were a diagnosis of either chronic or recurrent MDD in the context of a current Major Depressive Episode of at least moderate severity, defined as scoring 20 or above on the BDI-II (Beck, Steer, & Brown, 1996). Exclusion criteria included current alcohol or substance dependence or a history of psychosis, bipolar disorder, traumatic brain injury, intellectual disability or dementia.

Handedness was assessed using the Edinburgh Handedness Inventory (Oldfield, 1971) and an estimate of years of education was established via a brief conversation with the participant.

2.1.2. Control samples

For each depressed sample, a control group of equal size was recruited. Controls were healthy individuals with no significant history of anxiety or depression, and each control group was matched to the respective depressed group on age, sex and years of education. Exclusion criteria were as for the depressed participants with the additional specifications that controls had never met diagnostic criteria for a Major Depressive Episode, dysthymic disorder or an anxiety disorder (assessed by a clinical psychologist on the day of testing, using the SCID screening questions); and that they scored within the 'minimal' range on both mood measures at the time of testing: i.e., a score of less than 14 on the BDI-II (Beck, Steer, & Brown, 1996) and a score of less than 8 on the BAI (Beck & Steer, 1993). Handedness and estimated years of education were established as for the depressed samples.

2.1.3. Power, sample sizes and sample constitutions

An a priori power analysis was conducted using G*Power 3.1. (Faul, Erdfelder, Lang, & Buchner, 2007) based on an effect size estimate derived from a covert orienting study which compared validity effects between depressed and control participants (Pardo et al., 2006). The effect size of the group

comparison of validity effects in this study was very large ($\eta_p^2 = 0.38$), and with $\alpha = .05$ the minimum total sample size to achieve power of 0.95 was N = 24, or 12 participants per group. In hindsight, given that this effect size estimate depends on a single study, and considering the possibility that it may have been inflated by publication bias (e.g., Schäfer & Schwarz, 2019), a better strategy might have been to combine effect size estimates from less-relevant group comparisons between depressed and control participants in a range of attention tasks in larger-scale studies.

On the basis of the power calculation, a sample of sixteen depressed participants and sixteen matched never-depressed controls was recruited to each study. The exception was Study 2, in which a large number of observations per participant was collected to allow participant-level analyses, and in which the design required the sample size to be a multiple of twelve. Twelve participants were therefore recruited for each group in Study 2.

To facilitate recruitment in the context of the strict inclusion criteria, depressed participants who were willing to participate in one study were invited to participate in another. Specifically, all participants who took part in Study 1 also participated in Study 4, which took place during the same testing session. Ten of the sixteen depressed Study 4 participants returned 6 months later to participate in Study 5 (two more were excluded due to an improvement in their symptoms at the time of testing). An additional six depressed participants naïve to any other studies completed the sample.

A separate group of twelve depressed participants was recruited for Study 2. Of these, eight returned to participate in Study 6. An additional eight depressed participants naïve to any other studies were recruited to bring the total to sixteen.

This arrangement of participants ensured that all key findings were demonstrated in two separate groups of depressed individuals. In essence, Study 2 used an independent sample to test the conclusions of Study 1, while Study 6 used an independent sample to test the conclusions of Studies 4 and 5.

2.1.4. Ethical considerations

Ethical considerations relating to the recruitment of human participants include requirements that the risk of any harm or burden to participants is minimised; that confidentiality and data protection with respect to personal information is maintained; and that informed consent to participate in all aspects of the study is elicited, including respect for the right to withdraw at any stage without giving a reason (General Assembly of the World Medical Association, 2014). When recruiting individuals with depressive disorders, additional considerations may include a potentially increased risk of distress,

anxiety or fatigue relative to healthy controls in the context of a potentially reduced capacity for assertiveness, indicating that active efforts should be made at all stages of study participation to ensure that participants are comfortable and happy throughout the proceedings.

The researcher discussed study details and procedures fully and transparently with potential participants by telephone during the recruitment process and encouraged them to take time to decide whether to participate. Attendance details were carefully negotiated with interested parties (for example, discussing the best time of day to come in for individuals whose symptoms were subject to diurnal variation, or arranging transport for individuals anxious about public spaces). Before testing, informed consent was elicited verbally and in writing; and during testing, the researcher checked in informally at intervals regarding participants' mood and comfort. Occasionally an aspect of one of the studies precipitated a dip in mood (for example, a minority of depressed participants were distressed by the negative word list employed in Study 2) and where this occurred a positive mood induction (a break, a cup of tea, a walk in the garden, discussing or planning an enjoyable activity) was used to repair the dip. Participants were informed that if they should experience substantial distress during or after any of the studies, they would be provided with a safe space in which to calm down and offered a confidential consultation with the study researcher, who is a registered clinical psychologist with specialist experience of working clinically with individuals with affective disorders. This did not prove to be necessary, although signposting to statutory services and assistance with the referral process was provided for some participants at their request.

The tasks required participants to sit still for periods of 5 – 10 minutes with their arms in a specific position. The position was chosen to minimise discomfort, and regular breaks and opportunities to stretch or to walk around were provided to reduce any remaining risk of physical discomfort. When testing was complete, participants were debriefed and offered an opportunity to ask questions. Confidentiality and anonymity were ensured by allocating each participant a unique number to store with all study data. Data were stored securely and no personally identifiable information was linked to them.

All participants provided written informed consent before taking part in any study, and all received compensation of £6 per hour for their participation in addition to travel expenses of up to £3. The studies were conducted in accordance with ethical approval from the Cambridge Psychology Research Ethics Committee (PRE.2013.72). Appendix J includes copies of the approval letter (J.1), consent form (J.2) and study information sheets (J.3).

2.2. Interview and self-report measures

2.2.1. Structured Clinical Interview for DSM-V Axis I Disorders (SCID-I; First, Gibbon, Spitzer & Williams, 1996).

The SCID-I is a standardized diagnostic interview schedule designed to assist clinicians and researchers in making reliable Axis I psychiatric diagnoses according to the DSM. It is considered to be a gold-standard clinical assessment instrument, with good inter-rater reliability (e.g., Lobbestael, Leurgans, & Arntz, 2011), and is used widely in research. Example questions from the SCID-I can be found in Appendix I (Section I.1).

2.2.2. Beck Depression Inventory (BDI-II: Beck, Steer & Brown, 1996)

The BDI-II is a 21-item self-report measure assessing depressive symptomatology including low mood. Good internal consistency, test-retest reliability and convergent validity with standardised clinician assessment have been demonstrated (Beck et al., 1996) and the measure is widely used in research into depression, enabling comparison across studies. The BDI-II is in Appendix I.2.

2.2.3. Beck Anxiety Inventory (BAI: Beck, Epstein, Brown & Steer, 1988)

The BAI is a 21-item self-report measure assessing current or state anxiety symptomatology. Like the BDI-II it is widely used in research and its psychometric properties are well-established, including a relatively good ability to discriminate anxious from depressive presentations (Beck et al., 1988). The BAI is in Appendix I.3.

2.2.4. Edinburgh Handedness Inventory (EHI: Oldfield, 1971)

This widely-used 10-item self-report measure provides a quantitative estimate of handedness. The EHI is in Appendix I.4.

2.2.5. Multidimensional Assessment of Interoceptive Awareness (MAIA: Mehling, Price, Daubenmier, Acree, Bartmess & Stewart, 2012)

The MAIA is a 32-item self-report measure designed to provide a comprehensive assessment of (subjective) interoceptive and body awareness across eight theoretically-derived domains including attention regulation and emotional awareness. The authors report adequate psychometric properties and support for construct validity. This measure was employed solely in Study 6 (Chapter 8) in order to test a specific hypothesis. The MAIA is in Appendix I.5.

2.3. Experimental paradigms

Two novel paradigms were developed to address the research questions posed in the Rationale outlined in Chapter 1. The first paradigm consisted of a multimodal adaptive staircase designed to

measure perceptual sensitivity in the somatic and auditory modalities. The second paradigm consisted of a cross-modal covert attention (Posner) task, employing similar somatic and auditory stimuli as targets and cues. Studies 1 and 2 employed the perceptual sensitivity paradigm, while Studies 4-6 employed the covert attention task. These two paradigms will be discussed in turn.

2.3.1. Perceptual sensitivity paradigm

Materials

Somatic stimulation was delivered via one of two 10mm diameter vibrating tactors (310-103, Precision Microdrives) affixed to the participant's left and right ventral forearms using surgical tape (see Figure 2.1B for the layout of the experimental materials). The tactors were driven using an Arduino board (Arduino Uno, Arduino) connected to a desktop PC via a USB port and controlled via MATLAB (2009a, The Mathworks). Stimuli consisted of 200 ms periods of vibration which were varied in intensity. White noise (LAeq = 65dB) was continuously delivered via external speakers (described below) during somatic blocks to mask any sounds generated by the tactors when driven.

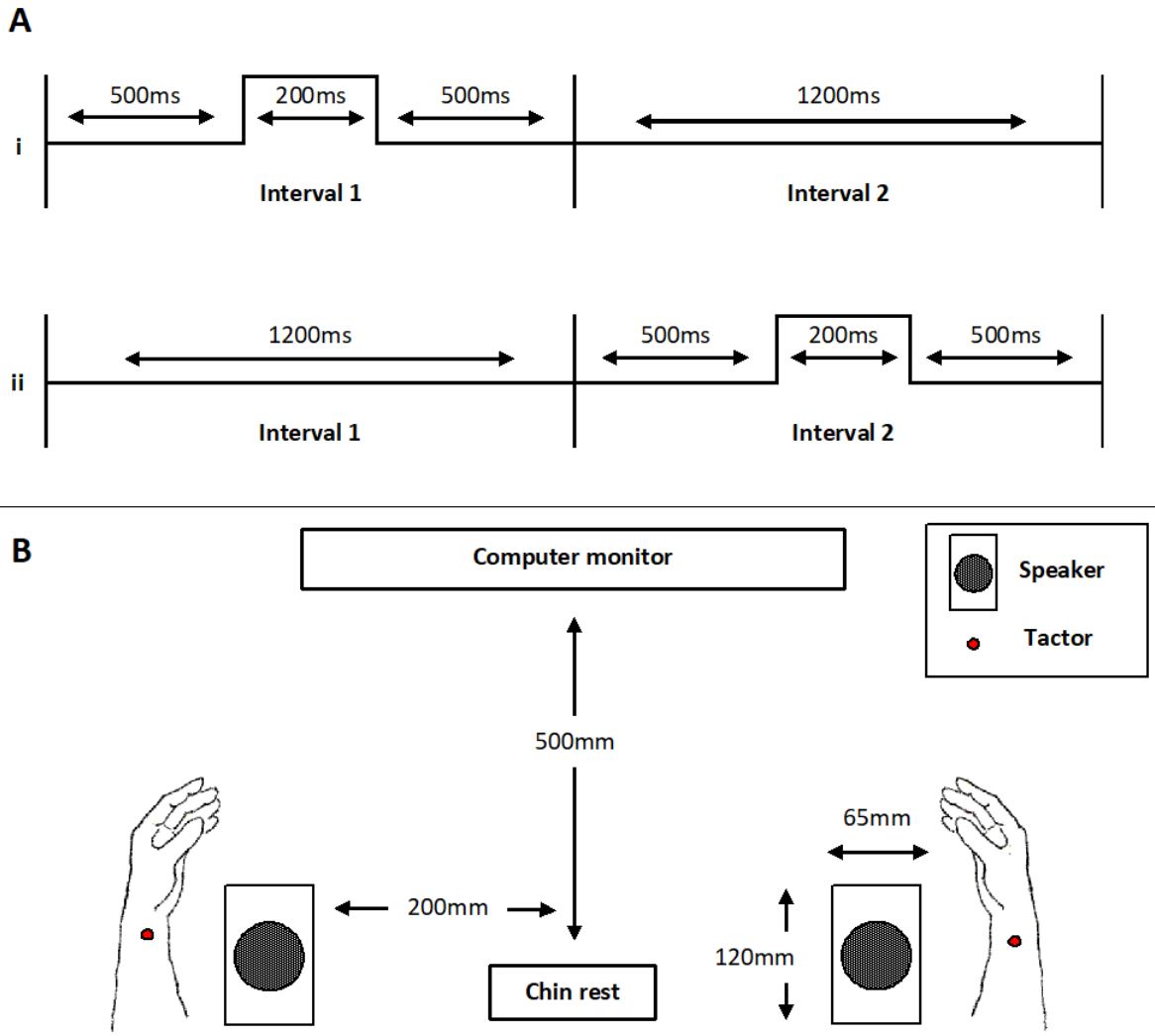


Figure 2.1: Experimental materials: perceptual sensitivity paradigm. A: a trial in the perceptual sensitivity paradigm. The stimulus is presented in either Interval 1 (i) or Interval 2 (ii). Sequence **i** or **ii** is randomly selected. **B**: Participants were seated at a table facing a computer monitor with forearms resting on small pads affixed to the table and head steadied by a chinrest. Tactors were affixed to the participant's left and right ventral forearms using surgical tape. Foot pedals were adjusted to a comfortable position under the table. Intervals were indicated by the appearance of the relevant interval name in the centre of the computer screen for the duration of each interval. Participants fixated on a cross in the centre of the screen between trials. Lights were dimmed during the task.

Auditory stimulation was delivered via one of two small mylar speakers (50mm diameter) fixed to the left and right of the participant (Figure 2.1B). The speakers were connected to a soundcard incorporated into a desktop PC running MATLAB (2009a, The Mathworks). Stimuli consisted of 440 Hz pure tones lasting 200ms, delivered via MATLAB and the psychophysics toolbox (Brainard, 1997; Pelli, 1997). All aspects of the stimuli were kept constant throughout the experiment with the exception of their intensity.

Given that finger movements can generate somatic sensations in the wrist area, responses during all blocks were made using foot pedals for left and right feet, to avoid the possibility of interference with somatic detection on the wrist.

Procedure

Perceptual sensitivity for somatic and auditory information was estimated using an adaptive staircase paradigm (Levitt, 1971), in which participants were asked to make a series of judgements regarding the presence or absence of a stimulus presented at near-threshold intensity. The aim of the task was to enable comparison of thresholds between depressed and non-depressed groups rather than to identify an absolute threshold for any individual in either modality.

Stimulus intensity was varied according to a standard psychophysical 3-down 1-up adaptive staircase procedure (Levitt, 1971), where the accuracy of the previous series of responses determined increases or decreases in intensity until a set number of reverses had been completed. This procedure converges on a threshold intensity for each participant at which approximately 79% of stimuli are detected. A 1-up-1-down procedure was used until the first reverse in order to reduce the time taken to reach the proximity of each participant's threshold.

A two-alternative-forced-choice (2AFC) paradigm was used – requiring a positive response on each trial – in order to reduce the likelihood that individual differences in motivation or mood could introduce a systematic response bias between groups (Malone & Hemsley, 1977). Stimuli were presented during one of two randomly selected intervals (illustrated in Figure 2.1A). The beginning of

each trial was indicated by a visual signal on the computer screen, and its end by a question mark which remained visible until a response was made. Responses made prior to the appearance of the question mark were not recorded, and following a valid response there was an inter-trial interval of 1000ms before the next trial began. Participants were informed that one stimulus would occur in each trial, with a 50% chance of occurring in either interval.

Stimuli were demonstrated to participants before starting the first block, and an opportunity was given to practice responding.

2.3.2. Covert attention (Posner) paradigm

Materials

Visual stimuli consisted of 400 ms illuminations of one of two 3mm white light emitting diodes (LEDs) positioned to the left and right peripheries of the participant's visual field (see Figure 2.2 for the layout of the experimental materials). Somatic stimuli consisted of 400 ms bursts of 210 Hz vibration, delivered by one of two 10mm vibrating tactors (310-131, Precision Microdrives) affixed to the participants' left and right ventral forearms using surgical tape. Auditory stimuli consisted of 400 ms 440 Hz tones (60dB LAeq) delivered via one of two 50mm mylar speakers. LEDs, tactors and speakers were all connected via the parallel port data register to a desktop PC running MATLAB (The Mathworks, 2009a), and were controlled via a program written using Psychtoolbox (Kleiner, Brainard, & Pelli, 2007) to ensure precise stimulus onset and offset latencies.

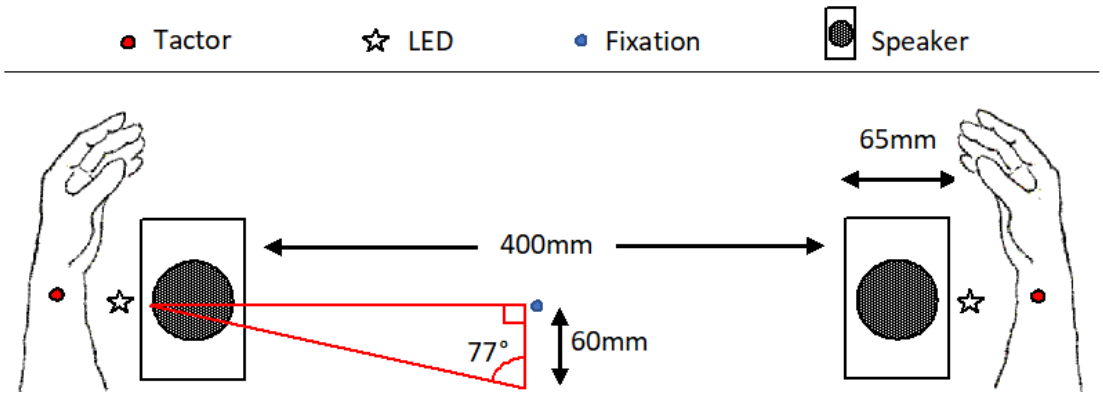


Figure 2.2: Experimental materials: covert attention paradigm. Tactors are affixed to the participant's left and right ventral forearms using surgical tape. The participant's wrists rest against padding fixed to the surface of the table and the outer sides of the speakers. LEDs are embedded in the padding, clearly visible and close to the ipsilateral speaker and tactor.

Trials began with cue onset followed by target onset with a variable stimulus onset asynchrony. Uncued trials began with target onset. Following target offset, the program paused until a response was made, triggering the start of the next trial. Inter-trial intervals were randomly varied between

1000 and 1500ms. Participant responses were made using foot pedals for the left and right feet, connected to the PC via the parallel port.

Procedure

Participants were seated at a table, with forearms resting on small pads affixed to the table and eyes resting on a central fixation dot (see Figure 2.2). Foot pedals were adjusted to a comfortable position under the table and lights were dimmed during the task. Participants were instructed to maintain fixation on the dot while responding as quickly and as accurately as possible to targets. The experimenter observed the participant throughout the task to ensure that central fixation was maintained.

In each trial, a target was presented to either the right or left side of fixation, and participants indicated its location as quickly and as accurately as possible using a spatially congruent foot pedal response. A cue was presented immediately before the target. Target and cue modality, stimulus-onset-asynchronies (SOAs) and the contingencies associated with cues were determined by the design of the specific studies. Trial types were presented within blocks in a randomised order, and reaction times and error data were collected by the program. In total participants completed 4 blocks in counterbalanced order in each study, with opportunities to rest provided between blocks.

2.4. Analyses

Classical analyses of variance (ANOVAs), regressions and t-tests were conducted using IBM SPSS Statistics for Windows (version 25). Bayesian statistical models were fit using a Markov Chain Monte Carlo (MCMC) approach, conducted using JAGS (Plummer, 2017), running with R (R Core Team, 2017) and the runjags (Denwood, 2016) and coda (Plummer, Best, Cowles, & Vines, 2006) packages. For each parameter estimate within each model, four chains were initialised at a range of starting points and run until convergence, assessed visually and according to the potential scale reduction factor ($\hat{R}$: Gelman & Rubin, 1992). Once adequate convergence was identified, chains were subsequently run until an estimated sample size near or above 10,000 samples was collected for each parameter of interest (Kruschke, 2014). Sensitivity analyses and posterior predictive checks for each model are described in Appendix A.

Analyses were a mix of Bayesian and classical inference, depending on task. Studies 1 and 2 were analysed using Bayesian inference, an approach chosen because of its flexibility in terms of parameter inclusion and the ease with which it can handle hierarchical and mixture modelling. Studies 4, 5 and 6 followed a classical design and were analysed using a classical ANOVA predetermined before data collection took place.

Study 3 simulations were created using MATLAB (R2018a, The Mathworks) and analysed using the same scripts and models as Studies 1 and 2. A Study 6 predictive processing model of the covert orienting task was created in R and optimized using JAGS.

Plots were produced using the packages ggplot2 (Wickham, 2016) and ggpubr (Kassambara, 2017).

Chapter 3. Study 1: Perceptual sensitivity in somatic and auditory signal detection in persistent depression

Study 1 employed the perceptual sensitivity paradigm described in the Method section in Chapter 2 to estimate perceptual thresholds for somatic and auditory stimuli on the left and right sides of space. Efforts were made to minimise the impact of attentional and response factors that might disproportionately affect depressed participants relative to healthy controls. Specifically, brief adaptive staircases were used because they can efficiently and reliably estimate thresholds from a relatively small number of trials (Leek, 2001), reducing the potential impact of group differences in the ability to sustain attention. The task was simple, and well-practiced beforehand, reducing load on working memory and executive function, and the testing room was quiet and dark, reducing potential distractions.

On the basis of the literature described in Chapter 1, it was hypothesised that persistently-depressed participants would demonstrate reduced perceptual sensitivity for auditory and somatic stimuli, and that this reduction in sensitivity would be particularly marked for somatic targets. An alternative hypothesis stated that previous reports of reduced perceptual sensitivity in depression resulted from systematic group differences in top-down attention and motivational factors rather than baseline perception, and that the current paradigm would succeed in minimising such differences. In this case, no group differences in perceptual sensitivity would be expected. The key index of perceptual sensitivity in Study 1 was a group-level perceptual threshold estimate derived by fitting a general linear mixed model with a logistic link function to the data. Such a model also yields a group-level estimate of the slope of the function, which can potentially provide insights into factors affecting task performance (Klein, 2001).

3.1. Study 1 design

Participant recruitment, materials and procedure were as described in the Methods in Chapter 2.

Four adaptive staircases were presented in sequence. Each staircase consisted entirely of stimuli of one modality and one laterality (somatic left, somatic right, auditory left, and auditory right) and staircase order was counterbalanced across participants using a Latin Square. Participants were verbally requested to pay attention to either the left or right side of space, depending on staircase, while the stimuli were presented. Each staircase continued until 8 reverses had been completed. Initial step sizes were 8dB for auditory stimulation and 2dB for somatic stimulation, reducing by an eighth with each reverse to increase the precision of the final estimate. Initial stimulus intensities were well

above normal perceptual thresholds (0.9 G for the somatic stimulus and 55dB LAeq for the auditory stimulus)

Stimuli were presented during one of two randomly selected time intervals. Intervals were indicated by a visual signal on the computer screen ("Interval 1" at fixation for the duration of the first interval, and "Interval 2" for the duration of the second). The stimulus was presented 500ms after onset of the visual signal. To mark the end of the second interval, a question mark appeared at fixation and remained visible until a response was made. Accurate responses were a left foot-press for a stimulus occurring in the first interval, and a right foot-press for a stimulus occurring in the second. Responses made prior to the appearance of the question mark were not recorded, and following a valid response there was an inter-trial interval of 1000ms before the next trial began.

Stimuli were demonstrated to participants before starting the first block, and an opportunity was given to practice depressing the foot pedals.

3.2. Study 1 model

A Bayesian analytic approach was employed. The data were fit to a generalised linear mixed model (GLMM) with a logistic link function, in which participant responses were pooled across groups in order to estimate logistic regression parameters by group and experimental condition (stimulus modality and laterality) with a random effect added to account for individual differences within groups.

Following initial attempts to fit the model (discussed below) a lapse parameter was added. In an influential paper, Wichmann and Hill (2001) showed that the occurrence of lapses (errors) at the upper asymptote of a psychometric function can severely bias threshold and slope estimates when the lapse rate is assumed to be zero. Their proposed solution is to model the lapse rate using a flat prior with a lower bound of 0 and an upper bound of 6%. We addressed evidence of bias in our GLMM slope estimates using a similar solution as a described in Section 3.3.3.

According to the model, the data are distributed as

$$y_{ijk} \sim Binomial(n_{jk}, \theta_{jk}) \quad (1)$$

where y_{ijk} denotes the i^{th} observation for the j^{th} participant in the k^{th} condition, n_{jk} denotes the total number of observations and θ_{jk} the rate of correct responses of participant j under condition k. K is equivalent to a design matrix including a group factor (2 levels), a modality factor (2 levels), and a laterality factor (2 levels).

Rate of correct responses θ_{jk} was modelled as a logistic transform of a combination of intercept and slope varying by condition k and a random factor Rj specific to the participant. Because the task was a 2AFC task, the lower asymptote was set at the guess rate, γ = 0.5. Following initial attempts to fit the model (discussed above) a lapse parameter λ was also added.

$$\theta_{jk} = \gamma + (1 - \gamma - \lambda_k) logistic(\beta 0_k + \beta 1_k x + R_j) \quad (2)$$

Lapse rates (λ) were modelled using a uniform prior (Wichmann & Hill, 2001) with a relatively permissive upper bound of 10% given that our participants were drawn from a clinical population. Lapse rates were allowed to vary by group and condition.

$$\lambda_k \sim Uniform(0,0.1) \quad (3)$$

Prior distributions for the slope and threshold coefficients were vague on the scale of the standardised data:

$$\beta 0_k \sim N(0, \sigma^{\beta 0^2}) \quad (4)$$

$$\beta 1_k \sim N(0, \sigma^{\beta 1^2}) \quad (5)$$

$$R_j \sim N(0, \sigma^{R^2}) \quad (6)$$

$$\sigma^R = \sqrt{\frac{1}{\tau^R}} \quad (7)$$

$$\tau^R \sim Gamma(0.001,0.001) \quad (8)$$

$$\sigma^{\beta 0} = \sigma^{\beta 1} = 2 \quad (9)$$

The predictor variable was binned into 8 steps, each step representing 4dB in the auditory staircases and 1dB in the somatic staircases; and standardised using z-score scaling. Sensitivity analyses and details of model fit are in Appendix A.1.

3.3. Study 1 results

3.3.1. Sample characteristics

All depressed participants were diagnosed with chronic, recurrent and/or treatment-resistant forms of depressive illness of at least moderate severity at the time of testing. Mean age of onset was 21.73 years old (SD 11.25) and the mean number of years since first diagnosis was 19.60 (SD 15.89). Six participants (37.5%) reported that their first onset of depression was in childhood. Six individuals

(37.5%) met criteria for at least one comorbid Axis 1 disorder at the time of testing, including Obsessive-Compulsive Disorder, Generalised Anxiety Disorder, Posttraumatic Stress Disorder and Anorexia (three participants met criteria for an anxiety disorder, two met criteria for an anxiety disorder and PTSD, and one met criteria for an eating disorder). Six participants (37.5%) were currently prescribed antidepressant medication (n=6 were prescribed an SSRI, n=2 were additionally prescribed an SNRI). No control participants were prescribed any form of psychotropic medication.

A series of t-tests demonstrated that there were no significant group differences with respect to the characteristics of age, years of education or handedness (see Table 3.1). As expected, depressed participants differed significantly from healthy controls with respect to self-reported symptoms of depression and anxiety.

Table 3.1: Study 1 demographic comparisons by group

	Depressed group (n = 16)	Control group (n=16)	2-tailed t-tests
Demographics: mean (SD)			
Sex	15 women	15 women	-
Age (years)	42.00 (18.11)	42.50 (17.41)	$t(30) = 0.08$, $p = 0.94$
Handedness (EHI)	68.14 (47.75)	80.06 (31.16)	$t(30) = 0.84$, $p = 0.41$
Education (years)	15.25 (2.86)	15.69 (2.41)	$t(30) = 0.47$, $p = 0.64$
Mood measures: mean (SD)			
Depression (BDI-II)	33.19 (5.06)	5.06 (2.70)	$t(30) = 20.77$, $p < 0.001$
Anxiety (BAI)	22.00 (10.00)	3.06 (2.64)	$t(17.09^{1}) = 7.32$, $p < 0.001$

[1] Degrees of freedom adjusted due to unequal variances

EHI = Edinburgh Handedness Inventory, BDI-II = Beck Depression Inventory-II, BAI = Beck Anxiety Inventory

3.3.2. GLMM

A total of 5033 observations was collected, an average of 40 per participant per condition.

Figure 3.1 shows the model fit to the data for each group in each condition (left panels), contrasts on the effects on the slope and threshold parameters (upper right panel), and lapse rate estimates by group and condition (lower right panel). As can be seen, there are credible main effects of modality on both threshold and slope, which are unsurprising given differing starting-points and step sizes across the two modalities. There are no other effects on either parameter. Of interest, there are no effects of group, and no interactions between group and any other factor, on either slope or threshold.

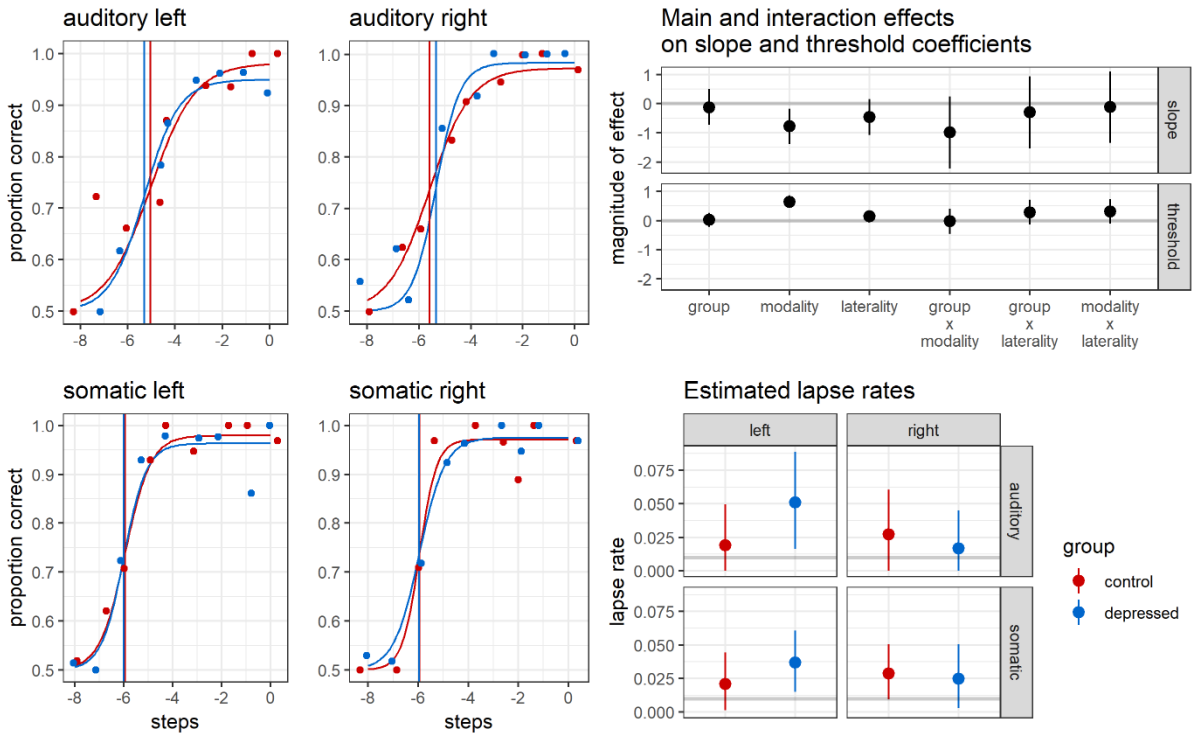


Figure 3.1: Study 1 GLMM outcomes by group, stimulus modality and laterality. Left panels: mean logistic curves and thresholds (vertical lines) estimated from the Study 1 GLMM, shown by stimulus modality and laterality. Points represent the observed data (proportion correct averaged over group) shown to the nearest step and jittered to avoid overlap. The step size for the auditory staircases is 4dB, for the somatic staircases 1dB. Upper right panel: contrasts on effects and interactions for the slope and threshold parameters. Lower right panel: estimated lapse rates by group and condition.

GLMM model comparison.

A variable selection procedure (Dellaportas, Forster, & Ntzoufras, 2002) was carried out in order to assess the contribution of the various factors, most importantly group membership, to the fit of the slope and threshold parameters. Eight models were included in the comparison comprising every possible combination of factors. Given the similarity of the effects on the slope and threshold parameters observed in the preceding model, each model tested its effects on both parameters simultaneously. The lapse rate was estimated for all models as above. Models are described in order of decreasing posterior credibility in Table 3.2.

Table 3.2: Study 1 posterior model probabilities and Bayes factors for GLMM variable selection procedure

Model	Factors included	Posterior model probability	Bayes factor relative to reference model
M	Modality	0.99997	7.56×10^{9}
ML	Modality and laterality	2.02×10^{-5}	1.53×10^{5}
GM	Group and modality	8.42×10^{-6}	6.37×10^{4}
REF	None (reference model)	1.32×10^{-10}	1
L	Laterality	9.42×10^{-13}	7.13×10^{-3}
G	Group	2.59×10^{-13}	1.96×10^{-3}
GML	Group, modality and laterality	1.81×10^{-14}	1.37×10^{-4}
GL	Group and laterality	2.74×10^{-17}	2.07×10^{-7}

Model REF is the simplest model comprising a single intercept and slope for both groups of participants in all conditions. It is used here as a reference model. The only models which provide a better account of the data are those which include modality and no more than one additional factor. An effect of modality alone is substantially more credible than any other explanation for the data, with the probability of the data under this model increased by a Bayes factor of 49519.76 relative to its nearest competitor.

With respect to hypothesised effects of group, the addition of a group parameter to any model in fact renders it substantially less probable (i.e., P(model G)<P(model REF), P(model GM)<P(model M), P(model GL)<P(model L) and P(model GML)<P(model ML)). This suggests that true group influences on perceptual performance are highly unlikely given the current data, and furthermore that the failure to identify group differences in slope and threshold parameters in the current dataset is not attributable to a lack of power.

3.3.3. Attentional lapses

The lapse rate in a psychophysics task is assumed to be independent of stimulus intensity but is most salient at highly detectable intensities, where errors are unlikely to reflect genuine perceptual limits but can nevertheless exert a disproportionate influence on model fit (Prins, 2012; Wichmann & Hill, 2001). A first attempt to fit the model, not including a lapse parameter, resulted in a credible interaction between group and laterality in the slope parameter (see Appendix C for details), observable in both stimulus modalities and reflecting a flattening of the slopes on the left in the depressed group and on the right in healthy controls. This flattening was reminiscent of the influence of unmodelled lapses in psychometric functions (Wichmann & Hill, 2001) and the associated group by laterality interaction was abolished once the lapse parameter was included in the model. The implication that lapse rates might be disproportionately high on the left in the depressed group and on the right in controls led us to examine asymptotic lapses more carefully.

To provide a direct index of attentional lapses, a count of errors occurring at the upper asymptotes was made. For the purposes of this count the upper asymptotes were conservatively defined as the portion of the curve to the right of the lowest-intensity point at which the percentage of correct responses was greater than or equal to the percentage of correct responses averaged over that data point and all higher-intensity data points. The resulting count of asymptotic lapses for each group in each laterality condition (summed over modality) is shown in Figure 3.2.

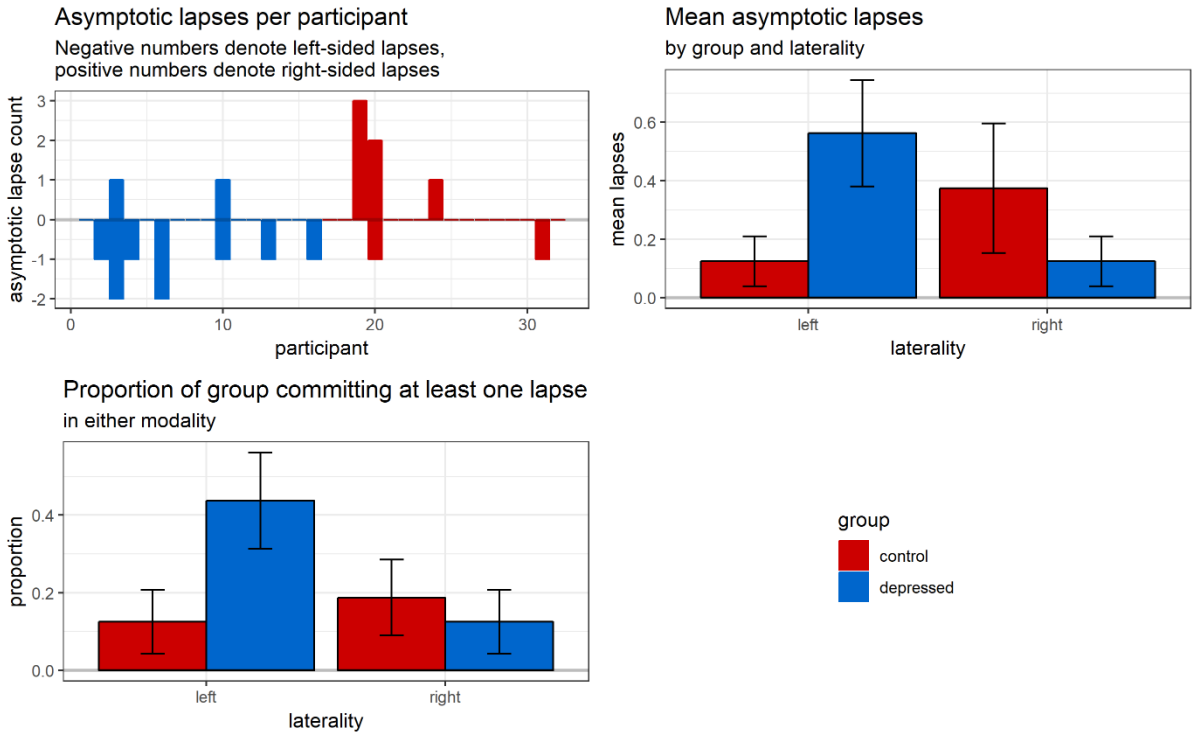


Figure 3.2: Study 1 asymptotic lapses by group and laterality. Error bars represent 1 standard error of the mean.

Likelihood ratio Chi-square tests confirmed that depressed participants were more than three times as likely as healthy controls to lapse at least once on the left (χ^2 (1) = 4.04, p = 0.044, odds ratio = 3.5), while there was no significant group difference in the likelihood of lapsing at least once on the right (χ^2 (1) = 0.24, p = 0.625, odds ratio = 0.67).

3.3.4. Medication-free analyses

All analyses were repeated excluding n=6 participants from the depressed group who were prescribed psychotropic medication at the time of the study. All outcomes of interest were unaffected (see Appendix B.1. for details).

3.4. Study 1 summary

In summary, under conditions which aimed to minimise any impact of differential attentional resource between groups, and when attentional fluctuations were accounted for, Study 1 provided no evidence for a systematic effect of persistent depression on perceptual threshold in either the somatic or auditory modalities. These findings argue against the existence of modality-specific perceptual disturbances resulting from persistent depression in terms of either somatic or auditory experience. In contrast to some previous studies (Adler & Gattaz, 1993; Malone & Hemsley, 1977; Marazziti et al., 1998; Yovell et al., 1995), and in a dissimilarity with the literature on interoception (Dunn et al., 2007; Dunn, Stefanovitch, et al., 2010; Furman et al., 2013), the current study suggests that persistent depression may not be associated with an increase in intrinsic sensory noise in the somatic or auditory modalities. However, these findings do not rule out the possibility that under conditions of greater attentional load, changes in perceptual sensitivity may arise as a secondary result of a primary disturbance of attention. In line with the hypothesis that depression may have an impact on voluntary perceptual attention, there was some indication in Study 1 of an increased tendency to left-sided attentional lapses in depressed participants, potentially indicating disproportionate difficulty in maintaining attention to the left side of space. This interpretation is a very preliminary one, however, given the sparse overall lapse count in the current data. In order to further test these hypotheses, Study 2 explicitly investigated the impact of potential group differences in voluntary attention on perceptual sensitivity, using a design that aimed to maximise any such group differences with respect to voluntary attention in general and to lateralised attentional asymmetries in particular.

Chapter 4. Study 2: Influence of voluntary attention on somatic and auditory signal detection in persistent depression

In contrast to Study 1, Study 2 had the explicit aim of maximising the impact of attentional factors which might be expected to moderate perception. Increasing the influence of attentional factors on task performance enables a detailed examination of depression-specific changes in attention, as well as providing insight into the impact of any such depression-specific attentional changes on perception. In addition, relinquishing the need to keep the task as brief as possible (to minimise attentional lapses or mind-wandering) allowed the collection of a larger number of observations, to enable participant-level analyses.

The paradigm was similar to that employed in Study 1, with a number of changes designed to increase the 'cost' of performing the task in terms of attentional resources. As before, each participant completed a left-sided staircase and a right-sided staircase for each condition. In contrast to the previous design, however, the left- and right-sided staircases were interleaved and presented in a randomised fashion such that any given trial had an equal probability of belonging to either staircase, and participants decided between spatial (left/right) rather than temporal intervals. This innovation required participants to pay attention simultaneously to both sides of space, increasing the spatial attentional load of the task. Importantly, it also provided the participants with redundant information, allowing them, in principle, to complete the task on the basis of the information provided by only one side of space. As a strategy for identifying "true" perceptual thresholds this is clearly problematic due to the risk of non-converging staircases (see García-Pérez & Alcalá-Quintana, 2011 for further discussion of this approach) but in the current context it offers a method of indexing hypothesised lateralised attentional biases. For example, a participant with a strong preference for the right side of space could complete the task by effectively treating the right-sided staircase as a yes-no task, responding "right" with high probability whenever a right-sided stimulus was detected, and "left" with high probability when no stimulus was detected on the right. This would induce a compensatory response bias towards the left at high levels of uncertainty: for example, following an attentional lapse, or when stimulus intensity was low. Given the lateralised effects suggested by Study 1, it was expected that depressed people would be disproportionately affected by increased spatial load, especially when responding to left-sided stimuli, and that this would be indexed by a compensatory left-sided response bias in depressed participants.

In addition to the increase in spatial load, attentional load was further increased by lengthening time-on-task. Study 2 quadrupled the total number of staircases completed by each participant to sixteen; in addition, each staircase was lengthened by two additional reverses and each block included two

staircases rather than one, more than doubling the length of time between breaks. The extended time-on-task was expected to impact depressed participants more than healthy controls given the documented effects of depression on sustained attention (e.g., Van Der Meere, Börger, & Van Os, 2007; Yang et al., 2015).

Competition for attentional resources was further provided by the introduction of depression-relevant, but task-irrelevant, distractor words of positive, negative and neutral valence. Distraction, and particularly distraction by depression-relevant negative words, was expected to disproportionately impact depressed participants, given the difficulty in disengaging from such material which is associated with the tendency to depressive rumination (e.g., Kaiser et al., 2018). Finally, reaction times were recorded in Study 2 as an additional index of attentional control (e.g., Bellgrove, Hester, & Garavan, 2004; Kelly, Uddin, Biswal, Castellanos, & Milham, 2008; Weissman, Roberts, Visscher, & Woldorff, 2006).

It was hypothesised that an increase in attentional 'cost' would result in a deterioration in overall performance and that this would be exacerbated in depressed individuals. Specifically, it was predicted 1) that increased time-on-task would result in an increase in the likelihood of attentional lapses among depressed participants relative to healthy controls; 2) that an individual preferentially tracking one side of space is likely to manifest a response bias for the less-attended side of space when stimuli are undetected, and that this would manifest in depressed participants as a left-sided response bias at low levels of stimulus intensity; and 3) that the introduction of distractor words would impact differentially on group performance with respect to word category, such that the attentional performance of depressed participants would be more disrupted by depression-relevant negative words relative to healthy controls.

In the absence, to our knowledge, of any existing investigations of this issue, it was an open question whether evidence of distraction or poor attentional control in depressed participants would be associated with a meaningful shift in perceptual thresholds.

4.1. Study 2 design

Participant recruitment, materials and procedure were as described in the Methods in Chapter 2.

Staircase step sizes were made constant (1dB in the somatic modality, 4dB in the auditory modality) for ease of analysis. Starting intensities were initially reduced to reflect this change (lead-ins would otherwise be doubled in length) but were varied where necessary in the course of testing to ensure

that all participants began the staircases at an intensity that they could comfortably detect. Staircases were lengthened from 8 to 10 reverses to provide more data and to increase time on task.

In contrast to Study 1, intervals were spatial rather than temporal. Each participant completed interleaved left- and right-sided staircases for each condition, making a judgement as to whether the stimulus in each trial had occurred on the left or the right side of space. Participants were alerted to the beginning of a trial by the appearance of either a fixation cross or an irrelevant word on the screen. After 500 ms, a stimulus was presented either on the left or the right, and participants responded using the spatially congruent foot pedal. Once a response had been made, the trial indicator vanished from the screen and a 1000ms inter-trial interval intervened before the beginning of the next trial. Response latencies were recorded by the program as an additional index of attentional lapses.

Each participant completed four blocks in each modality (each block consisting of two interleaved staircases as described above). During the first block of each modality, the trial indicator consisted of a fixation cross. In the three subsequent blocks (presented in counterbalanced order across participants), the indicator consisted of a word drawn at random (with replacement) from one of three word lists (positive, negative or neutral words), depending on block. Word lists are described in Appendix D.

Two brief practice blocks (one for each modality) were completed by each participant prior to beginning the task. The function of the practice blocks was to ascertain that the participant had understood the task and was able to utilise the foot-pedals comfortably. No feedback was given.

4.2. Study 2 models

4.2.1. Signal detection model

As described above, the key index of hypothesised lateralised attentional asymmetry in Study 2 was expected to be response bias, and a signal detection model is explicitly designed to quantify such biases in addition to generating estimates of perceptual sensitivity. Therefore, a signal detection model (Green & Swets, 1966; Lee & Wagenmakers, 2014) was fit to the data. In this model, indices of perceptual sensitivity (d': the standardised difference between the means of signal and noise distributions) and response bias (c: an index of the marginal probability of giving a particular response) were estimated for each participant in each condition, partially pooling variance through the use of a hierarchical model, taking into account individual differences, group membership and the stimulus features of modality and intensity.

Arbitrarily, hits were defined as correct left-sided responses while correct rejections were defined as correct right-sided responses.

According to the model, the data are distributed as

$$h_{jk} \sim Binomial(n^h_{jk}, \theta^h_{jk}) \tag{10}$$

$$f_{jk} \sim Binomial(n^f_{jk}, \theta^f_{jk}) \tag{11}$$

where h_{jk} denotes the number of hits (correct responses to left-sided stimuli), n^h_{jk} the total number of left-sided trials, and θ^h_{jk} the hit rate attributable to participant j in condition k. Similarly, f_{jk} denotes the number of false alarms (incorrect responses to right-sided stimuli), n^f_{jk} the total number of right-sided trials, and θ^f_{jk} the false alarm rate attributable to participant j in condition k.

Hit and false alarm rates θ^h and θ^f were reparameterised in terms of sensitivity (d') and response bias (c) in accordance with signal detection theory as shown below. ANOVA-like linear models (Kruschke, 2014) were placed on the d' and c estimates in order to estimate their variance components with respect to group membership and the experimental conditions. In contrast to the logistic model employed in Study 1, therefore, stimulus intensity was treated as a categorical rather than a continuous variable.

$$\theta^h_{jk} = \Phi\left(\left(\frac{\sqrt{2d'_{jk}}}{2}\right) - c_{jk}\right) \tag{12}$$

$$\theta^f_{jk} = \Phi\left(-\left(\frac{\sqrt{2d'_{jk}}}{2}\right) - c_{jk}\right) \tag{13}$$

$$d'_{jk} = \alpha^{d'}0 + \alpha^{d'}R_j + \alpha^{d'}F_k + \varepsilon^{d'}_{jk} \tag{14}$$

$$c_{jk} = \alpha^{c}0 + \alpha^{c}R_j + \alpha^{c}F_k + \varepsilon^{c}_{jk} \tag{15}$$

For both d' and c:

$$\alpha 0 \sim N(\mu, \sigma^{0^2}) \tag{16}$$

$$\alpha R_j \sim N(0, \sigma^{R^2}) \tag{17}$$

$$\alpha F_k \sim N(0, \sigma_f^{F^2}) \tag{18}$$

$$\varepsilon_{jk} \sim N(0, \sigma^{\varepsilon^2}) \quad (19)$$

For all σ:

$$\sigma \sim t(0,1,\nu)\ , \sigma \geq 0 \quad (20)$$

$$\nu \sim Gamma(2, 0.1) \quad (21)$$

where Φ is the cumulative distribution function (CDF) of the standard normal distribution, R represents a vector of random effects and F is equivalent to a design matrix with k conditions grouped into f factors including a group factor (2 levels), a modality factor (2 levels), and an intensity factor (4 levels). μ was estimated by averaging point estimates for the respective parameters over the whole dataset ($\mu^{d'}$ = 1.66, μ^{c} = 0.06).

Sensitivity analyses and posterior predictive checks are described in Appendix A.2.1.

4.2.2. Reaction time (RT) distributions mixture model

RT data was collected as an additional index of attentional lapses and to provide an additional source of insight into processes underlying group performance in the task. A mixture model was employed to tease out lapses from the main RT distribution for each participant in each condition.

The main RT distribution was modelled using a 3-parameter Weibull distribution following the suggestions of Rouder, Lu, Speckman, Sun, and Jiang (2005). This distribution is parameterised by a shift parameter ψ which determines the location of the distribution in time, a scale parameter θ which determines its breadth, and a shape parameter β which determines its skew. Following Rouder et al. (2005), we placed linear models on the shift and (reparameterised) scale parameters ψ and θ. A preliminary unrestricted random effects model suggested that group differences of interest resided in these parameters but not in the shape parameter β (see Appendix F.2.1.).

With respect to lapse estimation, Rouder et al. (2005) suggest that RTs not belonging to the main distribution (i.e., responses which result from fast guesses or attentional lapses) can be best accounted for by adding a pre-specified distribution such as a uniform distribution across the range of RTs to the model. In line with this suggestion, we expanded our model to become a 2-component mixture of the Weibull and a uniform likelihood with upper and lower limits at 0 and 6 seconds to capture lapses and fast guesses.

The likelihood of the data given the model was

$$P(y_{ijk}|\,\psi_{jk},\lambda_{jk},\beta_{jk,}\vartheta_m) = \vartheta_{lapse}Uniform(y_{ijk}|0,6) + \vartheta_{Weibull}Weibull(y_{ijk}|\,\psi_{jk},\lambda_{jk},\beta_{jk}) \quad (22)$$

where again following Rouder et al. (2005) the Weibull scale parameter θ has been reparameterised as a rate parameter λ for computational tractability using the transformation:

$$\lambda_{jk} = \theta_{jk}^{-\beta_{jk}} \quad (23)$$

and where y_{ijk} represents the i^{th} response of the j^{th} participant in the k^{th} condition. The mixture weights associated with each model component were estimated from the data using the following uninformative priors:

$$\vartheta_{lapse} \sim Uniform(0,1) \quad (24)$$

$$\vartheta_{Weibull} = 1 - \vartheta_{lapse} \quad (25)$$

Linear models were placed upon the ψ and λ parameters of the Weibull distribution as follows:

$$\psi_{jk} = \alpha^{\psi}0 + \alpha^{\psi}R_j + \alpha^{\psi}F_k + \varepsilon_{jk}^{\psi} \quad (26)$$

$$\lambda_{jk} = \alpha^{\lambda}0 + \alpha^{\lambda}R_j + \alpha^{\lambda}F_k + \varepsilon_{jk}^{\lambda} \quad (27)$$

$$\beta_{jk} \sim N(2, \sigma^{\beta^2}) \quad (28)$$

for both ψ and λ:

$$\alpha 0 \sim N(\mu^0, \sigma^{0^2}) \quad (29)$$

$$\alpha R_j \sim N(0, \sigma^{R^2}) \quad (30)$$

$$\alpha F_k \sim N(0, \sigma_f^{F^2}) \quad (31)$$

$$\varepsilon_{jk} \sim N(0, \sigma^{\varepsilon^2}) \quad (32)$$

For all σ:

$$\sigma \sim t(0,1,\nu)\,, \sigma \geq 0 \quad (33)$$

$$\nu \sim Gamma(2,0.1) \quad (34)$$

where R represents a vector of random effects and F is equivalent to a design matrix with k conditions grouped into f factors including a group factor (2 levels), a modality factor (2 levels), a laterality factor

(2 levels) and an intensity factor (4 levels). μ^0 was defined by averaging estimates for the respective parameters which had previously been derived using an unrestricted random effects model.

As described in the Results section below, the 2-component mixture model results indicated that RTs identified as probable "lapses" were bimodally distributed with an early peak around 500ms – i.e., earlier than the average shift estimate for the main Weibull distributions. To distinguish in a principled way between lapses and "fast guesses" therefore, an additional pre-specified distribution was added to the mixture model. This distribution was a standard half-normal likelihood placing high probability over the likely range of fast guesses or anticipations (≈ 0-200 ms) but very little probability over the likely range of attentional lapses (≈2-6 seconds).

The resulting 3-component mixture model was as follows:

$$P(y_{ijk}|\,\psi_{jk},\lambda_{jk},\beta_{jk,}\vartheta_m) = \vartheta_{lapse}Uniform(y_{ijk}|0{,}6) + \vartheta_{guess}N(y_{ijk}|0{,}1), y \geq 0 + \vartheta_{Weibull}Weibull(y_{ijk}|\,\psi_{jk},\lambda_{jk},\beta_{jk}) \quad (35)$$

$$\vartheta_{lapse} \sim Uniform(0{,}1) \quad (36)$$

$$\vartheta_{guess} \sim Uniform(0{,}1) \quad (37)$$

$$\vartheta_{Weibull} = 1 - (\vartheta_{lapse} + \vartheta_{guess}) \quad (38)$$

The development of the RT distributions mixture model is described in Appendix F. Sensitivity analyses and details of model fit are in Appendix A.2.2.

4.3. Study 2 results

4.3.1. Sample characteristics

All depressed participants were diagnosed with chronic or recurrent forms of depressive illness of at least moderate severity at the time of testing. Mean age of onset was 19.25 years old (SD 10.03) and the mean number of years since first diagnosis was 19.67 (SD 14.15). Eight participants (66.7%) reported that their first onset of depression was in childhood and 11 participants (91.7%) had suffered too many past depressive episodes to count. Six individuals (50%) met criteria for at least one comorbid Axis 1 disorder at the time of testing including Social Phobia, Generalised Anxiety Disorder, Anorexia, Binge Eating Disorder and Posttraumatic Stress Disorder (three participants met criteria for an anxiety disorder, one met criteria for an eating disorder, one met criteria for an anxiety disorder and an eating disorder, and one met criteria for an anxiety disorder, an eating disorder and PTSD). Six

participants (50%) were currently prescribed antidepressant medication. No members of the control group were prescribed any form of psychotropic medication.

A series of t-tests demonstrated that there were no significant group differences with respect to the characteristics of age, years of education or handedness (see Table 4.1). A maximum-likelihood chi-square test demonstrated that a trend towards a sex difference between groups did not reach statistical significance. As expected, depressed participants differed significantly from healthy controls with respect to self-reported symptoms of depression and anxiety.

Table 4.1: Study 2 demographic comparisons by group

	Depressed group (n = 12)	Control group (n = 12)	2-tailed t-tests
Demographics: mean (SD)			
Sex	10 women	6 women	χ^2 (1) = 3.10, p = 0.078
Age (years)	38.92 (17.36)	33.92 (17.53)	t(22) = 0.70, p = 0.49
Education (years)	15.33 (2.93)	16.75 (2.18)	t(22) = 1.34, p = 0.19
Handedness (EHI)	51.02 (74.08)	64.43 (57.35)	t(22) = 0.50, p = 0.63
Mood measures: mean (SD)			
Depression (BDI-II)	32.92 (13.43)	1.75 (2.14)	t(11.56[1]) = 7.94, p < 0.001
Anxiety (BAI)	21.00 (14.05)	1.17 (1.34)	t(11.20[2]) = 4.87, p< 0.001

[1,2] Degrees of freedom adjusted due to unequal variances.

EHI = Edinburgh Handedness Inventory, BDI-II = Beck Depression Inventory-II, BAI = Beck Anxiety Inventory

4.3.2. Signal detection model

In total, 20,242 observations were collected (somewhat over 200 per participant per condition). Within each modality, data were pooled across blocks following preliminary analyses indicating no effect of distractor presence or valence on perceptual thresholds in either modality (see Appendix E for details). Observations near the upper and lower asymptotes were binned to render estimates at the extremes more reliable. Specifically, participants performed at chance at -12dB in the auditory

condition and -6dB in the somatic condition and observations occurring at these and lower intensities were therefore pooled together in one category. Similarly, participants in the somatic condition performed at ceiling at 0, -1 and -2dB, and therefore these observations were pooled. Any observations occurring above the starting intensity were included in the starting intensity category in both modalities. This produced 4 levels of stimulus intensity in each modality.

Figure 4.1 shows the model outcomes in terms of the posterior distributions of d' and c, (upper and middle panels) and contrasts on the model coefficients (lower panels). The only credible effect on d' is a very strong effect of stimulus intensity as expected. A trend towards an interaction between modality and intensity is not credibly different from zero and, as in Study 1, there is no indication of any group effect on perceptual sensitivity. On c, there are substantial main effects of group and modality. The group effect reflects a marked tendency towards a left-sided response bias in depressed participants in both stimulus modalities as predicted, together with the opposite tendency in healthy controls. The modality effect reflects a tendency among all participants towards right-sided bias in response to auditory stimuli and left-sided bias in response to somatic stimuli. The reasons for this latter finding are unclear; but could include equipment or acoustic imbalances in the testing environment. Trends towards interactions between group and intensity and between modality and intensity are not credibly different from zero.

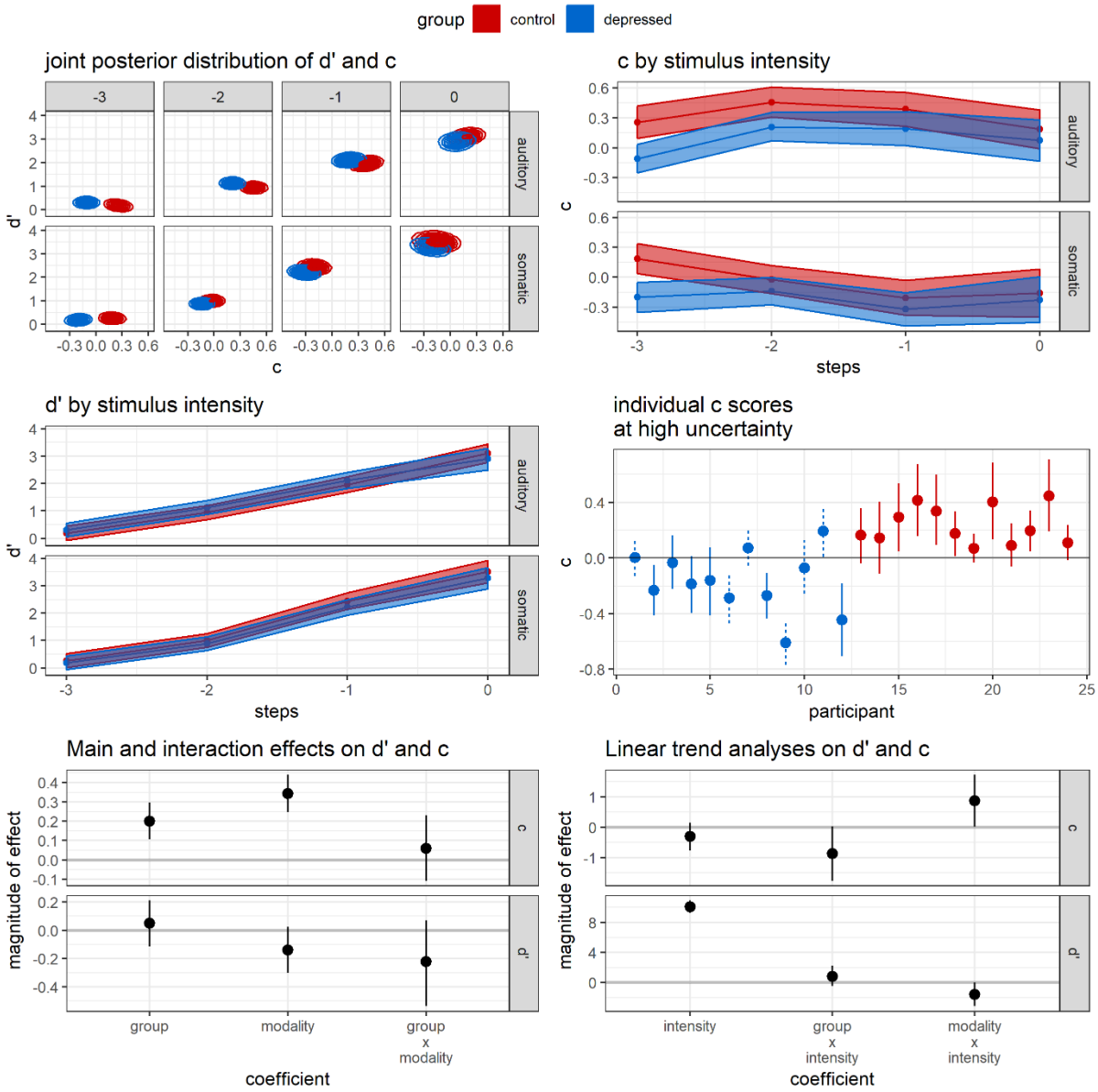


Figure 4.1: Study 2 hierarchical signal detection model outcomes by group, modality and stimulus intensity. The top left panel shows the joint posterior distribution of d' and c across stimulus intensity, averaged by group and modality , while the middle left and upper right panels respectively show the corresponding 95% credible intervals for the averaged estimates of d' and c across stimulus intensity. The middle right panel shows the individual participant estimates of c averaged over modality at the lowest level of stimulus intensity. Unbroken lines indicate that the participant was medication-free. The bottom panels show the main and interaction effects of the linear models on d' and c: in the bottom left panel simple contrasts on factors with 2 levels; in the bottom right panel linear trends on intensity and on the respective interactions of group and modality with intensity. The 3-way interaction (not shown) was not credibly different from zero. Points represent posterior distribution means, error bars 95% credible intervals.

Signal detection model comparison

A variable selection approach (Dellaportas et al., 2002) was used to confirm the influence of group on c, and the lack of a group influence on d'. For simplicity, only main effects were included in the model comparison, and only 4 models were compared: a model including an effect of group on both d' and c; a model including an effect of group on d' only; a model including an effect of group on c only; and a model including no effect of group on either parameter. Posterior model probabilities and Bayes Factors are shown in Table 4.2 and by convention indicate substantial evidence against a group effect on d', and strong evidence in favour of a group effect on c (Jeffreys, 1961).

Table 4.2: Study 2 posterior model probabilities and Bayes factors for signal detection model comparison.

	Model	Posterior model probability		Bayes factor
Model		c		
		Group effect	No group effect	
d'	Group effect	0.21	0.02	10.14
	No group effect	0.71	0.07	10.26
Bayes factor		0.29	0.29	

Medication-free analysis

All analyses were repeated excluding n=6 participants from the depressed group who were prescribed psychotropic medication at the time of the study. The key outcome of interest (the group difference in response bias) remained highly credible, and in fact its relative likelihood was increased by a factor of 7 by the exclusion of medicated participants. The evidence against a group difference in d' was reduced to an anecdotal level however (see Appendix B.2. for details).

Summary

Study 2, like Study 1, found no evidence for an influence of depression on perceptual sensitivity (although the evidence against such an influence was less credible when excluding medicated participants). However, the signal detection model identified a systematic left-sided response bias in depressed individuals which was reversed in healthy controls. In contrast to Study 1, examination of the data demonstrated no disproportionate tendency towards left-sided asymptotic lapses in the

depressed group; however, on the basis of accuracy data alone, it is possible that occasional lapses were masked by the strong response bias.

This hypothesis was investigated using the reaction time (RT) data collected during the Study 2 task. Unusually lengthy reaction latencies are often used as a proxy measure of attentional lapses (e.g., Weissman et al., 2006), and in line with this approach a distributional analysis was applied to the RT data. It was hypothesised that an increased tendency to left-sided lapses (represented by unusually lengthy RTs in response to left-sided stimuli) would be observed in the depressed group.

4.3.3. RT distributions mixture model

Guesses and lapses

A total of 817 RTs (5.32%) were identified as probable lapses (i.e., were more frequently categorised as belonging to the lapse than to the Weibull distribution). The distribution of these RTs over time was examined by group and laterality (shown in Figure 4.2: left panel). As can be seen, while the distribution of lapses does not seem to vary depending on stimulus laterality among healthy controls, for the depressed group it appears that fast guesses were more numerous in response to right-sided stimuli, while slower attentional lapses were more numerous in response to left-sided stimuli.

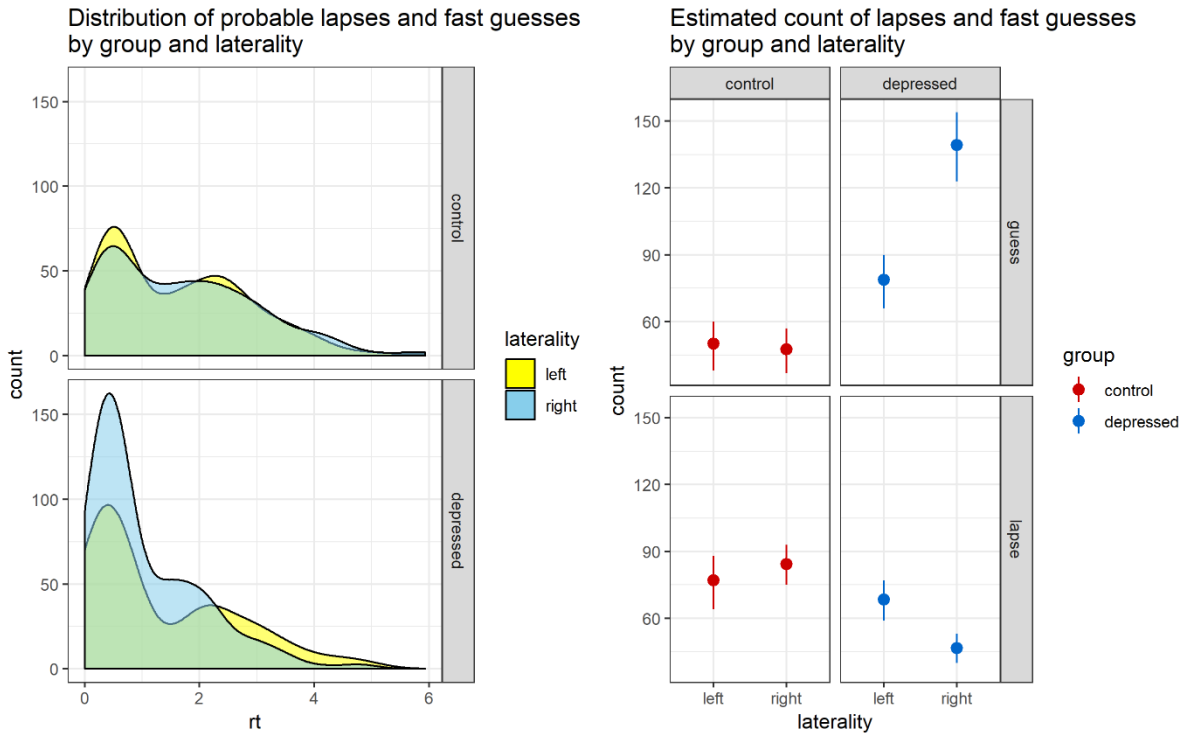


Figure 4.2: Study 2 distribution and count of fast guesses and attentional lapses by group and laterality. The left-hand side panel shows the distribution of probable lapses and guesses over time by group and stimulus laterality. The right-hand side panel shows the estimated counts of lapses and guesses once these have been independently captured by separate likelihood distributions. Points

represent the posterior distribution mean for each count by group and laterality, and error bars represent 95% high density intervals.

To distinguish between fast guesses and attentional lapses in a more principled way, an additional pre-specified distribution was added to the mixture model. This distribution was a standard half-normal likelihood placing high probability over the likely range of fast guesses (≈ 0-200 ms) but very little probability over the likely range of attentional lapses (≈2-6 seconds).

The posterior distributions of the total count of RTs categorised as guesses and lapses for each group in each laterality condition are shown in Figure 4.2 (right panel). As expected, lapses among the depressed group are credibly more numerous in trials where the stimulus appeared on the left side of space compared to trials where it appeared on the right, suggesting, as in Study 1, that depressed participants might have experienced disproportionate difficulty in maintaining attention to the left. Conversely, the depressed group was credibly more likely to respond unusually quickly when the stimulus appeared on the right. The finding of an influence of laterality (i.e., one dependent upon stimulus characteristics) among fast guesses indicates that a substantial proportion of fast responses must have been genuine responses to the stimulus rather than anticipations of it. This finding may suggest an attentional advantage for stimuli occurring on the right side of space, or perhaps a higher level of perceptual or motor preparation for right-sided stimuli relative to left-sided stimuli in depressed participants. Both guesses and lapses arising from left- and right-sided stimuli are comparable among the control group.

Although for convenience we refer to RTs categorised as consistent with the respective distributions as “guesses” and “lapses”, we do not intend these labels to denote certainty about the causal processes or mechanisms relating to either category, or to imply any assumptions about the underlying distributions. For example, we do not assume that all RTs in one category are drawn from the same underlying true distribution.

Weibull fits

Key outcomes of the Weibull fits to the bulk of the RT data are shown in Figure 4.3. As an illustration, Figure 4.3 (top panels) depicts Weibull distributions arising from the individual posterior parameter estimates averaged by group and over stimulus intensity. These are therefore not fits to actual data, but a visual representation of the effect of average group differences in parameter estimates in terms of the distribution of RTs. The averaged distributions in Figure 4.3 indicate that the responses of

depressed participants are in general faster and more efficiently distributed than those of healthy controls, as discussed below.

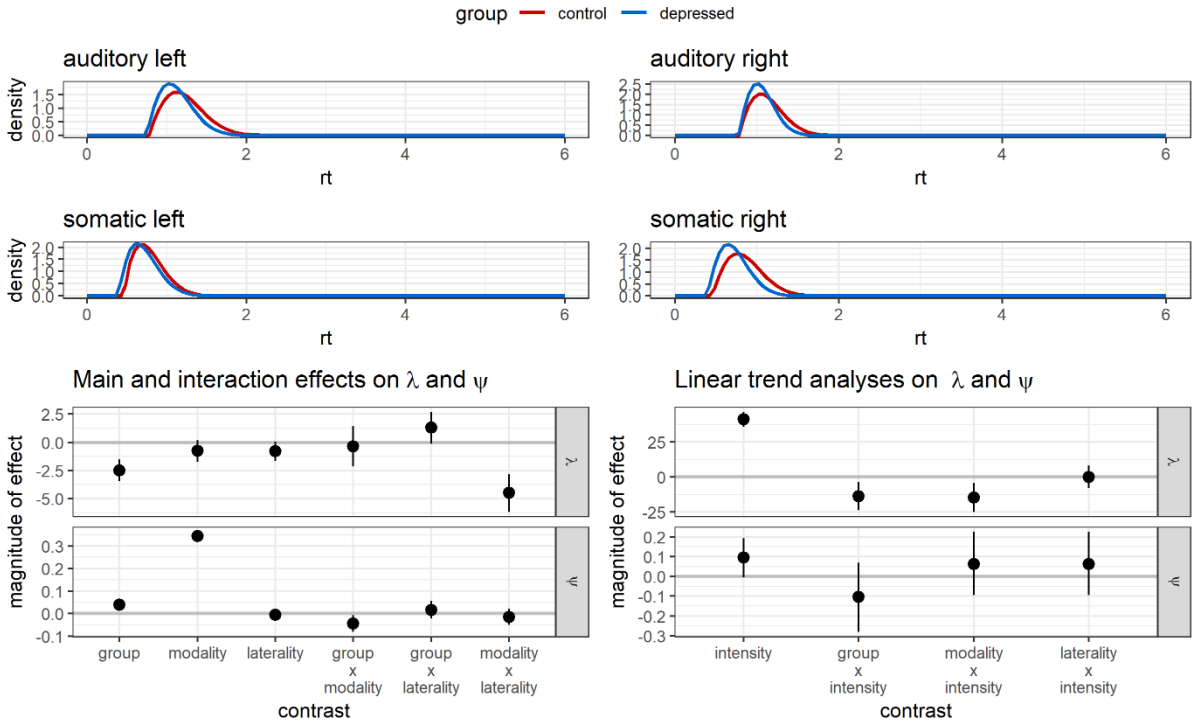


Figure 4.3: Study 2 Weibull distribution outcomes by group, stimulus modality and laterality. The top panels show the most probable Weibull distributions, given the data, averaged over participant and stimulus intensity and shown by group, modality and laterality. The lower panels show the magnitude of the main and interaction effects arising from the linear models on λ and ψ.

The lower panels of Figure 4.3 show the main and interaction effects arising from the linear models on the shift parameter ψ and the rate parameter λ in the Weibull model. On ψ, there was a credible main effect of group, indicating rather counter-intuitively that depressed participants demonstrated an ability to prepare and implement a response more quickly than healthy controls. There was also a strong main effect of modality, indicating a delayed lower bound on responses to auditory stimuli relative to somatic stimuli. This effect was not group-specific and may reflect timing differences in the respective perceptual processing systems. A trend towards an advantage for depressed participants when responding to somatic information was not credibly different from zero.

As the rate parameter λ increases, the scale parameter θ decreases. The effects on rate will therefore be discussed in terms of scale, given its greater ease of interpretation in the context of RT distributions. There was a credible effect of group on the scale of the estimated RT distributions, such that the distributions generated by depressed participants were relatively narrow. This, together with the

group effect on ψ, suggests that RTs in this group were both on average faster and more efficient in terms of reduced RT variability. A credible interaction between group and intensity indicated that the increase in efficiency in the depressed group was particularly marked at higher stimulus intensities.

The remaining effects on λ were not group-specific. Most markedly, there was a strong main effect of intensity, such that the spread of RTs was wider when stimulus intensity was lower, consistent with the greater effort or search required to detect lower-intensity stimuli. There were also credible interactions of modality by intensity (responses to auditory stimuli were relatively efficient at lower stimulus intensities, while the responses to somatic stimuli were relatively efficient at higher stimulus intensities) and modality by laterality (responses to right-sided auditory stimuli and left-sided somatic stimuli were relatively efficient). These effects are difficult to interpret and may be rather specific to the nature of the stimuli, the hardware used to produce the stimuli, and/or the acoustic environment of the testing lab.

4.4. Study 2 summary

Study 2 aimed to maximise the influence of attentional factors during the perceptual task to identify any group differences in attentional performance and to assess their impact, if any, on perceptual sensitivity. Taking the second question first, the findings suggest that even with the increased attentional load of the task in Study 2, there were still no credible overall group differences in perceptual sensitivity, although the marked response biases may suggest that the sensitivity estimates should be treated with some caution. In general, the results suggest that basic perceptual experience (as indexed by sensitivity to perceptual signals) under conditions of top-down attentional focus may in fact be rather robustly preserved in depression, even in the face of attentional challenges including lengthy time on task and the presence of depression-relevant negative distractors. There was also no evidence that stimulus modality interacted with depression status to affect any outcomes with respect to perceptual sensitivity.

Contrary to hypothesis, depressed individuals were not in any way disadvantaged relative to healthy controls by either the presence or the valence of task-irrelevant distractors. Nor, indeed, did the presence or the valence of distractors impact on attentional or perceptual performance in either group. Conceivably, the distractors were simply not distracting enough: any group differences may have been masked by a floor effect. The outcomes reported here do not allow any further conclusions to be drawn on this topic.

More generally, and once again contrary to our hypothesis, there was little straightforward evidence for any generic disruption to voluntary attention in the depressed group in the current study. Probable

lapses (as identified by the mixture model) were no higher in depressed participants than in healthy controls, and RTs among the depressed group were in fact credibly faster and less variable than those observed in controls, an outcome traditionally considered to denote *improved* attentional control (Bellgrove et al., 2004; Kelly et al., 2008; Sonuga-Barke & Castellanos, 2007)

Study 2 did, however, provide unequivocal evidence in support of the hypothesis that depression would be associated with a left-sided response bias, particularly under conditions of high uncertainty. Participant-level analyses demonstrated that neutral or left-sided bias under uncertainty was replicated in 83% (n=10) of persistently depressed participants – including 100% (n=7) of those who were medication-free – while right-sided bias was replicated in 100% (n=12) of healthy controls. This is a striking result, despite the small sample size, and unlikely to have occurred by chance. These lateralised response biases were particularly marked when stimulus detectability was low, but may also have existed at high values of d' when attention wandered, as implied by a disproportionate number of lapses on the left side of space in depressed participants as indexed by the RT distributions.

These findings (and the statement 'if I can't hear it, it's on the left' which was independently and spontaneously made by two depressed participants in Study 2) are inconsistent with standard signal detection theory, which assumes that absolute response bias is independent of sensitivity. The relationships between d', response bias and group observed here may be more readily interpreted in the context of the indecision model proposed by García-Pérez and Alcalá-Quintana (2010, 2011, 2017) which incorporates an interval of uncertainty together with a (potentially biased) guessing rule into the standard 2AFC difference model. A guessing rule biased to the left amongst depressed individuals relative to controls can provide a good account of the outcomes observed in the current study as follows: a small proportion of trials at broadly detectable stimulus intensities would nevertheless be expected to yield a d' close to 0 due to lapses of attention or to fluctuations in other variables contributing to its determination. A tendency to guess 'left' on these occasions would result in a mild leftwards bias among depressed participants relative to controls, as observed here at high and intermediate intensity levels. At the lowest intensity level, where signal is difficult to distinguish from noise, guesses are likely to form a much larger proportion of all responses and the resulting bias would be expected to be commensurately greater. A similarly biased guessing rule, in the opposite direction, can by the same token explain the pattern of results among healthy controls. A biased guessing rule, as suggested above, could also explain the difference between the two studies in terms of the proportion of left-sided asymptotic lapses committed by depressed participants as indexed by accuracy data. A lateralised bias in lapse rates would be expected to be masked by a similarly lateralised bias in guesses.

Assuming that participants employed biased response strategies to maximise the proportion of correct responses, these biases imply a differential level of confidence in the ability to detect a stimulus to one side or the other, assessing one side, perhaps, as disproportionately vulnerable to attentional lapses. In other words, the awareness (conscious or otherwise) that attention is less reliable to one side or the other could explain the use of a corresponding response bias as a compensatory strategy in a motivated participant responding to an undetected stimulus. An alternative explanation assumes that, as well as aiming to complete the task accurately, participants may also have been motivated to conserve attentional resources. In principle it is possible to complete the Study 2 task successfully using information from only one side of space, and the lateralised response bias could conceivably reflect a top-down decision to preferentially allocate attention to one side, with a consequent assumption that undetected stimuli were more likely to occur on the other. If this explanation is correct, control participants chose on average to allocate attentional resources to the left side of space, while depressed participants preferred the right. Following either explanation (response bias as a compensatory strategy, or response bias as part of a strategy for minimising task-related effort), the evident conclusion is that for control participants it is easier or less costly to maintain attention to the left side of space, while for depressed participants it is easier or less costly to maintain attention to the right.

A related finding arising from the analysis of the main RT distributions was that depressed participants systematically responded to stimuli more efficiently than healthy controls, in terms of both the speed and the variability of their responses. This finding is counter-intuitive at first glance and is unlikely on theoretical grounds to reflect a faster speed of processing, more efficient perceptual or motor preparation or improved attentional control in depressed participants relative to healthy controls (e.g., Hammar & Ardal, 2009). However, the theory regarding preferential allocation of attention to one side of space can account for this finding, if it is assumed that depressed participants relied on biased attention to a substantially greater extent than did controls. Under these circumstances, one might expect to see a faster and more efficient RT distribution, if only one side of space is carefully monitored; a higher proportion of speeded right-sided RTs, given the attentional advantage for stimuli occurring on the right; and a higher proportion of unusually lengthy left-sided “lapses”, given that a left-sided stimulus might be responded to by default only after the participant had satisfied themselves that they had heard nothing on the right.

These hypotheses are interesting, but at present have only circumstantial evidence to support them. Study 3 attempted a more precise specification of the mechanisms hypothesised to underlie the Study

1 and 2 results, with the aim of evaluating their ability to predict the observed outcomes through simulation.

Chapter 5. Study 3: A computational model of somatic and auditory signal detection in the Study 1 and 2 tasks

Computational models within behavioural science can be a valuable aspect of hypothesis generation and testing, motivating precise specification of hypothesised mechanisms underlying behaviour, and generating specific predictions with respect to behavioural outcomes. Study 3 employed a computational approach to evaluate the plausibility of the proposed interpretations of the Study 1 and 2 data through a process of modelling the hypothesised mechanisms, generating and analysing simulated datasets on the basis of these models, and comparing the results to the observed Study 1 and 2 outcomes. A Bayesian "agent" was chosen for its simplicity and intuitiveness (Vincent, 2015), and because Bayesian models of perceptual and attentional processes have demonstrated predictive power in simulating data generating processes in a number of domains (A. Clark, 2013; Friston, 2010; Knill & Pouget, 2004). Previous models have defined perceptual attention in terms of the precision of sensory distributions contributing to perception (e.g., Feldman & Friston, 2010; Vossel et al., 2013), and in the current study changes in attention (e.g., attentional lapses) were represented by changes in precision in relevant probability distributions. The simulations aimed to address three questions, as follows:

1) Can a single lapse model, together with a simple compensatory strategy, predict the patterns observed in the data in Studies 1 and 2?
2) Can a "depressed" agent reduce energy expenditure in the Study 2 paradigm by reducing attention to the left side of space without reducing overall perceptual sensitivity as a corollary? If so, what patterns of bias are produced?
3) Are there alternative explanations which can better predict the data?

These questions motivated the development of an agent for each study with comparable baseline perceptual sensitivity and response behaviour to that observed in human Study 1 and 2 participants. Variants of the two agents (lapsing agents, resource-conserving agents, agents with a constant lateralised attentional deficit and agents prone to false percepts) were then developed to address the questions detailed above in turn.

5.1. Study 3 design

Bayesian agents capable of simulating human performance on the Study 1 and 2 tasks were developed using MATLAB (R2018a, The Mathworks).

5.2. Study 3 models

5.2.1. Study 1 agent

The Study 1 task required participants to detect a stimulus occurring at random in one of two possible time intervals in each trial, while stimulus intensity was varied according to an adaptive staircase. The Study 1 agent likewise detected and responded to adaptive stimuli occurring in one of two intervals using a simple Bayesian model. In all respects other than the symbolic nature of stimulus and response the task was identical to that carried out by human participants in Study 1.

Stimulus

The stimulus was represented by an input describing its intensity in decibels, which was then translated into a location μ^{signal} on a sensitivity / detectability scale from 0 (undetectable) to 3 (clearly detectable). The translation was achieved by means of a sigmoid curve fitted to the relationship between stimulus intensity and d' in the observed data from the control group in Study 1: the translation therefore differed for the two modalities. As in the real task, the stimulus occurred at random in one of two possible intervals. A 'noise' event, occurring in the other interval, was represented on the sensitivity scale by the location $\mu^{noise} = 0$.

Generative model

The agent initially made a prior prediction about the likely detectability (θ) of the impending signal, informed by knowledge about the operation of the staircase and about stimulus detectability during previous trials. This prior was distributed as:

$$P(\theta) \sim N(\mu^{prior}, \sigma^{prior^2}) \tag{39}$$

where the initial value of $\mu^{prior} = 3$, and subsequent values were based on the posterior probabilities of previous trials. The precision of the prior was given a default value of 1.

The agent then received noisy inputs associated with the respective intervals as follows:

$$data^{signal} \sim N(\mu^{signal}, \sigma^{signal^2}) \tag{40}$$

$$data^{noise} \sim N(\mu^{noise}, \sigma^{noise^2}) \tag{41}$$

A likelihood function was calculated for each interval, giving the probability of the data acquired during that interval given the possible range of signal detectability as follows:

$$P(data|\theta, interval) = N(data, \theta, \sigma^{data^2}) \tag{42}$$

For simplicity, $\sigma^{signal} = \sigma^{noise} = \sigma^{data}$ in this application and represents a reparameterisation of a default precision of 4 for all likelihood functions.

Recognition model

The generative model was then inverted according to Bayes Theorem to give the posterior probability of signal detectability, given the data, for each interval:

$$P(\theta|data, interval) = \frac{P(data|\theta, interval)P(\theta)}{P(data|interval)} \quad (43)$$

where the overall probability of the data for each interval is given by:

$$P(data|interval) = \int P(data|\theta, interval)P(\theta)d\theta \quad (44)$$

The posterior distributions for each interval were treated as percepts upon which the agent based its responses. Figure 5.1 (top panels) shows the prior, likelihood and posterior distributions for both intervals (signal occurring in Interval 1, data shown in each interval as a black vertical line) in a hypothetical trial occurring at the outset of a staircase where the expected detectability of the signal is at its maximum of 3.

A posterior distribution placing little or no probability ($P(\theta=0)<0.01$) at 0 on the detectability scale was considered to be unambiguously detectable. A posterior distribution placing 50% or more probability below 0.25 on the detectability scale was considered to be undetectable. This cut-off was relatively arbitrary; but was chosen because it produced similar behaviour in the agent to that observed in the human participants.

Response decisions

When a percept was uniquely detectable during one interval, the agent gave the response associated with that interval with a probability of 1. When both percepts were undetectable, the agent "guessed" at random, drawing its response from a Bernoulli distribution with a rate of 0.5. In the more typical case of ambiguity, the agent drew upon Bayes Theorem a second time to weigh up the most likely causes of its perceptual experience. The probabilities of the data given the interval (as calculated in the previous section) were combined with the prior probability that the signal had occurred in either interval

$$P(interval) = 0.5 \quad (45)$$

to give the normalised posterior probability that the signal had occurred in each interval given the data:

$$P(interval|data) = \frac{P(interval)P(data|interval)}{\sum P(interval)P(data|interval)} \quad (46)$$

The agent then drew its response from a Bernoulli distribution with a rate reflecting the relative posterior probabilities.

Finally, the prior expectation of stimulus detectability $P(\theta) \sim N(\mu^{prior}, \sigma^{prior2})$ was updated based on the outcome of the trial. This was achieved by updating μ^{prior} with the maximum a posteriori estimate of the posterior distribution. The precision of the prior remained constant at 1 throughout the task for the sake of simplicity. Figure 5.1 (lower panel) shows a staircase generated by the agent using this process.

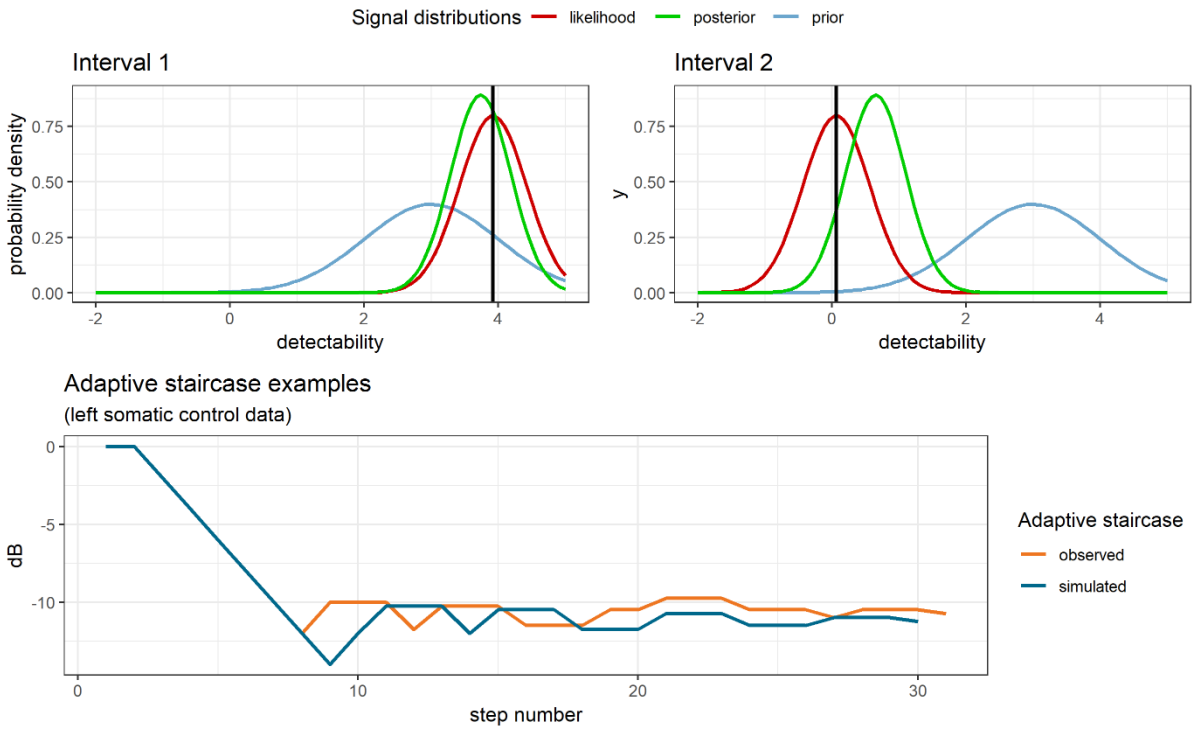


Figure 5.1: Study 3 simulated single trial and adaptive staircase. Upper panels show the prior, likelihood and posterior distributions for the two intervals in a hypothetical trial occurring at the outset of a staircase where the expected detectability of the signal is at its maximum of 3. The signal occurs during Interval 1, and for each interval the (noisy) input is shown as a black, vertical line. As can be seen, the posterior distribution ("percept") arising from the Interval 1 input is detectable, placing effectively no probability at zero. The corresponding "percept" arising from the Interval 2 input is ambiguous, with substantial probability at or below zero. On the basis of these outcomes, the agent

would select "interval 1" with a probability of 1. The lower panel shows a staircase simulated using this process (randomly selected from the total 128 staircases generated in the process of simulating a Study 1 dataset) plotted against a staircase (matched by group and condition) randomly selected from the observed Study 1 data.

5.2.2. Study 2 agent

The Study 1 task employed a single, uninterrupted staircase for each stimulus modality presented on each side of space. The task of the participant during all staircases was to decide in which of two possible time intervals the stimulus occurred. The Study 2 task differed from that in Study 1 in employing two distinct, interleaved staircases, one modulating the intensity of stimuli occurring on the left, and one modulating the intensity of stimuli occurring on the right. Either staircase could be in operation during any given trial, and the task of the participant was to make a judgement regarding which side of space a stimulus occurred in that trial, given current expectations about the likely intensity of a left-sided stimulus versus the likely intensity of a right-sided stimulus versus noise. To model this task, it was therefore necessary for the agent to develop two independent models, one relating to each staircase.

Stimulus

The representation of the stimulus was similar to that in the Study 1 simulation, and similarly employed modality-specific sigmoid transformations based upon the observed control sensitivity data to transform a representation of stimulus intensity (dB) into a location μ^{signal} on a sensitivity / detectability scale. The detectability scale ran from -3 (highly detectable left-sided stimulus) to 3 (highly detectable right-sided stimulus) with the range near 0 representing low detectability / high uncertainty. Staircase laterality in any given trial was chosen at random, and a "noise" event occurring in the alternative laterality was represented on the detectability scale by the location $\mu^{noise} = 0$.

Generative model

The agent in this task relied upon a more complex set of prior expectations resulting from the additional information provided by the existence of two independently varying staircases. The priors for the signal differed depending on staircase laterality, and additionally a prior was created to represent the expectation of noise:

$$P(\theta|laterality, input = signal) \sim N(\mu^{signal}_{laterality}, \sigma^{prior^2}) \quad (47)$$

$$P(\theta| input = noise) \sim N(\mu^{noise}, \sigma^{prior^2}) \quad (48)$$

The initial values of μ^{signal} were -3 and 3 depending on laterality, and subsequent values were based on the posterior probabilities of previous trials. μ^{noise} remained constant at 0 throughout the task. As before the precision of all priors had a default value of 1.

As before, the agent received noisy inputs associated respectively with each side of space as follows:

$$data^{signal} \sim N(\mu^{signal}, \sigma^{signal^2}) \tag{49}$$

$$data^{noise} \sim N(\mu^{noise}, \sigma^{noise^2}) \tag{50}$$

A likelihood function was calculated for each laterality and each possible input (signal or noise), as follows:

$$P(data|\theta, laterality, input) = N(data, \theta, \sigma^{data^2}) \tag{51}$$

As before, $\sigma^{signal} = \sigma^{noise} = \sigma^{data}$ in this application and represents a reparameterisation of a default precision of 4 for all likelihood functions.

Recognition model

As before, the generative model for the signal distributions was inverted according to Bayes Theorem to calculate the posterior probability of signal detectability, given the data, for each interval. Note that as in the previous model, this procedure assumes that the data arise from signal rather than from noise:

$$P(\theta|data, laterality, input = signal) = \frac{P(data|\theta, laterality, input = signal)P(\theta|laterality, input = signal)}{P(data|laterality, input = signal)} \tag{52}$$

where the probability of the data given laterality is given by:

$$P(data|laterality, input = signal) = \int P(data \,|\, \theta, laterality, input = signal)P(\theta|laterality, input = signal)d\theta \tag{53}$$

As before, the posterior distributions of signal detectability for each laterality were treated as percepts upon which the agent based its responses. The same criteria for detectability and undetectability were employed as in the Study 1 simulations.

Response decisions

When a percept was uniquely detectable on one side of space, the agent gave the response associated with that laterality with a probability of 1. When both percepts were undetectable, the agent "guessed" at random, drawing its response from a Bernoulli distribution with a rate of 0.5. In the case of ambiguity, the agent combined the signal and noise likelihoods calculated in the previous section with the known prior probability of a signal occurring on either side of space:

$$P(input = signal|laterality) = 0.5 \tag{54}$$

to give the normalised posterior probability that the signal had occurred on a given side of space, given the data, independently for each laterality. For each laterality:

$$P(input = signal|data, laterality) = \frac{P(data|input = signal, laterality)P(input = signal|laterality)}{\sum_{i=1}^{input} P(data|input, laterality)} \tag{55}$$

Importantly, this process yields two distinct posterior estimates, one based on evidence from the left side of space, and one based on evidence from the right. This innovation allows the agent to rely preferentially on evidence from one side of space or the other, although in the current (default) model final estimates of the averaged posterior probability

$$P(input = signal|data, laterality = left) = 1 - P(input = signal|data, laterality = right) \tag{56}$$

were calculated using a model-averaging procedure with weights of 0.5 for each model. The agent then drew its response from a Bernoulli distribution with a rate reflecting the relative posterior probabilities.

Finally, the prior expectation of stimulus detectability

$$P(\theta|laterality, input = signal) \sim N(\mu^{signal}_{laterality}, \sigma^{prior^2}) \tag{57}$$

was updated based on the outcome of the trial. This was achieved by updating μ^{signal} with the maximum a posteriori estimate of the posterior distribution for the laterality selected by the agent as the correct one for that trial. As before, the precision of all priors remained constant at 1 throughout the task.

5.2.3. Agent modifications

The agents were then modified in order to address the questions posed at the outset of Study 3.

Attentional lapse models

A simple model of attentional lapses was incorporated into the Study 1 agent described above. A proportion of trials occurring with rate λ were designated "lapse trials". A lapse trial was distinguished from fully attended trials in that the parameters, $\sigma^{signal} = \sigma^{noise} = \sigma^{data} = 10$ (i.e., the precision of the likelihoods was 0.01 rather than 4 as in fully attended trials). The practical effect of this change in precision is that signal and noise likelihoods become indistinguishable from each other even given a highly detectable input, and that due to the imprecision of the data the posterior distributions are to all intents and purposes indistinguishable from their priors. The attentional status of the agent in any given trial was determined by a draw from a Bernoulli distribution with rate λ.

"Depressed" agents were defined by lapse rates of $\lambda^{left} = 0.06$ and $\lambda^{right} = 0.01$. "Control" agents were defined by lapse rates of $\lambda^{left} = 0.01$ and $\lambda^{right} = 0.03$.

A similar lapse model, with both "depressed" and "control" λ values identical to the Study 1 agent, was incorporated into the Study 2 agent. Given that, in contrast to the Study 1 simulation, the agent "attended" to both sides of space simultaneously, the precision of the likelihoods was reduced for one side of space only during a lapse trial, unless a lapse coincidentally occurred on both sides at once. The Study 2 task also differed from the previous task in that its interleaved staircases afforded redundant information about each laterality based on evidence from the other, and therefore compensatory strategies could in principle be employed in response to lateralised attentional deficits. On this basis three variants of the lapsing agent were developed.

- Uncompensated lapses variant (Figure 5.3, Panel C). No compensatory strategies were employed.
- Intuited lapses variant (Figure 5.3, Panel D). The agent was able to "intuit" its lapses and accurately adjust its prior expectations about signal laterality on lapse trials only:

$$\mathrm{P}(\mathrm{laterality} = \mathrm{left}|\mathrm{lapse}) = \frac{\lambda^{\mathrm{left}}}{\lambda^{\mathrm{left}} + \lambda^{\mathrm{right}}} \quad (58)$$

- Compensated lapses variant (Figure 5.3, Panel E). The agent could not distinguish between lapses and trials in which there was no detectable signal, and so used the adjusted laterality prior described above as a biased guessing rule in any trial yielding no reliable data (i.e., lapse trials and those in which percepts on both sides of space were undetectable). Note that this strategy is overcompensatory in its overgeneral use of the guessing rule.

As before, "depressed" agents were defined by lapse rates of $\lambda^{left} = 0.06$ and $\lambda^{right} = 0.01$ and "control" agents were defined by lapse rates of $\lambda^{left} = 0.01$ and $\lambda^{right} = 0.03$.

Resource conservation models

Aspects of the Study 2 findings that are not addressed by the lapse account include the improved overall RT efficiency and the systematic increase in early responses to right-sided stimuli observed in the depressed group relative to healthy controls. As suggested above, these outcomes could arise from a strategy of directing attention predominantly to the right side of space with the aim of reducing task-related effort or conserving resources. Arguing against this hypothesis is the fact that no group difference in perceptual sensitivity was found, as might be expected if one group is systematically reducing its access to precise task-relevant information.

A resource-conservation variant of the Study 2 agent was created by attenuating the attention (precision) afforded to the left side of space commensurately with the expectation of the agent that that the left-sided percept would be difficult to detect. Since greater effort is required to detect low-intensity signals, greater cost-savings in energy terms may be made by titrating attention in this way.

The resource-conserving agent generated a prediction of the distribution of the next left-sided signal percept given the current prior and predicted data. The reduction in precision on the left (parameterised as $\Delta\sigma^{unattended}$) was a function of the probability density of the predicted posterior at 0 on the detectability scale as follows:

$$\Delta\sigma^{unattended} = \frac{1}{2}P(\theta = 0 \mid predicted\ data)^{1.5} \tag{59}$$

To maintain the relative precisions of prior and likelihood, they were adjusted using the following formula (reparameterised as a standard deviation)

$$\sigma^{unattended} = \sigma^{attended} + (\Delta\sigma^{unattended}\sigma^{attended}) \tag{60}$$

As a result, when a detectable left-sided percept was expected the precisions did not differ across space, but as expected left-sided stimulus detectability reduced, precision on the left side reduced proportionally. At the point where the left-sided stimulus was expected to be completely undetectable, left-sided precision was about ½ of the precision on the right. Three versions of this model were simulated as follows:

- Uncompensated resource conservation variant (Figure 5.3, Panel F). No compensatory strategies were employed.

- Precision-weighted resource conservation variant (Figure 5.3, Panel G). The agent used precision-weighting to rely increasingly on evidence generated from the right side of space as precision to the left was reduced, using the formula

$$w = \frac{\tau^{right}}{(\tau^{left} + \tau^{right})} \quad (61)$$

where τ is the precision of the posterior distributions and w is the weighting used for the right-lateralised posterior probability P(input=signal|data) relative to the left. In addition, in trials in which neither stimulus was unambiguously detectable, but the stimulus on the right was unambiguously undetectable, the agent adjusted the guess rate to 1 - w (i.e., when no detectable information is available on the attended right side of space, the agent increases its belief that the signal occurred on the left).

- Overcompensated resource-conservation variant (Figure 5.3, Panel H). This model was identical to the previous one except that w was multiplied by 1.2 to provide an over-compensatory precision-weighting strategy.

Alternative models

We also searched for competing explanations for our empirical findings.

Constant deficit models

Our first alternative hypothesis, relevant to both studies, suggests that left-sided perceptual performance in depression is affected not by discrete lapses, but by a small, constant increase in perceptual noise. Variants of the "depressed" agents for both studies were created in which the precisions of the likelihood and prior on the left side of space were consistently reduced by ¼ relative to the precisions of the likelihood and prior on the right side of space.

False percept models

Our second alternative hypothesis was that the response bias observed in depressed participants in Study 2 resulted not from a compensatory strategy, but from a tendency to false percepts on the left side of space. False percepts may arise when disproportionately precise prior expectations contribute to the generation of disproportionately precise (detectable) percepts despite a small or vague likelihood for the data. It is possible that the tendency to focus overly on the expectation of a signal is more likely to occur at lower levels of stimulus intensity, where participants may be straining to detect the target, and so two variants of the false percept agent were developed:

- Unmodulated false percept variant (Figure 5.3, Panel I). The precision of the left-sided expectation of a signal was increased by a small constant throughout the task
- Modulated false percept variant (Figure 5.3, Panel J). The precision of the left-sided expectation of a signal increased commensurately with the expectation that the right-sided stimulus would be undetectable as follows (where the probability refers to signal detectability on the right side of space):

$$\sigma^{left\ signal\ prior} = 1 - P(\theta = 0 \mid predicted\ data) \quad (62)$$

Each of the Study 1 variants was used to generate simulated datasets for 16 "depressed" participants and 16 "controls" for each block of the Study 1 design. Similarly, each of the Study 2 variants was used to generate simulated datasets for 12 "depressed" participants and 12 "controls" for each block and condition of the Study 2 design.

5.3. Results

5.3.1. Attentional lapse models

Question 1: Can a single lapse model, together with a simple compensatory strategy, predict the patterns observed in the data in both studies?

The simulated Study 1 data for the lapsing agents was fit to the GLMM described in Study 1. The results (shown in Figure 5.2) closely match those derived from the observed Study 1 data (Figure 3.1). As with the observed Study 1 data, an attempt to fit a version of the model without any lapse parameter resulted in a credible group by laterality interaction in the slope parameter which was abolished when the lapse parameter was included.

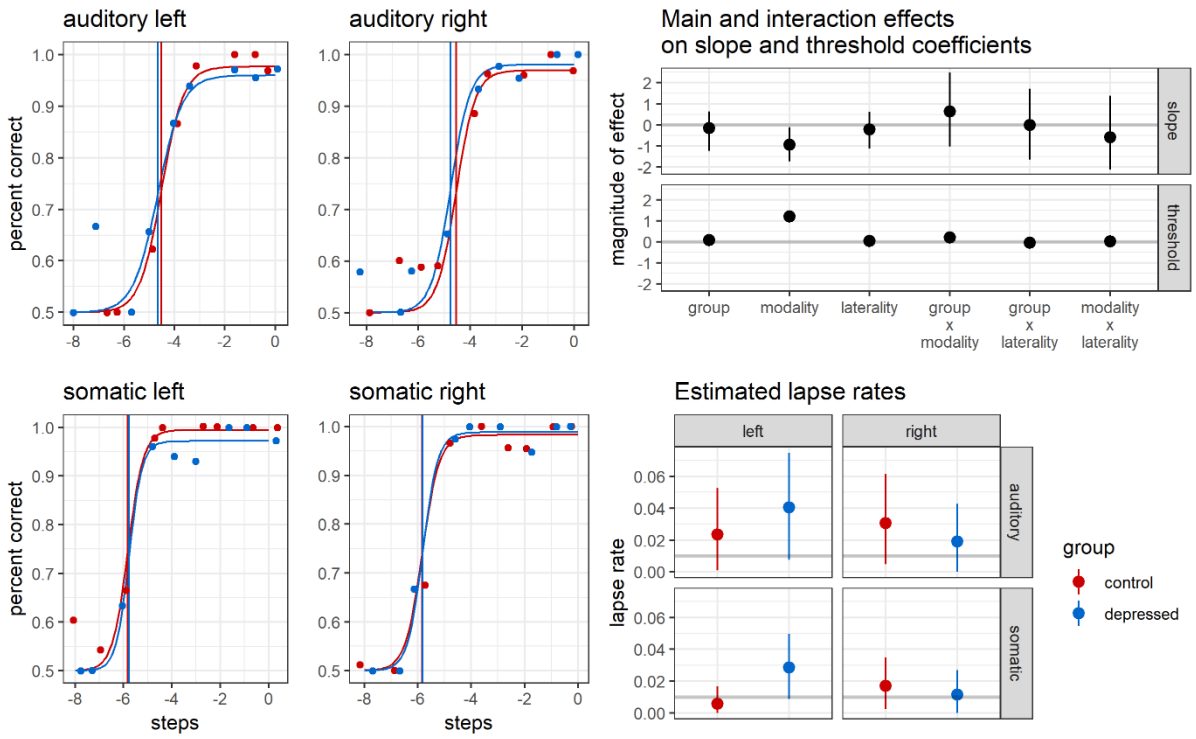


Figure 5.2: Study 3 simulated Study 1 GLMM outcomes by group, stimulus modality and laterality (lapse model). Left panels: mean logistic curves and thresholds (vertical lines) estimated from the simulated data fit to the Study 1 GLMM model, shown by stimulus modality and laterality. Points represent the simulated data (proportion correct averaged over group) shown to the nearest step and jittered to avoid overlap. The step size for the auditory staircases is 4dB, for the somatic staircases 1dB. Upper right panel: contrasts on effects and interactions for the slope and threshold parameters. Lower right panel: estimated lapse rates by group and condition. Compare to observed data analysis in Figure 3.1.

The three simulated Study 2 datasets derived from the lapsing agents were independently analysed using the Study 2 hierarchical signal detection model, and results are shown in Figure 5.3 (panels C, D and E). The uncompensated lapses variant generated systematic right-sided bias in the "depressed" agents which was reduced to near zero at the lowest levels of stimulus intensity (Panel C). The intuited lapses variant induced mild left-sided bias in the "depressed" agents, which was broadly constant across all stimulus intensity levels (Panel D). The compensated lapses variant (Panel E), however, closely resembles the observed data (shown in Panel A), with a leftward bias in the "depressed" agents evident across the whole range of stimulus intensity, and particularly marked when stimulus intensity is low.

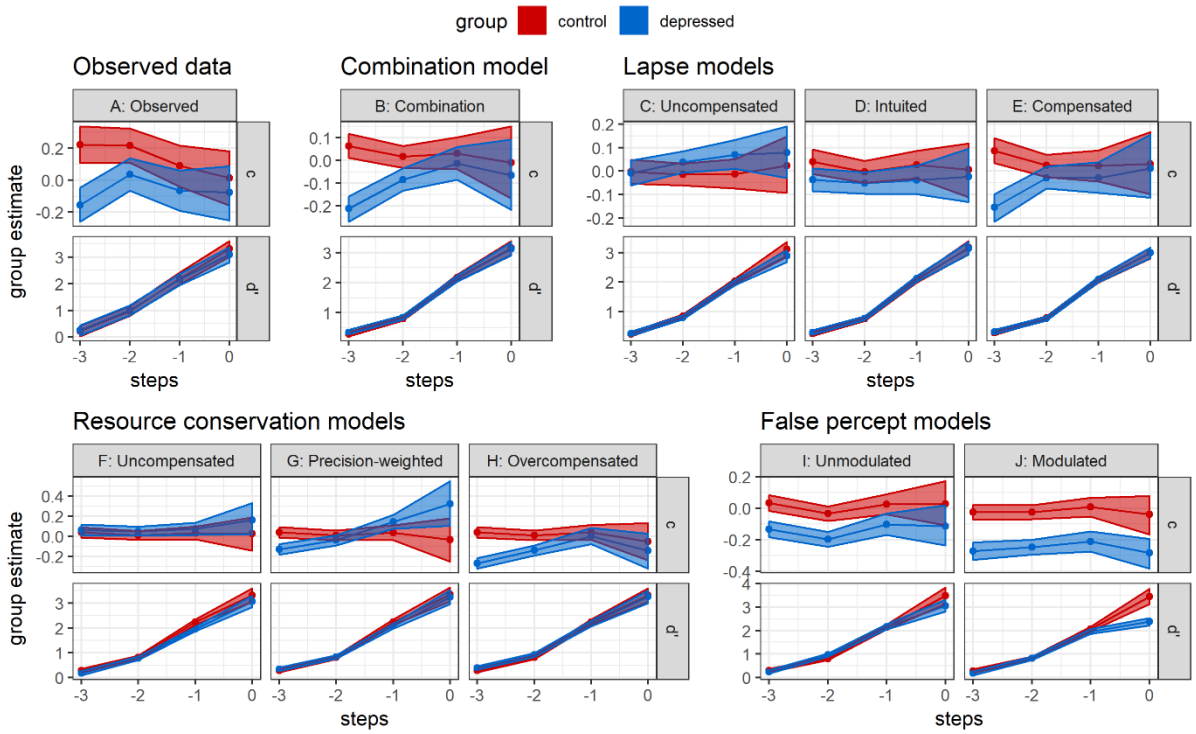


Figure 5.3: Study 3 simulated Study 2 signal detection model outcomes by group and stimulus intensity. Posterior distributions of the estimates of d' and c by group and stimulus intensity, averaged over modality, for various simulations. Panel A represents the observed Study 2 outcomes for comparison. Points represent the mean posterior estimate for each parameter given group and condition. Ribbons represent the 95% credible interval of the posterior distributions. Posterior distributions are broader for the observed data than for the simulated data, because for clarity no individual differences were incorporated in the various iterations of the agent in each simulation.

In summary, simulated data closely resembling the observed data were generated for both Study 1 and Study 2 by an identical lapse model, with the addition in the Study 2 simulation of a simple compensatory strategy: a biased guessing rule. Such a strategy implies that depressed participants are aware at some level of reduced left-sided attentional performance; but does not rely on an ability to accurately intuit lapses. This model appears to provide a good account of the observed data from human participants generated in both studies and is therefore parsimonious as well as internally consistent.

5.3.2. Resource conservation models

Question 2: Can a "depressed" agent reduce energy expenditure in the Study 2 paradigm by reducing attention to the left side of space without reducing overall perceptual sensitivity as a corollary? If so, what patterns of bias are produced?

The datasets arising from the resource-conservation simulations were independently analysed using the Study 2 hierarchical signal detection model. The posterior distributions of the averaged d' and c

parameters for each variant are shown in Figure 5.3 (panels F, G and H). As can be seen in panel F, an uncompensated loss of precision to the left induced a marked right-sided bias which was greatest in response to high-intensity stimuli and reduced to near zero when stimuli were undetectable. As expected, there was also a substantial loss of sensitivity which manifested as a credible group difference in d'. This group difference in sensitivity was abolished by the compensatory strategy of (accurately) precision-weighting the left- and right-lateralised posterior probabilities (panel G). The pattern of bias arising from this compensatory strategy is midway between the pattern seen in the uncompensated resource conservation simulation and that seen in the observed data. The final variant, employing an over-compensatory precision-weighting strategy (panel H), generated data similar to the observed data in terms of group influences on both sensitivity and bias.

In summary, these models critically demonstrate that it is possible to conserve resources by reducing sensory precision to the left when undertaking this task with no loss of apparent sensitivity if response decisions are informed by precision-weighting of the posterior distributions. The pattern of bias arising from this strategy is consistent with the observed data in that left-sided bias increases with increasing uncertainty, but an overcompensatory precision-weighting strategy is required to predict the observed patterns of bias across the whole range of stimulus intensity.

5.3.3. Alternative models

Question 3: Are there alternative explanations which can better predict the data? Specifically, how does a constant deficit model or a false percept model compare to the lapse or resource conservation models?

Constant deficit model

The outcomes differed substantially from those in the observed data. In the simulated Study 1 dataset a group by laterality interaction was observed in the threshold rather than the slope parameter (Figure 5.4, left and upper right panels), and inclusion of a lapse parameter in the model did not affect the credibility of this interaction. In the simulated Study 2 datasets, loss of sensitivity in an uncompensated version was not corrected by a compensatory strategy of precision-weighting, and patterns of bias did not correspond to those seen in the observed data (Figure 5.4, lower right panel).

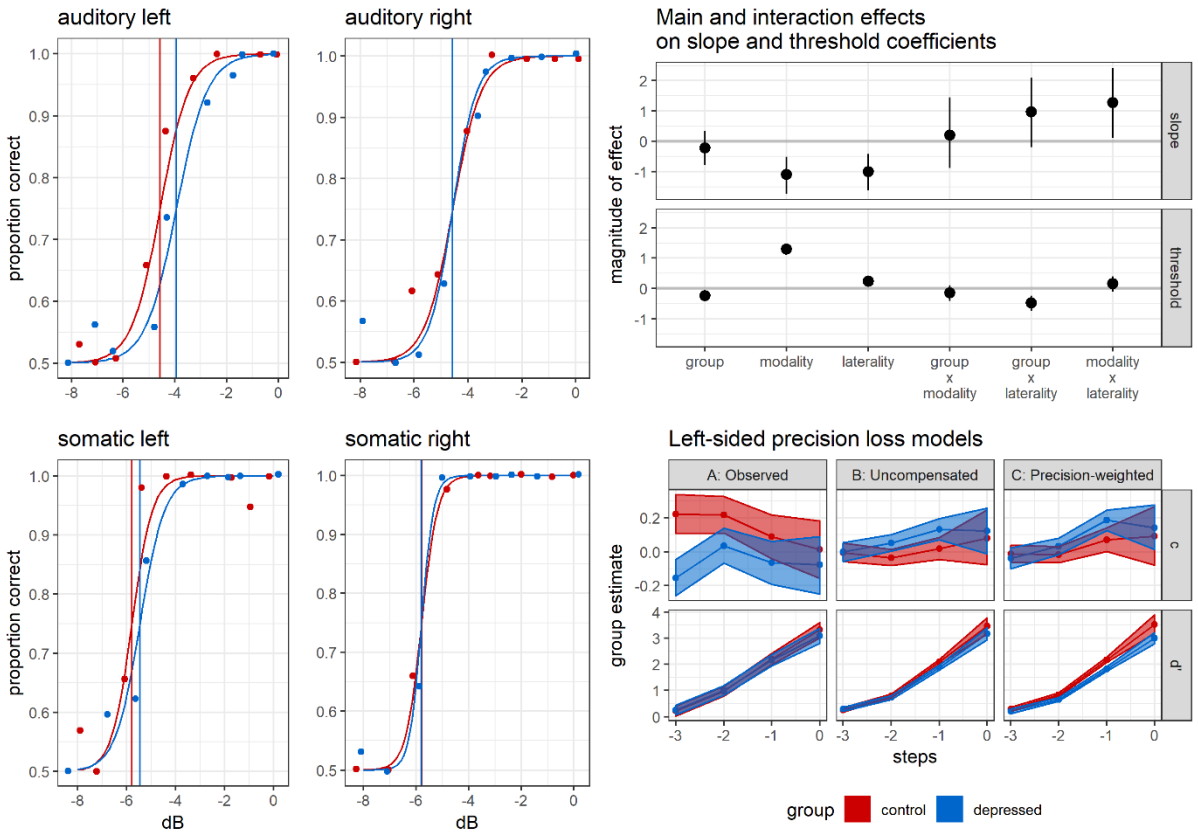


Figure 5.4: Study 3 simulated Study 1 GLMM and Study 2 signal detection model outcomes (constant deficit model). Left panels: mean logistic curves and thresholds (vertical lines) estimated from the simulated data fit to the Study 1 GLMM model, shown by stimulus modality and laterality. Points represent the simulated data (proportion correct averaged over group) shown to the nearest step and jittered to avoid overlap. The step size for the auditory staircases is 4dB, for the somatic staircases 1dB. Upper right panel: contrasts on effects and interactions for the Study 1 GLMM slope and threshold parameters. Compare to observed data analysis in Figure 3.1. Lower right panel: posterior distributions of the estimates of d' and c by group and stimulus intensity, averaged over modality, for the Study 2 constant deficit simulation.

<u>False percept model</u>

The datasets arising from the resource-conservation simulations were independently analysed using the Study 2 hierarchical signal detection model. The posterior distributions of the averaged d' and c parameters for each variant are shown in Figure 5.3 (panels I and J). In both variants, detectable false percepts were generated on the left side of space at higher levels of stimulus intensity, and confidence was increased in ambiguous left-sided percepts relative to ambiguous right-sided percepts. As a result, sensitivity was markedly reduced at the highest level of stimulus intensity, while a constant pattern of left-sided bias was produced, inconsistent with the observed data. It may be the case that a more sophisticated mechanism for updating prior precision would allow the model to predict the data more accurately.

5.3.4. Combination model

In summary, the simulations described above indicate that both a lapse account and a resource-conservation account can provide plausible predictions of the observed data. In Study 1, in the absence of any opportunity for resource conservation, the lapse account appears the more probable explanation. In Study 2, both accounts are plausible, and each is consistent with a different aspect of the reaction time data. Perhaps the most likely solution is that a combination of these processes can account for the Study 2 data. Figure 5.3 (Panel B), for example, depicts averaged outcomes over the compensated lapse model and the overcompensated resource conservation strategy, and displays a similar pattern of sensitivity and bias to the observed data. Neither of our alternative hypotheses provided as good a prediction of the observed data as the lapse and resource conservation models.

5.4. Study 3 summary

Study 3 aimed to investigate possible mechanisms underlying the observed pattern of results from Studies 1 and 2 using a series of simulations. Although simulations cannot give conclusive insights into the psychological mechanisms underlying the observed results in the experimental studies, they can provide a proof-of-principle with respect to hypotheses about how such mechanisms could theoretically operate. The hypotheses supported by the outcomes of the current study are intrinsically parsimonious by virtue of having been implemented in such a basic Bayesian agent, although of course more complex models could produce equal or better quality of data prediction. Despite its simplicity, the basic agent was able to generate data patterns very similar to those observed in the human data in two different studies by using a single lapse model with a lateralised bias and a proportionally biased guessing rule as a compensatory strategy. This provides some support for the plausibility of the lapse model as a theory about how the observed data were generated. In addition, a resource conservation model importantly demonstrated that the Study 2 task could be successfully completed with no loss of sensitivity by relying predominantly on evidence from the right side of space even when this drastically reduced perceptual precision on the unattended left side of space. This model also succeeded in predicting patterns of bias observed in the data, under conditions where its precision-weighting compensatory strategy was *over-compensatory*. Both the lapse model and the resource conservation model provided better predictions of the observed data than either a deficit model of left-sided precision loss or a false percept model.

The simulations provide support for the contention that the observed data may have been generated in part by a compensatory strategy. The pattern of bias in the observed data could not be modelled directly through precision loss or lapses on either side of space because these exerted their smallest effect on bias when stimulus intensity was low. On the other hand, compensatory models utilising

biased guess rates or evidence weighting were able to produce a large effect on bias at low stimulus intensity. In fact, accurate compensation did not accurately predict the observed data in either the lapse model or in the resource conservation model. In order to produce left-sided bias across the whole range of stimulus intensity with a larger effect at the lowest level of intensity, it was necessary to *over*compensate. This might suggest a relatively broad loss of confidence in the ability to attend to one laterality, or a strategy designed to compensate both for the occasional lapse and for intermittent attention to that side of space. In addition, the simulations provide support for the difference model with guessing proposed by García-Pérez and Alcalá-Quintana (2010), given that all simulations which successfully modelled the bias at high uncertainty observed in Study 2 included some form of biased guessing rule.

An additional finding of interest was a relationship between indices of left-sided neglect in both Study 1 and Study 2 and anhedonic symptomatology over and above the contribution of depression. Details of this analysis can be found in Appendix G.

In summary, the simulations suggest not only that a lateralised attentional deficit is a plausible model for the performance of persistently depressed individuals in these tasks, but also that these individuals may be engaging in heuristic strategies as a means of compensation or resource conservation in order to maintain apparent task performance despite a (voluntary or involuntary) reduction in the availability of task-relevant sensory data.

Despite indications of a generic loss of sensory precision as part of a resource-conservation strategy in depressed participants, this series of three studies provides no evidence for a modality-specific loss of somatic precision, either with respect to baseline perceptual sensitivity, or arising from failures in voluntary attention. Study 4 investigated the possibility that somatic signals exert a unique effect on involuntary attentional capture among persistently-depressed participants relative to controls.

Chapter 6. Study 4: Attentional capture by auditory and somatic stimuli during covert attentional orienting in persistent depression

Study 4 employed the covert attention (Posner) paradigm described in the Method section in Chapter 2 to investigate involuntary attentional capture by somatic signals in persistently depressed and control samples. In this task, targets are presented either to the left or right of fixation while preceding cues can be either spatially valid (occurring on the same side of space) or invalid (occurring on the opposite side of space) with respect to the target. The reaction time difference between responses to targets where cues are valid and responses where cues are invalid provides an index of attentional capture by those cues, sometimes known as the validity effect. If non-predictive somatic stimuli are employed as cues, this task can therefore yield a measure of the extent of stimulus-driven attentional capture by task-irrelevant somatic information, potentially indexing a key trait or tendency underlying day-to-day bodily awareness. An otherwise identical control condition employs auditory cues to dissociate modality-specific from supra-modal effects.

Study 4 attempts to address three specific questions. First, is persistent depression associated with a shift in the strength of stimulus-driven attentional capture by somatic signals? Secondly, is any such shift genuinely modality-specific? And finally, what are the implications of any such shift in terms of the salience of somatic experience in persistent depression? Specifically, are somatic signals amplified or attenuated through their interactions with attention in persistently-depressed relative to healthy individuals?

Comparison of the attentional performance of persistently depressed participants with healthy controls in the context of somatic versus auditory cues can yield: first, an estimate of the extent to which depression is associated with disruption in attentional performance across modalities; second, an estimate of the extent to which depression is associated with attentional disruption in response to somatic cues in particular; and third, an estimate of the direction of any effect of attentional disruption. If depressed individuals are habituated to downregulating or failing to optimize the precision of somatic signals (attenuated bodily awareness) they should demonstrate a reduced validity effect for somatic cues relative to auditory ones. If, on the other hand, they are sensitized to somatic signals (amplified bodily awareness), they should demonstrate an increased validity effect.

6.1. Study 4 design

Participant recruitment, materials and procedure were as described in the Methods in Chapter 2.

Participants were instructed to maintain central fixation while responding as quickly and as accurately as possible to peripheral visual targets, and to ignore all other stimuli. In each trial, a visual target was presented to either the right or left side of fixation, and participants indicated the location of the target using a spatially congruent foot pedal response. A spatially valid (50%) or invalid (50%) cue was presented immediately before the target in either the auditory or the somatic modality, depending on block. There were thus two levels of stimulus validity (valid / invalid), two levels of target laterality (left / right), and two levels of cue modality (auditory/somatic). Within each block, five levels of stimulus onset asynchrony (SOA) between cue and target were employed (50ms, 100ms, 200ms, 300ms or 500ms). Eight trials were presented for each combination of SOA, validity and laterality, and there were additionally eight uncued trials for each laterality, totalling 176 trials per block. Trial types (validity, laterality) were presented within blocks in a randomized order, and in total participants completed 4 blocks (2 somatic, 2 auditory) in counterbalanced order. Reaction times and error data were collected by the program. During somatic blocks, continuous white noise was delivered via the peripheral speakers to mask any sound associated with tactor vibration.

Two brief practice blocks were completed in order to check participants' understanding of the task and enable them to become familiar with the equipment.

6.2. Study 4 results

6.2.1. Sample characteristics

All depressed participants were diagnosed with chronic, recurrent and/or treatment-resistant forms of depressive illness of at least moderate severity at the time of testing. Mean age of onset was 21.73 years old (SD 11.25) and the mean number of years since first diagnosis was 19.60 (SD 15.89). Six participants (37.5%) reported that their first onset of depression was in childhood. Six individuals (37.5%) met criteria for at least one comorbid Axis 1 disorder at the time of testing, including Obsessive-Compulsive Disorder, Generalised Anxiety Disorder, Posttraumatic Stress Disorder and Anorexia (three participants met criteria for an anxiety disorder, two met criteria for an anxiety disorder and PTSD, and one met criteria for an eating disorder). Six participants (37.5%) were currently prescribed antidepressant medication (n=6 were prescribed an SSRI, n=2 were additionally prescribed an SNRI). No control participants were prescribed any form of psychotropic medication.

A series of t-tests demonstrated that the depressed and control groups were comparable with respect to the characteristics of age, years of education and handedness (see Table 6.1). As expected, depressed participants differed significantly from healthy controls with respect to self-reported symptoms of depression and anxiety.

Table 6.1: Study 4 demographic comparisons by group

	Depressed group (n = 16)	Control group (n = 16)	2-tailed t-tests
Demographics: mean (SD)			
Sex	15 women	15 women	-
Age (years)	42 (18.11)	42.5 (17.41)	t(30) = -0.08, p = 0.94
Handedness (EHI)	68.14 (47.75)	80.06 (31.16)	t(30) = -0.84, p = 0.41
Education (years)	15.25 (2.86)	15.69 (2.41)	t(30) = -0.47, p = 0.64
Mood measures: mean (SD)			
Depression (BDI-II)	33.19 (5.06)	5.06 (2.70)	t(30) = 20.77, p < 0.001
Anxiety (BAI)	22.00 (10.00)	3.06 (2.64)	t(17.09[1]) = 7.32, p < 0.001

[1] Degrees of freedom adjusted due to unequal variances

EHI = Edinburgh Handedness Inventory, BDI-II = Beck Depression Inventory-II; BAI = Beck Anxiety Inventory

6.2.2. Reaction times

Reaction times (RTs) greater than 1500ms were assumed to reflect equipment failure or misuse (typically a failure to fully depress the foot pedal), and trials with these latencies were eliminated from both the RT and error data. Subsequently, responses in which RTs were more than 3 standard deviations away from the mean for each participant (assumed to reflect anticipations and misfires) were eliminated from both RT and error data. Individualised rather than generic cut-offs were employed due to a high level of between-subject variability. In total, 2.48% of responses were disallowed, with no significant effect of group on the total number of disallowed trials (t(30) = 1.16, p = 0.26, d = 0.41).

Examination of the remaining data revealed an acceptable error rate of 0.80%. Incorrect responses were eliminated from the RT data. In total, 21795 observations remained.

No statistically significant interactions between group and stimulus-onset-asynchrony (SOA) were found in initial analyses (ps > 0.08); therefore, for simplicity, SOA categories are collapsed in the analysis reported here. Uncued trials are not analysed.

A repeated-measures ANOVA with a between-participants factor of group and within-participants factors of cue modality, block, cue validity and target laterality was carried out on the RT data.

Within-participants effects

The ANOVA revealed that there was no significant main effect of modality ($F(1, 30) = 0.02$, $p = 0.89$, $\eta_p^2 = 0.001$), indicating that on average participants responded with comparable speed during somatic and auditory blocks. A main effect of block ($F(1, 30) = 8.78$, $p = 0.006$, $\eta_p^2 = 0.23$), indicated that responses were speeded during later blocks relative to earlier ones, probably reflecting a practice effect. There was a large main effect of validity ($F(1, 30) = 97.74$, $p < 0.001$, $\eta_p^2 = 0.77$) demonstrating, as expected, that invalid cues were associated with slowed responses relative to valid cues. There was also a moderate effect of laterality ($F(1, 30) = 6.05$, $p = 0.02$, $\eta_p^2 = 0.17$), indicating that left-sided responses were somewhat slowed relative to right-sided responses. There were no other statistically significant within-participants effects (all ps > 0.1: see Appendix I.1.1 for details).

Group effects

There was a significant main effect of group, indicating that depressed participants responded on average more slowly than healthy controls ($F(1, 30) = 6.36$, $p = 0.017$, $\eta_p^2 = 0.18$). Importantly, an interaction between modality and group ($F(1, 30) = 9.64$, $p = 0.004$, $\eta_p^2 = 0.24$) indicated that the slowing in the depressed participants was especially strong in somatic blocks ($F(1, 30) = 9.89$, $p = 0.004$, $\eta_p^2 = 0.25$), and did not reach statistical significance during auditory blocks ($F(1, 30) = 3.55$, $p = 0.069$, $\eta_p^2 = 0.11$) (see Figure 6.1, upper left panel). A 3-way interaction between block, validity and group ($F(1, 30) = 4.98$, $p = 0.033$, $\eta_p^2 = 0.14$) reflected increased validity effects in the depressed group relative to healthy controls in later blocks ($F(1, 30) = 5.05$, $p = 0.032$, $\eta_p^2 = 0.14$) but not in earlier ones ($F(1, 30) = 0.28$, $p = 0.60$, $\eta_p^2 = 0.009$: Figure 6.1, lower right panel). There were no other statistically significant interactions between group and any other effect (all ps > 0.1: Appendix I.1.1).

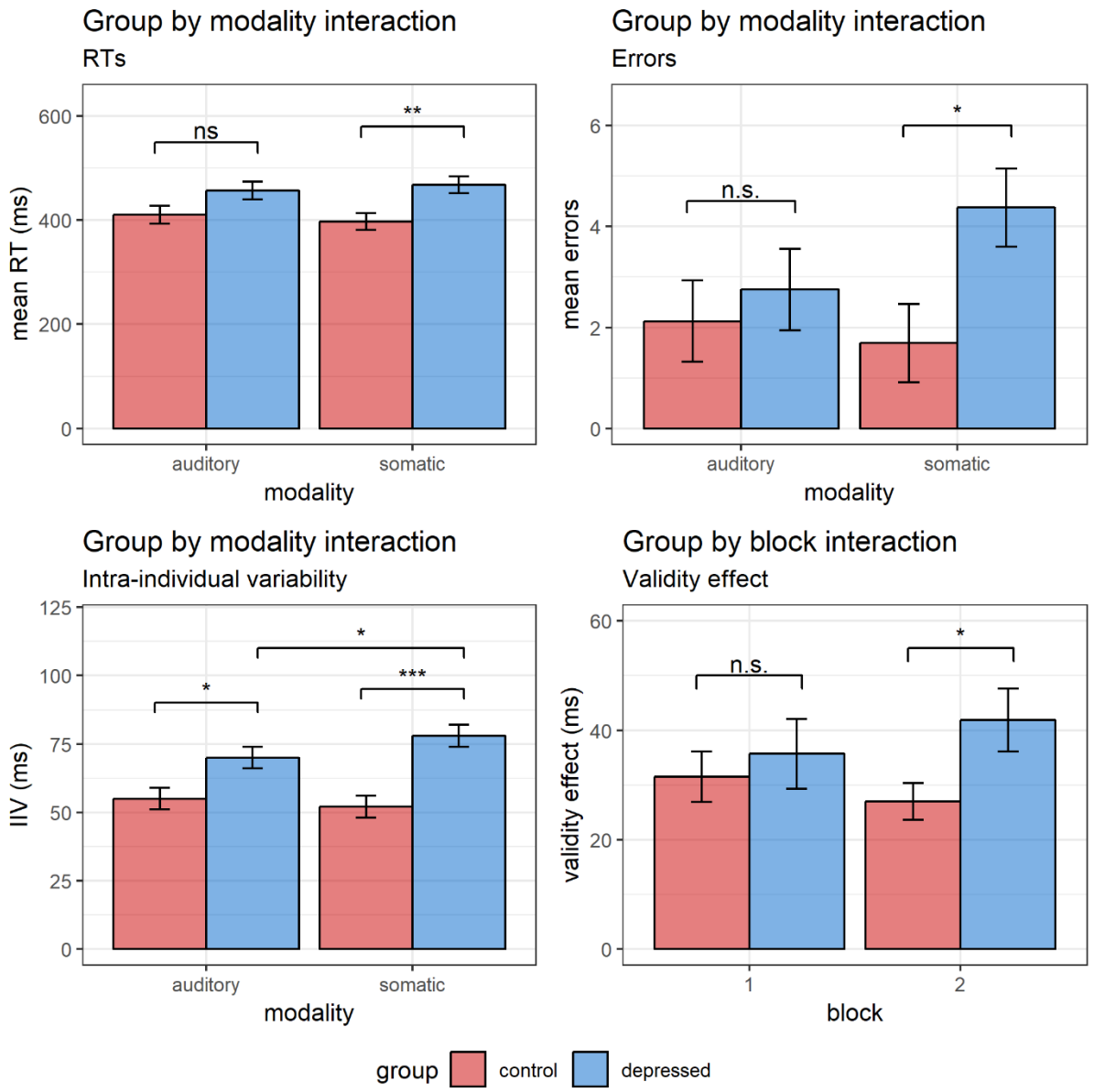


Figure 6.1: Study 4 outcomes of interest. Error bars represent one standard error of the mean. Asterisks represent p-values less than 0.05 (*), 0.01 (**) and 0.001(***). The upper left panel shows an interaction between group and modality in overall reaction time, indicating relatively slowed responses among depressed participants following somatic cues. The upper right and lower left panels show the same effect respectively in error rates (depressed participants are more prone to errors following a somatic cue) and in intra-individual variability (depressed participants are more variable in their responses following a somatic cue). The lower right panel shows the interaction between group, validity and block, indicating that depressed participants displayed increased validity effects relative to controls during later blocks of the task.

Summary

In summary, for the RT data an interaction between group and cue modality indicated a specific disadvantage for depressed individuals when cues were somatic, regardless of cue validity. Both

groups demonstrated speeded responses in later blocks relative to earlier ones, suggestive of a practice effect; and both groups showed a modest disadvantage for left-sided responses, possibly muscular, given that a predominantly right-handed sample is likely to be predominantly right-footed also (Augustyn & Peters, 1986). The expected effect of cue validity was strongly present in both groups and exacerbated in depressed participants relative to healthy controls in later blocks, possibly indicating a group-specific change in supra-modal attentional control over time. There was no evidence, however, of differential validity effects for somatic versus auditory cues across groups.

6.2.3. Errors

Given the modality x group interaction in the RT data, errors were examined to rule out the possibility of a speed-accuracy trade-off. Error data were collapsed together into modality categories and a modality x group ANOVA was conducted on the resulting scores.

There was no significant main effect of modality ($F(1, 30) = 1.58$, $p = 0.22$, $\eta_p^2 = 0.05$) and no significant main effect of group ($F(1, 30) = 2.67$, $p = 0.11$, $\eta_p^2 = 0.08$). There was, however, an interaction between modality and group ($F(1, 30) = 4.78$, $p = 0.037$, $\eta_p^2 = 0.14$) in the same direction as that found in the RT data; i.e. the depressed group made more errors following somatic cues (see Figure 6.1, upper right panel).

Independent samples t-tests confirmed that the depressed group made significantly more errors during somatic blocks than did controls (corrected $t(17.89) = 2.46$, $p = 0.024$, $d = 0.87$) with no evidence of any group difference in error rates during auditory blocks ($t(30) = 0.55$, $p = 0.59$, $d = 0.19$).

6.2.4. Intra-individual variability (IIV)

The pattern of slowed reaction times *and* increased error rates in the depressed group specifically in response to somatic cues suggests a reduction in attentional efficiency under these circumstances. This hypothesis was investigated further by calculating an index of intra-individual variability (IIV) in RT scores. IIV is a phenomenon which is thought to reflect attentional control, such that increased variability is associated with reduced control or efficiency (e.g., Bellgrove et al., 2004; Weissman et al., 2006)

A modality-specific IIV score was determined for each participant by calculating the standard deviation of RTs within each trial category and averaging across all categories within each modality. A modality x group ANOVA was then conducted on the IIV scores.

The ANOVA found no main effect of modality ($F(1, 30) = 1.48$, $p = 0.23$, $\eta_p^2 = 0.05$). There was, however, a large main effect of group ($F(1,30) = 15.33$, $p < 0.001$, $\eta_p^2 = 0.34$), indicating increased IIV among

depressed participants relative to healthy controls. There was also a significant interaction between modality and group ($F(1, 30) = 5.60$, $p = 0.025$, $\eta_p^2 = 0.16$) indicating a disproportionate increase in IIV during somatic blocks in the depressed group (see Figure 6.1, lower left panel).

Independent samples t-tests confirmed that IIV was increased in depressed participants relative to healthy controls during auditory blocks ($t(30) = 2.49$, $p = 0.019$, $d = 0.87$) but that this effect was more marked during somatic blocks ($t(30) = 4.98$, $p < 0.001$, $d = 1.71$). Furthermore, depressed individuals were significantly more variable in their responses during somatic blocks than they were during auditory blocks ($t(15) = 2.16$, $p = 0.048$, $d = 0.44$), while there was no support for the variability displayed by healthy controls differing across modalities ($t(15) = 1.03$, $p = 0.32$, $d = 0.23$).

6.2.5. Medication-free analyses

To rule out the potentially confounding factor of medication status, all analyses were repeated excluding (n=6) depressed individuals who were prescribed psychotropic medication at the time of the study. The results are detailed in Appendix B.3. All key group effects remained statistically significant, with the exception of the error analysis, in which statistical significance did not survive a correction for unequal variances but effect sizes remained large. In summary, there is no evidence to suggest that group effects in this study are attributable to psychotropic medication status.

6.2.6. Correlation analysis

An additional analysis was undertaken to rule out the possibility that the observed effects of modality on performance in the depressed group were accounted for by anxiety symptomatology rather than by depression *per se*. The somatic IIV score was used as the dependent variable because this outcome represented the most marked difference between groups. Partial correlations demonstrated that the relationship between somatic IIV and BDI score, covarying BAI score, remained significant ($r_{partial}(29) = 0.55$, $p = 0.001$), while the relationship between somatic IIV and BAI score, controlling for BDI score, was non-significant ($r_{partial}(29) = -0.10$, $p = 0.59$).

6.3. Study 4 summary

We hypothesised that an influence of depression (in either direction) on the salience of somatic signals would be indexed by group differences in validity effects following somatic cues in Study 4. Contrary to prediction, the observed group difference in validity effect was not modality-specific and occurred only after relatively lengthy time on task. Nevertheless, our hypothesis was partially supported by a marked and largely modality-specific effect of somatic cues on attentional performance in general in the depressed group relative to healthy controls. Specifically, decrements in performance indexed by global markers of attentional control, including longer reaction times, higher error rates and increased

intra-individual variability, were observed in depressed participants during somatic blocks regardless of cue validity. This pattern of responses, particularly RT variability, has been interpreted in relevant literatures as diagnostic of a breakdown in the efficiency of attention regulation (e.g., Bellgrove et al., 2004; Kelly et al., 2008; Sonuga-Barke & Castellanos, 2007). Reduced attentional efficiency in depression is not, in itself, a novel finding; indeed, concentration difficulties are a considered to be a core symptom of the illness (American Psychiatric Association, 2013), but to our knowledge this is the first report demonstrating that such problems may be accentuated in the somatic modality.

In the absence of a significant interaction between group, cue modality and validity, the question of whether depression is associated with an increase or a decrease in the salience of somatic signals cannot be directly answered. Sensitization to somatic signals might draw attention away from the visual targets and entail greater effort to ignore them; conversely, attenuation or habitual ignoring might weaken their alerting effect, reducing anticipation of and preparation for the impending target, while increasing the risk of mind-wandering. Either situation could account for the pattern of results demonstrated here. In addition, a possible alternative explanation for these findings is that white noise (played continuously during somatic blocks only) could have been particularly distracting for depressed individuals and responsible for their performance decrements observed during these blocks. Study 5 was therefore designed to clarify these issues.

Chapter 7. Study 5: Relative salience of somatic and auditory stimuli in attentional capture during covert attentional orienting in persistent depression

Study 4 presented evidence for a marked influence of unwanted or ignored somatic stimuli on attentional orienting in depressed individuals relative to never-depressed controls. However, there are competing interpretations of this finding with respect to the implications regarding somatic salience in persistent depression. Specifically, amplified somatic salience may have rendered somatic cues more distracting or more likely to capture limited attentional resources in the effort to ignore them; or alternatively attenuated somatic salience may have reduced the alerting effect of somatic cues or otherwise failed to recall attention during mind-wandering. The design of Study 4 did not allow for comparison of these possible explanations. In Study 5, the direction of any interaction between cue modality and salience-driven attentional capture was examined in detail by manipulating cue relevance. Relevant or predictive cues (for example, cues that are valid 75% of the time) are advantageous to attend to and therefore less likely to be ignored than irrelevant cues such as those employed in Study 4. In a task employing relevant cues, the amplification and attenuation hypotheses generate opposing predictions. The amplification hypothesis suggests that relevant somatic cues will be highly salient and therefore predicts increased validity effects in depressed participants relative to healthy controls. The attenuation hypothesis predicts that depressed individuals will be less able to utilise relevant somatic cues and will therefore demonstrate reduced validity effects relative to healthy controls. The results of Study 5 should therefore provide clear support for one hypothesis over the other. Additionally, to rule out the alternative white noise explanation for reduced attentional efficiency in depression in Study 4, white noise was continuously delivered during all blocks in Study 5, regardless of cue modality.

7.1. Study 5 design

Participant recruitment, materials and procedure were as described in in the Method section in Chapter 2.

Experimental design parameters other than cue relevance were identical to those described in Study 4. The key manipulation characterising Study 5 was the use of relevant cues, i.e., blocks in which 75% of cues were valid. During a given block, 12 trials employing valid cues were presented for each level of SOA and laterality, yielding a total of 120 trials. 4 trials employed invalid cues for every level of SOA and laterality, yielding a further 40 trials. As in Study 4, 8 additional trials per laterality were uncued, bringing the total number of trials to 176 per block. Participants were presented with one block in which cues were relevant and somatic, and one block in which they were relevant and auditory. In

addition, one block of irrelevant (50% valid) somatic cues and one block of irrelevant auditory cues were presented. Irrelevant blocks were identical to those employed in Study 4. The order of block presentation was counterbalanced using a Latin square.

Experimental procedure was similar to that employed during Study 4, with a key difference in the instructions given. In contrast to Study 4 participants, Study 5 participants were informed about cue contingencies at the outset of the experiment and were also told at the beginning of each block whether subsequent cues would be 'helpful' (relevant cues) or 'unhelpful' (irrelevant cues). No further instructions were given to Study 5 participants regarding how they should respond to the cues.

In contrast to Study 4, white noise was delivered via both external speakers throughout all blocks regardless of cue modality.

7.2. Study 5 results

7.2.1. Sample characteristics

All depressed participants were diagnosed with chronic or recurrent forms of depressive illness. Mean age of onset was 28.57 years old (SD 15.21) and the mean number of years since first diagnosis was 23.10 (SD 16.60). Three participants (18.75%) reported that their first onset of depression was in childhood. Five individuals (31.25%) met criteria for at least one comorbid Axis 1 disorder at the time of testing, including Generalised Anxiety Disorder, Obsessive-Compulsive Disorder, Social Phobia, and Posttraumatic Stress Disorder (two participants met criteria for an anxiety disorder, one met criteria for PTSD, and two met criteria for an anxiety disorder and PTSD). Ten participants (62.5%) were currently prescribed antidepressant medication. One control participant was also prescribed psychotropic medication (amitriptyline for migraine).

Independent samples t-tests demonstrated no significant group differences in demographic characteristics including age, handedness and years of education. As expected, there were significant group differences in self-reported depression and anxiety (see Table 7.1).

Table 7.1: Study 5 demographic comparisons by group

	Depressed group (n = 16)	Control group (n = 16)	2-tailed t-tests
Demographics: mean (SD)			
Sex	12 women	12 women	-

Age (years)	51.69 (14.79)	50.31 (14.60)	t(30) = 0.27, p = 0.79
Handedness (EHI)	50.76 (69.75)	62.34 (65.59)	t(30) = -0.48, p = 0.63
Education (years)	15.25 (3.34)	16.50 (2.28)	t(30) = -1.24, p = 0.23
Mood measures: mean (SD)			
Depression (BDI-II)	32.63 (8.82)	2.06 (2.38)	$t(17.17^{1}) = 13.39$, $p < 0.001$
Anxiety (BAI)	19.96 (12.53)	1.44 (1.26)	$t(15.31^{2}) = 5.88$, $p < 0.001$

[1,2] Degrees of freedom adjusted due to unequal variances

EHI = Edinburgh Handedness Inventory, BDI-II = Beck Depression Inventory-II, BAI = Beck Anxiety Inventory

7.2.2. Reaction times

The data were cleaned according to the criteria employed in Study 4. In total, 2.14% of responses were assumed to have occurred as a result of anticipations, misfires and equipment failure and disallowed. There was no effect of group on the total number of disallowed trials (t(30) = -0.07, p = 0.94, d = 0.03). Examination of the remaining data revealed an acceptable error rate of 0.48%. Incorrect responses were removed from the RT data. In total, 21940 observations remained.

As in Study 4, no statistically significant interactions between group and SOA were found in initial analyses (ps > 0.1); therefore, SOA categories are collapsed in the analysis reported here. Uncued trials were not analysed.

A repeated-measures ANOVA with a between-participants factor of group and within-participants factors of cue relevance, cue modality, cue validity and target laterality was carried out on the RT data.

Within-participant effects

As expected, there was a large main effect of cue validity ($F(1, 30) = 72.79$, $p < 0.001$, $\eta_p^2 = 0.71$) with faster latencies to valid cues. The ANOVA also revealed a substantial interaction between cue relevance and cue validity ($F(1, 30) = 18.60$, $p < 0.001$, $\eta_p^2 = 0.38$) indicating that validity effects were larger in blocks where cues were relevant. A four-way interaction between relevance, modality, validity and laterality ($F(1, 30) = 5.15$, $p = 0.031$, $\eta_p^2 = 0.15$) indicated that in relevant blocks only, validity effects were larger on the left when cues were somatic and larger on the right when cues were

auditory. This effect is difficult to interpret on theoretical grounds. There were no other statistically significant within-participant effects (all ps > 0.05: see Appendix I.2.1 for details).

Group effects

Only one statistically significant group effect emerged from the RT analysis: an interaction between modality, validity and group ($F(1, 30) = 4.65$, $p = 0.039$, $\eta_p^2 = 0.13$). This indicated that depressed individuals demonstrated significantly increased validity effects relative to controls in response to somatic cues ($F(1,30) = 4.44$, $p = 0.043$, $\eta_p^2 = 0.13$), but not to auditory cues ($F(1, 30) = 0.77$, $p = 0.39$, $\eta_p^2 = 0.03$). Furthermore, within the depressed group validity effects were significantly larger in response to somatic cues than to auditory ones ($F(1,15) = 5.13$, $p = 0.039$, $\eta_p^2 = 0.26$), whilst validity effects among healthy controls did not differ from one modality to the other ($F(1, 15) = 0.12$, $p = 0.74$, $\eta_p^2 = 0.008$). See Figure 7.1 (left panel).

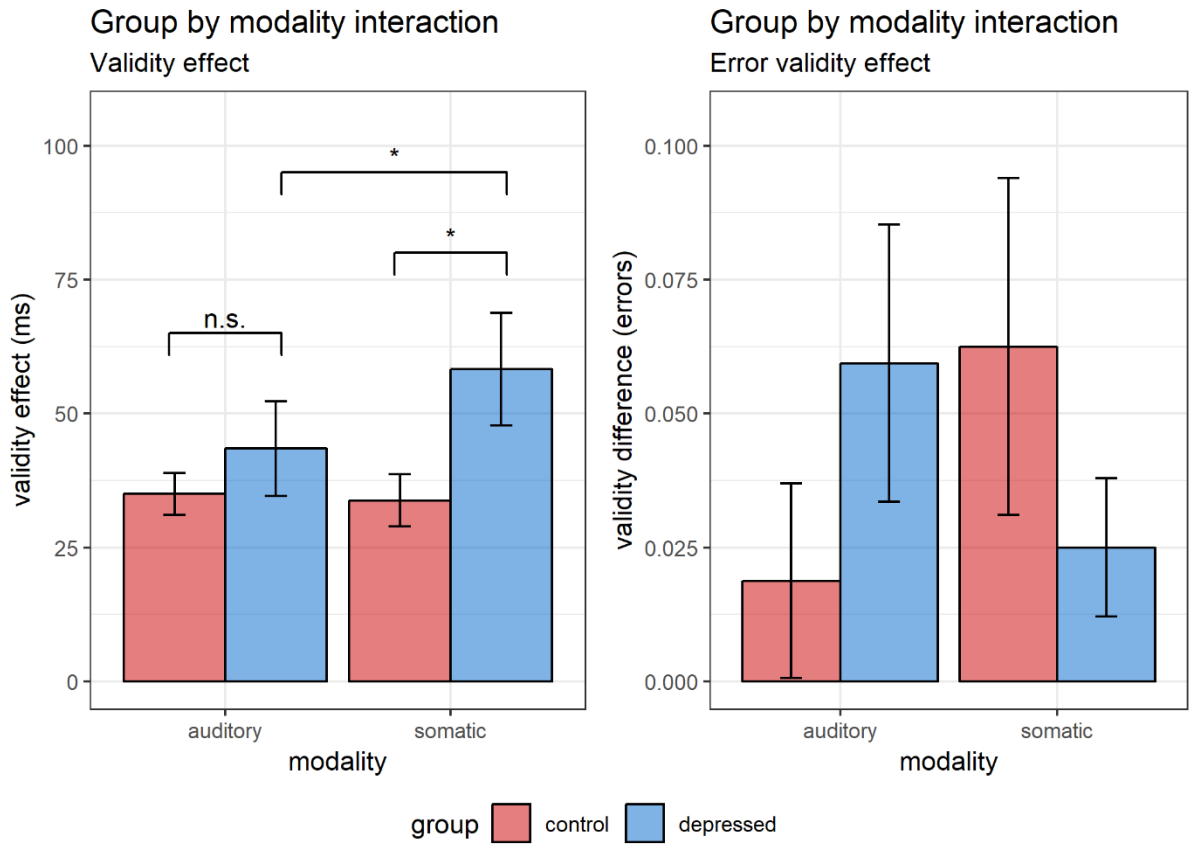


Figure 7.1: Study 5 outcomes of interest by group and cue modality. Error bars represent one standard error of the mean. Asterisks represent p-values less than 0.05. The left panel shows validity effects by group and modality, indicating that validity effects following somatic cues are exacerbated in depressed participants relative to healthy controls. Validity effects following somatic cues are significantly larger than those following auditory cues in depressed participants. "Error validity effects"

in the right panel were calculated by subtracting errors following valid cues from errors following invalid cues (shown by group and modality). This pattern of results is in the opposite direction to the RT outcomes, with depressed participants showing reduced influence of somatic cues on error rates relative to the influence of auditory cues. Control participants show the opposite pattern.

There were no other significant interactions between group and any other effect (all ps > 0.05: see Appendix I.2.1). Of note, in contrast to Study 4, now that relevant cues were employed there was no significant group by modality interaction in reaction time as a whole ($F(1,30) = 0.59$, $p = 0.45$, $\eta_p^2 = 0.02$). While the main effect of group observed in Study 4 did not reach significance, there was a trend in the same direction ($F(1, 30) = 3.56$, $p = 0.069$, $\eta_p^2 = 0.11$), suggesting somewhat slowed responses in the depressed group relative to healthy controls.

7.2.3. Errors

Following Study 4, errors were pooled according to modality and validity and an ANOVA with the factors of modality, validity and group was performed on the resulting scores. The ANOVA revealed a main effect of validity ($F(1,30) = 7.76$, $p = 0.009$, $\eta_p^2 = 0.21$) indicating that error rates were higher following an invalid cue relative to a valid one. Of interest, there was also an interaction between group, modality and validity ($F(1,30) = 7.79$, $p = 0.009$, $\eta_p^2 = 0.21$), indicating that auditory cues had greater influence than somatic cues on error rates among the depressed group, while the opposite pattern was observable in the control group (see Figure 7.1, right panel). No contrasts between group and condition met statistical significance however (ps > 0.05). There were no other significant effects (all ps > 0.4: see Appendix I.2.2).

7.2.4. IIV

A group x modality x validity ANOVA was also conducted on IIV scores, calculated using the method described in Study 4. The ANOVA revealed a significant main effect of modality, indicating that somatic cues were associated with greater response variability within the sample as a whole ($F(1, 30) = 4.54$, $p = 0.041$, $\eta_p^2 = 0.13$). There was also an interaction between modality and validity ($F(1,30) = 5.15$, $p = 0.031$, $\eta_p^2 = 0.15$) indicating that across the whole sample greater variability was associated with valid auditory cues and with invalid somatic cues. There were no other significant main or interaction effects (all ps > 0.1: see Appendix I.2.3).

7.2.5. Medication-free analyses

In order to rule out the potentially confounding factor of medication status on observed group differences, the RT analysis was repeated excluding 10 depressed individuals and 1 member of the control group who were prescribed psychotropic medication at the time of the study. The effect size

of the critical group difference (the interaction between modality, validity and group) actually increased, although it no longer reached statistical significance as a result of the markedly reduced power ($F(1, 19) = 3.78$, $p = 0.067$, $\eta_p^2 = 0.17$). This suggests that medication status is unlikely to account for this finding.

7.2.6. Correlation analysis

As in Study 4, an additional analysis was undertaken to rule out the possibility that the observed group difference in somatic validity effect was accounted for by anxiety symptomatology rather than by depression per se. Partial correlations demonstrated that the relationship between somatic validity effect and BDI score, controlling for BAI score, remained statistically significant ($r_{partial}(29) = 0.42$, $p = 0.019$), while the relationship between somatic validity and BAI score, controlling for BDI score, was not ($r_{partial}(29) = -0.21$, $p = 0.26$).

7.3. Study 5 summary

Study 5, employing relevant cues, demonstrated increased validity effects for somatic relative to auditory information in the depressed group, implying disproportionate attentional capture by somatic signals. The direction of the effect therefore provides support for the hypothesis that the salience of somatic signals is amplified, rather than attenuated, for depressed participants.

Of interest, the error data also yielded an interaction between group, modality and validity, but in the opposite direction. This "error validity effect" – the result of subtracting error rates following valid cues from error rates following invalid cues – was largest for depressed participants when cues were auditory, with healthy controls showing the opposite pattern. This finding would also be consistent with the amplification theory of somatic stimuli in depression, if it is assumed that depressed participants find disproportionately salient somatic cues easier to distinguish from targets than their auditory counterparts. Less distinctive cues may be more frequently mistaken for targets and responded to accordingly, a process which would be expected to yield few errors following valid cues but relatively many following invalid ones. Conversely, a highly salient cue may be highly distinguishable from the target, with the result that error rates are less dependent on cue validity.

In contrast to Study 4, there was no evidence of reduced attentional efficiency in the depressed group, despite the fact that white noise was played continuously throughout all blocks. This suggests that white noise was not responsible for the loss of attentional efficiency observed in the depressed group during somatic blocks in Study 4, although as a null result it must be interpreted cautiously. The significant group x modality x validity effect, observed here with constant white noise, also suggests that the modality effect in Study 4 was not dependent on the difference in white noise.

In summary, the results of Studies 4 and 5 taken together suggest that somatic signals have disproportionate salience for persistently-depressed individuals relative to healthy controls. In addition, increased validity effects in depressed participants in both studies – occurring supra-modally with longer time-on-task in Study 4, and uniquely following somatic cues in Study 5 – may indicate (following Yu & Dayan, 2003) an attenuation of the sensory precision of visual targets relative to the precision of expectations set up by the cue. Study 6 was designed with the aim of replicating these findings and exploring them further, using a computational model to tease apart the respective influences of sensory precision and salience, and to provide estimates of their magnitude in depressed participants relative to controls.

Chapter 8. Study 6: Computational model of the salience and precision of sensory signals during covert attentional orienting in persistent depression

Studies 4 and 5 supported the hypothesis that somatic signals hold disproportionate salience for persistently-depressed individuals relative to healthy controls. In addition, increased validity effects were observed in depressed participants in both studies – occurring supra-modally with longer time-on-task in Study 4; and following particularly salient cues in Study 5. A possible interpretation of these disparate interactions is that a group difference in validity effect emerges most strongly under conditions of higher effort or task difficulty. If this is the case, it should be possible to replicate this effect reliably by rendering the task more difficult: in Study 6 cue and target stimuli switched roles between blocks to increase the difficulty of target discrimination. In addition, systematically increased validity effects in persistently-depressed participants relative to controls may indicate (following Yu & Dayan, 2003) an attenuation of the sensory precision of visual targets relative to the precision of expectations set up by the cue.

Study 6 was therefore designed with the aim of replicating the Study 4 and 5 findings with respect to the impact of depression on both somatic salience and the magnitude of validity effects, and directly investigating the hypothesis that persistent depression may be associated with attenuated salience and precision in the representation of sensory signals across sensory modalities. An established computational model developed by Feldman and Friston (2010) provides a framework for modelling sensory precision in the context of the Posner covert attention task, and in Study 6 an adapted version of this model was optimized with data derived from the experimental task to estimate its underlying parameters for depressed participants in comparison to controls.

Feldman and Friston (2010) additionally used their model to simulate electroencephalogram (EEG) data from human participants recorded during attentional tasks. Event-related brain potentials (ERPs) are EEG recordings collected during stimulus presentation or task performance; and provide an index of cognitive processing with high temporal specificity. Early (P1 and N1) ERP components are positively modulated by attention and are thought to reflect sensory or perceptual processing (e.g., Luck, Woodman, & Vogel, 2000) while the later P3 component has an amplitude that is inversely related to the probability of the stimulus, and positively related to its salience (Nieuwenhuis, Aston-Jones, & Cohen, 2005): it has been suggested that the P3 indexes prediction error (Feldman & Friston, 2010) or context updating (Donchin & Coles, 1988). Of interest, a substantial body of literature (reviewed in Bruder, Kayser, & Tenke, 2012) suggests that acute depression is associated with reductions in the amplitude of the P3 component. Feldman and Friston (2010) relate early and late ERP components to

simulated sensory and contextual prediction error arising from their model; employing the same approach we used our optimized model to simulate ERP components in depressed populations engaged in similar tasks.

As in Studies 4 and 5, persistently-depressed and control groups participated in a variant of the covert attention paradigm described in the Methods in Chapter 2, and a classical ANOVA was performed to check that our basic predictions were met. The data were then used to optimize a predictive processing model of the task, closely based on that of Feldman and Friston (2010). We developed a range of model variants, each locating key group differences in a different combination of model parameters; and performed a model comparison to identify the most probable version of the model, given the data. We predicted that persistently depressed participants would demonstrate larger validity effects than healthy controls, reflecting an overreliance on prior expectation relative to sensory prediction error. Following Studies 4 and 5, we predicted that in comparison to controls, the salience of somatic cues and targets would be amplified among depressed participants relative to the salience of auditory stimuli. Finally, we predicted that larger validity effects would translate into reduced sensory precision across stimulus modalities among depressed participants when fit to the model.

8.1. Study 6 design

Participant recruitment, materials and procedure were as described in the Method section in Chapter 2.

Participants were instructed to maintain central fixation while responding as quickly and as accurately as possible to targets. In each trial, a target was presented to either the right or left side of fixation, and participants indicated the location of the target using a spatially congruent foot pedal response. A spatially valid, neutral or invalid cue was presented immediately before the target. 8 trials were presented for every combination of SOA (3 levels: 100ms, 300ms, 500ms), validity (3 levels: valid, neutral, invalid) and laterality (2 levels: left, right) and there were additionally 8 uncued trials for each laterality, totalling 160 trials per block. Trial types were presented within blocks in a randomized order, and in total participants completed 4 blocks counterbalanced using a Latin Square. In one block, targets were auditory and cues were somatic; in a second, targets were somatic and cues were auditory. In the remaining two blocks, targets were visual and cues were auditory or somatic respectively. During all blocks, continuous white noise was delivered via the peripheral speakers to mask any sound associated with tactor vibration.

Four brief practice blocks (reflecting the 4 experimental blocks) were completed to check participants' understanding of the task and to familiarise them with the equipment.

8.2. Study 6 model

The model was closely derived from Feldman and Friston's (2010) predictive processing model of covert attention. This model allows hidden states to bias sensory precision towards the left or right side of space prior to target presentation depending on the location of a cue. Evidence for the presence of a target is accumulated through an updating process utilising precision-weighted prediction errors. A response is triggered once the posterior probability that the target is present reaches a given level (80% in the original model). This probability is a function of both the location and the scale (i.e., inverse precision) of the target estimate. Therefore, the hidden states encoding precision affect both target recognition and the confidence associated with it, with a consequent effect on reaction times.

Because our experimental paradigm differed slightly from the canonical Posner paradigm modelled by Feldman and Friston, some adaptations were made to the model framework. First, we replaced the single precision gain-control parameter γ with modality-specific parameters γ_{target} and γ_{cue} intended to reflect bottom-up salience attributes of the different stimuli in addition to top-down salience reflecting their prescribed role as cue or target in a given trial. Secondly, given that all cues in our study were exogenous, we omitted the high-precision central channel which produced endogenous cueing in the original model. The basic form of our adapted model is illustrated in Figure 8.1.

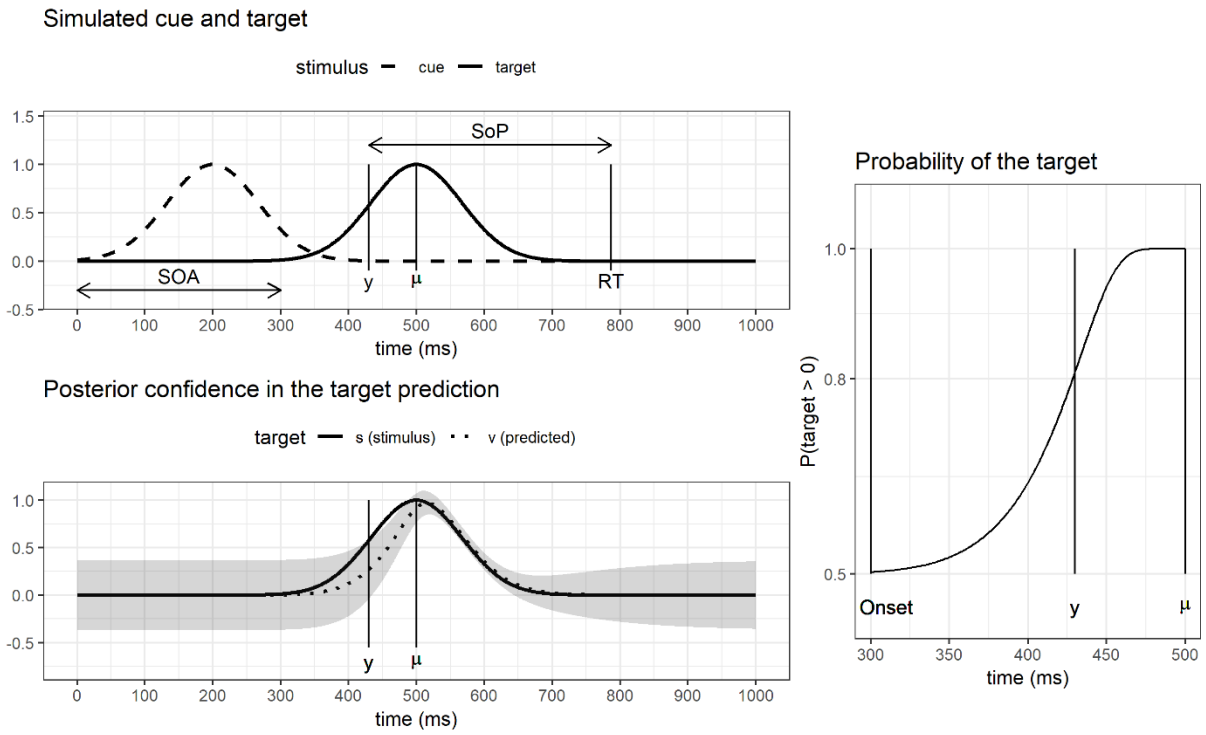


Figure 8.1: Study 6 computational model - cue, target and target probability over the course of a single trial. The upper left panel shows a simulated cue and target (SOA=300ms) situated within a single trial. y represents the point at which 80% confidence in the presence of the target is achieved. Speed of processing (SoP) components contribute to the remainder of the RT. The lower left panel shows the same simulated target (s) and the associated prediction of the underlying hidden cause (v). This prediction is a Gaussian function, varying over time, with mean shown by the dotted line, and standard deviation shown by the surrounding grey area. The uncertainty associated with the expectation of v reflects the estimated precision of the sensory data, which is affected by cue validity: here the target follows a neutral cue. The right panel shows the resulting posterior confidence in the presence of the target (the probability that v is greater than 0) over time.

Cues and targets were auditory, somatic or visual stimuli presented well above perceptual threshold for 400ms intervals. For the purposes of the model, all stimuli were simulated using a Gaussian function with a standard deviation of 67ms and with the mean (μ) located at the midpoint of the veridical stimulus (i.e., 200ms from the start of the trial for a cue, and 300, 500 or 700ms for a target depending on SOA). This generated simulated stimuli of approximately 400ms duration with an onset appropriate to their category and condition (Figure 8.1, upper left panel). Each trial was modelled as lasting for 1 second and was comprised of one thousand 1ms time-bins.

Sensory data resulting from cue or target presentation is compared to the representation of its cause v, inducing prediction error ε. Prediction error, weighted by its precision Π, drives changes in the representation of v over time. The denominator Π + C (where C is a constant) is included in the

weighting to ensure that the weight does not drop below 0 or exceed 1. Precision Π is derived from the log-precision π which is the sum of hidden state x and basal sensory precision parameter τ. Hidden state x represents state-dependent expectations of sensory precision, and its changes over time are driven by the causes v weighted by salience parameters γ, and decay at rate ϑ. A spatial component is introduced by the validity indicator which determines the impact of an invalid, neutral or valid cue on x, given that x represents the side of space containing the target.

$$s = v + \varepsilon \tag{63}$$

$$\xi = \varepsilon\left(\frac{\Pi}{\Pi + C}\right) \tag{64}$$

$$\dot{v} = \xi \tag{65}$$

$$\Pi = \exp(\pi) \tag{66}$$

$$\pi = x + \tau \tag{67}$$

$$\dot{x} = \gamma_{target} v_{target} + validity(\gamma_{cue} v_{cue}) - \vartheta x \tag{68}$$

$$validity \in -1, 0, 1 \tag{69}$$

Priors for the parameters to be estimated were flat and broad relative to the posterior estimates as follows:

$$\tau \sim Uniform(0,5) \tag{70}$$

$$\gamma_{cue} \sim Uniform(0,1) \tag{71}$$

$$\gamma_{target} \sim Uniform(0.01,1) \tag{72}$$

$$\vartheta \sim Uniform(0,0.01) \tag{73}$$

The limits on the priors for γ_{target} and ϑ reflect the model constraint that x's decay must be slower than its accumulation (Feldman and Friston, 2010).

8.2.1. Data standardization

Given model assumptions, the raw RTs can be thought of as the result of a mixture of processes, including the (standardized) perceptual recognition process captured by the model, the additional contribution of modality-specific perceptual speed-of-processing lags, and the latencies associated

with motor preparation and motor response implementation. The sum-total of all perceptual and motor speed-of-processing factors SoP (Figure 8.1, upper left panel) was estimated as follows:

$$SoP = RT - y \tag{74}$$

where y represents the process of perceptual recognition described in the model and specifically the point in peristimulus time at which 80% confidence in the presence of the target is achieved. Although neither SoP nor y are known, the estimation is rendered more tractable by adding a constant d to both RT and y, where d is defined as the difference between the point of 80% confidence and target mean μ. Equation 12 can therefore be rearranged as

$$SoP = RT + d - \mu \tag{75}$$

d is determined by the underlying model parameters and therefore can be estimated by fixing those parameters at reasonable values. For the purposes of this estimation we used only neutrally-cued data and followed the original model in fixing confidence at 80% and basal precision (τ) at 2. Decay parameter ϑ was fixed at 0.01. SoP can be estimated in this way either for the sample as a whole, or independently by group.

8.2.2. Model optimization

Feldman and Friston (2010) simulated RTs by finding the point in peri-stimulus time at which the posterior probability of the target reached 80%, i.e., finding t where

$$P(v_t > 0) = 0.8 \tag{76}$$

This timepoint can be identified by applying the CDF of the standard normal distribution to a z-score derived from the mean and standard deviation of v_t

$$P(v_t > 0) = 1 - \Phi\left(\frac{0 - v_t}{\sqrt{\exp(-\pi)}}\right) = 0.8 \tag{77}$$

Rearranging, we can derive an estimate of precision at the point of 80% confidence from the data y:

$$\hat{\pi}_y = -\log\left(\left(\frac{v_y}{-\Phi^{-1}(0.8)}\right)^2\right) \tag{78}$$

where y enters the model as an index indicating the timepoint at which 80% confidence, and hence (ultimately) a response, is achieved. The model is optimized by minimizing the difference δ between each estimate of precision derived from the data and its counterpart derived from the model parameters:

$$\delta = \hat{\pi}_y - \pi_y \quad (79)$$

hence δ can act as an informal index of model fit.

8.3. Study 6 results

8.3.1. Sample characteristics

All depressed participants were diagnosed with chronic or recurrent forms of depressive illness. Six individuals (37.5%) met criteria for chronic depression and 10 (62.5%) met criteria for recurrent depression. Of these, two participants described respective histories of 9 and 15 past episodes of depression; the remainder reported that they had experienced too many depressive episodes to count. Nine participants (56.25%) reported that their first depressive episode occurred in childhood. Mean age of onset was 19.00 years old (SD 6.81) and the mean number of years since first diagnosis was 18.19 (SD 12. 49). Eleven individuals (68.75%) met criteria for at least one comorbid Axis 1 disorder including Obsessive-Compulsive Disorder, Social Phobia, Generalised Anxiety Disorder, Anorexia and Binge Eating Disorder (five participants met criteria for one anxiety disorder, three met criteria for two anxiety disorders, and one met criteria for three anxiety disorders. One participant met criteria for an eating disorder, and one met criteria for an anxiety disorder and an eating disorder). Nine depressed participants (56.25%) were prescribed psychotropic medication at the time of testing (n=4 were prescribed an SSRI, one of these with an additional sedative-hypnotic; n=1 was prescribed an SNRI; n=1 a tetracyclic; n=1 a sedative-hypnotic, n=1 an atypical antipsychotic and a sedative-hypnotic; and n=1 a mood stabiliser, and SNRI and a neuroleptic).

Two members of the control group were also prescribed psychotropic medication, for sleep (a sedative-hypnotic) and pain (unspecified), respectively.

A series of t-tests demonstrated that there were no significant group differences with respect to the matched characteristics of age and years of education (see Table 8.1). There was a non-significant trend towards a group difference in handedness: handedness was therefore included as a covariate in the analysis as described below. As expected, depressed participants differed significantly from never-depressed controls with respect to self-reported symptoms of depression and anxiety.

Table 8.1: Study 6 demographic comparisons by group

	Depressed group n=16	Control group n=16	2-tailed t-tests

Demographics: mean (SD)			
Sex	14 women	14 women	-
Age (years)	37.19 (16.56)	38.44 (17.27)	t(30) = -0.21, p = 0.84
Handedness (EHI)	55.83 (67.42)	90.69 (18.99)	t(17.37[1]), p = 0.062
Education (years)	16.31 (2.30)	15.81 (3.41)	t(30) = 0.49, p = 0.63
Mood measures: mean (SD)			
Depression (BDI-II)	31.75 (12.06)	2.81 (2.59)	t(16.38[2]) = 9.39, p < 0.001
Anxiety (BAI)	24.13 (14.88)	1.69 (1.78)	t(15.43[3]) = 5.99, p< 0.001

[1,2,3] Degrees of freedom adjusted due to unequal variances

EHI = Edinburgh Handedness Inventory, BDI-II = Beck Depression Inventory-II, BAI = Beck Anxiety Inventory

8.3.2. Analysis of variance

For simplicity, only cued trials were included in the analyses (total 18432 trials). RTs shorter than 200ms or longer than 1500ms were assumed to result from anticipations or misfires and removed from the dataset (197 observations; 1.07%). An additional 73 errors (0.4%) were also removed.

A repeated-measures ANOVA with a between-participants factor of group and within-participants factors of cue modality, cue validity, SOA and target laterality was carried out. The data were pooled across target modalities for simplicity and because the design was not fully crossed. A Greenhouse-Geisser correction was employed where the assumption of sphericity was not met.

Within-participants effects

There was a marked effect of cue validity ($F(1.57, 47) = 65.76$, $p < 0.001$, $\eta_p^2 = 0.69$) in the expected direction, indicating that participants displayed robust validity effects (see Figure 8.2). There was also a large effect of SOA ($F(1.68, 50.31) = 243.23$, $p < 0.001$, $\eta_p^2 = 0.89$) indicating that RTs decreased as SOAs increased. There was an interaction between cue modality and SOA ($F(2, 60) = 23.13$, $p < 0.001$, $\eta_p^2 = 0.44$) suggesting that responses to targets with auditory cues were speeded relative to targets with somatic cues but only at longer SOAs; and an interaction between validity and SOA ($F(4, 120) = 8.92$, $p < 0.001$, $\eta_p^2 = 0.23$) indicating that validity effects were smallest at the longest SOA. There was an interaction between validity and laterality ($F(2,60) = 3.29$, $p = 0.044$, $\eta_p^2 = 0.10$) suggesting that

responses to left-sided targets were speeded relative to right-sided targets only when cues were neutral; and finally an interaction between SOA and laterality ($F(1.65, 49.36) = 7.13$, $p = 0.002$, $\eta_p^2 = 0.19$), suggesting that left-sided responses were slightly quicker at shorter SOAs while right-sided responses were slightly quicker at the longest. There was also a non-significant trend towards a main effect of modality ($F(1,30) = 3.96$, $p = 0.056$, $\eta_p^2 = 0.12$) suggesting that responses to targets with auditory cues were (unreliably) faster than responses to targets with somatic cues. There were no other significant main effects or interactions (all ps>0.1: see Appendix I.3 for details).

Group effects

There was a statistically significant interaction between group and cue validity ($F(1.57, 60) = 4.37$, $p = 0.026$, $\eta_p^2 = 0.13$) indicating exacerbated validity effects in the depressed group relative to healthy controls, as predicted (see Figure 8.2). There was no main effect of group (p>0.5), and no other significant interactions between group and any other factors (all ps>0.08).

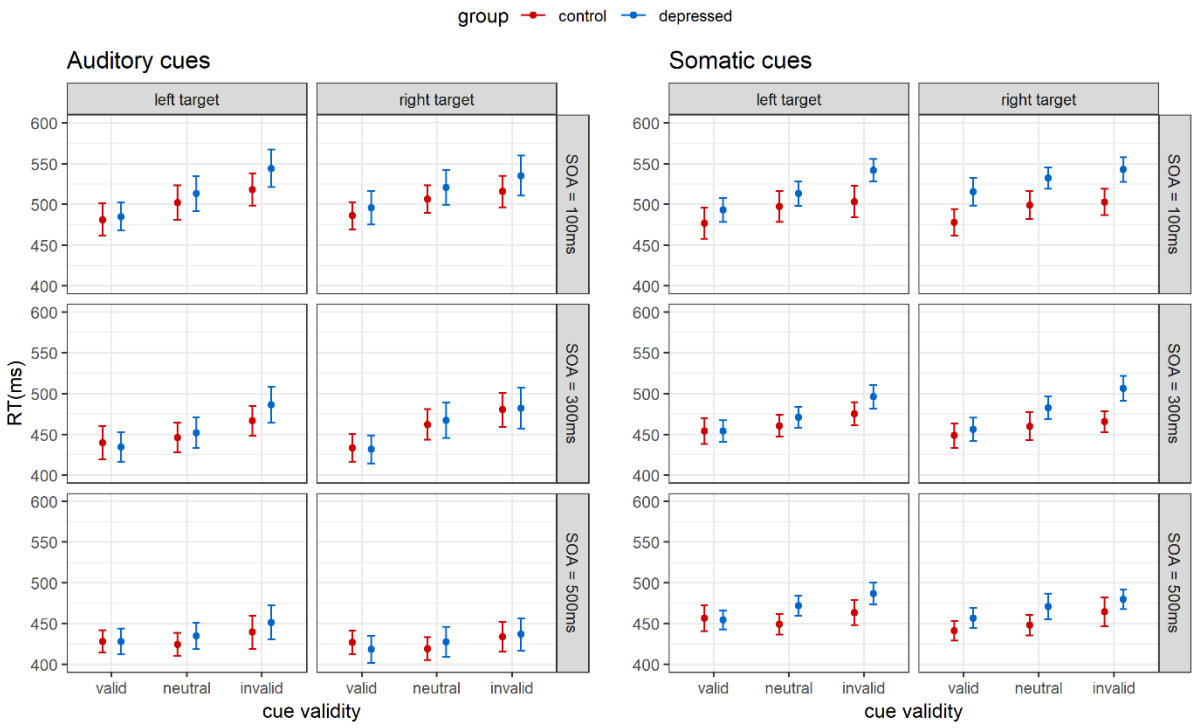


Figure 8.2: Study 6 reaction times by group and cue validity. RTs (ms) are panelled by cue modality, SOA and target laterality. Error bars represent 1 standard error of the mean (between-groups error). Validity effects are exacerbated in the depressed group relative to healthy controls.

Handedness

Due to a non-significant trend towards a group difference in handedness (see Table 8.1 above) the analysis was re-run as an ANCOVA with handedness (EHI score) as a covariate. There was no main

effect of handedness ($p > 0.6$) and no interaction of handedness with any other factor ($ps > 0.09$). All outcomes of interest were unaffected by its inclusion (see Appendix H for details).

8.3.3. Model fitting and selection

The same data, averaged by group and condition, were then used to optimize a model of precision-weighted predictive processing in the covert orienting paradigm.

Speed of processing estimation

Speed of processing (SoP) components, estimated for the whole sample, are shown in Table 8.2.

Table 8.2: Study 6 estimated sum of perceptual and motor speed of processing RT components by target modality and SOA.

	Perceptual and motor SoP components (ms)		
SOA	*Auditory target*	*Somatic target*	*Visual target*
100	478	452	287
300	432	394	244
500	430	357	222

Model variations

A series of model variations was developed to investigate the most probable source, given overall model assumptions, of the group difference in validity identified in the classical analysis (Figure 8.2). All model variations were nested within the overall model described above.

1. Salience model: group difference in γ

In the first model, SoP estimates were based on the sample as a whole; confidence was fixed at 80%; and a single estimate of basal precision parameter τ was derived for the whole sample. Salience parameters γ were estimated independently for each group.

2. Basal precision model: group difference in τ

In the second model, SoP estimates were based on the sample as a whole, confidence was fixed at 80%, and salience parameters γ were estimated for the whole sample. Basal precision parameter τ was estimated independently for each group.

3. Confidence model: group difference in α

The preceding models both posit group differences in mechanisms contributing to perceptual precision. An alternative hypothesis suggests that depressed participants differ from healthy controls not in terms of perception itself, but in requiring a higher level of confidence (i.e., more time for evidence accumulation) before being willing to commit to a response. In the third model, therefore, a confidence parameter α was estimated for each group as follows:

$$\alpha \sim Uniform(0.5,1) \tag{80}$$

The confidence parameter α overlapped substantially with basal precision parameter τ, due to their similarity in roles. An increase in τ increases the precision of the conditional confidence in the target, pulling the lower bound of the confidence estimate away from 0. Similarly, a reduction in α, by definition, pulls the lower bound of the confidence estimate in the same direction, reducing the amount of precision required to attain the cut-off. Only the unique contribution of τ to the prediction of cue and target differentiates the two parameters. Due to this overlap, attempts to estimate the two parameters simultaneously were found to lead to difficulties with convergence, and so τ was fixed at 2 for both groups. SoP estimates and salience parameters γ were estimated for the sample as a whole.

4. Speed of processing model: group difference in SoP

The fourth model assumed that confidence and precision parameters did not differ by group, and that group differences were solely accounted for by differences in perceptual and motor speed of processing. SoP and its consequences for data y were estimated independently for the two groups. Confidence was fixed at 80%, and precision parameters γ and τ were estimated for the whole sample.

Combination models

All possible combinations of these models were also considered (a total of 15 models). Models in which both τ and α varied by group were discarded following initial runs which demonstrated that these functionally similar parameters traded off each other when both were allowed to vary within the same model, causing difficulties with convergence. The remaining 11 models were compared in terms of fit (Appendix A.3., Figure A.6).

It was observed that the addition of a group difference in SoP to any other group difference or combination of differences worsened the fit of the model, without any compensatory gains in terms of reduced model complexity. Five models which included group differences in SoP and at least one other parameter were discarded for this reason. Six models remained: the four index models described above, and two combination models as follows:

5. Salience and precision model: group differences in γ and τ

This model assumes that group differences are present in both state-dependent and basal precision parameters (i.e., salience parameters γ and basal precision parameter τ). These parameters were allowed to vary by group, while confidence was held constant at 80% and SoP was estimated for the whole sample.

6. Salience and confidence model: group differences in γ and α

This model locates group differences in the salience parameters γ and the confidence parameter α. Basal precision was held constant at 2 and SoP was estimated for the whole sample.

Bayesian model comparison

All six models were entered into a Bayesian model comparison using the product space method (Carlin & Chib, 1995). The model comparison proceeded by fitting each model to the data y averaged by group, cue modality, cue validity and SOA; i.e., pooled over target modality as in the ANOVA (and for the same reasons). Posterior model probabilities are shown in Table 8.3. Bayesian model comparison penalises model complexity in addition to rewarding good fit, and so the basal precision model has a higher posterior probability than the more complex salience model, despite the latter's better fit (Appendix A.3., Figure A.6). However, the best-fitting model was also the most probable one, providing a better description of the data by a Bayes factor of 13.02 relative to its nearest competitor. This model was the salience and precision model, in which both the salience parameter γ and the basal sensory precision parameter τ varied by group.

Table 8.3: Study 6 posterior model probabilities for predictive processing model of covert orienting

Model		Location of group difference	Posterior probability
5	Salience and precision model	γ and τ	0.93
6	Salience and confidence model	γ and α	0.07
2	Basal precision model	τ	2.70×10^{-12}
1	Salience model	γ	1.28×10^{-14}
3	Confidence model	α	8.63×10^{-18}
4	Speed of processing model	SoP	8.34×10^{-23}

8.3.4. Salience and precision model

Parameter estimates for the best-fitting (salience and precision) model were derived by fitting the model to the data averaged by group, cue modality, cue validity and SOA and pooled over target modality as before. This approach yielded estimates for the basal precision parameter τ and the decay parameter ϑ, and for salience parameter γ by category (i.e., by whether a stimulus was assigned to cue or target status during a given trial). It could not yield an estimate for target salience by modality due to the pooling. In order to derive these modality-specific estimates, the model was independently fit to the data for each cue modality, averaged by group, target modality, cue validity and SOA. To ensure consistency, τ and ϑ were held constant at the most probable values derived from the pooled analysis. A posterior predictive check on model fit is shown in Appendix A.3 (Figure A.7).

Figure 8.3 shows the resulting parameter estimates. As can be seen, the depressed group and the control groups differ credibly in stimulus salience (γ) as a function of both stimulus relevance (cue vs target) and modality (auditory vs somatic) stimulus salience. When compared by stimulus category (cue versus target) averaging over modality, the γ estimates indicate that depressed participants assign higher salience to cues and lower salience to targets relative to healthy controls; suggesting, perhaps, a deficit in the ability to discriminate or filter stimuli by behavioural relevance. When compared by stimulus modality (averaging over category) the γ estimates suggest that depressed participants assign a disproportionate salience to somatic stimuli in the context of a weakened influence of auditory stimuli relative to healthy controls, consistent with our hypothesis.

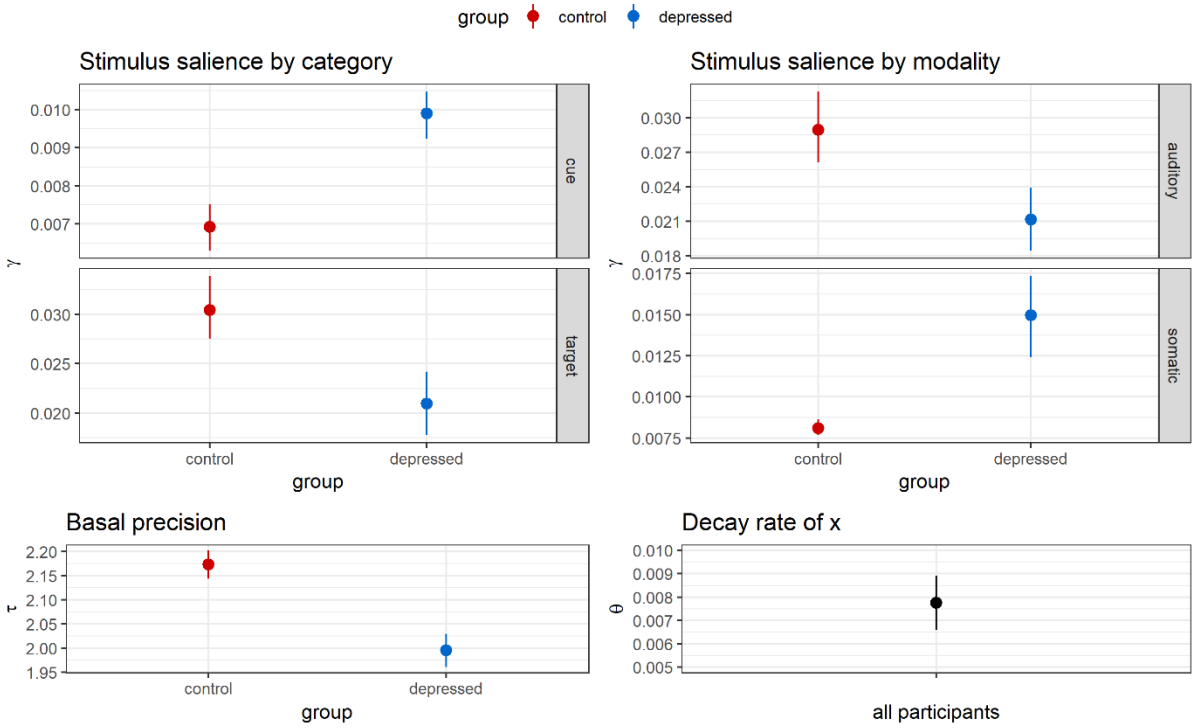


Figure 8.3: Study 6 salience and precision model parameters by group. Panels show parameter estimates for the salience and precision model. Points represent the mean of the posterior distribution for each parameter: error bars are 95% credible intervals.

Estimates for the basal precision parameter τ also differ between groups, with a credibly smaller estimate for the depressed group relative to healthy controls.

The consequences of these group differences in target salience and basal precision for perception and action in the context of a covert attention trial are illustrated in Figure 8.4. The upper row of panels in Figure 8.4 shows the consequences for a trial when the target is preceded by a valid cue (not shown), while the lower row shows the consequences when the cue is invalid. The depicted trial is one in which the SOA is 100ms; parameters are averaged over cue and target modality.

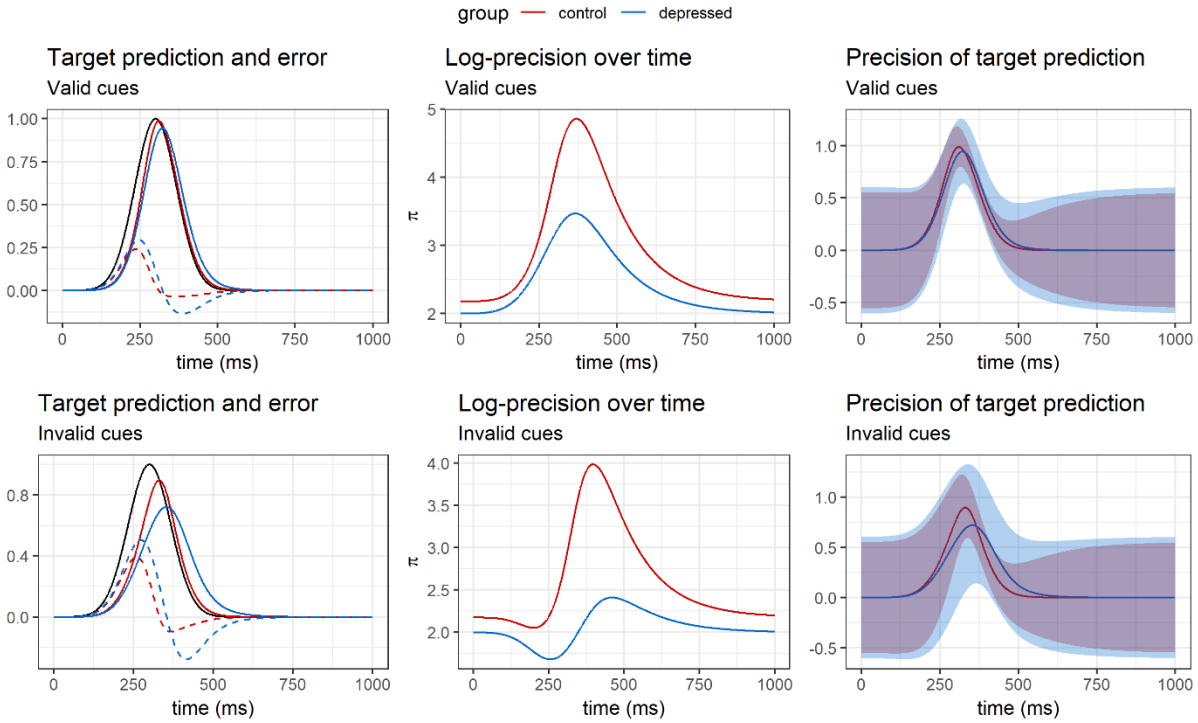


Figure 8.4: Study 6 consequences for perception of group differences in salience and precision. Targets are represented following valid cues (top row) and invalid cues (bottom row). Targets s (black lines), target predictions v (unbroken coloured lines) and absolute prediction error ε (dashed lines) are shown by group in the leftmost panels; log-precision by group over the course of the trial in the central panels, and the estimated precision of the target predictions (90% confidence regions) by group in the rightmost panels. The depicted trial represents an SOA of 100ms, and parameters are averaged over target and cue modality. Cues are not shown for greater readability of the plots.

The leftmost panels of Figure 8.4 show the target s (black line) together with the target predictions v as perceived by healthy controls (red line) and depressed participants (blue line). Absolute prediction

error ε for the respective groups is shown by dashed lines. When cues are valid, absolute prediction error is relatively small for both groups; when they are invalid it is increased for both groups, but disproportionately so for depressed participants. This impact on perception is driven by reduced precision of the prediction error which dampens its ability to influence posterior beliefs.

The reduction in log sensory precision in depressed participants relative to healthy controls is depicted in the central panels of Figure 8.4. Regardless of cue validity, sensory precision is reduced in the depressed group due to the combination of a reduction in the basal sensory precision level τ together with reduced influence of the target salience parameter γ_{target}. When the cue is invalid, sensory precision suffers yet further in the depressed group due to the disproportionate influence of γ_{cue} in reallocating precision to the opposite side of space. The rightmost panels of Figure 8.4 combine the target predictions from the leftmost panels with the sensory precision estimates of the middle panels to show the target predictions ν surrounded by 90% conditional confidence regions which are inversely proportional to the estimated precision of the sensory data over time. Conditional confidence is reduced for the depressed group relative to healthy controls regardless of cue validity, but the reduction is disproportionately large when cues are invalid, necessitating a compensatory increase in evidence accumulation which can account for the group x validity effects in RT observed in the classical analysis.

Participant-level analyses

The analyses described above were conducted on data averaged across participants within groups. As a check on the conclusions, the model was independently fit to the individual data of each of the 32 participants and participant-level parameter estimates derived using an identical procedure to that used to derive the group-level estimates. The outcomes of the participant-level analyses (Appendix A.3., Figure A.8) demonstrate that group differences in parameter estimates remain reliable when participant-level estimates are entered into a group comparison, and therefore suggest that the conclusions drawn from the group-level analysis are robust.

Medication-free analyses

The ANOVA and group comparisons based on participant-level parameter estimates were repeated, including only the 21 participants who were medication-free at the time of the study. No substantive differences in outcomes were identified (see Appendix B.5. for details).

Additional analyses

Somatic salience, anxiety and interoceptive sensibility

The finding that somatic stimuli have increased salience for depressed individuals relative to healthy controls is consistent with the outcomes of Studies 4 and 5, but nevertheless requires explanation. One possibility is that somatic stimuli are salient among depressed participants as a result of relatively high levels of anxiety in this group (Dunn, Stefanovitch, et al., 2010). An alternative hypothesis suggests that if depressed individuals habitually suppress or attenuate endogenous interoceptive or bodily signals, exogenous somatic or bodily prediction error arising from a novel task may be relatively unexpected and hence more surprising. In this case the tendency to be aware of interoceptive experience should be negatively associated with relative somatic salience.

As an initial test of this hypothesis, participants completed a Multidimensional Assessment of Interoceptive Awareness (MAIA: Mehling et al., 2012). Self-reported interoceptive awareness, also known as interoceptive sensibility (Garfinkel et al., 2015) was estimated using the total MAIA score. Interoceptive sensibility was reliably decreased in the depressed group relative to controls ($t(30) = -5.54$, $p < 0.001$). Interoceptive sensibility (total MAIA score) and anxiety (BAI score) were then simultaneously regressed onto relative somatic salience. Both interoceptive sensibility (β=-0.26, $p = 0.011$) and anxiety (β=0.008, $p = 0.03$) predicted unique variance in relative somatic salience, in the expected directions. With respect to overall model fit, adjusted $R^2 = .373$. Relationships are shown in Figure 8.5 (upper panels).

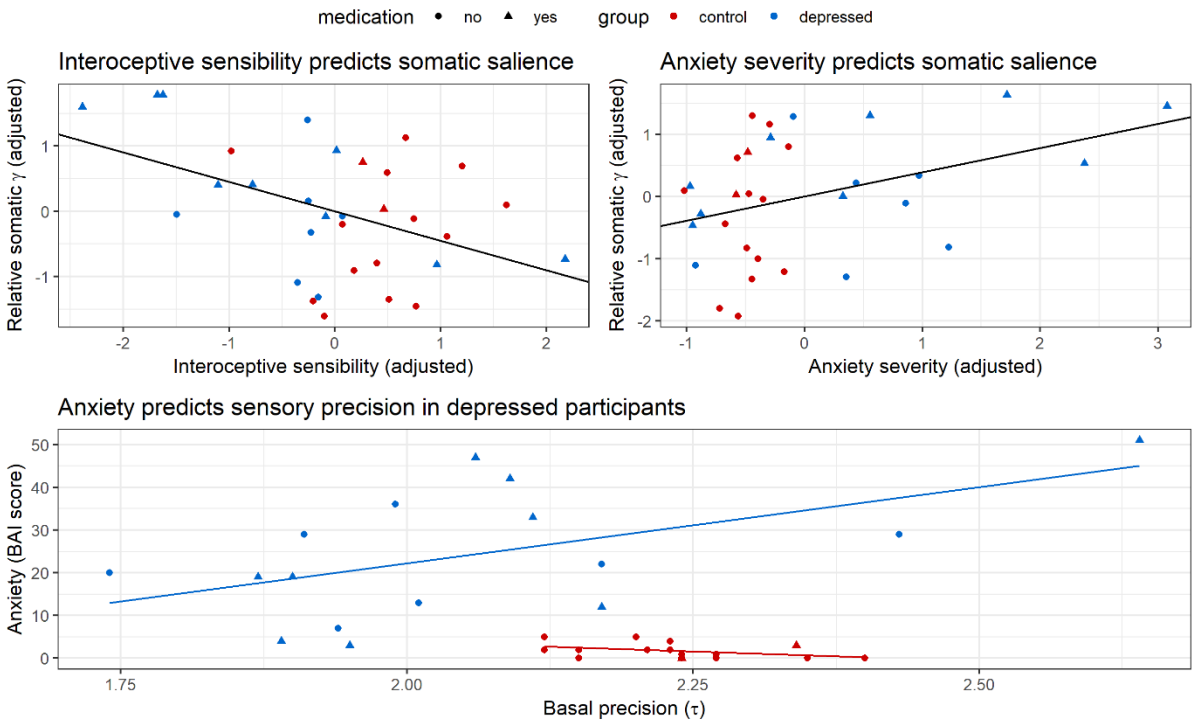


Figure 8.5: Study 6 additional analyses – relationships of somatic salience with interoceptive sensibility and anxiety severity, and of sensory precision with anxiety severity. Upper panels: partial correlation plots. On the left, interoceptive sensibility is negatively associated with relative somatic salience, adjusting for the influence of anxiety severity. On the right, anxiety severity is positively associated with relative somatic salience, adjusting for the influence of interoceptive sensibility. Lower panel: despite relatively low basal precision on average in the depressed group, a positive relationship between participant-level estimates of basal precision and anxiety severity is apparent among depressed participants; the same relationship is not present in healthy controls.

Basal sensory precision and anxiety

Assuming that the basal precision parameter τ reflects a tonic level of arousal, external focus, or scanning attention, a question of interest was the relationship between this parameter and anxiety levels. Figure 8.5 (lower panel) shows individual τ estimates plotted against BAI scores for depressed participants (in blue) and controls (in red). Although τ estimates in the depressed group are in general smaller than those in controls, higher levels of anxiety in depression are associated with higher τ ($r(16) = 0.54$, $p = 0.033$), an association that is not present in controls ($r(16) = -.41$, $p = 0.11$). This may suggest that depression and anxiety exert opposing influences on basal precision, although the numbers here are too small to draw firm conclusions.

Electrophysiology predictions

In addition to simulating prediction error on the hidden causes of sensory experience (v), Feldman and Friston (2010) simulated prediction error on the hidden states themselves (x). Prediction error on the hidden states arises from failures in predicting stimuli with the expected precision; and it is therefore exacerbated following an invalid cue. Feldman and Friston (2010) suggest that this form of prediction error signals a surprising or novel context. They further draw a parallel between the encoding of both sensory and contextual prediction error in their model and the electrophysiological correlates of the Posner paradigm, relating sensory prediction error to early (P1 and N1) responses which reflect perceptual processes; and contextual prediction error (i.e., the prediction errors on the hidden states encoding precision) to later P3 responses. They show that as a result of its low precision, simulated sensory prediction error is suppressed in response to invalidly cued targets, mirroring the attenuation in early perceptual components in response to invalidly cued targets observed in EEG studies (Luck et al., 2000). The low precision of the sensory prediction error in response to invalidly cued targets drives an increase in simulated contextual prediction error, which Feldman and Friston relate to the increase in amplitude of P3 components seen in response to invalid targets (Mangun & Hillyard, 1991) and in oddball paradigms in EEG studies (Pritchard, 1981).

Under the same assumptions, we can make explicit predictions about event-related potentials (ERPs) in depressed participants on the basis of simulations derived from our optimized model parameters. Prediction errors on the sensory predictions v (hidden causes) and context x (hidden states) from our own simulations are shown in Figure 8.6. Examining the prediction errors for the control group, we see a similar pattern to that observed by Feldman and Friston: invalid cues suppress sensory precision relative to valid cues, suppressing precision-weighted sensory prediction error (ξ) and enhancing contextual prediction error. In the depressed group, precision-weighted prediction error in response to validly-cued targets is almost comparable to that seen in healthy controls, although its suppression in response to invalid cues is greater. The most marked group differences are seen in contextual prediction error, which is suppressed in the depressed group relative to healthy controls, particularly in response to invalidly-cued targets. This suppression results from low target salience in the depressed group, causing an absolute reduction in sensory precision but reducing expected precision commensurately more. According to the theory advanced by Feldman and Friston (2010), this is analogous to a reduced or suppressed P3 amplitude in depressed participants relative to healthy controls, particularly in response to invalidly-cued or low-probability targets. In fact, reduced P3 amplitudes in response to targets in oddball tasks have been consistently observed in depression (e.g., Bruder et al., 2012).

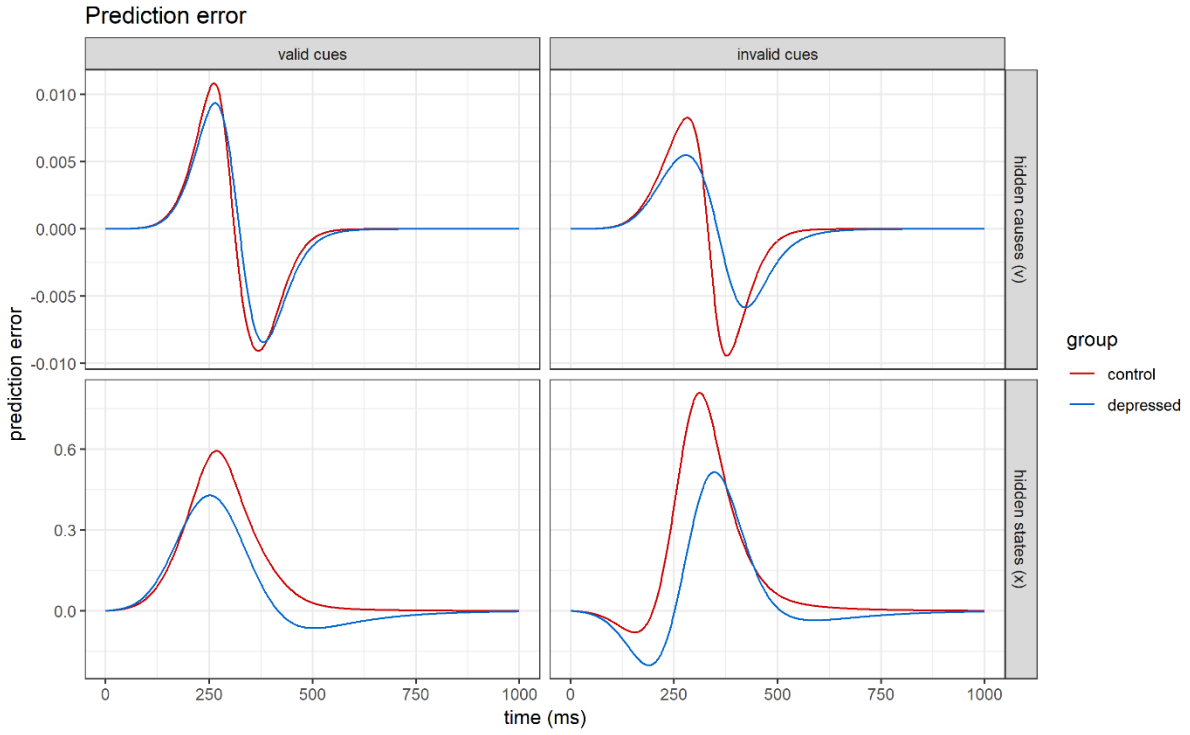


Figure 8.6: Study 6 simulated prediction error on sensory predictions and context. Control participants show a facilitation of precision-weighted sensory prediction error (ξ) in response to

validly-cued relative to invalidly-cued targets. However, contextual prediction error (prediction error on the hidden states encoding precision) is exacerbated following an invalid cue, reflecting a failure to optimize stimulus precision. Depressed participants show a similar facilitation of precision-weighted sensory prediction error (ξ) in response to validly-cued targets; but a relative attenuation of contextual prediction error, particularly following invalidly-cued targets. Given model assumptions, this outcome is consistent with ERP evidence in this population.

8.4. Study 6 summary

In Study 6, a classical analysis of variance of RTs from a cross-modal covert attention task (Posner, 1980) was conducted before the data were fit to a predictive processing model in order to derive estimates of sensory precision and stimulus salience in persistently depressed individuals relative to never-depressed controls. As expected, the classical statistical analysis demonstrated a group difference in the size of the validity effect, defined as the latency difference between validly- and invalidly-cued targets. Precision and salience parameters estimated by optimising the predictive processing model with the empirical data indicated that depressed participants demonstrated reduced sensory precision, reduced target salience, and increased somatic salience relative to controls. Study 6 therefore succeeded in replicating the key outcomes of Studies 4 and 5. Additional analyses suggested that amplified somatic salience in depressed individuals might reflect relatively high anxiety and relatively low interoceptive sensibility. In addition, although attenuated in the depressed group overall, basal precision estimates were positively associated in this group with anxiety severity, suggesting the hypothesis that anxiety and low mood might influence basal precision in opposite directions.

Chapter 9. Discussion

This chapter will discuss the findings of each set of studies in turn. The theoretical and clinical implications of the study outcomes will be considered, and finally, the limitations of the current series of studies will be discussed and recommendations made for future research.

9.1. Summary of Study findings

Study 1 (Chapter 3) and Study 2 (Chapter 4) aimed to investigate the hypothesis that auditory and somatic perceptual sensitivity is reduced in depressed participants relative to healthy controls, under conditions of optimal voluntary attention (Study 1) and attentional burden (Study 2) respectively. Both studies found that perceptual sensitivity in both the somatic and the auditory modalities was unaffected by depression status. Similarly, no systematic impact of depression on overall attentional performance was identified in either study. Nevertheless, the two studies, taken together, suggested that depressed participants exhibited a subtle left-sided neglect of space which manifested as a disproportionate tendency towards left-sided attentional lapses in Study 1 and as a preference for attending to the right as indexed by lateralised response bias In Study 2. In both studies, these indices of left-sided neglect were positively associated with anhedonia over and above the influence of depression severity (Appendix G). Faster and less variable reaction times in the depressed group in Study 2 also suggested that this group might be engaging in some form of resource conservation strategy during task performance. Study 3 (Chapter 5) provided proof-of-principle for the theory that the attentional performance of depressed participants in both studies could be accounted for by left-sided lapses with a biased guessing rule as a compensatory strategy; and by a resource-conservation strategy predicated on reducing voluntary attention to the left side of space and compensating by greater reliance on evidence from the right. Such a strategy would predict both response bias and, in theory, increased reaction time efficiency as observed in the depressed group in Study 2. These outcomes support the theory that persistent depression is associated with subtle left-sided hemineglect, and also suggest that sensory precision may be reduced in persistently-depressed individuals as part of a voluntary or involuntary resource conservation strategy.

Study 4 (Chapter 6), Study 5 (Chapter 7) and Study 6 (Chapter 8) examined attentional capture by irrelevant and relevant sensory signals in the context of a covert orienting (Posner) task. Study 4 aimed to identify the extent to which unattended somatic stimuli capture attention or awareness in persistently-depressed individuals relative to healthy controls. Study 5 built on Study 4 and tested the hypothesis that the salience of somatic stimuli is amplified in depression rather than attenuated. Study 6 aimed to replicate the findings of the previous two studies and additionally to directly test the

hypothesis that supra-modal sensory precision is reduced in persistent depression through a computational modelling approach. Each of these studies provided evidence suggesting that unattended somatic stimuli may be disproportionately salient to in persistent depression. Each of these studies also demonstrated exacerbated validity effects in depressed participants under different conditions. Study 6 additionally estimated underlying precision and salience parameters of a computational model optimized by the data, and found that given model assumptions, depressed participants demonstrated reduced sensory precision, reduced target salience, and increased somatic salience relative to controls.

9.2. Perceptual sensitivity in signal detection

Study 1 was, to our knowledge, the first study to compare somatic thresholds between depressed participants and healthy controls in a non-nociceptive context. The study's outcomes strongly suggested that once the influence of attentional lapses was taken into account, somatic sensitivity was unaffected by depression status. Similarly, after attention was accounted for, no influence of depression on auditory sensitivity was apparent. Study 2 replicated these findings. However, discernible group-specific effects of voluntary attention on some aspects of perceptual performance (manifested as attentional lapses and response bias) were present in all variants of this task in both studies, adding weight to the proposal that attentional and motivational processes rather than perceptual sensitivity may have contributed to group differences in previous investigations of somatic and auditory perception (e.g., Malone & Hemsley, 1977). Given the relatively small number of participants employed in both studies; and given the possibility that sensitivity performance in depressed participants in Study 2 was inflated by the intelligent use of heuristic compensatory strategies; interpretation must be cautious. However, even the hypothesised compensatory strategies rely on good quality right-sided data for their success, and overall the evidence does not support the theory that depressive symptoms are related to absolute changes in perception in the studied modalities under conditions where voluntary attention to sensory targets is successfully maintained.

9.3. Voluntary attention to sensory signals

The two experimental studies were consistent in identifying a reliable deficit in attentional outcomes on the left side of space in depressed participants across a range of different attentional indices. This deficit emerged in asymptotic error data in Study 1, in response bias in Study 2 and in the 'lapse' component of the mixture model used to analyse the Study 2 RT data. Specifically, both studies found direct evidence for a disproportionate number of lapses on the left side of space in depression, in addition to the more indirect evidence supporting a lateralised lapse model from Study 3 simulations.

There was also evidence, although less marked and less consistent, for the opposite tendency towards right-sided attentional lapses and response bias in healthy controls.

Importantly, there was no evidence whatsoever for any influence of stimulus modality on these attentional outcomes. Stimuli in both the somatic and auditory modalities were subject to disproportionate left-sided lapses among depressed participants in Study 1, and stimuli of both modalities were subject to lateralised response biases in the same population in Study 2. Finally, the efficient reaction time distributions observed in depressed participants in Study 2, and which contributed to the resource conservation theory, similarly occurred in response to targets of both modalities. This lack of modality-specificity supports the theory that lapses and biases in these studies arose from deficits in a supra-modal process such as voluntary attention. The findings also indicate that persistently depressed participants in these studies were as capable of successfully directing voluntary attention to somatic stimuli as they were to auditory stimuli. This finding is somewhat at odds with the literature on interoceptive accuracy in heartbeat perception tasks, which have typically found that depressed individuals have a reduced ability to accurately track interoceptive stimuli relative to healthy controls (Dunn et al., 2007; Dunn, Stefanovitch, et al., 2010; Furman et al., 2013). The inconsistency between this literature and the current studies may arise from a number of possible causes. One possibility is that the crucial difference is in the distinction between interoceptive and somatic signals: it is very plausible that depression may be associated with an increase in interoceptive, but not somatic, sensory noise. Another is that the context of an adaptive staircase (in which potentially wandering attention is relatively likely to be recalled by an increase in stimulus intensity following an error) scaffolds the performance of depressed participants and mitigates against attentional lapses in a way which is not possible in a heartbeat detection paradigm. It is also the case that comparison of the perceptual performance of depressed individuals across modalities is greatly complicated in studies of interoception by the difficulties inherent in identifying genuinely comparable control stimuli with respect to variable and endogenously-determined interoceptive stimuli such as heartbeats; any lack of modality-specificity in the observed attenuation of awareness may thus be very difficult to capture.

As shown by the simulations in Study 3, the observed lateralised response biases in Study 2 are consistent either with a compensatory strategy involving a biased guess rate employed in response to lateralised differentials in confidence in attentional performance; or alternatively, with a top-down strategy intended to conserve resources by enabling task completion whilst allowing attention to be attenuated on one side of space. These possibilities are not mutually exclusive and further research will be required to separate them. In either case, the implication is clear that it is in some way more

difficult or 'costly' for depressed individuals to attend to the left side of space, and, to a lesser extent, more difficult or costly for healthy controls to attend to the right.

9.4. Attentional capture by sensory signals

Studies 4, 5 and 6 investigated attentional capture by sensory signals. In contrast to the previous investigations into perceptual sensitivity and voluntary attention, all three studies of bottom-up attentional capture identified interactions between depression status and stimulus modality, suggestive of group differences in the relative salience of somatic information. In fact, in Studies 4 and 5 these interactions were more marked than the impact of depression on any other aspect of performance, despite the reliance of the task on functions such as concentration and speed of processing, well known to be vulnerable to disturbance in depression. In Study 6 the interaction between group and stimulus modality was not reliable in the classical analysis, perhaps due to a lack of power; but it nevertheless emerged strongly in the estimated salience parameter of the computational model. A possible non-specific explanation for these findings is that a modality processing differential common to all participants is exacerbated in depression (if, for example, somatic information represents greater attentional load, depressed individuals could be disproportionately affected due to reduced global processing capacity), but this explanation is unlikely given that healthy controls showed few effects of cue modality in their responses. Taken together, the results of all three studies are most parsimoniously explained by the hypothesis that somatic information exerts a particular, modality-specific influence on attentional orienting in major depression. Furthermore, among persistently-depressed participants, and relative to auditory cues, Study 4 found that somatic cues were disproportionately distracting; Study 5 found that somatic cues captured attention to a disproportionate extent; and Study 6 found that somatic cues were associated with disproportionate salience in a predictive processing model. All three studies, therefore, presented evidence that somatic stimuli are uniquely salient to persistently depressed individuals.

Studies 4-6 also provided evidence of an influence of persistent depression on attentional orienting at a supra-modal level. Increased validity effects were observed in the depressed groups relative to controls in all three studies, although manifesting slightly differently in each study. In Study 4, increased validity effects were seen in depressed participants relative to controls in later blocks; that is, with extended time-on-task. In Study 5, the group difference in validity effects was specific to responses following somatic cues. In Study 6, the group difference in validity effects was unqualified by any other factor. Given that all three studies additionally provided support for the theory that somatic cues had disproportionate salience for depressed participants, the most parsimonious explanation for these assorted effects is that the group by cue validity interaction in all three studies

was particularly reliable under conditions of greater effort or difficulty (extended time-on-task in Study 4, high cue salience in Study 5, and cue/target switches with each new block in Study 6). The evidence of increased validity effects in depressed participants in all three studies replicates a similar finding using a visuo-spatial covert orienting task (Pardo et al., 2006) and additionally generalises it to a cross-modal paradigm including auditory and somatic stimuli.

9.5. Theoretical implications

9.5.1. Somatic salience in persistent depression

A clear implication arising from the current findings relates to the utility of somatic stimuli in the study of persistent depression. In all three studies indexing attentional capture, somatic stimuli differentiated the performance of depressed individuals from that of controls, indicating that such stimuli succeeded in capturing some attribute specific to bodily information processing in this population. It is possible, tentatively, to suggest on this basis that somatic stimuli may be capable of providing a relatively tractable analogue for the study of interoceptive processing in depressive disorders. Alternatively, somatic processing may prove to be subject to the influence of depression entirely independently of any such influence on interoceptive processing; but if this is the case then the findings presented here suggest that it may be important to investigate somatic processing in persistent depression in its own right. Much work remains to be done in identifying the nature of the relationships between depression, somatosensation and interoception, but the current studies go some way towards establishing the relevance of somatosensation to the study of bodily awareness and precision in depression.

Existing formulations of disturbed somatic processes in depression posit an attenuation of somatic experience (e.g., Bylsma et al., 2008), although the self-reports of depressed individuals demonstrate that at least some forms of unpleasant somatic experience can be highly salient during depressive episodes (Ratcliffe, 2014). While a disturbance of somatic awareness was evident in all three studies of attentional capture, the natures of these respective disturbances provide somewhat different insights.

In Study 4, the instruction to ignore salient but irrelevant somatic cues seems to have precipitated a significant reduction of general attentional efficiency in depressed individuals. Although discussion of the cognitive or neurological mechanisms which may underlie this effect is speculative, a substantial and potentially relevant literature exists which relates similar patterns of reduced attentional efficiency to activity in the default mode network (DMN) of the brain (Kelly et al., 2008; Sonuga-Barke & Castellanos, 2007; Weissman et al., 2006). The DMN is known to be active during rest and ‘mind-

wandering' (e.g., Schooler et al., 2011), and deactivated in response to attentional demands, operating in opposition to a task-positive brain network (TPN) which mediates focused attention (Fox et al., 2005). Attentional lapses, as indexed by lengthy and variable reaction times (Weissman et al., 2006) and errors (Eichele et al., 2008; Li, Yan, Bergquist, & Sinha, 2007) during a variety of tasks have been associated with reduced DMN deactivation, while intra-individual variability in response times during an attention task has also been shown in healthy participants to relate to the strength of anticorrelations between the DMN and the TPN (Kelly et al., 2008). Such findings suggest that consistent attentional performance may depend upon efficient DMN deactivation, implying that DMN dysregulation could underlie inconsistent performance such as that observed in depressed participants in Study 4. It is well-established that abnormal patterns of intra-and extra-network resting-state functional connectivity can operate with respect to the DMN in depression (Kaiser, Andrews-Hanna, Wager, & Pizzagalli, 2015; Mulders, van Eijndhoven, Schene, Beckmann, & Tendolkar, 2015), and functional imaging studies have further demonstrated that depressed groups can be characterised by reduced DMN deactivation during focused attention, certainly when emotionally relevant stimuli are involved (Grimm et al., 2009; Sheline et al., 2009). It is plausible, therefore, that reductions in attentional efficiency in response to somatic cues could reflect reduced DMN deactivation under these conditions in depressed participants. It is possible to speculate further that an association of unwanted somatic stimuli with threat or emotion in individuals with persistent or recurrent histories of depression could exacerbate failures of DMN deactivation during blocks in which irrelevant cues are somatic, accounting for the greater response variability in these blocks.

An alternative account suggests that high response variability in the depressed group could result from peristimulus efforts to refocus attention centrally in the attempt to ignore cues as instructed. It may be the case that relative difficulty in optimising target precision at the expense of the precision of irrelevant cues, as suggested by the outcomes of the Study 6 computational model, could motivate the use of a clumsier strategy of endogenous attentional shifts among depressed participants. Heightened response variability following somatic cues would then indicate greater difficulty in ignoring such cues and more vigorous resulting efforts to endogenously control the locus of attention. Participants were not asked to provide any information about the cognitive strategies that they had used during the task and so further explication of this finding must await additional research.

In Study 5, on the other hand, participants were not instructed to ignore the cues, and cues were on average predictive of target location. Under these circumstances, no significant reductions in overall attentional efficiency were observed, but there was instead a depression-specific exacerbation of validity effects with respect to somatic cues. This finding suggests that attention within the depressed

group was disproportionately captured by such cues, consistent with the hypothesis that the salience of somatic sensation may be amplified in persistent depression rather than attenuated. There is a well-documented and often disabling impact of somatic symptomatology in persistent depression (Ratcliffe, 2014; Vaccarino et al., 2008); and increased attentional capture by somatic signals may reflect their heightened salience in this population as a result of their frequently threatening or problematic nature. The proposed increase in the salience, or threat value, of somatic signals in persistent depression is also consistent with the proposal that they may be disproportionately likely to trigger cognitive avoidance or control strategies.

Both Studies 4 and 5 suggest, therefore, that somatic cues were associated with stronger salience for depressed participants, relative to auditory cues. Additional support for this proposal is provided by the estimated bottom-up stimulus salience parameters in the Study 6 computational model. Specifically, in Study 6, the model outcomes suggested that depressed participants found somatic stimuli disproportionately salient in comparison to controls, while the opposite pattern was observed for auditory stimuli. The finding that somatic cues are uniquely distracting or salient for depressed participants is thus consistent across all three studies, but requires some explanation, particularly given a body of literature indicating *reduced* bodily awareness in depressive disorders (Dunn et al., 2007; Dunn, Stefanovitch, et al., 2010; Furman et al., 2013; Harshaw, 2015). The regression analysis undertaken in Study 6 with respect to relative somatic salience suggested that (at least) two mechanisms contributed to this outcome: first, an index of physiological anxiety symptom severity predicted relative somatic salience, suggesting, perhaps uncontroversially, that more anxious individuals are likely to find bodily signals more salient. Given that depressed participants were by definition more likely to be anxious than healthy controls, this accounts in part for the group difference. Secondly, an index of interoceptive sensibility (self-reported interoceptive awareness) was negatively associated with relative somatic salience, suggesting that individuals who reported less awareness of interoceptive sensation day-to-day were more surprised (in a Bayesian sense) by somatic stimuli in our task. Because depressed participants reported reduced interoceptive sensibility relative to controls, this relationship also contributed to the group difference. It is possible that increased surprise at novel bodily sensations can result from habitual downregulation of interoceptive and other bodily signals, an explanation which can accommodate both the increased salience of the novel stimuli employed in the current studies, and the reduced salience of endogenously-occurring interoceptive signals such as heartbeats observed in tasks indexing interoceptive awareness (Dunn et al., 2007; Furman et al., 2013). Alternatively, higher salience of unwanted bodily signals may motivate more habitual cognitive and behavioural avoidance of such signals (e.g., Borkovec & Lyonfields, 1993; Hayes,

Wilson, Gifford, Follette, & Strosahl, 1996; Moore & Garland, 2004), reflected in lower interoceptive sensibility. A more targeted approach, employing a wider range of interoceptive measures (Garfinkel et al., 2015), is needed to investigate this question further.

In theoretical terms, our finding that somatic stimuli are disproportionately salient in the context of attenuated generic sensory precision is broadly consistent with proposals by Paulus and Stein (2010) that bodily signals are both noisy and amplified in depressive disorders. The relative salience of somatic signals may also relate to clinical observations regarding the ubiquity of motivated and explicit attempts to downregulate interoceptive experience in anxiety and depression, in contrast to the more implicit mechanisms involved in the reduced precision of signals occurring in other sensory modalities. For example, while attention to sensory information of all kinds may be constrained or attenuated in depression in order to reduce energy expenditure or to regulate arousal, the disproportionate salience or threat of somatic signals may render this process more difficult, necessitating the employment of additional, more explicit emotional avoidance strategies. Studies employing dynamic causal modelling could be of great utility in developing our understanding of these processes.

9.5.2. Mechanisms of attentional disturbance in persistent depression

Despite clinical and theoretical consensus implicating attentional disturbance as a key feature of depression, surprisingly little is known regarding the mechanisms or substrates underlying this disturbance. The current findings may contribute to our understanding of this issue. Studies 1 and 2, indexing voluntary attention, identified subtle left-sided neglect in persistently depressed groups. Studies 4, 5 and 6, indexing attentional orienting, identified increased validity effects in persistently depressed groups suggestive of disproportionate difficulty in reorienting attention towards the targets following an invalid cue. These findings suggest the specific involvement of a right-lateralised attention network in the brain subserving stimulus-driven attention.

An extensive literature indicates that stimulus-driven attention towards novel, salient or behaviourally-relevant sensory events is subserved by a right-lateralised ventral attention network (VAN) in the brain consisting of the right temporoparietal junction (TPJ), anterior insula and frontal operculum, and inferior and middle frontal gyri (Corbetta et al., 2008; Corbetta & Shulman, 2002; Downar, Crawley, Mikulis, & Davis, 2001; Fox et al., 2005; Kucyi, Hodaie, & Davis, 2012). Activity in this ventral attention network has been hypothesised to have the functions of maintaining vigilance (Langner & Eickhoff, 2013), facilitating attention to salient or behaviourally relevant signals, and acting as an attentional circuit-breaker subserving task-switching when key environmental contingencies change (Corbetta & Shulman, 2002). The TPJ (a key node of this network) has also been associated

with context updating and the tracking of prediction error (Geng & Vossel, 2013; Mengotti et al., 2017).

Damage to, or disconnection of, the VAN is associated with unilateral neglect, a neurological condition which is characterised by deficits in arousal and vigilance and a tendency to ignore stimuli occurring on one side of space, typically the left (Corbetta, 2014; He et al., 2007). This failure to attend to the left contrasts with the left hemi-spatial advantage (known as "pseudoneglect") which is often observed in healthy participants (Benwell, Thut, Learmonth, & Harvey, 2013; Jewell & McCourt, 2000; Voyer, Voyer, & Tramonte, 2012) and which is thought to reflect right-hemisphere dominance in attention. However, it has also been demonstrated that a mild and transitory form of left-sided neglect can be induced in healthy participants under conditions of low arousal, high fatigue or lengthy time on task (Bareham, Manly, Pustovaya, Scott, & Bekinschtein, 2014; Dodds et al., 2008; Fimm, Willmes, & Spijkers, 2006; Manly, Dobler, Dodds, & George, 2005; Paladini et al., 2016). It has been proposed (Benwell, Harvey, & Thut, 2014; Newman, O'Connell, & Bellgrove, 2013) that transitory neglect in healthy participants results from resource depletion within the VAN, a hypothesis with some support from EEG source localisation studies implicating the TPJ, a key node of the VAN, in these effects (Benwell et al., 2014; Foxe, McCourt, & Javitt, 2003).

As described above, there is evidence from our own studies and from previous literature that depression is associated with left-sided neglect (Bruder et al., 1989; Liotti & Mayberg, 2001; Liotti et al., 1991), and with relative difficulty in reorienting attention following an invalid cue (Pardo et al., 2006), in addition to existing evidence that depression is associated with a loss of vigilance (Rock et al., 2014). These deficits may indicate ventral attention network disturbance or hypoactivity, comparable, perhaps, to that displayed by healthy controls under conditions of low arousal or resource depletion. Perhaps related is the finding that resting-state parietal alpha is frequently greater over the right hemisphere than the left in depression (Blackhart, Minnix, & Kline, 2006; Bruder et al., 1997; Kentgen et al., 2000); an imbalance that has been attributed to reduced arousal in this population (Heller, 1993). Of interest, the opposite pattern has been observed in anxious individuals, perhaps reflecting increased arousal or hypervigilance for threat (Bruder et al., 1997; Kemp et al., 2010; Metzger et al., 2004).

In summary, then, it may be the case that persistent depression is characterised by a specific disturbance of stimulus-driven attention, specialised for the detection of behaviourally-relevant signals occurring in the environment, and subserved by right-lateralised ventral parietal and frontal brain regions. The extent to which these brain regions may be implicated with respect to disturbances

of salience processing and precision estimation in this population remains a question for future research.

9.5.3. Salience in persistent depression

A striking finding from the Study 6 predictive processing model was the relative attenuation of target salience and amplification of cue salience among depressed participants in comparison to healthy controls, suggesting that this group may have been less able to discriminate targets or to potentiate target processing relative to the processing of irrelevant cues. This finding is of great theoretical interest, given the centrality of salience processing to information processing in general.

In order to register and adapt to shifting environmental contingencies, it is necessary for the brain, in its creation of an online inferential working model of that environment, to monitor a constant stream of incoming sensory information and to amplify those aspects of it that are relevant for model updating. Salience within predictive processing accounts has been defined as Bayesian surprise (Itti & Baldi, 2009; Parr & Friston, 2019), which in terms of Bayesian probability distributions is the extent of the change from prior to posterior belief occasioned by the observation of new data. Salient data, therefore, are data which are both precise and informative with respect to existing goals or expectancies, whether because of their motivational significance or due to their novelty and unexpectedness. Saccades, foraging, and exploration are all examples of experimental actions which have the function of eliciting salient information: at a phenomenological level, Parr and Friston (2019) equate salience with intrinsic motivation, which is associated with spontaneous exploration, interest and curiosity (Oudeyer & Kaplan, 2009). According to these definitions, a reduction or loss of specificity in the salience of sensory signals arising in the environment appears very consistent with the phenomenology of persistent depression.

A key neuromodulator underpinning salience processing in the brain is noradrenaline (NA). NA is largely synthesised in the locus coeruleus (LC) and supplied throughout the brain via widespread efferent projections (Amaral & Sinnamon, 1977). LC activity has a tonic mode, associated with arousal and wakefulness, and a phasic mode, in which discharge occurs in response to salient or novel events. High tonic activity is associated with scanning attention and behavioural flexibility, while phasic activity is observed during focused attention and is thought to potentiate the cortical response to motivationally significant sensory information (Berridge & Waterhouse, 2003). Phasic LC discharge is typically observed when tonic activity is moderate, and, like focused task performance, is suppressed when tonic firing rates are either low or high (Aston-Jones, Rajkowski, & Cohen, 1999). It has been proposed that high tonic firing occurs in response to contextual uncertainty, disengaging task-focus

and promoting exploration in order to collect new data (Aston-Jones & Cohen, 2005), while phasic activity may operate as a network reset, dynamically reconfiguring neural networks in response to stimuli which signal shifts in environmental contingencies in order to facilitate rapid behavioural adaptation (Bouret & Sara, 2005). Yu and Dayan (Dayan & Yu, 2006; Yu & Dayan, 2005) have proposed that the function of NA release is to signal unexpected uncertainty, indicating a need to reset model expectations and to amplify relevant sensory signals to inform a new model of the current context . A related theory was recently advanced by Sales, Friston, Jones, Pickering, and Moran (2019), who have modelled both tonic and phasic LC activity as responses to prediction error which potentiate flexible belief updating.

As a key aspect of salience processing, NA plays a central role in detecting and responding to both threat and potential reward (Berridge & Waterhouse, 2003), and the noradrenergic system is therefore extremely responsive to stress (e.g., Morilak et al., 2005). During acute stress, NA is released both centrally and peripherally, and high tonic LC activity may disengage task-focused attention and promote bottom-up sensory signals in a manner consistent with hypervigilance or scanning for threat (Valentino & Van Bockstaele, 2008). Over the longer-term, both acute and chronic stress induce plasticity in the NA system with likely implications for mood and anxiety disorders (Borodovitsyna, Joshi, & Chandler, 2018), and although the precise relationships between chronic stress, changes in NA signalling and depression are not yet clear (Maletic, Eramo, Gwin, Offord, & Duffy, 2017), there is robust evidence for noradrenergic system disruption in individuals with depressive illness (e.g., Leonard, 2001; Moret & Briley, 2011).

A possible electrophysiological marker of NA function is the P3 wave of the event-related potential (ERP) in EEG studies, a late component that is typically observed in oddball tasks and in response to attended, novel or salient stimuli (Pritchard, 1981). Its amplitude is inversely related to the probability of the stimulus, and positively related to its salience (Nieuwenhuis et al., 2005), and it has been suggested that it indexes prediction error (Feldman & Friston, 2010) or context updating (Donchin & Coles, 1988). On the basis of similarities in the observed response patterns, Nieuwenhuis et al. (2005) have suggested that the P3 is an electrophysiological correlate of phasic LC activity. Of interest, a substantial literature suggests that the amplitude of the P3 wave is typically blunted in depression, (Bruder et al., 2012; Klawohn, Santopetro, Meyer, & Hajcak, 2020), consistent with the proposal that salience registration and associated context updating may be dampened in depressive illness.

In line with this proposal, in our Study 6 electrophysiological simulation, following Feldman and Friston (2010) and based on parameter estimates derived from our empirical data, we found that of all

simulated ERP components, the one that was attenuated most drastically in the depressed group was the one considered to be analogous to the P3 in response to an unexpected target. This attenuation reflected a failure to fully update context representations and was the result of reduced target salience which contributed to a dampening of both sensory precision and its expectation in depressed participants. This simulation suggests the hypothesis that as a result of disturbed salience processing, persistent depression may be characterised by failures in the updating of online working models of the current context or environment. In line with this proposal, perseverative errors in set-shifting tasks and difficulties in inhibiting irrelevant information in working memory updating tasks have been repeatedly observed in depressed individuals (Gotlib & Joormann, 2010; Harvey et al., 2004; Le, Borghi, Kujawa, Klein, & Leung, 2017; Rock et al., 2014; Snyder, 2013) and may provide an alternative index of the same difficulties in salience attribution and subsequent context updating.

9.5.4. Sensory precision in persistent depression

All three studies examining covert attentional orienting found evidence of large validity effects in depressed participants relative to healthy controls. Given that validity effects reflect the influence of the cue, which adjusts prior expectations regarding the probable location of the target, these findings provide some support for the suggestion that perception and action in persistent depression are characterised by an overreliance on prior beliefs relative to sensory prediction error[1]. This hypothesis is reflected in the outcomes of the Study 6 computational model, which demonstrated a supra-modal attenuation of sensory precision in the depressed group relative to healthy controls; underpinned by a generic reduction in basal sensory precision regardless of the modality or salience characteristics of the stimuli in any given trial. This finding is consistent with predictive processing models which posit that depression is characterised by reduced sensory precision in the interoceptive realm (Barrett et al., 2016; Paulus et al., 2019), but generalises this reduction to other sensory modalities including the somatic, auditory and visual modalities. Of interest, although estimates of basal precision were reduced on average in depressed participants relative to healthy controls, among the depressed group they were positively associated with anxiety scores. This may suggest that high arousal or hypervigilance associated with anxiety has an opposing influence on basal sensory precision relative to the dampening effect of longstanding depression; however, a larger study better able to characterise different presentations of anxiety and depression symptomatology will be required to

[1] The relevant prior in this scenario (when cues are non-predictive) is the expectation that, following a sensory event, other sensory events are likely to occur in the same location

confirm such a hypothesis. Importantly, these findings indicate that reduced sensory precision in persistent depression may generalise across sensory modalities.

Reduced sensory precision resulting from resource conservation strategies during top-down attention also emerged as a plausible explanation for the Study 2 findings. It is unclear, on the basis of the current evidence, whether such strategies are implicit or explicit and how frequently they are employed during day-to-day perception and action by individuals with persistent depressive illnesses. A functional imaging study which may provide information relevant to this question employed dynamic causal modelling to investigate attentional filtering of irrelevant visual information in depression (Desseilles et al., 2009; Desseilles et al., 2011). Depressed participants and healthy controls performed a selective attention task under conditions of high and low attentional load. Control participants demonstrated parietal inhibition of activity in visual cortex both directly and via inhibition of forward connections within visual cortex, but only in the high-load condition. This outcome was consistent with the hypothesis that in healthy individuals cognitive control processes suppress irrelevant sensory input under conditions of attentional challenge. In depressed participants, however, a similar parietal modulation of visual cortex was observed in both the high- and low-load conditions, demonstrating that even a pop-out task requiring minimal focused attention can recruit top-down suppression of irrelevant sensory input during a depressive episode. Assuming that this observation generalises more broadly to attentionally undemanding day-to-day situations, it might imply not only that relatively high levels of cognitive effort are required for precise perception even of attended sensory information in depression, but also that extraneous sensory information that would be available to a healthy individual may not be available to a depressed individual in the same circumstances. This interpretation is consistent with the hypothesis that the precision of sensory signals may be suppressed or attenuated in persistent depression during focused attention as a result of implicit or explicit resource conservation strategies.

The above studies imply that optimizing the precision of sensory information may be relatively costly in energy terms, or otherwise requires resources that are less available in persistent depression due, perhaps, to the effects of chronic stress on relevant neurobiological systems. At a neural level, it has been proposed that the optimization of sensory precision is underpinned by the cholinergic system (Parr & Friston, 2019; Yu & Dayan, 2003). Acetylcholine (ACh) transmission regulates the gain control of sensory channels in selective attention, enhances cortical sensitivity to salient sensory information, and contributes to top-down cortical control under conditions of attentional challenge (Ballinger, Ananth, Talmage, & Role, 2016; Sarter, Hasselmo, Bruno, & Givens, 2005; Schmitz & Duncan, 2018). Prefrontal cholinergic signalling has been associated with both slow volume transmission and fast

phasic activity, perhaps contributing to maintenance and switching of task set respectively (Sarter & Lustig, 2019; but see Sarter & Lustig, 2020), and while thalamic cholinergic signalling may enhance the processing of salient sensory signals (Kim, Müller, Bohnen, Sarter, & Lustig, 2017), cortical cholinergic circuits may have the opposing function of inhibiting irrelevant sensory information and reducing distractibility and behavioural flexibility in order to maintain existing context representations and task set (Kim, Müller, Bohnen, Sarter, & Lustig, 2019; Thiele & Bellgrove, 2018).

There is evidence that both stress and depression modulate cholinergic activity (Dulawa & Janowsky, 2019; Han et al., 2017; Higley & Picciotto, 2014): in particular, an extensive literature implicates chronically elevated central cholinergic signalling in depression. Although both the causes and consequences of a putative hypercholinergic state in depression remain unclear, it is possible to speculate that such a state could be consistent with excessive top-down control of afferent sensory inputs, or with the effort required to maintain the task-set associated with an outdated context by habitual suppression of inconsistent sensory evidence; consistent with an overemphasis on prior precision at the expense of sensory precision. In an interesting simulation of a related situation, Avery, Nitz, Chiba, and Krichmar (2012), following Yu and Dayan (2005), tracked interactions between NA and ACh in an agent undertaking a behavioural task involving both expected and unexpected uncertainty. A simulated lesion to the LC was found to lead to perseverative errors resulting from failures in context updating, which also contributed to an increase of PFC activity and to persistently elevated ACh levels which no longer accurately tracked uncertainty.

9.6. Clinical implications

The finding that persistently depressed individuals may be at a disadvantage in model updating due to a pervasive attenuation of sensory precision has clinical implications, particularly with respect to psychological therapies for this population. Cognitive Behaviour Therapy (Beck et al., 1979) provides a powerful rationale for identifying, examining and updating rigid and entrenched prior expectations, but much less emphasis is placed within cognitive-behavioural approaches upon the related necessity to amplify data quality and sensory precision commensurately. Conversely, the MBCT approach (Segal et al., 2002) provides an equally powerful rationale for engaging in extensive practice in amplifying sensory precision; but allows any updating of prior expectations or beliefs about context to occur incidentally, without theorising or scaffolding this process. Evidence of a loss of sensory precision and salience in persistently depressed participants suggests that explicit practice in the amplification of sensory precision could be usefully incorporated into traditional CBT for this population; while also providing an additional rationale for engaging in meditative practices as part of an MBCT approach.

Evidence for the disproportionate salience of somatic signals in persistently depressed individuals also has clinical relevance, particularly if, as suggested in Study 6, high somatic salience arises from a combination of threat and emotional avoidance or downregulation associated with somatic signals. Current CBT practice is very effective in its formulation of beliefs, predictions and avoidance behaviours in the external milieu, but is to some extent lacking in a language and rationale for bringing the same lens to bear on the internal milieu, despite the likely relevance of interoceptive and bodily experience to depression and its persistence. Nevertheless, relevant techniques could very easily be generalised, much as techniques for the updating of verbal beliefs have been generalised to accommodate beliefs and meanings instantiated in visual imagery (Hackmann, Bennett-Levy, & Holmes, 2011). The current findings may also suggest an increased emphasis on body-focused interventions such as relaxation practices and body-focused meditation practices with persistently-depressed populations.

9.7. Limitations and future research

The most important limitation of all the studies described here is in the modest sample sizes that they employed. As described in the Rationale in Chapter 1, the decision to employ small but precisely defined samples was made with the aim of studying the mechanisms specifically characterising severe and persistent depressive illnesses. Effect sizes may have been maximised and statistical noise reduced by the use of this strategy, and it is reassuring that key outcomes were consistent across different studies. Nevertheless, replication with larger samples would be an advantage before drawing firm conclusions. In addition, given the heterogeneity of depression and its frequent association with anxiety, it may be important to establish not only the replicability of our findings but also the extent to which they generalise to different presentations: for example, the extent to which depression history and persistence influences sensory precision and salience versus the acute presence of a major depressive episode, and the direction of any influence of anxiety both acutely and in the longer-term.

While the present studies suggest that paradigms including somatic stimuli can provide a fruitful approach to the investigation of bodily awareness or precision in depression, further work is needed to provide a clearer understanding of the mechanisms involved. In particular, the significance of the findings in terms of interoception is unclear: although (as discussed in Chapter 1) there are good reasons to believe that somatic and visceral or interoceptive stimuli may share representations at a relevant level of processing (Craig, 2010), this hypothesis requires direct comparison of interoceptive and exteroceptive somatic paradigms for confirmation. Thus, although the current series of studies may inform concepts of general bodily awareness in depression, it is possible that it speaks only to specifically exteroceptive somatic processing. Further research is needed to elucidate these

relationships and to investigate the brain networks implicated in these outcomes. In addition, the findings raise questions as to the meaning or significance of increased salience of somatic signals in persistent depression, and future research which attempts to understand these questions may prove to have relevance for the development of psychological interventions for this population; as, for example, has been the case for various anxiety disorders (D. A. Clark & Beck, 2011).

More generally, the studies presented here were all either behavioural or computational, and therefore our understanding of the neurobiological mechanisms underlying the findings is presently speculative. A future step will be to identify relationships between behavioural and neural outcomes in this population using a wider range of methods. The evidence from the current studies suggests that investigation of right-lateralised ventral frontal and parietal areas specialised for stimulus-driven attention may be particularly fruitful.

With respect to the investigation and modelling of behavioural and neurobiological processes relating to salience, precision-weighting and model updating, a wide range of relevant and informative paradigms has emerged over recent years (e.g., de Lange, Heilbron, & Kok, 2018; Filipowicz, Glaze, Kable, & Gold, 2020; Zhao et al., 2019) which could be effectively adapted for the study of persistent depression in order to support and extend the current findings. For example, in a reward-learning context, (Haarsma et al., 2020) recently demonstrated disrupted precision-weighting in participants with psychosis using a prediction task in which the precision of information contributing to belief updating was explicitly manipulated. A particularly interesting question is with regards to the relationship between precision optimization and salience in persistently-depressed individuals. Attenuation of one may follow from attenuation of the other, or both may arise from related neurobiological causes such as a disturbance of the neuromodulatory systems underpinning them. Simulation studies have employed paradigms and models which separate these processes and examine their interactions, and these approaches could provide a basis for future work in the field of depression (Avery et al., 2012; Yu & Dayan, 2005).

With respect to the identification of left-sided neglect in a persistently-depressed population, further research to confirm this finding and to explore the extent to which it generalises across depressive presentations would be valuable. In particular, it may be useful to identify whether this potential marker has any predictive power in terms of prognosis or treatment response.

The identification of resource conservation strategies as a likely contributor to reduced sensory precision in persistent depression is a particularly interesting finding from a practical point of view, particularly given their unique association with anhedonia (described in Appendix G). Further research

examining the conditions under which such strategies are deployed and their consequences in terms of perceptual and hedonic experience could be highly relevant to the development of novel psychological interventions for this population.

Finally, sensory attention and precision in persistent depression may be a particularly worthwhile object of study from a clinical perspective, because they have the advantage of being consciously modifiable and are thus potential targets for psychological treatment. Indeed, as described above, interventions such as MBCT (Segal et al., 2002), with a substantial focus on the training of sensory attention, have already proved effective in the acute (Kenny & Williams, 2007) or prophylactic (e.g., Kuyken et al., 2015) treatment of more persistent forms of depression. The "active ingredients" which contribute to the effectiveness of MBCT are a matter of debate at present: it is very possible that our findings have relevance for this question. Combining future investigations of sensory precision with such interventions or intervention components may facilitate the development of more powerful and targeted approaches to persistent depressive disorders.

9.8. Conclusion

In conclusion, this series of studies demonstrates the utility of exteroceptive somatic paradigms in the study of bodily awareness in depression. The results indicate that somatic awareness is specifically disrupted in persistent forms of depression and that the locus of the disruption is at an attentional rather than a perceptual level. They also suggest that, at least in some circumstances, the salience of somatic sensation is amplified, rather than attenuated, in persistent depression. The studies further provide support for the proposal that sensory precision and salience processing may be attenuated in persistent depression across sensory modalities (despite relatively heightened bottom-up salience of somatic stimuli), with a consequent reduction in the ability to flexibly update online inferential models of both the internal and external environment. These findings suggest new avenues for investigation of stimulus-driven attention, salience, precision, and model-updating in persistent depression, and have practical relevance in clinical terms.

References

Adler, G., & Gattaz, W. F. (1993). Pain perception threshold in major depression. *Biol Psychiatry, 34*(10), 687-689.

Adolfi, F., Couto, B., Richter, F., Decety, J., Lopez, J., Sigman, M., . . . Ibanez, A. (2017). Convergence of interoception, emotion, and social cognition: A twofold fMRI meta-analysis and lesion approach. *Cortex, 88*, 124-142. doi:10.1016/j.cortex.2016.12.019

Ainley, V., Apps, M. A., Fotopoulou, A., & Tsakiris, M. (2016). 'Bodily precision': a predictive coding account of individual differences in interoceptive accuracy. *Philos Trans R Soc Lond B Biol Sci, 371*(1708). doi:10.1098/rstb.2016.0003

Allen, N. B., & Badcock, P. B. (2006). Darwinian models of depression: A review of evolutionary accounts of mood and mood disorders. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 30*(5), 815-826.

Amaral, D. G., & Sinnamon, H. M. (1977). The locus coeruleus: neurobiology of a central noradrenergic nucleus. *Progress in neurobiology, 9*(3), 147-196.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders (DSM-5®)*: American Psychiatric Publishing.

General Assembly of the World Medical Association. (2014). World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. *310*(20), 2191-2194.

Aston-Jones, G., & Cohen, J. D. (2005). An integrative theory of locus coeruleus-norepinephrine function: adaptive gain and optimal performance. *Annu. Rev. Neurosci., 28*, 403-450.

Aston-Jones, G., Rajkowski, J., & Cohen, J. (1999). Role of locus coeruleus in attention and behavioral flexibility. *Biol Psychiatry, 46*(9), 1309-1320.

Augustyn, C., & Peters, M. (1986). On the relation between footedness and handedness. *Perceptual and Motor Skills, 63*(3), 1115-1118.

Avery, M. C., Nitz, D. A., Chiba, A. A., & Krichmar, J. L. (2012). Simulation of cholinergic and noradrenergic modulation of behavior in uncertain environments. *Frontiers in computational neuroscience, 6*, 5.

Ballinger, E. C., Ananth, M., Talmage, D. A., & Role, L. W. (2016). Basal forebrain cholinergic circuits and signaling in cognition and cognitive decline. *Neuron, 91*(6), 1199-1218.

Bär, K.-J., Terhaar, J., Boettger, M. K., Boettger, S., Berger, S., & Weiss, T. (2011). Pseudohypoalgesia on the skin: a novel view on the paradox of pain perception in depression. *Journal of clinical psychopharmacology, 31*(1), 103-107.

Bareham, C. A., Manly, T., Pustovaya, O. V., Scott, S. K., & Bekinschtein, T. A. (2014). Losing the left side of the world: rightward shift in human spatial attention with sleep onset. *Scientific reports, 4*(1), 1-5.

Barrett, L. F., Quigley, K. S., & Hamilton, P. (2016). An active inference theory of allostasis and interoception in depression. *Philos Trans R Soc Lond B Biol Sci, 371*(1708). doi:10.1098/rstb.2016.0011

Beck, A. T. (2008). The evolution of the cognitive model of depression and its neurobiological correlates. *American journal of psychiatry, 165*(8), 969-977.

Beck, A. T., & Bredemeier, K. (2016). A unified model of depression: Integrating clinical, cognitive, biological, and evolutionary perspectives. *Clinical Psychological Science, 4*(4), 596-619.

Beck, A. T., Epstein, N., Brown, G., & Steer, R. A. (1988). An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol, 56*(6), 893-897.

Beck, A. T., Rush, A., Shaw, B., & Emery, G. (1979). *Cognitive therapy of depression*: Guilford press.

Beck, A. T., & Rush, A. J. (1978). Cognitive approaches to depression and suicide.

Beck, A. T., & Steer, R. (1993). Beck Anxiety Inventory Manual. The Psychological Corporation. *San Antonio, TX*.

Beck, A. T., Steer, R. A., Ball, R., & Ranieri, W. (1996). Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients. *J Pers Assess, 67*(3), 588-597. doi:10.1207/s15327752jpa6703_13

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). Manual for the Beck Depression Inventory–Second Edition. *San Antonio, TX: The Psychological Corporation*.

Bellgrove, M. A., Hester, R., & Garavan, H. (2004). The functional neuroanatomical correlates of response variability: evidence from a response inhibition task. *Neuropsychologia, 42*(14), 1910-1916. doi:10.1016/j.neuropsychologia.2004.05.007

Ben-Tovim, D. I., & Schwartz, M. S. (1981). Hypoalgesia in depressive illness. *The British Journal of Psychiatry, 138*(1), 37-39.

Bennett-Levy, J. E., Butler, G. E., Fennell, M. E., Hackman, A. E., Mueller, M. E., & Westbrook, D. E. (2004). *Oxford guide to behavioural experiments in cognitive therapy*: Oxford University Press.

Benwell, C. S., Harvey, M., & Thut, G. (2014). On the neural origin of pseudoneglect: EEG-correlates of shifts in line bisection performance with manipulation of line length. *Neuroimage, 86*, 370-380.

Benwell, C. S., Thut, G., Learmonth, G., & Harvey, M. (2013). Spatial attention: differential shifts in pseudoneglect direction with time-on-task and initial bias support the idea of observer subtypes. *Neuropsychologia, 51*(13), 2747-2756.

Berridge, C. W., & Waterhouse, B. D. (2003). The locus coeruleus–noradrenergic system: modulation of behavioral state and state-dependent cognitive processes. *Brain research reviews, 42*(1), 33-84.

Blackhart, G. C., Minnix, J. A., & Kline, J. P. (2006). Can EEG asymmetry patterns predict future development of anxiety and depression?: A preliminary study. *Biological psychology, 72*(1), 46-50.

Borkovec, T. D., & Lyonfields, J. D. (1993). Worry: Thought suppression of emotional processing.

Borodovitsyna, O., Joshi, N., & Chandler, D. (2018). Persistent stress-induced neuroplastic changes in the locus coeruleus/norepinephrine system. *Neural plasticity, 2018*.

Bouret, S., & Sara, S. J. (2005). Network reset: a simplified overarching theory of locus coeruleus noradrenaline function. *Trends Neurosci, 28*(11), 574-582.

Brainard, D. H. (1997). The Psychophysics Toolbox. *Spat Vis, 10*(4), 433-436.

Brown, H., Friston, K. J., & Bestmann, S. (2011). Active inference, attention, and motor preparation. *Front Psychol, 2*, 218.

Bruder, G. E., Fong, R., Tenke, C. E., Leite, P., Towey, J. P., Stewart, J. E., . . . Quitkin, F. M. (1997). Regional brain asymmetries in major depression with or without an anxiety disorder: a quantitative electroencephalographic study. *Biol Psychiatry, 41*(9), 939-948.

Bruder, G. E., Kayser, J., & Tenke, C. E. (2012). Event-related brain potentials in depression: Clinical, cognitive, and neurophysiological implications.

Bruder, G. E., Quitkin, F. M., Stewart, J. W., Martin, C., Voglmaier, M. M., & Harrison, W. M. (1989). Cerebral laterality and depression: differences in perceptual asymmetry among diagnostic subtypes. *Journal of abnormal psychology, 98*(2), 177.

Bubl, E., Ebert, D., Kern, E., van Elst, L. T., & Bach, M. (2012). Effect of antidepressive therapy on retinal contrast processing in depressive disorder. *The British Journal of Psychiatry, 201*(2), 151-158.

Bubl, E., Kern, E., Ebert, D., Bach, M., & Van Elst, L. T. (2010). Seeing gray when feeling blue? Depression can be measured in the eye of the diseased. *Biol Psychiatry, 68*(2), 205-208.

Bubl, E., Kern, E., Ebert, D., Riedel, A., van Elst, L. T., & Bach, M. (2015). Retinal dysfunction of contrast processing in major depression also apparent in cortical activity. *European archives of psychiatry and clinical neuroscience, 265*(4), 343-350.

Bubl, E., Tebartz Van Elst, L., Gondan, M., Ebert, D., & Greenlee, M. W. (2009). Vision in depressive disorder. *The World Journal of Biological Psychiatry, 10*(4-2), 377-384.

Burton, H., Videen, T. O., & Raichle, M. E. (1993). Tactile-vibration-activated foci in insular and parietal-opercular cortex studied with positron emission tomography: mapping the second somatosensory area in humans. *Somatosens Mot Res, 10*(3), 297-308.

Bylsma, L. M., Morris, B. H., & Rottenberg, J. (2008). A meta-analysis of emotional reactivity in major depressive disorder. *Clin Psychol Rev, 28*(4), 676-691. doi:10.1016/j.cpr.2007.10.001

Carlin, B. P., & Chib, S. (1995). Bayesian model choice via Markov chain Monte Carlo methods. *Journal of the Royal Statistical Society: Series B (Methodological), 57*(3), 473-484.

Cauda, F., D'Agata, F., Sacco, K., Duca, S., Geminiani, G., & Vercelli, A. (2011). Functional connectivity of the insula in the resting brain. *Neuroimage, 55*(1), 8-23. doi:10.1016/j.neuroimage.2010.11.049

Cerliani, L., Thomas, R. M., Jbabdi, S., Siero, J. C., Nanetti, L., Crippa, A., . . . Keysers, C. (2012). Probabilistic tractography recovers a rostrocaudal trajectory of connectivity variability in the human insular cortex. *Hum Brain Mapp, 33*(9), 2005-2034. doi:10.1002/hbm.21338

Chica, A. B., Bartolomeo, P., & Lupiáñez, J. (2013). Two cognitive and neural systems for endogenous and exogenous spatial attention. *Behavioural brain research, 237*, 107-123.

Clark, A. (2013). Whatever next? Predictive brains, situated agents, and the future of cognitive science. *Behavioral and brain sciences, 36*(3), 181-204.

Clark, D. A., & Beck, A. T. (2011). *Cognitive therapy of anxiety disorders: Science and practice*: Guilford Press.

Cloutman, L. L., Binney, R. J., Drakesmith, M., Parker, G. J., & Lambon Ralph, M. A. (2012). The variation of function across the human insula mirrors its patterns of structural connectivity: evidence from in vivo probabilistic tractography. *Neuroimage, 59*(4), 3514-3521. doi:10.1016/j.neuroimage.2011.11.016

Coghill, R. C., Talbot, J. D., Evans, A. C., Meyer, E., Gjedde, A., Bushnell, M. C., & Duncan, G. H. (1994). Distributed processing of pain and vibration by the human brain. *J Neurosci, 14*(7), 4095-4108.

Cohen, R., Lohr, I., Paul, R., & Boland, R. (2001). Impairments of attention and effort among patients with major affective disorders. *J Neuropsychiatry Clin Neurosci, 13*(3), 385-395.

Corbetta, M. (2014). *Hemispatial neglect: clinic, pathogenesis, and treatment.* Paper presented at the Seminars in neurology.

Corbetta, M., Kincade, J. M., & Shulman, G. L. (2002). Neural systems for visual orienting and their relationships to spatial working memory. *J Cogn Neurosci, 14*(3), 508-523.

Corbetta, M., Patel, G., & Shulman, G. L. (2008). The reorienting system of the human brain: from environment to theory of mind. *Neuron, 58*(3), 306-324. doi:10.1016/j.neuron.2008.04.017

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci, 3*(3), 201-215. doi:10.1038/nrn755

Craig, A. D. (2009). How do you feel--now? The anterior insula and human awareness. *Nat Rev Neurosci, 10*(1), 59-70. doi:10.1038/nrn2555

Craig, A. D. (2010). The sentient self. *Brain Struct Funct, 214*(5-6), 563-577. doi:10.1007/s00429-010-0248-y

Croy, I., Symmank, A., Schellong, J., Hummel, C., Gerber, J., Joraschky, P., & Hummel, T. (2014). Olfaction as a marker for depression in humans. *J Affect Disord, 160*, 80-86.

Damasio, A. R. (2006). *Descartes' error*: Random House.

Dantzer, R., O'Connor, J. C., Freund, G. G., Johnson, R. W., & Kelley, K. W. (2008). From inflammation to sickness and depression: when the immune system subjugates the brain. *Nat Rev Neurosci, 9*(1), 46-56. doi:10.1038/nrn2297

Davis, K. D., Kwan, C. L., Crawley, A. P., & Mikulis, D. J. (1998). Functional MRI study of thalamic and cortical activations evoked by cutaneous heat, cold, and tactile stimuli. *J Neurophysiol, 80*(3), 1533-1546.

Dayan, P., & Yu, A. J. (2006). Phasic norepinephrine: a neural interrupt signal for unexpected events. *Network: Computation in Neural Systems, 17*(4), 335-350.

de Lange, F. P., Heilbron, M., & Kok, P. (2018). How do expectations shape perception? *Trends Cogn Sci, 22*(9), 764-779.

Deen, B., Pitskel, N. B., & Pelphrey, K. A. (2011). Three systems of insular functional connectivity identified with cluster analysis. *Cereb Cortex, 21*(7), 1498-1506. doi:10.1093/cercor/bhq186

Dellaportas, P., Forster, J. J., & Ntzoufras, I. (2002). On Bayesian model and variable selection using MCMC. *Statistics and Computing, 12*(1), 27-36.

Denwood, M. J. (2016). runjags: An R package providing interface utilities, model templates, parallel computing methods and additional distributions for MCMC models in JAGS. *Journal of Statistical Software, 71*(9), 1-25.

Desseilles, M., Balteau, E., Sterpenich, V., Dang-Vu, T. T., Darsaud, A., Vandewalle, G., . . . Schmidt, C. (2009). Abnormal neural filtering of irrelevant visual information in depression. *Journal of Neuroscience, 29*(5), 1395-1403.

Desseilles, M., Schwartz, S., Dang-Vu, T. T., Sterpenich, V., Ansseau, M., Maquet, P., & Phillips, C. (2011). Depression alters "top-down" visual attention: a dynamic causal modeling comparison between depressed and healthy subjects. *Neuroimage, 54*(2), 1662-1668.

Dichter, G. S., Smoski, M. J., Kampov-Polevoy, A. B., Gallop, R., & Garbutt, J. C. (2010). Unipolar depression does not moderate responses to the Sweet Taste Test. *Depress Anxiety, 27*(9), 859-863.

Dijkerman, H. C., & de Haan, E. H. (2007). Somatosensory processes subserving perception and action. *Behav Brain Sci, 30*(2), 189-201; discussion 201-139. doi:10.1017/S0140525X07001392

Dodds, C. M., van Belle, J., Peers, P. V., Dove, A., Cusack, R., Duncan, J., & Manly, T. (2008). The effects of time-on-task and concurrent cognitive load on normal visuospatial bias. *Neuropsychology, 22*(4), 545.

Donchin, E., & Coles, M. G. (1988). Is the P300 component a manifestation of context updating? *Behavioral and brain sciences, 11*(3), 357-374.

Downar, J., Crawley, A. P., Mikulis, D. J., & Davis, K. D. (2001). The effect of task relevance on the cortical response to changes in visual and auditory stimuli: an event-related fMRI study. *Neuroimage, 14*(6), 1256-1267.

Dozois, D. J., & Beck, A. T. (2008). Cognitive schemas, beliefs and assumptions *Risk factors in depression* (pp. 119-143): Elsevier.

Dulawa, S. C., & Janowsky, D. S. (2019). Cholinergic regulation of mood: from basic and clinical studies to emerging therapeutics. *Mol Psychiatry, 24*(5), 694-709.

Dunn, B. D., Dalgleish, T., Ogilvie, A. D., & Lawrence, A. D. (2007). Heartbeat perception in depression. *Behav Res Ther, 45*(8), 1921-1930. doi:10.1016/j.brat.2006.09.008

Dunn, B. D., Galton, H. C., Morgan, R., Evans, D., Oliver, C., Meyer, M., . . . Dalgleish, T. (2010). Listening to your heart. How interoception shapes emotion experience and intuitive decision making. *Psychol Sci, 21*(12), 1835-1844. doi:10.1177/0956797610389191

Dunn, B. D., Stefanovitch, I., Evans, D., Oliver, C., Hawkins, A., & Dalgleish, T. (2010). Can you feel the beat? Interoceptive awareness is an interactive function of anxiety- and depression-specific symptom dimensions. *Behav Res Ther, 48*(11), 1133-1138. doi:10.1016/j.brat.2010.07.006

Eichele, T., Debener, S., Calhoun, V. D., Specht, K., Engel, A. K., Hugdahl, K., . . . Ullsperger, M. (2008). Prediction of human errors by maladaptive changes in event-related brain networks. *Proc Natl Acad Sci U S A, 105*(16), 6173-6178. doi:10.1073/pnas.0708965105

Eickhoff, S. B., Lotze, M., Wietek, B., Amunts, K., Enck, P., & Zilles, K. (2006). Segregation of visceral and somatosensory afferents: an fMRI and cytoarchitectonic mapping study. *Neuroimage, 31*(3), 1004-1014. doi:10.1016/j.neuroimage.2006.01.023

Evans, M. D., Hollon, S. D., DeRubeis, R. J., Piasecki, J. M., Grove, W. M., Garvey, M. J., & Tuason, V. B. (1992). Differential relapse following cognitive therapy and pharmacotherapy for depression. *Arch Gen Psychiatry, 49*(10), 802-808.

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G* Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior research methods, 39*(2), 175-191.

Feldman, H., & Friston, K. (2010). Attention, uncertainty, and free-energy. *Front Hum Neurosci, 4*, 215.

Fennell, M. J. (2004). Depression, low self-esteem and mindfulness. *Behav Res Ther, 42*(9), 1053-1067.

Fennell, M. J., & Teasdale, J. D. (1982). Cognitive therapy with chronic, drug-refractory depressed outpatients: A note of caution. *Cognitive Therapy and Research, 6*(4), 455-459.

Filipowicz, A. L., Glaze, C. M., Kable, J. W., & Gold, J. I. (2020). Pupil diameter encodes the idiosyncratic, cognitive complexity of belief updating. *Elife, 9*, e57872.

Fimm, B., Willmes, K., & Spijkers, W. (2006). The effect of low arousal on visuo-spatial attention. *Neuropsychologia, 44*(8), 1261-1268.

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. (2002). *Structured clinical interview for DSM-IV-TR axis I disorders, research version, patient edition*. Retrieved from

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., & Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences, 102*(27), 9673-9678.

Foxe, J. J., McCourt, M. E., & Javitt, D. C. (2003). Right hemisphere control of visuospatial attention: line-bisection judgments evaluated with high-density electrical mapping and source analysis☆. *Neuroimage, 19*(3), 710-726.

Francis, S. T., Kelly, E. F., Bowtell, R., Dunseath, W. J., Folger, S. E., & McGlone, F. (2000). fMRI of the responses to vibratory stimulation of digit tips. *Neuroimage, 11*(3), 188-202. doi:10.1006/nimg.2000.0541

Friston, K. (2010). The free-energy principle: a unified brain theory? *Nature reviews neuroscience, 11*(2), 127.

Furman, D. J., Waugh, C. E., Bhattacharjee, K., Thompson, R. J., & Gotlib, I. H. (2013). Interoceptive awareness, positive affect, and decision making in major depressive disorder. *J Affect Disord, 151*(2), 780-785. doi:10.1016/j.jad.2013.06.044

Fustos, J., Gramann, K., Herbert, B. M., & Pollatos, O. (2013). On the embodiment of emotion regulation: interoceptive awareness facilitates reappraisal. *Soc Cogn Affect Neurosci, 8*(8), 911-917. doi:10.1093/scan/nss089

García-Pérez, M. A., & Alcalá-Quintana, R. (2010). The difference model with guessing explains interval bias in two-alternative forced-choice detection procedures. *Journal of Sensory Studies, 25*(6), 876-898.

García-Pérez, M. A., & Alcalá-Quintana, R. (2011). Interval bias in 2AFC detection tasks: sorting out the artifacts. *Attention, Perception, & Psychophysics, 73*(7), 2332-2352.

García-Pérez, M. A., & Alcalá-Quintana, R. (2017). The indecision model of psychophysical performance in dual-presentation tasks: Parameter estimation and comparative analysis of response formats. *Front Psychol, 8*, 1142.

Garfinkel, S. N., Manassei, M. F., Hamilton-Fletcher, G., In den Bosch, Y., Critchley, H. D., & Engels, M. (2016). Interoceptive dimensions across cardiac and respiratory axes. *Philosophical Transactions of the Royal Society B: Biological Sciences, 371*(1708), 20160014.

Garfinkel, S. N., Seth, A. K., Barrett, A. B., Suzuki, K., & Critchley, H. D. (2015). Knowing your own heart: distinguishing interoceptive accuracy from interoceptive awareness. *Biological psychology, 104*, 65-74.

Gelman, A., & Rubin, D. B. (1992). Inference from iterative simulation using multiple sequences. *Statistical science, 7*(4), 457-472.

Geng, J. J., & Vossel, S. (2013). Re-evaluating the role of TPJ in attentional control: contextual updating? *Neuroscience & Biobehavioral Reviews, 37*(10), 2608-2620.

Ghaziri, J., Tucholka, A., Girard, G., Houde, J. C., Boucher, O., Gilbert, G., . . . Nguyen, D. K. (2015). The Corticocortical Structural Connectivity of the Human Insula. *Cereb Cortex*. doi:10.1093/cercor/bhv308

Golaszewski, S. M., Siedentopf, C. M., Koppelstaetter, F., Fend, M., Ischebeck, A., Gonzalez-Felipe, V., . . . Gerstenbrand, F. (2006). Human brain structures related to plantar vibrotactile stimulation: a functional magnetic resonance imaging study. *Neuroimage, 29*(3), 923-929. doi:10.1016/j.neuroimage.2005.08.052

Gotlib, I. H., & Joormann, J. (2010). Cognition and depression: current status and future directions. *Annual review of clinical psychology, 6*, 285-312.

Green, D. M., & Swets, J. A. (1966). *Signal detection theory and psychophysics* (Vol. 1): Wiley New York.

Grimm, S., Boesiger, P., Beck, J., Schuepbach, D., Bermpohl, F., Walter, M., . . . Northoff, G. (2009). Altered negative BOLD responses in the default-mode network during emotion processing in depressed subjects. *Neuropsychopharmacology, 34*(4), 932-943. doi:10.1038/npp.2008.81

Haarsma, J., Fletcher, P., Griffin, J., Taverne, H., Ziauddeen, H., Spencer, T., . . . Diederen, K. (2020). Precision weighting of cortical unsigned prediction error signals benefits learning, is mediated by dopamine, and is impaired in psychosis. *Mol Psychiatry*, 1-14.

Hackmann, A., Bennett-Levy, J., & Holmes, E. A. (2011). *Oxford guide to imagery in cognitive therapy*: Oxford university press.

Hammar, A., & Ardal, G. (2009). Cognitive functioning in major depression--a summary. *Front Hum Neurosci, 3*, 26. doi:10.3389/neuro.09.026.2009

Hammen, C. (2005). Stress and depression. *Annu. Rev. Clin. Psychol., 1*, 293-319.

Han, S., Yang, S. H., Kim, J. Y., Mo, S., Yang, E., Song, K. M., . . . Lee, H. W. (2017). Down-regulation of cholinergic signaling in the habenula induces anhedonia-like behavior. *Scientific reports, 7*(1), 1-13.

Harshaw, C. (2015). Interoceptive dysfunction: Toward an integrated framework for understanding somatic and affective disturbance in depression. *Psychological bulletin, 141*(2), 311.

Harvey, P., Le Bastard, G., Pochon, J., Levy, R., Allilaire, J., Dubois, B., & Fossati, P. (2004). Executive functions and updating of the contents of working memory in unipolar depression. *J Psychiatr Res, 38*(6), 567-576.

Hayes, S. C., Wilson, K. G., Gifford, E. V., Follette, V. M., & Strosahl, K. (1996). Experiential avoidance and behavioral disorders: A functional dimensional approach to diagnosis and treatment. *J Consult Clin Psychol, 64*(6), 1152.

He, B. J., Snyder, A. Z., Vincent, J. L., Epstein, A., Shulman, G. L., & Corbetta, M. (2007). Breakdown of functional connectivity in frontoparietal networks underlies behavioral deficits in spatial neglect. *Neuron, 53*(6), 905-918.

Hegerl, U., & Hensch, T. (2014). The vigilance regulation model of affective disorders and ADHD. *Neuroscience & Biobehavioral Reviews, 44*, 45-57.

Heller, W. (1993). Neuropsychological mechanisms of individual differences in emotion, personality, and arousal. *Neuropsychology, 7*(4), 476.

Higley, M. J., & Picciotto, M. R. (2014). Neuromodulation by acetylcholine: examples from schizophrenia and depression. *Current opinion in neurobiology, 29*, 88-95.

Hollon, S. D., DeRubeis, R. J., Shelton, R. C., Amsterdam, J. D., Salomon, R. M., O'Reardon, J. P., . . . Freeman, B. B. (2005). Prevention of relapse following cognitive therapy vs medications in moderate to severe depression. *Arch Gen Psychiatry, 62*(4), 417-422.

Hu, L., Zhang, L., Chen, R., Yu, H., Li, H., & Mouraux, A. (2015). The primary somatosensory cortex and the insula contribute differently to the processing of transient and sustained nociceptive and non-nociceptive somatosensory inputs. *Hum Brain Mapp, 36*(11), 4346-4360. doi:10.1002/hbm.22922

Hunter, E. C., Sierra, M., & David, A. S. (2004). The epidemiology of depersonalisation and derealisation. A systematic review. *Soc Psychiatry Psychiatr Epidemiol, 39*(1), 9-18. doi:10.1007/s00127-004-0701-4

Ibanez, A., Gleichgerrcht, E., & Manes, F. (2010). Clinical effects of insular damage in humans. *Brain Structure and Function, 214*(5-6), 397-410.

Itti, L., & Baldi, P. (2009). Bayesian surprise attracts human attention. *Vision research, 49*(10), 1295-1306.

Jakab, A., Molnar, P. P., Bogner, P., Beres, M., & Berenyi, E. L. (2012). Connectivity-based parcellation reveals interhemispheric differences in the insula. *Brain Topogr, 25*(3), 264-271. doi:10.1007/s10548-011-0205-y

James, W. (1894). Discussion: The physical basis of emotion. *Psychol Rev, 1*(5), 516.

Jeffreys, H. (1961). *The theory of probability*: OUP Oxford.

Jewell, G., & McCourt, M. E. (2000). Pseudoneglect: a review and meta-analysis of performance factors in line bisection tasks. *Neuropsychologia, 38*(1), 93-110.

Judd, L. L. (1997). The clinical course of unipolar major depressive disorders. *Arch Gen Psychiatry, 54*(11), 989-991.

Judd, L. L., Akiskal, H. S., Maser, J. D., Zeller, P. J., Endicott, J., Coryell, W., . . . Mueller, T. I. (1998a). Major depressive disorder: a prospective study of residual subthreshold depressive symptoms as predictor of rapid relapse. *J Affect Disord, 50*(2-3), 97-108.

Judd, L. L., Akiskal, H. S., Maser, J. D., Zeller, P. J., Endicott, J., Coryell, W., . . . Mueller, T. I. (1998b). A prospective 12-year study of subsyndromal and syndromal depressive symptoms in unipolar major depressive disorders. *Arch Gen Psychiatry, 55*(8), 694-700.

Kabat-Zinn, J. (2013). *Full catastrophe living, revised edition: how to cope with stress, pain and illness using mindfulness meditation*: Hachette uK.

Kaiser, R. H., Andrews-Hanna, J. R., Wager, T. D., & Pizzagalli, D. A. (2015). Large-Scale Network Dysfunction in Major Depressive Disorder: A Meta-analysis of Resting-State Functional Connectivity. *JAMA Psychiatry, 72*(6), 603-611. doi:10.1001/jamapsychiatry.2015.0071

Kaiser, R. H., Snyder, H. R., Goer, F., Clegg, R., Ironside, M., & Pizzagalli, D. A. (2018). Attention bias in rumination and depression: Cognitive mechanisms and brain networks. *Clinical Psychological Science, 6*(6), 765-782.

Kassambara, A. (2017). ggpubr:"ggplot2" based publication ready plots. *R package version 0.1, 6*.

Keedwell, P. (2008). *How sadness survived: The evolutionary basis of depression*: Radcliffe Publishing.

Keller, M. B., Klerman, G. L., Lavori, P. W., Coryell, W., Endicott, J., & Taylor, J. (1984). Long-term outcome of episodes of major depression: clinical and public health significance. *Jama, 252*(6), 788-792.

Keller, M. B., & Shapiro, R. W. (1981). Major depressive disorder. Initial results from a one-year prospective naturalistic follow-up study. *J Nerv Ment Dis, 169*(12), 761-768.

Keller, M. B., Shapiro, R. W., Lavori, P. W., & Wolfe, N. (1982). Relapse in major depressive disorder: analysis with the life table. *Arch Gen Psychiatry, 39*(8), 911-915.

Kelly, A. M., Uddin, L. Q., Biswal, B. B., Castellanos, F. X., & Milham, M. P. (2008). Competition between functional brain networks mediates behavioral variability. *Neuroimage, 39*(1), 527-537. doi:10.1016/j.neuroimage.2007.08.008

Kemp, A., Griffiths, K., Felmingham, K., Shankman, S. A., Drinkenburg, W., Arns, M., . . . Bryant, R. (2010). Disorder specificity despite comorbidity: resting EEG alpha asymmetry in major depressive disorder and post-traumatic stress disorder. *Biological psychology, 85*(2), 350-354.

Kendler, K. S., Kessler, R. C., Neale, M. C., Heath, A. C., & Eaves, L. J. (1993). The prediction of major depression in women: toward an integrated etiologic model. *American journal of psychiatry, 150*, 1139-1139.

Kendler, K. S., Thornton, L. M., & Gardner, C. O. (2000). Stressful life events and previous episodes in the etiology of major depression in women: an evaluation of the "kindling" hypothesis. *American journal of psychiatry, 157*(8), 1243-1251.

Kenny, M., & Williams, J. (2007). Treatment-resistant depressed patients show a good response to mindfulness-based cognitive therapy. *Behav Res Ther, 45*(3), 617-625.

Kentgen, L. M., Tenke, C. E., Pine, D. S., Fong, R., Klein, R. G., & Bruder, G. E. (2000). Electroencephalographic asymmetries in adolescents with major depression: influence of comorbidity with anxiety disorders. *Journal of abnormal psychology, 109*(4), 797.

Kessler, R. C., & Bromet, E. J. (2013). The epidemiology of depression across cultures. *Annual review of public health, 34*, 119-138.

Kessler, R. C., Nelson, C. B., McGonagle, K. A., Liu, J., Swartz, M., & Blazer, D. G. (1996). Comorbidity of DSM–III–R major depressive disorder in the general population: results from the US National Comorbidity Survey. *The British Journal of Psychiatry, 168*(S30), 17-30.

Khalsa, S. S., Adolphs, R., Cameron, O. G., Critchley, H. D., Davenport, P. W., Feinstein, J. S., . . . Mehling, W. E. (2018). Interoception and mental health: a roadmap. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 3*(6), 501-513.

Khil, L., Rahe, C., Wellmann, J., Baune, B. T., Wersching, H., & Berger, K. (2016). Association between major depressive disorder and odor identification impairment. *J Affect Disord, 203*, 332-338.

Kim, K., Müller, M. L., Bohnen, N. I., Sarter, M., & Lustig, C. (2017). Thalamic cholinergic innervation makes a specific bottom-up contribution to signal detection: Evidence from Parkinson's disease patients with defined cholinergic losses. *Neuroimage, 149*, 295-304.

Kim, K., Müller, M. L., Bohnen, N. I., Sarter, M., & Lustig, C. (2019). The cortical cholinergic system contributes to the top-down control of distraction: Evidence from patients with Parkinson's disease. *Neuroimage, 190*, 107-117.

Klauenberg, S., Maier, C., Assion, H.-J., Hoffmann, A., Krumova, E. K., Magerl, W., . . . Juckel, G. (2008). Depression and changed pain perception: hints for a central disinhibition mechanism. *Pain, 140*(2), 332-343.

Klawohn, J., Santopetro, N. J., Meyer, A., & Hajcak, G. (2020). Reduced P300 in depression: Evidence from a flanker task and impact on ERN, CRN, and Pe. *Psychophysiology*, e13520.

Klein, S. A. (2001). Measuring, estimating, and understanding the psychometric function: A commentary. *Percept Psychophys, 63*(8), 1421-1455.

Kleiner, M., Brainard, D., & Pelli, D. (2007). What's new in Psychtoolbox-3?

Knill, D. C., & Pouget, A. (2004). The Bayesian brain: the role of uncertainty in neural coding and computation. *Trends Neurosci, 27*(12), 712-719.

Kruschke, J. (2014). *Doing Bayesian data analysis: A tutorial with R, JAGS, and Stan*: Academic Press.

Kucyi, A., Hodaie, M., & Davis, K. D. (2012). Lateralization in intrinsic functional connectivity of the temporoparietal junction with salience-and attention-related brain networks. *J Neurophysiol, 108*(12), 3382-3392.

Kuyken, W., Hayes, R., Barrett, B., Byng, R., Dalgleish, T., Kessler, D., . . . Cardy, J. (2015). Effectiveness and cost-effectiveness of mindfulness-based cognitive therapy compared with maintenance antidepressant treatment in the prevention of depressive relapse or recurrence (PREVENT): a randomised controlled trial. *The Lancet, 386*(9988), 63-73.

Langner, R., & Eickhoff, S. B. (2013). Sustaining attention to simple tasks: a meta-analytic review of the neural mechanisms of vigilant attention. *Psychological bulletin, 139*(4), 870.

Le, T. M., Borghi, J. A., Kujawa, A. J., Klein, D. N., & Leung, H.-C. (2017). Alterations in visual cortical activation and connectivity with prefrontal cortex during working memory updating in major depressive disorder. *NeuroImage: Clinical, 14*, 43-53.

Lee, M. D., & Wagenmakers, E.-J. (2014). *Bayesian cognitive modeling: A practical course*: Cambridge university press.

Leek, M. R. (2001). Adaptive procedures in psychophysical research. *Percept Psychophys, 63*(8), 1279-1292.

Leonard, B. E. (2001). Stress, norepinephrine and depression. *Journal of psychiatry & neuroscience: JPN, 26*(Suppl), S11.

Levitt, H. (1971). Transformed up-down methods in psychoacoustics. *J Acoust Soc Am, 49*(2), Suppl 2:467+.

Leweke, F., Leichsenring, F., Kruse, J., & Hermes, S. (2012). Is alexithymia associated with specific mental disorders? *Psychopathology, 45*(1), 22-28. doi:10.1159/000325170

Li, C. S., Yan, P., Bergquist, K. L., & Sinha, R. (2007). Greater activation of the "default" brain regions predicts stop signal errors. *Neuroimage, 38*(3), 640-648. doi:10.1016/j.neuroimage.2007.07.021

Liotti, M., & Mayberg, H. S. (2001). The role of functional neuroimaging in the neuropsychology of depression. *Journal of Clinical and Experimental Neuropsychology, 23*(1), 121-136.

Liotti, M., Sava, D., Rizzolatti, G., & Caffarra, P. (1991). Differential hemispheric asymmetries in depression and anxiety: a reaction-time study. *Biol Psychiatry, 29*(9), 887-899.

Lobbestael, J., Leurgans, M., & Arntz, A. (2011). Inter-rater reliability of the Structured Clinical Interview for DSM-IV Axis I disorders (SCID I) and Axis II disorders (SCID II). *Clinical Psychology & Psychotherapy, 18*(1), 75-79.

Luck, S. J., Woodman, G. F., & Vogel, E. K. (2000). Event-related potential studies of attention. *Trends Cogn Sci, 4*(11), 432-440.

Ma, S. H., & Teasdale, J. D. (2004). Mindfulness-based cognitive therapy for depression: replication and exploration of differential relapse prevention effects. *J Consult Clin Psychol, 72*(1), 31.

Maletic, V., Eramo, A., Gwin, K., Offord, S. J., & Duffy, R. A. (2017). The role of norepinephrine and its α-adrenergic receptors in the pathophysiology and treatment of major depressive disorder and schizophrenia: a systematic review. *Frontiers in psychiatry, 8*, 42.

Malone, J., & Hemsley, D. (1977). Lowered responsiveness and auditory signal detectability during depression. *Psychological Medicine, 7*(4), 717-722.

Mangun, G. R., & Hillyard, S. A. (1991). Modulations of sensory-evoked brain potentials indicate changes in perceptual processing during visual-spatial priming. *Journal of Experimental Psychology: Human perception and performance, 17*(4), 1057.

Manly, T., Dobler, V. B., Dodds, C. M., & George, M. A. (2005). Rightward shift in spatial awareness with declining alertness. *Neuropsychologia, 43*(12), 1721-1728.

Marazziti, D., Castrogiovanni, P., Rossi, A., Rosa, C., Ghione, S., Di Muro, A., . . . Cassano, G. B. (1998). Pain threshold is reduced in depression. *International Journal of Neuropsychopharmacology, 1*(1), 45-48.

Marsala, S. Z., Pistacchi, M., Tocco, P., Gioulis, M., Fabris, F., Brigo, F., & Tinazzi, M. (2015). Pain perception in major depressive disorder: A neurophysiological case–control study. *Journal of the neurological sciences, 357*(1-2), 19-21.

Mazzola, L., Faillenot, I., Barral, F. G., Mauguiere, F., & Peyron, R. (2012). Spatial segregation of somato-sensory and pain activations in the human operculo-insular cortex. *Neuroimage, 60*(1), 409-418. doi:10.1016/j.neuroimage.2011.12.072

Mehling, W. E., Price, C., Daubenmier, J. J., Acree, M., Bartmess, E., & Stewart, A. (2012). The multidimensional assessment of interoceptive awareness (MAIA). *PLoS One*.

Mengotti, P., Dombert, P. L., Fink, G. R., & Vossel, S. (2017). Disruption of the right temporoparietal junction impairs probabilistic belief updating. *Journal of Neuroscience, 37*(22), 5419-5428.

Metzger, L. J., Paige, S. R., Carson, M. A., Lasko, N. B., Paulus, L. A., Pitman, R. K., & Orr, S. P. (2004). PTSD arousal and depression symptoms associated with increased right-sided parietal EEG asymmetry. *Journal of abnormal psychology, 113*(2), 324.

Mialet, J.-P., Pope, H., & Yurgelun-Todd, D. (1996). Impaired attention in depressive states: a non-specific deficit? *Psychological Medicine, 26*(5), 1009-1020.

Moore, R. G., & Garland, A. (2004). *Cognitive therapy for chronic and persistent depression*: John Wiley & Sons.

Moret, C., & Briley, M. (2011). The importance of norepinephrine in depression. *Neuropsychiatric disease and treatment, 7*(Suppl 1), 9.

Morilak, D. A., Barrera, G., Echevarria, D. J., Garcia, A. S., Hernandez, A., Ma, S., & Petre, C. O. (2005). Role of brain norepinephrine in the behavioral response to stress. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 29*(8), 1214-1224.

Moroz, B., Nuller, I., Ustimova, I., & Andreev, B. (1990). Study of pain sensitivity based on the indicators of electro-odontometry in patients with depersonalization and depressive disorders. *Zhurnal nevropatologii i psikhiatrii imeni SS Korsakova (Moscow, Russia: 1952), 90*(10), 81-82.

Mula, M., Pini, S., & Cassano, G. B. (2007). The neurobiology and clinical significance of depersonalization in mood and anxiety disorders: A critical reappraisal. *J Affect Disord, 99*(1-3), 91-99.

Mulders, P. C., van Eijndhoven, P. F., Schene, A. H., Beckmann, C. F., & Tendolkar, I. (2015). Resting-state functional connectivity in major depressive disorder: A review. *Neurosci Biobehav Rev, 56*, 330-344. doi:10.1016/j.neubiorev.2015.07.014

Newman, D. P., O'Connell, R. G., & Bellgrove, M. A. (2013). Linking time-on-task, spatial bias and hemispheric activation asymmetry: a neural correlate of rightward attention drift. *Neuropsychologia, 51*(7), 1215-1223.

NICE. (2009). Depression in adults: recognition and management: The National Institute for Health and Care Excellence London.

Nieuwenhuis, S., Aston-Jones, G., & Cohen, J. D. (2005). Decision making, the P3, and the locus coeruleus--norepinephrine system. *Psychological bulletin, 131*(4), 510.

Nolen-Hoeksema, S. (2004). The response styles theory. *Depressive rumination, 107*.

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia, 9*(1), 97-113.

Ostrowsky, K., Magnin, M., Ryvlin, P., Isnard, J., Guenot, M., & Mauguiere, F. (2002). Representation of pain and somatic sensation in the human insula: a study of responses to direct electrical cortical stimulation. *Cereb Cortex, 12*(4), 376-385.

Oudeyer, P.-Y., & Kaplan, F. (2009). What is intrinsic motivation? A typology of computational approaches. *Frontiers in neurorobotics, 1*, 6.

Padesky, C. A. (1994). Schema change processes in cognitive therapy. *Clinical Psychology & Psychotherapy, 1*(5), 267-278.

Paladini, R. E., Diana, L., Nyffeler, T., Mosimann, U. P., Nef, T., Müri, R. M., & Cazzoli, D. (2016). The asymmetrical influence of increasing time-on-task on attentional disengagement. *Neuropsychologia, 92*, 107-114.

Papageorgiou, C., & Wells, A. (2000). Treatment of recurrent major depression with attention training. *Cognitive and Behavioral Practice, 7*(4), 407-413.

Pardo, J. V., Pardo, P. J., Humes, S. W., & Posner, M. I. (2006). Neurocognitive dysfunction in antidepressant-free, non-elderly patients with unipolar depression: Alerting and covert orienting of visuospatial attention. *J Affect Disord, 92*(1), 71-78.

Pariante, C. M., & Lightman, S. L. (2008). The HPA axis in major depression: classical theories and new developments. *Trends Neurosci, 31*(9), 464-468. doi:10.1016/j.tins.2008.06.006

Parr, T., & Friston, K. (2019). Attention or salience? *Current opinion in psychology, 29*, 1-5.

Paulus, M. P., Feinstein, J. S., & Khalsa, S. S. (2019). An active inference approach to interoceptive psychopathology. *Annual review of clinical psychology, 15*, 97-122.

Paulus, M. P., & Stein, M. B. (2010). Interoception in anxiety and depression. *Brain Struct Funct, 214*(5-6), 451-463. doi:10.1007/s00429-010-0258-9

Pause, B. M., Miranda, A., Göder, R., Aldenhoff, J. B., & Ferstl, R. (2001). Reduced olfactory performance in patients with major depression. *J Psychiatr Res, 35*(5), 271-277.

Paykel, E. S., Scott, J., Teasdale, J. D., Johnson, A. L., Garland, A., Moore, R., . . . Abbott, R. (1999). Prevention of relapse in residual depression by cognitive therapy: a controlled trial. *Arch Gen Psychiatry, 56*(9), 829-835.

Pelli, D. G. (1997). The VideoToolbox software for visual psychophysics: transforming numbers into movies. *Spat Vis, 10*(4), 437-442.

Petzschner, F. H., Weber, L. A., Wellstein, K. V., Paolini, G., Do, C. T., & Stephan, K. E. (2019). Focus of attention modulates the heartbeat evoked potential. *Neuroimage, 186*, 595-606.

Pizzagalli, D. A., Jahn, A. L., & O'Shea, J. P. (2005). Toward an objective characterization of an anhedonic phenotype: a signal-detection approach. *Biol Psychiatry, 57*(4), 319-327.

Plummer, M. (2017). JAGS version 4.3. 0 user manual. 28 June 2017.

Plummer, M., Best, N., Cowles, K., & Vines, K. (2006). CODA: convergence diagnosis and output analysis for MCMC. R News 6 (1), 7–11 (2006).

Posner, M. I. (1980). Orienting of attention. *Q J Exp Psychol, 32*(1), 3-25.

Posternak, M. A., Solomon, D. A., Leon, A. C., Mueller, T. I., Shea, M. T., Endicott, J., & Keller, M. B. (2006). The naturalistic course of unipolar major depression in the absence of somatic therapy. *J Nerv Ment Dis, 194*(5), 324-329.

Preusser, S., Thiel, S. D., Rook, C., Roggenhofer, E., Kosatschek, A., Draganski, B., . . . Pleger, B. (2015). The perception of touch and the ventral somatosensory pathway. *Brain, 138*(Pt 3), 540-548. doi:10.1093/brain/awu370

Prins, N. (2012). The psychometric function: The lapse rate revisited. *Journal of Vision, 12*(6), 25-25.

Pritchard, W. S. (1981). Psychophysiology of P300. *Psychological bulletin, 89*(3), 506.

Ratcliffe, M. (2014). The phenomenology of depression and the nature of empathy. *Med Health Care Philos, 17*(2), 269-280. doi:10.1007/s11019-013-9499-8

Rock, P., Roiser, J., Riedel, W., & Blackwell, A. (2014). Cognitive impairment in depression: a systematic review and meta-analysis. *Psychological Medicine, 44*(10), 2029-2040.

Rottenberg, J., Joormann, J., Brozovich, F., & Gotlib, I. H. (2005). Emotional intensity of idiographic sad memories in depression predicts symptom levels 1 year later. *Emotion, 5*(2), 238.

Rouder, J. N., Lu, J., Speckman, P., Sun, D., & Jiang, Y. (2005). A hierarchical model for estimating response time distributions. *Psychonomic Bulletin & Review, 12*(2), 195-223.

Sales, A. C., Friston, K. J., Jones, M. W., Pickering, A. E., & Moran, R. J. (2019). Locus Coeruleus tracking of prediction errors optimises cognitive flexibility: An Active Inference model. *PLoS computational biology, 15*(1), e1006267.

Sarter, M., Hasselmo, M. E., Bruno, J. P., & Givens, B. (2005). Unraveling the attentional functions of cortical cholinergic inputs: interactions between signal-driven and cognitive modulation of signal detection. *Brain research reviews, 48*(1), 98-111.

Sarter, M., & Lustig, C. (2019). Cholinergic double duty: cue detection and attentional control. *Current opinion in psychology, 29*, 102-107.

Sarter, M., & Lustig, C. (2020). Forebrain cholinergic signaling: Wired and phasic, not tonic, and causing behavior. *Journal of Neuroscience, 40*(4), 712-719.

Sayar, K., Kirmayer, L. J., & Taillefer, S. S. (2003). Predictors of somatic symptoms in depressive disorder. *Gen Hosp Psychiatry, 25*(2), 108-114.

Schachter, S., & Singer, J. E. (1962). Cognitive, social, and physiological determinants of emotional state. *Psychol Rev, 69*, 379-399.

Schäfer, T., & Schwarz, M. A. (2019). The meaningfulness of effect sizes in psychological research: Differences between sub-disciplines and the impact of potential biases. *Front Psychol, 10*, 813.

Schandry, R. (1981). Heart beat perception and emotional experience. *Psychophysiology, 18*(4), 483-488.

Schmitz, T. W., & Duncan, J. (2018). Normalization and the cholinergic microcircuit: a unified basis for attention. *Trends Cogn Sci, 22*(5), 422-437.

Schooler, J. W., Smallwood, J., Christoff, K., Handy, T. C., Reichle, E. D., & Sayette, M. A. (2011). Meta-awareness, perceptual decoupling and the wandering mind. *Trends Cogn Sci, 15*(7), 319-326.

Schwenzer, M., Zattarin, E., Grözinger, M., & Mathiak, K. (2012). Impaired pitch identification as a potential marker for depression. *BMC psychiatry, 12*(1), 32.

Segal, Z. V., Williams, J. M. G., & Teasdale, J. D. (2002). *Mindfulness-based cognitive therapy for depression*. New York: Guilford Press.

Seth, A. K. (2013). Interoceptive inference, emotion, and the embodied self. *Trends Cogn Sci, 17*(11), 565-573. doi:10.1016/j.tics.2013.09.007

Sheline, Y. I., Barch, D. M., Price, J. L., Rundle, M. M., Vaishnavi, S. N., Snyder, A. Z., . . . Raichle, M. E. (2009). The default mode network and self-referential processes in depression. *Proc Natl Acad Sci U S A, 106*(6), 1942-1947. doi:10.1073/pnas.0812686106

Siedentopf, C. M., Heubach, K., Ischebeck, A., Gallasch, E., Fend, M., Mottaghy, F. M., . . . Golaszewski, S. M. (2008). Variability of BOLD response evoked by foot vibrotactile stimulation: influence of vibration amplitude and stimulus waveform. *Neuroimage, 41*(2), 504-510. doi:10.1016/j.neuroimage.2008.02.049

Snyder, H. R. (2013). Major depressive disorder is associated with broad impairments on neuropsychological measures of executive function: a meta-analysis and review. *Psychological bulletin, 139*(1), 81.

Solomon, D. A., Keller, M. B., Leon, A. C., Mueller, T. I., Lavori, P. W., Shea, M. T., . . . Maser, J. D. (2000). Multiple recurrences of major depressive disorder. *American journal of psychiatry, 157*(2), 229-233.

Sonuga-Barke, E. J., & Castellanos, F. X. (2007). Spontaneous attentional fluctuations in impaired states and pathological conditions: a neurobiological hypothesis. *Neurosci Biobehav Rev, 31*(7), 977-986. doi:10.1016/j.neubiorev.2007.02.005

Sotsky, S. M., Glass, D. R., Shea, M. T., Pilkonis, P. A., Collins, F., Elkin, I., . . . Moyer, J. (2006). Patient predictors of response to psychotherapy and pharmacotherapy: findings in the NIMH Treatment of Depression Collaborative Research Program. *Focus, 148*(2), 997-290.

Spence, C. (2010). Crossmodal spatial attention. *Annals of the New York Academy of Sciences, 1191*(1), 182-200.

Steiner, J. E., Lidar-Lifschitz, D., & Perl, E. (1993). Taste and odor: reactivity in depressive disorders, a multidisciplinary approach. *Perceptual and Motor Skills, 77*(3_suppl), 1331-1346.

Stephan, K. E., Manjaly, Z. M., Mathys, C. D., Weber, L. A., Paliwal, S., Gard, T., . . . Seth, A. K. (2016). Allostatic self-efficacy: a metacognitive theory of dyshomeostasis-induced fatigue and depression. *Front Hum Neurosci, 10*, 550.

Swiecicki, L., Zatorski, P., Bzinkowska, D., Sienkiewicz-Jarosz, H., Szyndler, J., & Scinska, A. (2009). Gustatory and olfactory function in patients with unipolar and bipolar depression. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 33*(5), 827-834.

Team, R. C. (2017). R: A language and environment for statistical computing [Internet]. Vienna, Austria; 2014.

Teasdale, J. D., Segal, Z. V., Williams, J. M. G., Ridgeway, V. A., Soulsby, J. M., & Lau, M. A. (2000). Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *J Consult Clin Psychol, 68*(4), 615.

Terhaar, J., Boettger, M. K., Schwier, C., Wagner, G., Israel, A.-K., & Bär, K.-J. (2010). Increased sensitivity to heat pain after sad mood induction in female patients with major depression. *European Journal of Pain, 14*(5), 559-563.

Terhaar, J., Viola, F. C., Bar, K. J., & Debener, S. (2012). Heartbeat evoked potentials mirror altered body perception in depressed patients. *Clin Neurophysiol, 123*(10), 1950-1957. doi:10.1016/j.clinph.2012.02.086

Thase, M. E., Reynolds, C. F., Frank, E., & Simons, A. D. (1994). Response to cognitive-behavioral therapy in chronic depression. *Journal of Psychotherapy Practice & Research*.

Thiele, A., & Bellgrove, M. A. (2018). Neuromodulation of attention. *Neuron, 97*(4), 769-785.

Trivedi, M. H., Rush, A. J., Wisniewski, S. R., Nierenberg, A. A., Warden, D., Ritz, L., . . . McGrath, P. J. (2006). Evaluation of outcomes with citalopram for depression using measurement-based care in STAR* D: implications for clinical practice. *American journal of psychiatry, 163*(1), 28-40.

Vaccarino, A. L., Sills, T. L., Evans, K. R., & Kalali, A. H. (2008). Prevalence and association of somatic symptoms in patients with Major Depressive Disorder. *J Affect Disord, 110*(3), 270-276. doi:10.1016/j.jad.2008.01.009

Valentino, R. J., & Van Bockstaele, E. (2008). Convergent regulation of locus coeruleus activity as an adaptive response to stress. *Eur J Pharmacol, 583*(2-3), 194-203.

Van Der Meere, J., Börger, N., & Van Os, T. (2007). Sustained attention in major unipolar depression. *Perceptual and Motor Skills, 104*(3_suppl), 1350-1354.

Vincent, B. T. (2015). Bayesian accounts of covert selective attention: a tutorial review. *Attention, Perception, & Psychophysics, 77*(4), 1013-1032.

Vos, T., Abajobir, A. A., Abate, K. H., Abbafati, C., Abbas, K. M., Abd-Allah, F., . . . Abera, S. F. (2017). Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet, 390*(10100), 1211-1259.

Vossel, S., Mathys, C., Daunizeau, J., Bauer, M., Driver, J., Friston, K. J., & Stephan, K. E. (2013). Spatial attention, precision, and Bayesian inference: a study of saccadic response speed. *Cerebral cortex, 24*(6), 1436-1450.

Voyer, D., Voyer, S. D., & Tramonte, L. (2012). Free-viewing laterality tasks: A multilevel meta-analysis. *Neuropsychology, 26*(5), 551.

Warriner, A. B., Kuperman, V., & Brysbaert, M. (2013). Norms of valence, arousal, and dominance for 13,915 English lemmas. *Behavior research methods, 45*(4), 1191-1207.

Weissman, D. H., Roberts, K. C., Visscher, K. M., & Woldorff, M. G. (2006). The neural bases of momentary lapses in attention. *Nat Neurosci, 9*(7), 971-978. doi:10.1038/nn1727

Wells, K. B., Burnam, M. A., Rogers, W., Hays, R., & Camp, P. (1992). The course of depression in adult outpatients: results from the Medical Outcomes Study. *Arch Gen Psychiatry, 49*(10), 788-794.

Wichmann, F. A., & Hill, N. J. (2001). The psychometric function: I. Fitting, sampling, and goodness of fit. *Percept Psychophys, 63*(8), 1293-1313.

Wickham, H. (2016). *ggplot2: elegant graphics for data analysis*: Springer.

Wiech, K., Jbabdi, S., Lin, C. S., Andersson, J., & Tracey, I. (2014). Differential structural and resting state connectivity between insular subdivisions and other pain-related brain regions. *Pain, 155*(10), 2047-2055. doi:10.1016/j.pain.2014.07.009

Williams, J. M. G., Crane, C., Barnhofer, T., Brennan, K., Duggan, D. S., Fennell, M. J., . . . Von Rohr, I. R. (2014). Mindfulness-based cognitive therapy for preventing relapse in recurrent depression: a randomized dismantling trial. *J Consult Clin Psychol, 82*(2), 275.

Wohleb, E. S., Franklin, T., Iwata, M., & Duman, R. S. (2016). Integrating neuroimmune systems in the neurobiology of depression. *Nat Rev Neurosci, 17*(8), 497-511. doi:10.1038/nrn.2016.69

Yang, X., Ma, X., Huang, B., Sun, G., Zhao, L., Lin, D., . . . Ma, X. (2015). Gray matter volume abnormalities were associated with sustained attention in unmedicated major depression. *Compr Psychiatry, 63*, 71-79.

Yovell, Y., Sackeim, H. A., Epstein, D. G., Prudic, J., Devanand, D., Settembrino, J. M., & Bruder, G. E. (1995). Hearing Loss and Asymmetry in Major. *Neurosciences, 7*, 82-89.

Yu, A., & Dayan, P. (2003). Acetylcholine, Norepinephrine, and Spatial Attention. *Computer Science Preprint Archive, 2003*(6), 18-26.

Yu, A., & Dayan, P. (2005). Uncertainty, neuromodulation, and attention. *Neuron, 46*(4), 681-692.

Zhao, S., Chait, M., Dick, F., Dayan, P., Furukawa, S., & Liao, H.-I. (2019). Pupil-linked phasic arousal evoked by violation but not emergence of regularity within rapid sound sequences. *Nat Commun, 10*.

zu Eulenburg, P., Baumgartner, U., Treede, R. D., & Dieterich, M. (2013). Interoceptive and multimodal functions of the operculo-insular cortex: tactile, nociceptive and vestibular representations. *Neuroimage, 83*, 75-86. doi:10.1016/j.neuroimage.2013.06.057

Appendix A: Sensitivity analyses and model fit

A.1. Study 1 GLMM

Sensitivity analyses

A series of sensitivity analyses was conducted to assess the sensitivity of the estimates to the choice of priors. In the first, a robust version of the model was implemented by replacing the normal priors on the β coefficients with t distributions. For all β

$$\beta \sim t(0,2,\nu = 5) \tag{81}$$

Two further sensitivity analyses included weakly informative hyperpriors on the scale of the priors for the coefficients as follows. For all σ^{β}

$$\sigma^{\beta} \sim t(0,1,\nu = 5), \sigma^{\beta} \geq 0 \tag{82}$$

$$\sigma^{\beta} = \sqrt{\frac{1}{\tau^{\beta}}}\ ,\ \tau^{\beta} \sim Gamma(0.001,0.001) \tag{83}$$

All sensitivity analyses produced comparable parameter estimates to the original analysis, indicating robustness to the choice of priors.

Posterior predictive check

The results of a posterior predictive check on the fit of the model are shown in Figure A.1 Fit is good and error relatively small close to the threshold where the majority of observations are clustered. Error is higher at the lower asymptote where observations are relatively sparse.

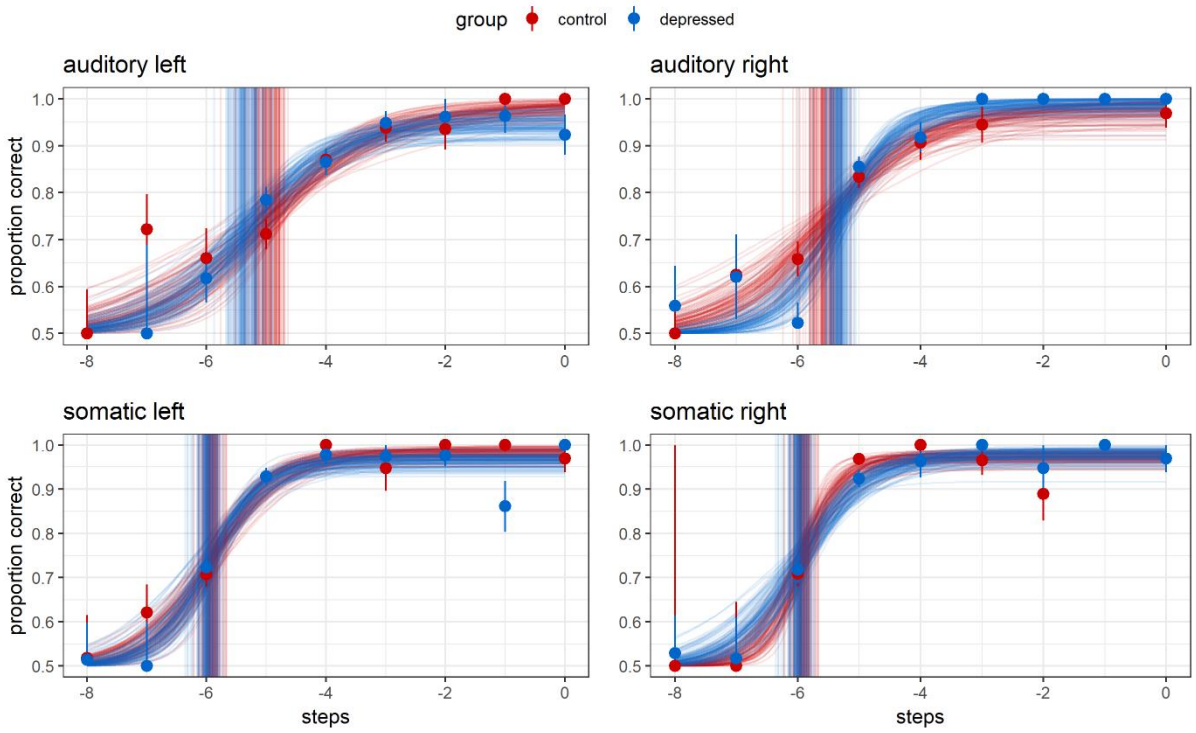


Figure A.1: Study 1 GLMM: posterior predictive check. Panels show logistic curves and estimated thresholds (vertical lines) for 100 simulations based on draws from the posterior distributions of model parameters for each group and condition. Points represent the observed data ± 1 standard error.

A.2. Study 2

A.2.1. Study 2 signal detection model

Sensitivity analyses

Study 2 hierarchical signal detection model. A series of sensitivity analyses were conducted to assess the sensitivity of the estimates to the choice of priors. In the first, a robust version of the model was implemented replacing the normal priors on the α coefficients with t distributions. For all α (except α0, for which the location parameter of the prior was μ as before)

$$\alpha \sim t(0, \sigma, \nu = 5) \tag{84}$$

The second sensitivity analysis placed a hyperprior on the scale of the prior for the precision of the coefficients of the fixed factors, to allow all factor coefficients to exert shrinkage upon each other rather than shrinkage solely occurring between levels of the same factor. For all σ^F

$$\sigma_f^F \sim t\left(0, \sigma^{shrinkage}, \nu\right),\ \sigma_f^F \geq 0 \tag{85}$$

$$\sigma^{shrinkage} \sim\ t(0,1,\nu)\ ,\ \sigma^{shrinkage} \geq 0 \tag{86}$$

The final sensitivity analysis replaced all folded t prior distributions for σ with Gamma (0.001,0.001) priors for τ where

$$\sigma = \sqrt{\frac{1}{\tau}} \tag{87}$$

None of the alternative prior distributions substantively affected the model outcomes.

Posterior predictive check

Model fit was assessed by comparing d' and c estimates derived from the model to point estimates derived directly from the Study 2 data. 1000 random draws were made from the posterior distributions of d' and c for each participant in each condition to create 1000 simulated datasets which were then compared with point estimates of d' and c, calculated directly from the observed data as follows:

$$\hat{d}' = \frac{\Phi^{-1}(\hat{\rho}_1) + \Phi^{-1}(\hat{\rho}_2)}{\sqrt{2}} \tag{88}$$

$$\hat{c} = -0.5(\Phi^{-1}(\hat{\rho}_1) - \Phi^{-1}(\hat{\rho}_2)) \tag{89}$$

where $\hat{p}_1$ is the proportion of correct responses following a left-sided stimulus, and $\hat{p}_2$ is the proportion of correct responses following a right-sided stimulus. p estimates of 0.99 or 0.01 were substituted for estimates of 1 or 0 respectively, in order to avoid infinite estimates of d' or c (NB this adjustment employed a constant rather than a proportion of trials due to the highly variable trial Ns resulting from the adaptive paradigm).

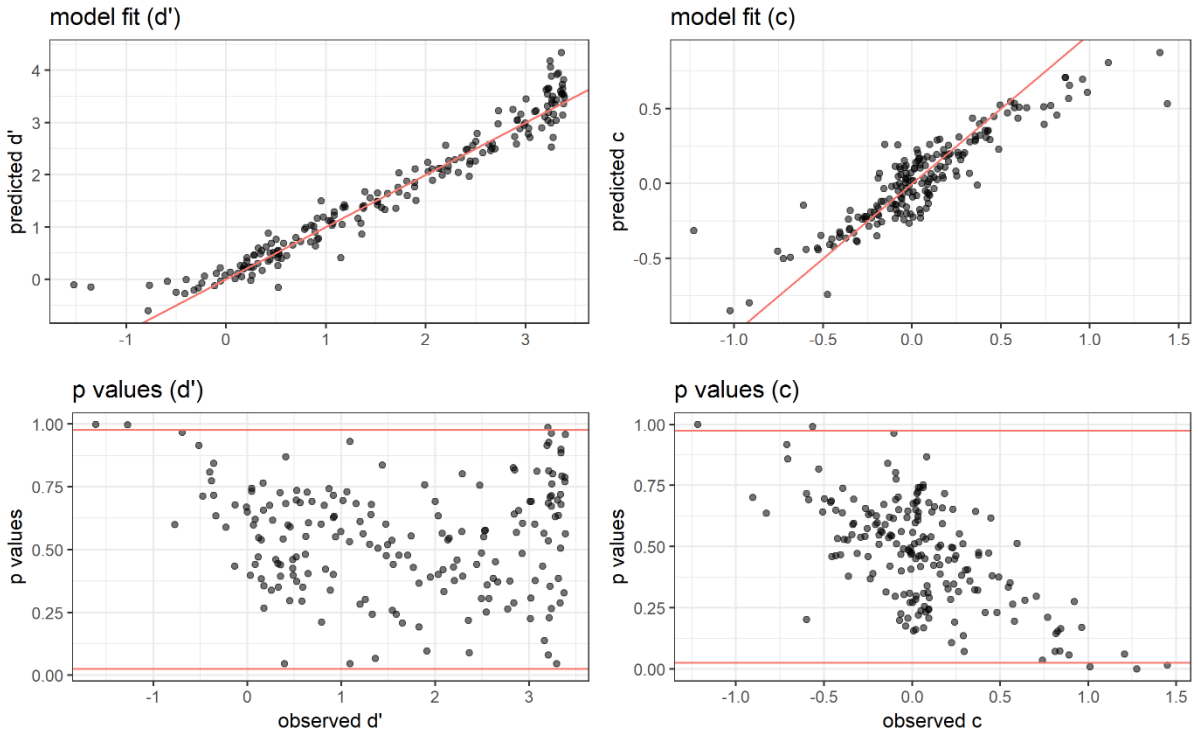


Figure A.2: Study 2 signal detection model: posterior predictive check. Model predictions for d' are consistent with (top left panel) and no more extreme than (bottom left panel) point estimates derived from the observed data. Predictions for c are somewhat more conservative than observed point estimates with respect to large positive or negative values of c, but in general are consistent with (top right panel) and no more extreme than (bottom right panel) the study observations.

Figure A.2 shows the point estimates by participant and condition plotted against the mean model-derived predicted data by participant and condition (upper panels) and against p-values respectively derived from the formulae:

$$P(d'^{simulated} \geq \hat{d}'^{observed}) \tag{90}$$

$$P(c^{simulated} \geq \hat{c}^{observed}) \tag{91}$$

Examination of the p-values indicates that for the vast majority of d' and c estimates the predicted data are no more extreme than the observed data. In the case of d', the model predictions tend to be larger than occasional point estimates less than 0, suggesting that the model has succeeded in avoiding large theoretically impossible negative predictions of d'. In the case of c, the model predicts somewhat larger values when point estimates are very small, and somewhat smaller values when point estimates are very large, suggesting that its estimates have been affected by shrinkage and are therefore more conservative than those calculated directly from the data. The positive relationships apparent between mean model predictions and observed point estimates plotted by participant and condition suggest that the model is succeeding in predicting participant and condition effects.

The same simulated data are presented in Figure A.3, averaged over group and condition.

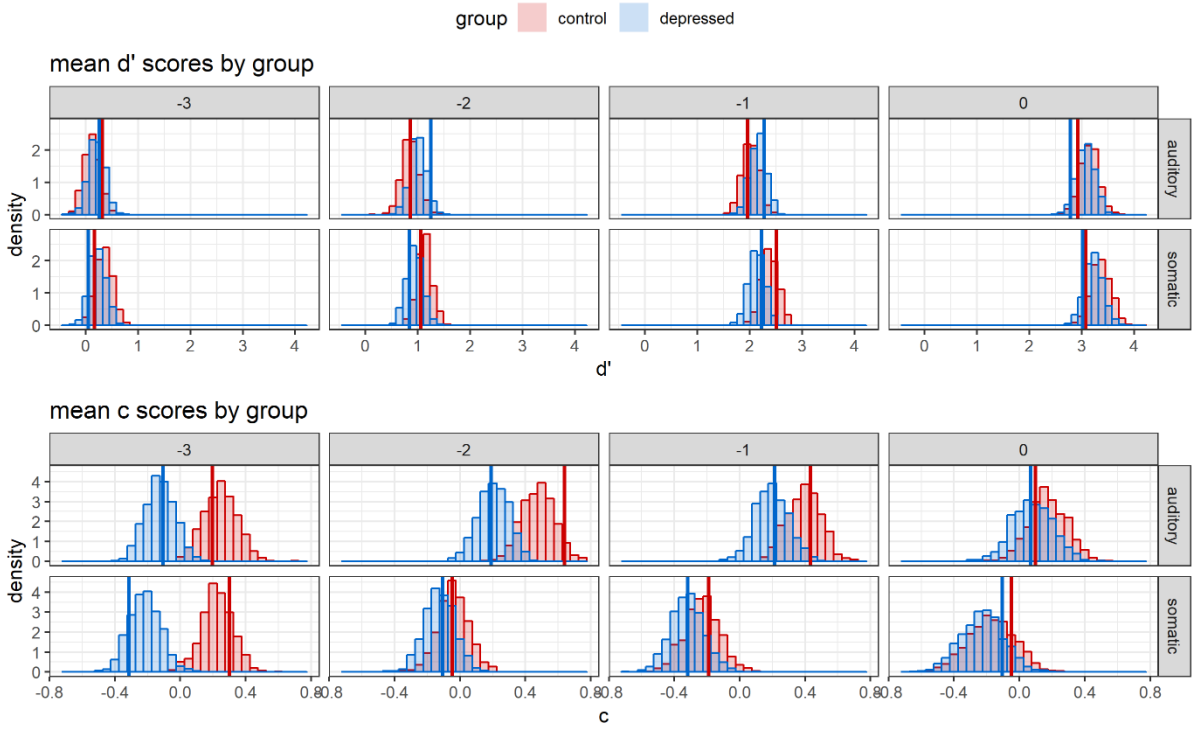


Figure A.3: Study 2 signal detection model: group-level posterior predictive check. Histograms show the distributions of 1000 model predictions for values of d' and c averaged by group and condition. Vertical lines show the point estimates for d' and c averages derived from the observed data. In general the model predictions are reasonably consistent with the point estimates.

A.2.2. Study 2 RT distributions mixture model

Sensitivity analysis

The mixture model with a linear model placed upon two Weibull parameters was derived from an unrestricted random effects model with gamma priors described below in Appendix F.2. The outcomes of the linear model and the unrestricted model were very consistent, in terms both of the distribution of lapses and fast guesses, and in terms of the effects on the Weibull parameters.

Posterior predictive check

Model fit was assessed by comparing observed RTs to simulated RTs derived from underlying 3-parameter Weibull distributions predicted by the model. A random draw was made from the posterior distribution of each Weibull parameter for each participant in each condition, and reaction times in the same proportion to those occurring in the observed data were simulated by making draws from the resulting Weibull distributions. This process was repeated 1000 times to create 1000 simulated

datasets. Figure A.4 shows the observed RT means plotted against the predicted RT means for each participant in each condition and against p-values derived from the formula

$$P(\overline{RT}_{jk}^{predicted} \geq \overline{RT}_{jk}^{observed}) \quad (92)$$

Examination of the p values indicates that the predicted data are no more extreme than the observed data. The positive relationship apparent between model predictions and observed data suggest that the model is succeeding in predicting participant and condition effects. The bottom-left panel Figure A.4 shows a quantile-quantile plot in which the quantiles of the observed data (excluding probable lapses and fast guesses) are plotted against the quantiles of 50 simulated datasets. The simulated data are comprised of 50 randomly chosen Weibull-derived datasets drawn from the set of 1000 described above. As can be seen from the QQ plot, this predicted distribution is similar to the distribution of the observed data. This provides some reassurance that the Weibull is an appropriate distribution for modelling these data.

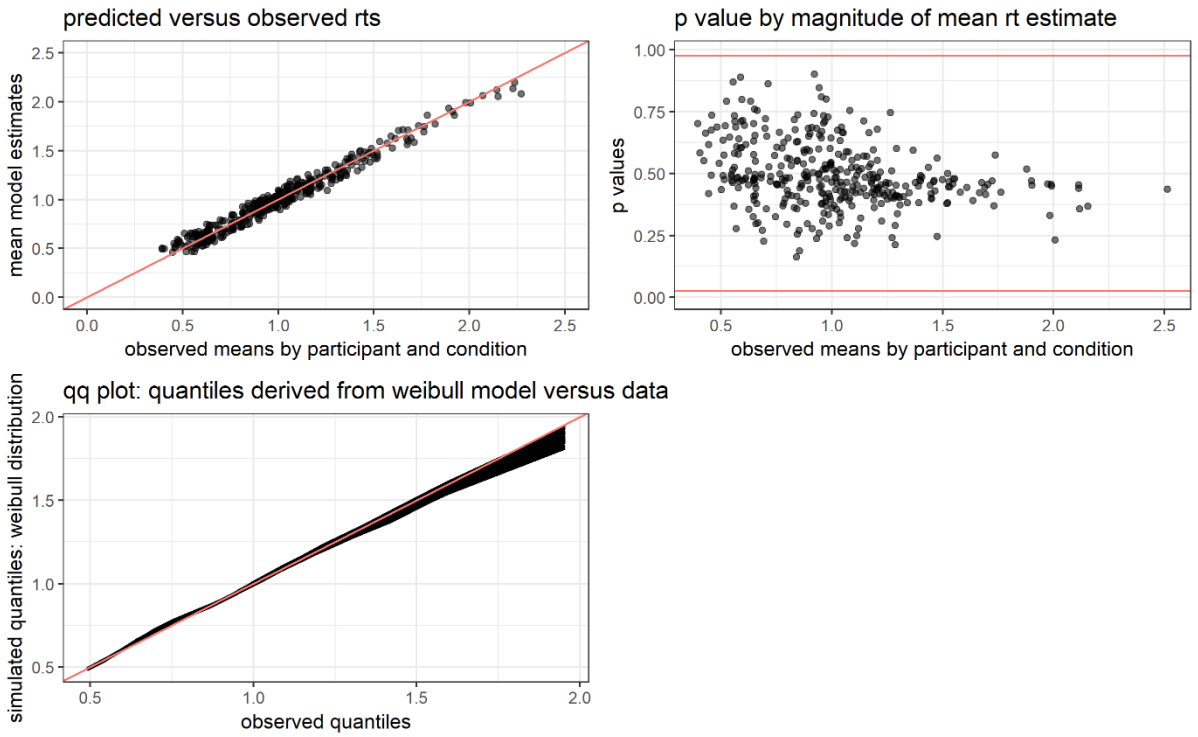


Figure A.4: Study 2 Weibull fit to RT data: posterior predictive check. Posterior predictive check on the Weibull fit to the RT data with linear models on the ψ and λ parameters. Predicted mean RTs are in general consistent with (top left panel) and no more extreme than (top right panel) observed mean RTs by participant and condition. The QQ plot (bottom left panel) indicates that the observed data distribution (excluding probable lapses and fast guesses) is similar to a predictive distribution derived from the Weibull component of the mixture model (50 simulations shown).

The fit of the linear models on ψ and λ was also checked against the individual-level parameter estimates. A random draw was made from the posterior distribution of each component of the linear model on ψ, and these were combined with each other and with a draw from the relevant noise distribution to produce a posterior predictive estimate of ψ for each participant in each condition. The process was then repeated 1000 times. A similar process produced posterior predictive estimates of λ. The estimates (averaged by group and over laterality for brevity) are shown in the form of histograms in Figure A.5. Vertical lines represent mean individual estimates of the parameters, averaged by group and over laterality. In summary, the individual Weibull fits are consistent with the observed data, and the predictions of the linear models are consistent with the individual Weibull fits.

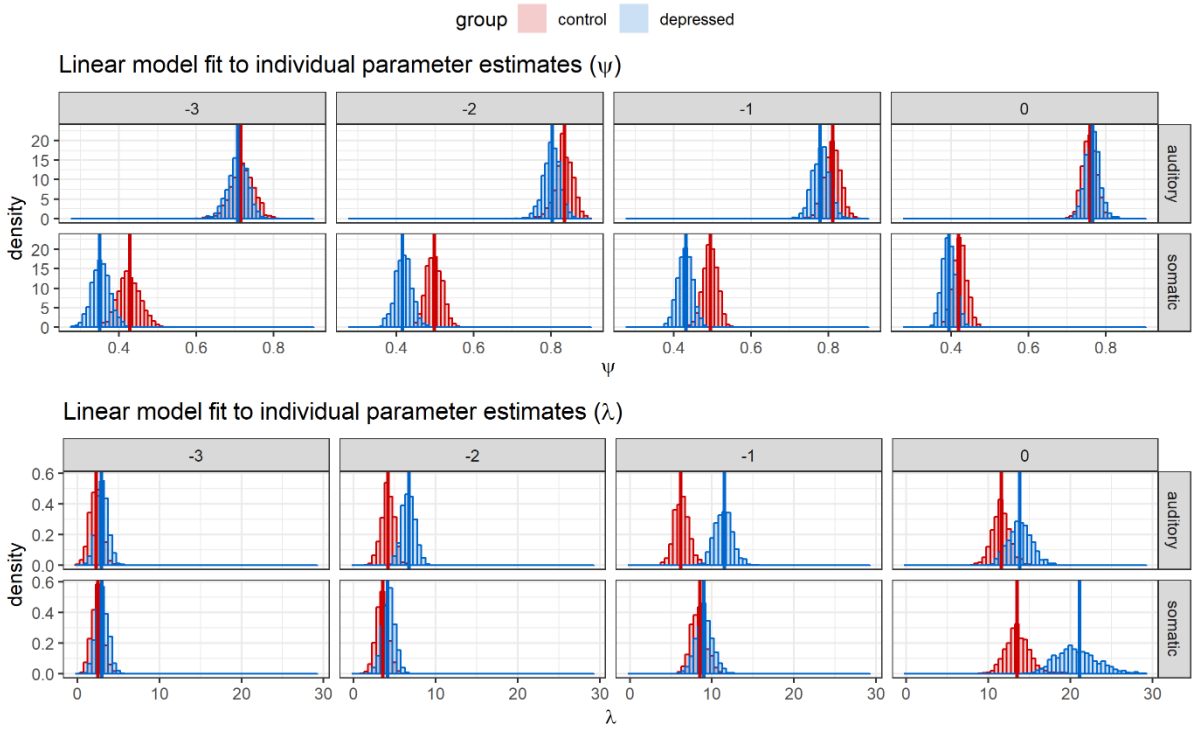


Figure A.5: Study 2 fit of the linear models on Weibull parameters ψ and λ to the individual estimates. Histograms show 1000 draws from the posterior distributions of the linear model components, combined into 1000 posterior predictive estimates of each parameter by group and condition. Lines represent the mean individual parameter estimates, averaged by group and condition.

A.3. Study 6 computational model

Model fit

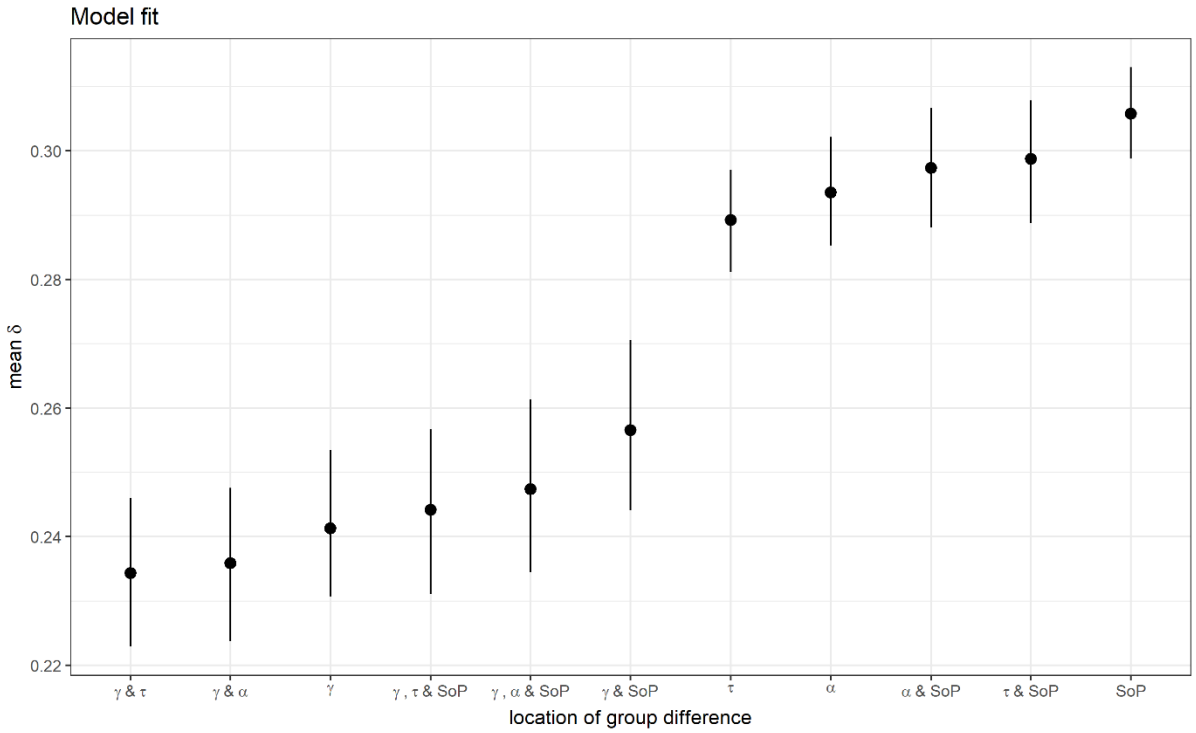


Figure A.6: Study 6 predictive processing model fits. Mean absolute δ estimates for each of the 11 viable models. Points represent the mean of the posterior distribution for δ and error bars are 95% credible intervals. Model fit improves as δ approaches zero.

Posterior predictive check

The mean posterior estimates of the salience and precision model parameters for each group and condition were used to generate predicted RTs which are plotted against observed RTs averaged over group and condition (Figure A.7). Although examination of the plot suggests that some variance due to effects of group and condition may be unaccounted for by the model (for example, RTs in response to the longest SOA condition are slightly underestimated; there may be signs of an interaction between group and SOA) on the whole the model has succeeded in predicting average response times for both groups within each condition within a few milliseconds.

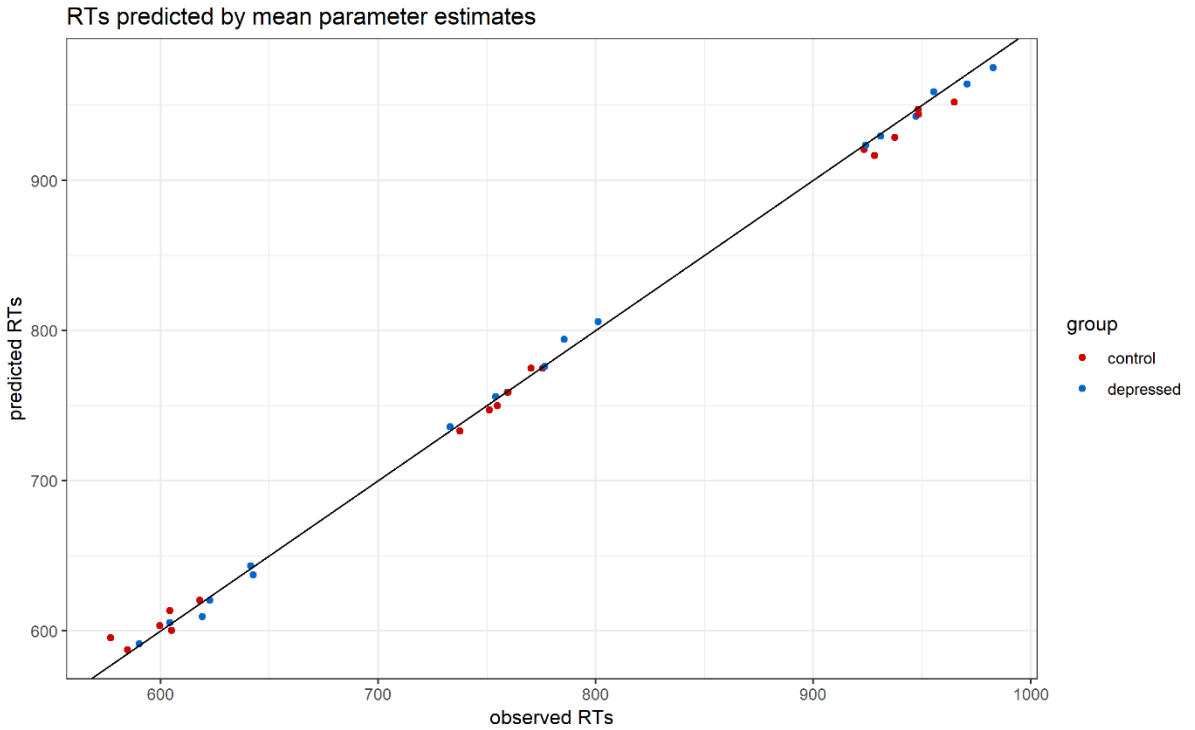


Figure A.7: Study 6 predictive processing model: posterior predictive check. Posterior predictive data plotted against observed data. RTs are calculated from the beginning of the trial (rather than from target presentation) in order to allow comparison across SOA categories.

Participant-level estimates

Participant-level parameter estimates are shown in Figure A.8. Independent-samples t-tests were carried out on the individual estimates for τ and for the ratio of somatic to auditory salience and the ratio of target to cue salience. Welch t-tests correcting for unequal variances confirmed that τ was reliably smaller in the depressed group than in healthy controls ($t(18.75) = -3.00$, $p = 0.007$, $d = 1.03$), as was the ratio of target γ to cue γ ($t(15.81) = -2.60$, $p = 0.02$, $d = 0.92$). A standard t-test confirmed that the ratio of somatic γ to auditory γ was reliably larger in depressed participants than in healthy controls ($t(32) = 4.10$, $p < 0.001$, $d = 1.44$).

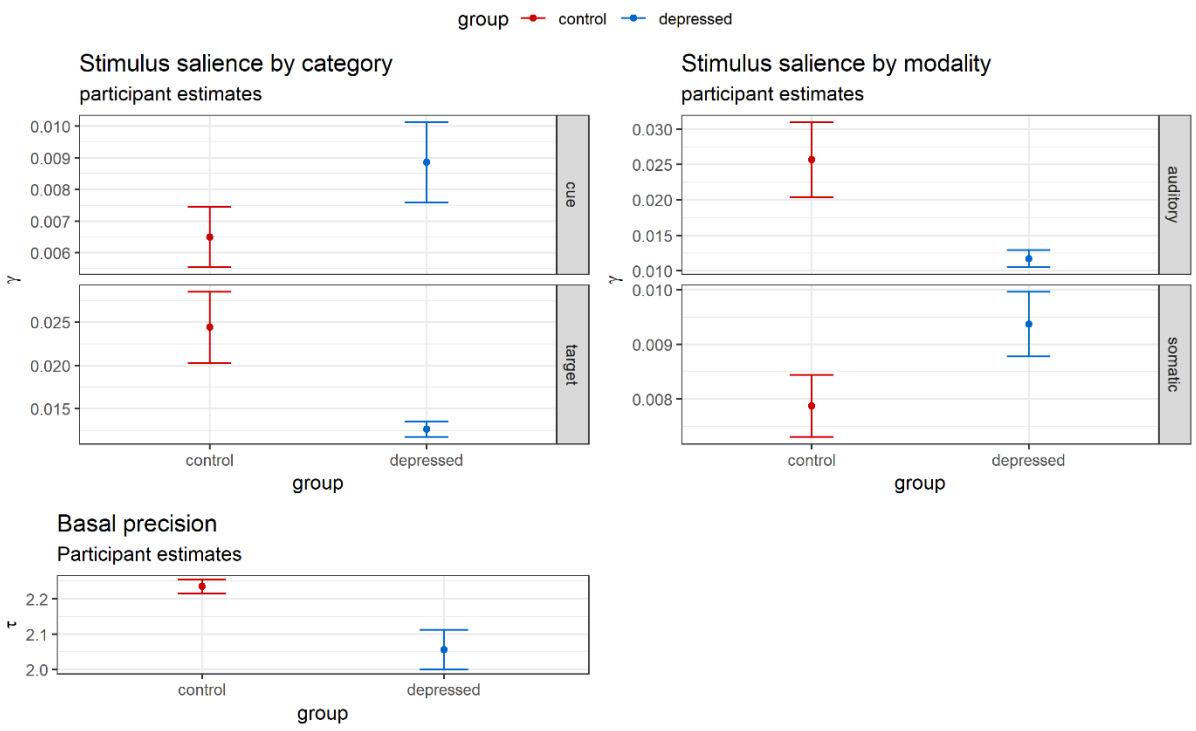


Figure A.8: Study 6 salience and precision model participant-level parameter estimates. Points represent group averages for participant-level estimates, error bars are 1 standard error of the mean (between-groups error).

Appendix B: Medication-free analyses

B.1. Study 1 GLMM

The analyses described in Study 1 were repeated including n=10 unmedicated depressed participants and n=16 healthy controls. Outcomes did not differ from the whole-group analyses described in the main study. Figure B.1 shows the model outcomes. Table B.1 shows the outcomes of the variable selection procedure, which do not differ from those derived from the whole-group variable selection analysis. As in the main analysis, when the lapse rate was restricted to zero disproportionate left-sided lapses among the depressed sample contributed to a credible interaction between group x laterality in the slope parameter which was abolished by the inclusion of a lapse parameter.

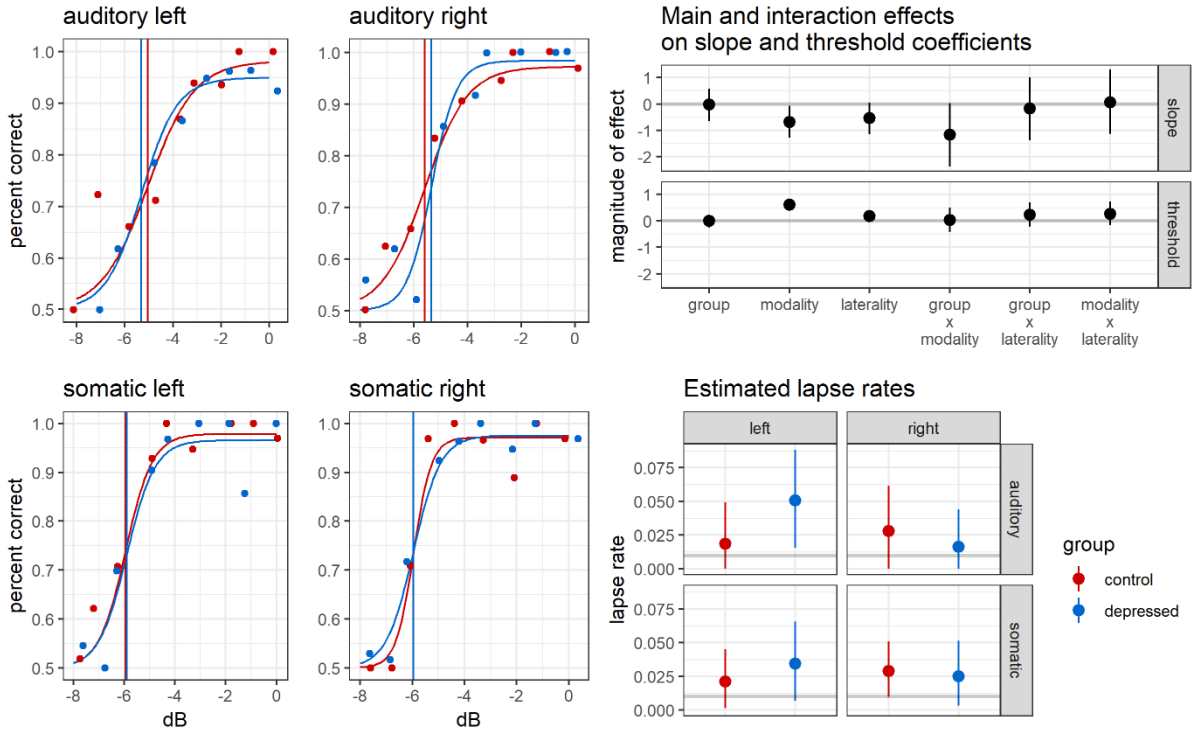


Figure B.1: Study 1 GLMM outcomes: medication-free subsample. Left panels: mean logistic curves and thresholds (vertical lines) shown by stimulus modality and laterality. Points represent the observed data (proportion correct averaged over group) shown to the nearest step and jittered to avoid overlap. The step size for the auditory staircases is 4dB, for the somatic staircases 1dB. Upper right panel: contrasts on effects and interactions for the slope and threshold parameters. Lower right panel: estimated lapse rates by group and condition.

Table B.1: Study 1 posterior model probabilities and Bayes factors for GLMM variable selection procedure (medication-free subsample)

Model	Effects included	Posterior model probability	Bayes factor relative to reference model
M	Modality	0.99992	6.68×10^{9}
ML	Modality and laterality	5.70×10^{-5}	3.80×10^{5}
GM	Group and modality	2.12×10^{-5}	1.42×10^{5}
REF	None (reference model)	1.50×10^{-10}	1
L	Laterality	4.32×10^{-12}	2.89×10^{-2}
G	Group	6.62×10^{-13}	4.42×10^{-3}
GML	Group, modality and laterality	9.35×10^{-14}	6.25×10^{-4}
GL	Group and laterality	9.04×10^{-17}	6.04×10^{-7}

B.2. Study 2 signal detection analysis

The signal detection analysis described in Study 2 was repeated including n=6 unmedicated depressed participants and n=12 healthy controls. Outcomes with respect to bias did not substantively differ from the whole-group analyses described in the main study (Figure B.2), although the interaction between group and intensity, which was marginal in the main analysis, became credible in the medication-free analysis. This outcome demonstrates that bias effects are strongest when uncertainty is high (i.e., at low intensity levels) as expected. With respect to sensitivity, a credible effect of group on d' emerged, indicating that healthy controls had slightly higher perceptual sensitivity than unmedicated depressed participants. However, the variable selection procedure (Table B.2) demonstrated that no group difference in d' remained the most probable explanation for this data, although the Bayes Factor is reduced relative to the whole-group analysis. It is also worth noting that bias affects sensitivity and the marked bias observed in these data indicates that sensitivity estimates should be treated with caution. Note that the relative likelihood of group differences in bias is substantially increased in the medication-free analysis compared to to the main analysis.

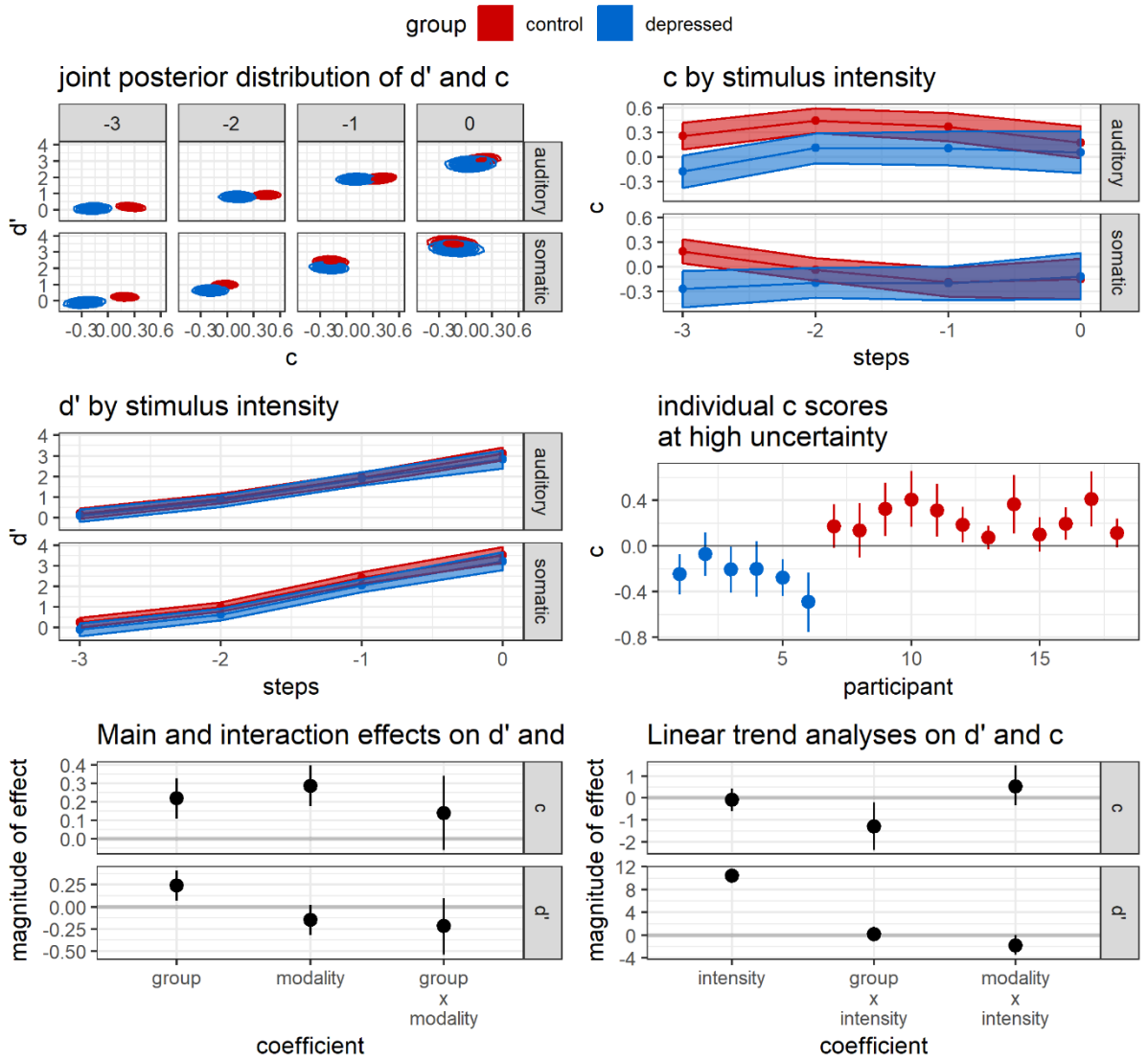


Figure B.2: Study 2 signal detection model outcomes: medication-free subsample. The top left panel shows the joint posterior distribution of d' and c across stimulus intensity, averaged by group and modality, while the middle left and upper right panels respectively show the corresponding 95% credible intervals for the averaged estimates of d' and c across stimulus intensity. The middle right panel shows the individual participant estimates of c averaged over modality at the lowest level of stimulus intensity. The bottom panels show the main and interaction effects of the linear models on d' and c: in the bottom left panel simple contrasts on factors with 2 levels; in the bottom right panel linear trends on intensity and on the respective interactions of group and modality with intensity.

Table B.2: Study 2 posterior model probabilities and Bayes factors for signal detection model comparison (medication-free subsample)

	Model	Posterior model probability	Bayes factor

Model		c		
		Group effect	No group effect	
d'	Group effect	0.29	0.004	77.58
	No group effect	0.70	0.009	77.31
Bayes factor		0.41	0.41	

B.3. Study 4 ANOVAs

Six medicated participants, all belonging to the depressed group, were excluded from the sensitivity analysis. Group effects were re-examined with n = 26 (10 depressed participants and 16 control participants) unmedicated participants included in the analysis.

B.3.1. Reaction time data

The overall main effect of group was no longer statistically significant ($F(1, 24) = 2.97$, $p = 0.098$, $\eta_p^2 = 0.11$), but the interaction between modality and group persisted ($F(1, 24) = 5.49$, $p = 0.028$, $\eta_p^2 = 0.19$). As in the main analysis, there was a statistically significant group difference in RT during somatic blocks ($F(1, 24) = 4.74$, $p = 0.04$, $\eta_p^2 = 0.17$), but not during auditory blocks ($F(1, 24) = 1.57$, $p = 0.22$, $\eta_p^2 = 0.06$).

The 3-way interaction between block, validity and group apparent in the main analysis remained statistically significant ($F(1, 30) = 8.76$, $p = 0.007$, $\eta_p^2 = 0.27$) with a group difference in validity effect occurring during later blocks ($F(1, 24) = 5.25$, $p = 0.031$, $\eta_p^2 = 0.18$), but not during earlier ones ($F(1, 24) = 0.007$, $p = 0.94$, $\eta_p^2 < 0.001$).

As in the main analysis, no other group effects reached statistical significance.

B.3.2. Error data

The modality x group interaction no longer reached statistical significance ($F(1, 24) = 3.16$, $p = 0.088$, $\eta_p^2 = 0.12$), and group differences in somatic errors did not survive a correction for unequal variances (corrected $t(10.10) = 1.84$, $p = 0.085$, $d = 0.91$). Effect sizes, however, remained medium-large.

As in the main analysis, there was no evidence for any group difference in errors during auditory blocks ($t(24) = 0.36$, $p = 0.72$, $d = 0.14$).

B.3.3. IIV

The modality x group interaction persisted ($F(1, 24) = 6.25$, $p = 0.02$, $\eta_p^2 = 0.21$). The group difference in IIV during auditory blocks no longer reached statistical significance ($t(24) = 1.76$, $p = 0.092$, $d = 0.69$) but the group difference in IIV during somatic blocks remained highly significant ($t(24) = 3.66$, $p = 0.001$, $d = 1.40$). Within the depressed group, IIV remained significantly greater during somatic than during auditory blocks ($t(9) = -2.37$, $p = 0.042$, $d = 0.51$).

B.5. Study 6 analyses

Nine depressed participants (56.25%) and two healthy controls (12.5%) were prescribed psychotropic medication at the time of the study, and were excluded from the medication-free analysis.

B.5.1. Classical analysis

As in the main analysis, the data were subjected to a repeated-measures ANOVA with the factors of Group, Cue Modality, Cue Validity, SOA and Target Laterality. The data was pooled across target modalities and a Greenhouse-Geisser correction was employed where the assumption of sphericity was not met.

Within-participant effects

The key outcomes remained highly significant in the medication-free analysis, including the effect of cue validity ($F(1.29, 24.45) = 72.81$, $p < 0.001$, $\eta_p^2 = 0.79$) and the effect of SOA ($F(1.24, 23.46) = 182.35$, $p < 0.001$, $\eta_p^2 = 0.91$). The interactions between cue modality and SOA ($F(2, 38) = 18.00$, $p < 0.001$, $\eta_p^2 = 0.49$) and between validity and SOA ($F(4, 76) = 8.42$, $p < 0.001$, $\eta_p^2 = 0.31$) also remained. However, the interactions between validity and laterality, and between SOA and laterality, no longer met criteria for statistical significance ($ps>0.1$).

Group effects

The interaction between group and cue validity was substantially strengthened by the exclusion of medicated participants ($F(1.29, 24.45) = 8.41$, $p = 0.005$, $\eta_p^2 = 0.31$). As in the main analysis, no main effect of group was observed ($p > 0.8$), or interactions between group and any other factor ($ps > 0.1$).

B.5.2. Salience and precision model parameter estimation

The participant-level estimates for the medication-free participants are plotted in Figure B.3. Independent-samples t-tests were carried out on the individual estimates for τ and for the ratio of somatic to auditory salience and the ratio of target to cue salience. Although the group difference in τ was no longer statistically significant due to a loss of power, the effect size was in fact increased relative to the whole-sample analysis: ($t(6.82) = -2.31$, $p = 0.055$, $d = 1.21$; Welch t-test). The group

difference in the ratio of target γ to cue γ remained statistically significant (t(16.36) = -3.20, p = 0.005, d = 1.25; Welch t-test), as did the group difference in the ratio of somatic to auditory salience (t(19) = 2.36, p = 0.029, d = 1.16).

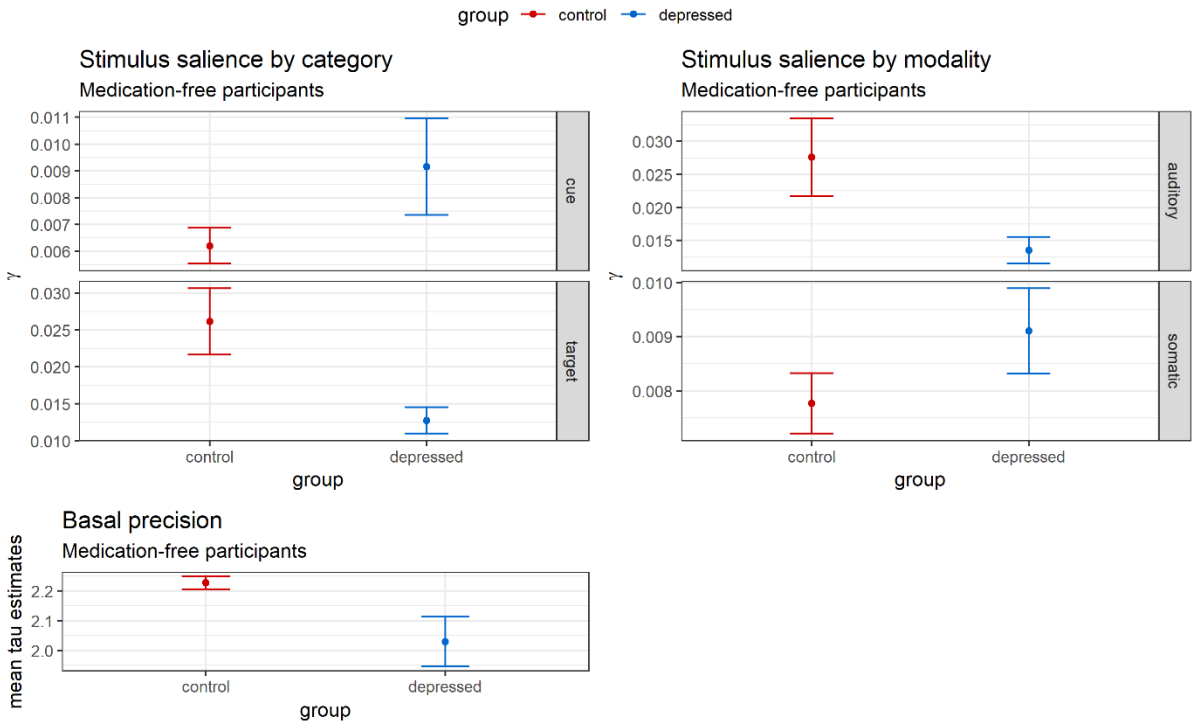


Figure B.3: Study 6 participant-level parameter estimates: medication-free subsample. Participant-level parameter estimates for medication-free participants. Points represent group averages for participant-level estimates, error bars are 1 standard error of the mean (between-groups error).

Appendix C: Study 1 GLMM without a lapse parameter

When the lapse parameter is constrained to zero, the model is characterised by flattening of the logistic curve for both groups in all conditions (Figure C.1, upper panels). In both modalities the flattening is exacerbated for the depressed group on the left and for the control group on the right, leading to a credible group by laterality interaction in the slope parameter (Figure C.1, lower panels). This interaction is abolished once a lapse parameter is included in the model as described in the main text.

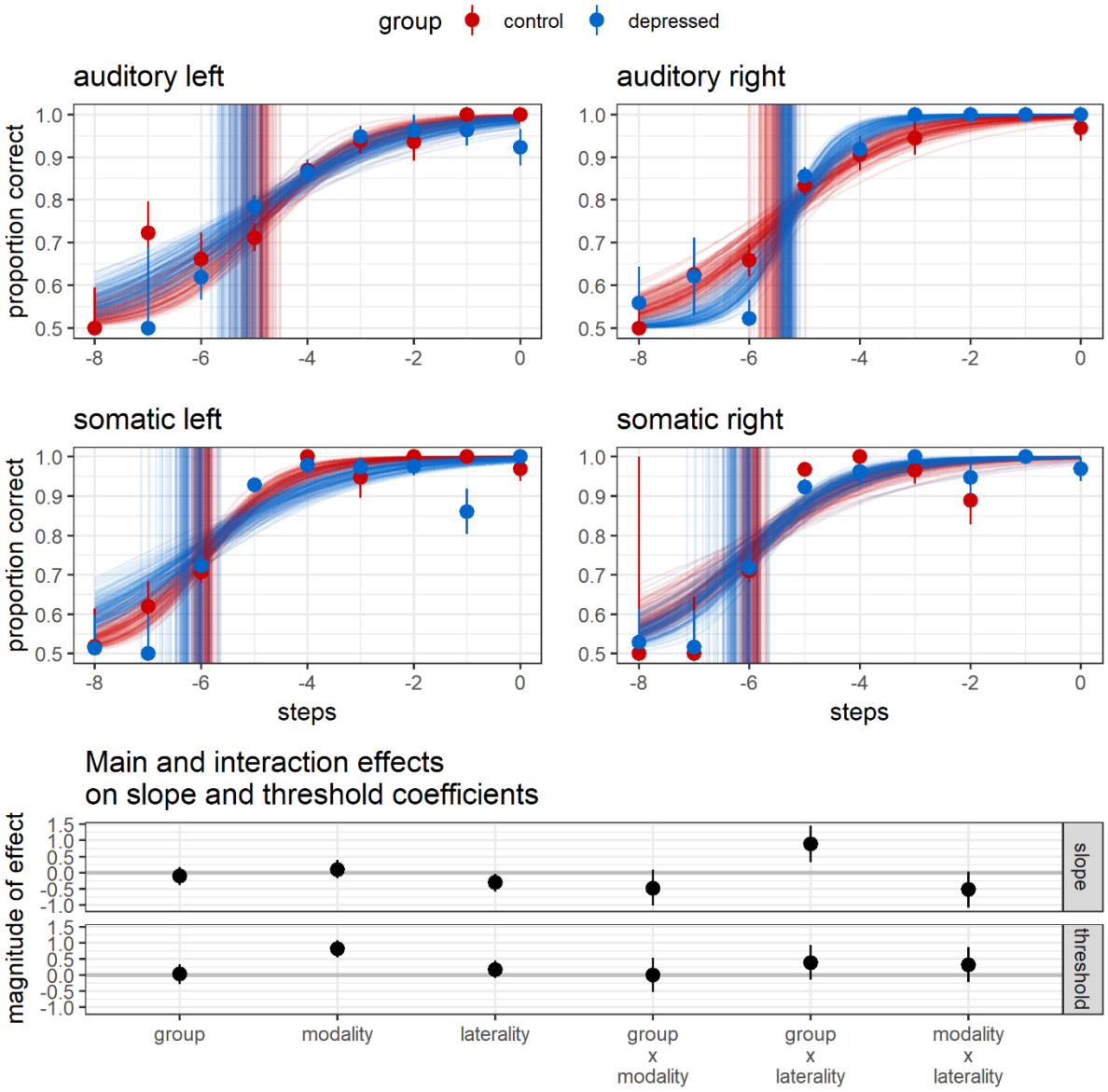


Figure C.1: Study 1 GLMM fits and outcomes when the lapse parameter is constrained to zero. Upper panels: lines represent 100 simulations based on draws from the posterior distributions of the model parameters. Points represent the observed data ± 1 standard error. Lower panels: contrasts on the main and interaction effects on the slope and threshold parameters. There is a credible interaction

between group and laterality on the slope parameter as a result of flattening on the left in the depressed group and the right in healthy controls.

A formal model comparison using the product space method (Carlin & Chib, 1995) indicated that the observed data were much more likely to have occurred under the model including a lapse parameter relative to the model without, by a Bayes factor of 1.34×10^8. Therefore, the model with lapses was accepted as the better explanation of the data, and the group by laterality interaction observed in the slope parameter of the latter model was assumed to be accounted for by group by laterality effects in the incidence of lapses at the upper asymptote.

Appendix D: Study 2 distractor word lists

Distractor words were drawn from three lists consisting respectively of 82 depression-relevant negative words, 82 positive antonyms, and 82 neutral words (see Table D.1), all selected from the stimulus set compiled by Warriner, Kuperman, and Brysbaert (2013). One-way ANOVAs demonstrated that word lists were adequately matched on word length and frequency. Independent samples t-tests confirmed that negative words were both more negative in valence ($t(162) = 24.22$, $p < 0.001$, $d = 1.77$) and more arousing ($t(162) = 7.86$, $p < 0.001$, $d = 1.27$) than neutral words, while positive words were both more positive in valence ($t(162) = 18.63$, $p < 0.001$, $d = 1.64$) and more arousing ($t(141.54) = 6.47$, $p < 0.001$, $d = 0.90$) than neutral words. Affective ratings differed significantly between negative and positive words ($t(162 = 40.72$, $p < 0.001$, $d = 1.90$) but arousal ratings did not ($t(146.42) = 0.08$, $p = 0.94$, $d = 0.01$). Welch's t-tests correcting for unequal variances were used for the positive-neutral and negative-positive arousal comparisons.

Table D.1: Distractor word lists by valence

Negative words	Positive words	Neutral words
Worthless	Valued	Elastic
Useless	Effective	Definite
Inadequate	Confident	Fluid
Contempt	Compassion	Observation
Disapproval	Approval	Viewpoint
Disparagement	Tenderness	Journey
Ridicule	Appreciation	Temperature
Blame	Acceptance	Notification
Criticize	Praise	Discuss
Bad	Welcome	Tiled
Fault	Achievement	Arrival

Mistake	Skill	Episode
Wrong	Justified	Audible
Lazy	Active	Solid
Selfish	Generous	Rapid
Hopeless	Hopeful	Woven
Despair	Joy	Motion
Desperate	Relaxed	Varnished
Trapped	Independent	Layered
Stuck	Calm	Short
Helpless	Influential	Ductile
Burden	Benefit	Demonstration
Affliction	Blessing	Postponement
Broken	Fulfilled	Narrow
Ruined	Lively	Wide
Frustration	Satisfaction	Volume
Anger	Excitement	Compartment
Resentment	Anticipation	Domain
Sadness	Happiness	Topic
Guilt	Innocence	Discourse
Shame	Respect	Measurement
Humiliation	Dignity	Length
Pain	Peace	Width

Suffering	Comfort	Fastening
Misery	Cheerfulness	Consistency
Distress	Pleasure	Mixture
Loneliness	Closeness	Magnitude
Alone	Popular	Habitual
Failure	Success	Portion
Disappoint	Delight	Indicate
Bleak	Warm	Broad
Relentless	Gentle	Unofficial
Rubbish	Treasure	Carpet
Complain	Soothe	Arrange
Dislike	Cherish	Lift
Rejected	Loved	Sent
Incompetent	Competent	Glossy
Incapable	Capable	Regular
Loss	Gain	Pause
Regret	Contentment	Passage
Exhausted	Energetic	Oval
Defeat	Victory	Arrangement
Beaten	Proud	Occasional
Vulnerable	Strong	Informal
Betrayed	Nurtured	Brought

Threat	Safety	Texture
Powerless	Powerful	Formal
Miserable	Fun	Proximal
Boring	Interesting	Brief
Unpleasant	Pleasant	Extended
Fail	Succeed	Proceed
Isolated	Supported	Viewed
Paralysing	Exhilarating	Entering
Illness	Health	Sequence
Wounded	Flourishing	Moist
Injured	Robust	Dry
Ailment	Vigour	Compartment
Poison	Wellness	Angle
Sick	Fit	Rectangular
Infected	Healthy	Folded
Weakness	Strength	Velocity
Disgusting	Attractive	Medium
Polluted	Pure	Plastic
Diseased	Thriving	Scanned
Dreary	Inspiring	Neutral
Dull	Vibrant	Substantial
Aching	Comfortable	Stationary

Hurt	Healed	Borrowed
Pathetic	Admirable	Ajar
Stupid	Bright	Powdery
Harm	Kindness	Situation
Contaminated	Fresh	Spatial

Appendix E: Study 2 analysis of distractor effects

Before pooling data across blocks for the Bayesian analyses, classical analyses were carried out on threshold estimates and variability data to ascertain that there was no meaningful influence of distractor presence or valence on outcomes.

E.1. Perceptual threshold

Perceptual thresholds were estimated by finding the average of the intensities (in dB, i.e., relative to the index starting point) at the last 6 reverses in each staircase for each individual (Wetherill and Levitt, 1965). Thresholds were normally distributed (2 outliers skewed control data in the somatic condition but their removal did not affect the outcome of the analysis). A repeated-measures group x distractor x laterality ANOVA was carried out on the data for each modality. These analyses revealed no effect of distractor (Greenhouse-Geisser-corrected $F(2.06, 45.26) = 0.46$, $p = 0.64$, $\eta_p^2 = 0.02$) and no interactions between group and valence ($F(3, 66) = 0.68$, $p = 0.57$, $\eta_p^2 = 0.03$), valence and laterality ($F(3, 66) = 1.70$, $p = 0.18$, $\eta_p^2 = 0.07$) or group, valence and laterality ($F(3, 66) = 0.51$, $p = 0.68$, $\eta_p^2 = 0.02$) in the somatic condition; and no effect of valence (Greenhouse-Geisser-corrected $F(2.17, 47.81) = 1.19$, $p = 0.32$, $\eta_p^2 = 0.05$) and no interactions between group and valence (Greenhouse-Geisser-corrected $F(2.17, 47.81) = 1.18$, $p = 0.33$, $\eta_p^2 = 0.05$), valence and laterality ($F(3, 66) = 1.44$, $p = 0.24$, $\eta_p^2 = 0.06$) or group, valence and laterality ($F(3, 66) = 0.91$, $p = 0.44$, $\eta_p^2 = 0.04$).

E.2. Intra-individual variability

Intra-individual variability (IIV) was calculated as the standard deviation of the stimulus intensity (dB) at all reverses for each staircase. The data was transformed from decibels to steps to facilitate comparison across modalities, and a repeated-measures ANOVA examining modality x valence x laterality x group effects on IIV was conducted. There was no main effect of valence ($F(1, 22) = 0.25$, $p = 0.86$, $\eta_p^2 = 0.011$) and no interaction between valence and group ($F(1, 22) = 0.90$, $p = 0.45$, $\eta_p^2 = 0.039$), valence and modality ($F(1, 22) = 0.20$, $p = 0.90$, $\eta_p^2 = 0.009$), valence and laterality ($F(1, 22) = 0.47$, $p = 0.71$, $\eta_p^2 = 0.021$), valence, group and modality ($F(1, 22) = 1.24$, $p = 0.30$, $\eta_p^2 = 0.053$), valence, group and laterality ($F(1, 22) = 0.50$, $p = 0.68$, $\eta_p^2 = 0.022$) , or valence, group, modality and laterality ($F(1, 22) = 0.77$, $p = 0.51$, $\eta_p^2 = 0.034$).

E.3. Summary

In summary, all findings relating to valence were null, with effect sizes ranging between $\eta_p^2 = 0.009$ and $\eta_p^2 = 0.053$, suggesting that neither group was significantly distracted by either the presence or the valence of distractor words.

Appendix F: Study 2 RT mixture model development

F.1. Block analysis

The dataset consisted of 20,242 reaction times, generated by 24 participants in response to stimuli with 2 levels of modality, 2 levels of laterality, 4 levels of intensity and 4 categories of distractor. In order to perform a robust distributional analysis it was necessary to pool RTs with respect to some stimulus characteristics. Given the lack of any effect of distractor on accuracy performance detailed above, an initial block (distractor valence) comparison was run to compare Weibull parameters across blocks to ascertain whether pooling would be appropriate.

Thirteen RTs (0.06%) were longer than 6 seconds (mean = 18.79 seconds, sd = 19.88 seconds). These were assumed to represent equipment failure or a short break in proceedings rather than attentional lapses, and were removed from the analysis.

F.1.1. Block analysis model

The initial analysis used a Weibull distribution (Rouder et al., 2005) to estimate parameters for the distributions of responses for each participant in each block in each modality, pooling responses by stimulus laterality and intensity. A uniform likelihood for lapses and fast guesses was also included so that the resulting model was a mixture model with m=2 components, distributed as

$$P(y_{ijk}|\,\psi_{jk},\lambda_{jk},\beta_{jk,}\vartheta_m) = \vartheta_{lapse}Uniform(y_{ijk}|0,6) + \vartheta_{Weibull}Weibull(y_{ijk}|\,\psi_{jk},\lambda_{jk},\beta_{jk}) \quad (93)$$

$$\lambda_{jk} = \theta_{jk}^{-\beta_{jk}} \quad (94)$$

where y_{ijk} denotes the i^{th} observation for the j^{th} participant in the k^{th} condition; $\psi_{jk,}$ θ_{jk} and β_{jk} respectively denote the shift, scale and shape parameters of a Weibull distribution fit to the data of the j^{th} participant in the k^{th} condition; and λ_{jk} represents the rate of the distribution (i.e., a relatively tractable reparameterization of θ_{jk}). K is equivalent to a design matrix including a modality factor (2 levels), and a block factor (4 levels).

Mixture weights are distributed as

$$\vartheta_{lapses} \sim Uniform(0,0.1) \quad (95)$$

$$\vartheta_{Weibull} = 1 - \vartheta_{lapses} \quad (96)$$

And priors as

$$\psi_{jk} \sim Gamma(\eta_1, \eta_2) \quad (97)$$

$$\lambda_{jk} \sim Gamma(\zeta_1, \zeta_2) \quad (98)$$

$$\beta_{jk} \sim Gamma(\xi_1, \xi_2) \quad (99)$$

for all shape and rate parameters:

$$\{\eta_1, \eta_2, \zeta_1, \zeta_2, \xi_1, \xi_2\} \sim Gamma(0.001, 0.001) \quad (100)$$

We gave our model a gamma prior on ψ rather than the uniform distribution employed by Rouder et al. (2005) to allow our lapse mixture component to identify anticipations and fast guesses occurring prior to the true shift of the distribution.

F.1.2. Block analysis results

Estimates of the 3 Weibull parameters are shown by block in Figure F.1, averaged over participants and stimulus modality. All parameter estimates overlap for the three later blocks (positive, negative and neutral word blocks) suggesting that the RT distributions arising from these blocks are comparable to each other. However, the RT distributions in the first block, in which the distractor was a fixation cross, start credibly later (ψ) and are credibly more skewed (β) than distributions in the later blocks.

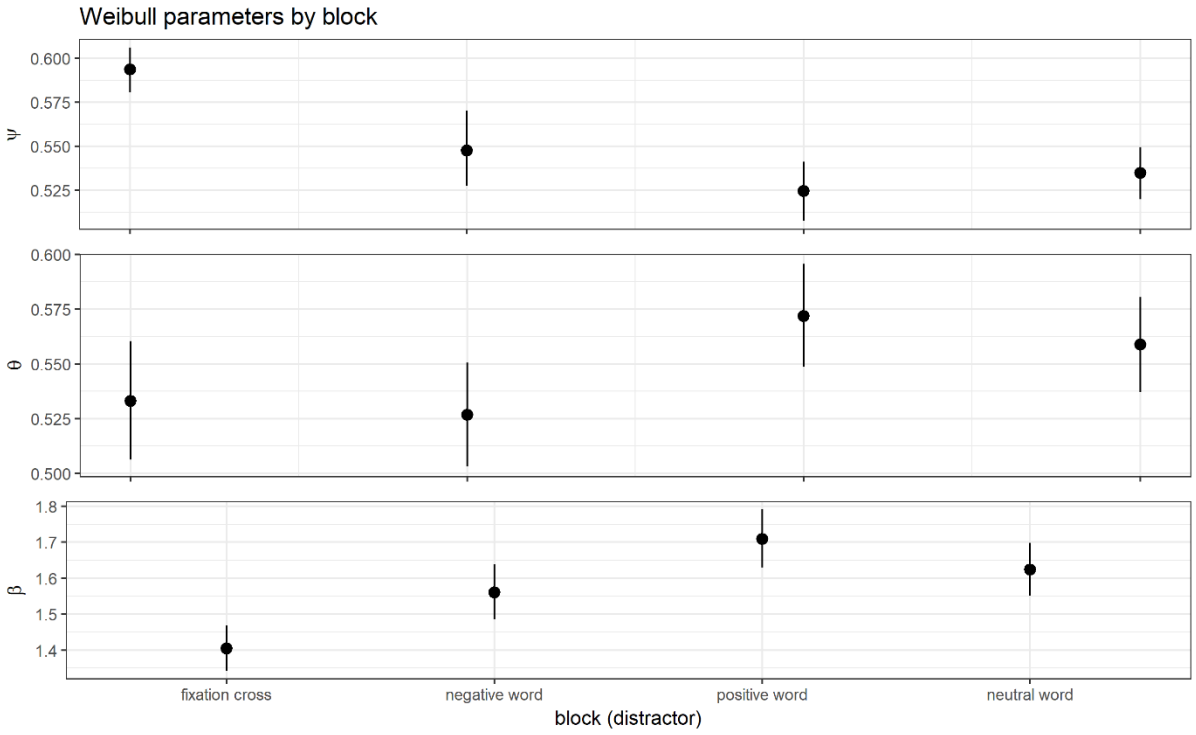


Figure F.1: Study 2 block analysis - estimated mean Weibull parameters by block. Points are the posterior distribution means of each parameter in each block, averaged over participant and modality. Error bars represent 95% credible intervals.

These estimates suggest that with the exception of the first block – which could perhaps be seen as a practice block with respect to the development of a predictable pattern of response times - the distributions are comparable across blocks. The possibility remains that interactions might exist between block and various stimulus characteristics: unfortunately, we did not have sufficient data to estimate the effect of any such interactions on distribution parameters directly. Instead, an additional classical analysis was carried out on the mean RTs.

A repeated-measures ANOVA (valence x modality x laterality x group) was performed on the reaction time data, averaged over participant and condition. This revealed a significant main effect of valence ($F(3, 66) = 6.89$, $p < 0.001$, $\eta_p^2 = 0.24$), which was investigated using repeated contrasts. Consistent with the Bayesian analysis above, these indicated that participants responded to stimuli during the first block (fixation cross) more slowly ($F(1, 22) = 12.11$, $p = 0.002$, $\eta_p^2 = 0.36$) than to stimuli during later blocks (distractor words). Later blocks did not differ from each other: ($F(1, 22) = 0.72$, $p = 0.40$, $\eta_p^2 = 0.032$, and $F(1, 22) = 0.008$, $p = 0.93$, $\eta_p^2 < 0.001$). The main effect of valence did not interact with group ($F(3, 66) = 0.76$, $p = 0.52$, $\eta_p^2 = 0.033$), modality ($F(3, 66) = 1.29$, $p = 0.29$, $\eta_p^2 = 0.055$), laterality (Greenhouse-Geisser-adjusted $F(2.36, 51.82) = 0.53$, $p = 0.62$, $\eta_p^2 = 0.024$), group x laterality (Greenhouse-Geisser-adjusted $F(2.36, 51.82) = 1.10$, $p = 0.35$, $\eta_p^2 = 0.048$), or group x modality ($F(3,66) = 0.61$, $p = 0.61$, $\eta_p^2 = 0.027$). There was a statistically significant interaction between valence, modality, and laterality (Greenhouse-Geisser-adjusted $F(2.25, 49.49) = 3.56$, $p = 0.031$, $\eta_p^2 = 0.139$) which apparently reflected responses to auditory stimuli that were somewhat slowed, and responses to somatic stimuli that were somewhat speeded, when stimuli occurred on the left relative to the right and when distractor words were positive. Given the lack of any compelling theoretical explanation for this result, the fact that it did not generalise to the perceptual sensitivity data (see Appendix E), and the multiple comparisons from which it arose, the most parsimonious explanation for it appears to be Type 1 error. In summary, the classical analyses support the Bayesian analyses in the conclusion that the initial block is distributed differently from subsequent blocks, which do not differ meaningfully from one another.

As a result of these analyses, the decision was made to treat the first block as a practice block with respect to reaction times and to exclude it from the whole-distribution analysis described here. The remainder of the blocks were pooled together to provide a total sample of 15344 observations.

F.2. Mixture model with unrestricted Weibull component.

Once RTs were pooled across blocks, a second preliminary model was developed including coefficients on stimulus laterality and intensity. This model was a mixture with an unrestricted Weibull component for the main distributions and predetermined likelihoods for lapses and fast guesses as in the linear model reported above. The likelihood for the mixture model was as follows:

$$P(y_{ijk}|\,\psi_{jk},\lambda_{jk},\beta_{jk,}\vartheta_m) = \vartheta_{lapse}Uniform(y_{ijk}|0,6) + \vartheta_{guess}N(y_{ijk}|0,1) + \vartheta_{Weibull}Weibull(y_{ijk}|\psi_{jk},\lambda_{jk},\beta_{jk}) \quad (101)$$

where y_{ijk} represents the i^{th} response of the j^{th} participant in the k^{th} condition. K is equivalent to a design matrix including a modality factor (2 levels), a laterality factor (2 levels), and an intensity factor (4 levels). The mixture weights are distributed as

$$\vartheta_{lapse} \sim Uniform(0,1) \quad (102)$$

$$\vartheta_{guess} \sim Uniform(0,1) \quad (103)$$

$$\vartheta_{Weibull} = 1 - (\vartheta_{lapse} + \vartheta_{guess}) \quad (104)$$

and the priors as

$$\psi_{jk} \sim Gamma(\eta_1,\eta_2) \quad (105)$$

$$\lambda_{jk} \sim Gamma(\zeta_1,\zeta_2) \quad (106)$$

$$\beta_{jk} \sim Gamma(\xi_1,\xi_2) \quad (107)$$

for all shape and rate parameters:

$$\{\eta_1,\eta_2,\zeta_1,\zeta_2,\xi_1,\xi_2\} \sim Gamma(0.001,0.001) \quad (108)$$

F.2.1. Unrestricted model results

There were effects of laterality on lapse and guess counts in the depressed group which were similar to those derived using the linear model described in the main paper (Figure F.2, upper panels). The distributions of the estimated participant-level Weibull parameters were explored and it was identified that group effects of interest might be present in the shift (ψ) and scale (θ) parameters. For example, Figure F.2 (lower panels) shows that estimates of the group averages for each of these

parameters were credibly different from each other. For the shape (β) parameter, by contrast, the credible intervals for the overall group means overlap.

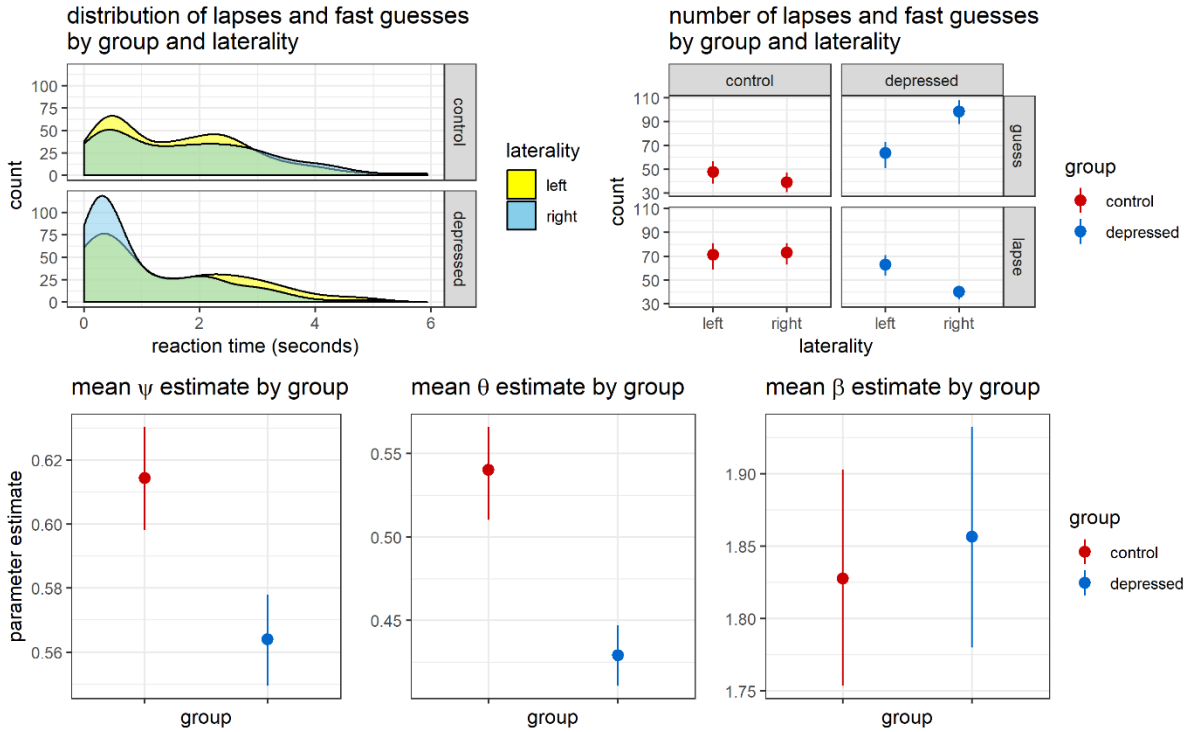


Figure F.2: Study 2 unrestricted Weibull mixture model outcomes. The top left panel shows the distribution of probable lapses and fast guesses by group and laterality. The top right panel shows the estimated count of the same. The bottom panels show posterior estimates of the overall group averages of the Weibull parameters. Points represent the mean of the posterior distribution, error bars are 95% credible intervals. Group differences in average parameter estimates are apparent in the ψ and θ parameters, but not the β parameter.

Of interest, these comparisons suggest that depressed participants were quicker to respond to targets relative to healthy controls both in terms of the onset of the response distributions and their breadth. The decision was made to develop a third model with normal priors and with linear models on the shift and scale parameters to investigate the apparent group differences in more detail. This model is described in detail in the main thesis (Chapter 4, Section 4.2.2).

Appendix G: Unique influence of anhedonia on left-sided neglect in persistent depression

The outcomes of Studies 1 and 2 tended towards the conclusion that a lateralised deficit in sensory attention could be present in the context of persistent, moderate-severe depressive illness. Theoretically, however, a question of potentially greater interest is in the relationship between indices of attentional disruption and the phenomenon of anhedonia. Anhedonia – the loss of interest and pleasure in previously valued activities or stimuli – is a central feature of depression and on phenomenological grounds may reflect a loss of sensory precision or a failure to orient attention towards behaviourally-relevant stimuli in the environment.

This question was investigated by conducting partial correlations between indices of lateralised attentional bias and anhedonia scores derived from the BDI using a subset of items (Pizzagalli, Jahn, & O'Shea, 2005) in each of the two studies while controlling for overall depression severity. The best available participant-level estimate of lateralised attentional bias in Study 1 was the absolute count of left-sided asymptotic attentional lapses (see Figure 3.2), while in Study 2 a more robust index of participant-level attentional bias was provided by maximum a posteriori estimates of response bias under the highest level of uncertainty (as shown in Figure 4.1). These outcomes were regressed on depression severity (indexed by total BDI-II score) to derive residuals which were then correlated with residuals derived from independent regressions of anhedonia on total BDI score for the two studies respectively.

G.1. Anhedonia analyses

A partially Bayesian approach to the estimation of the partial correlations was undertaken by using Bayesian regression models to estimate residuals and then taking a point estimate (i.e., the mean of the residual distribution) in order to conduct a Bayesian Pearson's correlation following Lee and Wagenmakers (2013). To estimate residuals for the Study 1 partial correlation, a linear regression of anhedonia subscale score on total BDI score was conducted, together with a Poisson regression of left lapse count on total BDI score. To estimate residuals for the Study 2 partial correlation, two independent linear regressions were conducted of anhedonia subscale score on total BDI score, and of response bias under uncertainty on BDI score respectively. All three linear regressions were modelled as follows:

G.1.1. Linear regression

According to the model, the (standardised) data is distributed as

$$y_i \sim N(\mu, \sigma^2) \tag{109}$$

where y_i denotes the outcome for the i^{th} participant and where

$$\mu = \beta 0 + \beta 1 x_i \quad (110)$$

$$\sigma \sim Cauchy(0,2), \sigma \geq 0 \quad (111)$$

$$\beta 0 \sim N(0, \sigma^{\beta 0^2}) \quad (112)$$

$$\beta 1 \sim N(0, \sigma^{\beta 1^2}) \quad (113)$$

$$\sigma^{\beta 0} = \sigma^{\beta 1} = 2 \quad (114)$$

As expected, there was a credible association between anhedonia and depression severity in both studies. A trend towards an association between left-sided response bias and depression severity was not credibly different from zero (Figure G.1, lower panels). Residuals were calculated for each regression and a point estimate for each residual derived from the mean of the posterior distribution for that residual.

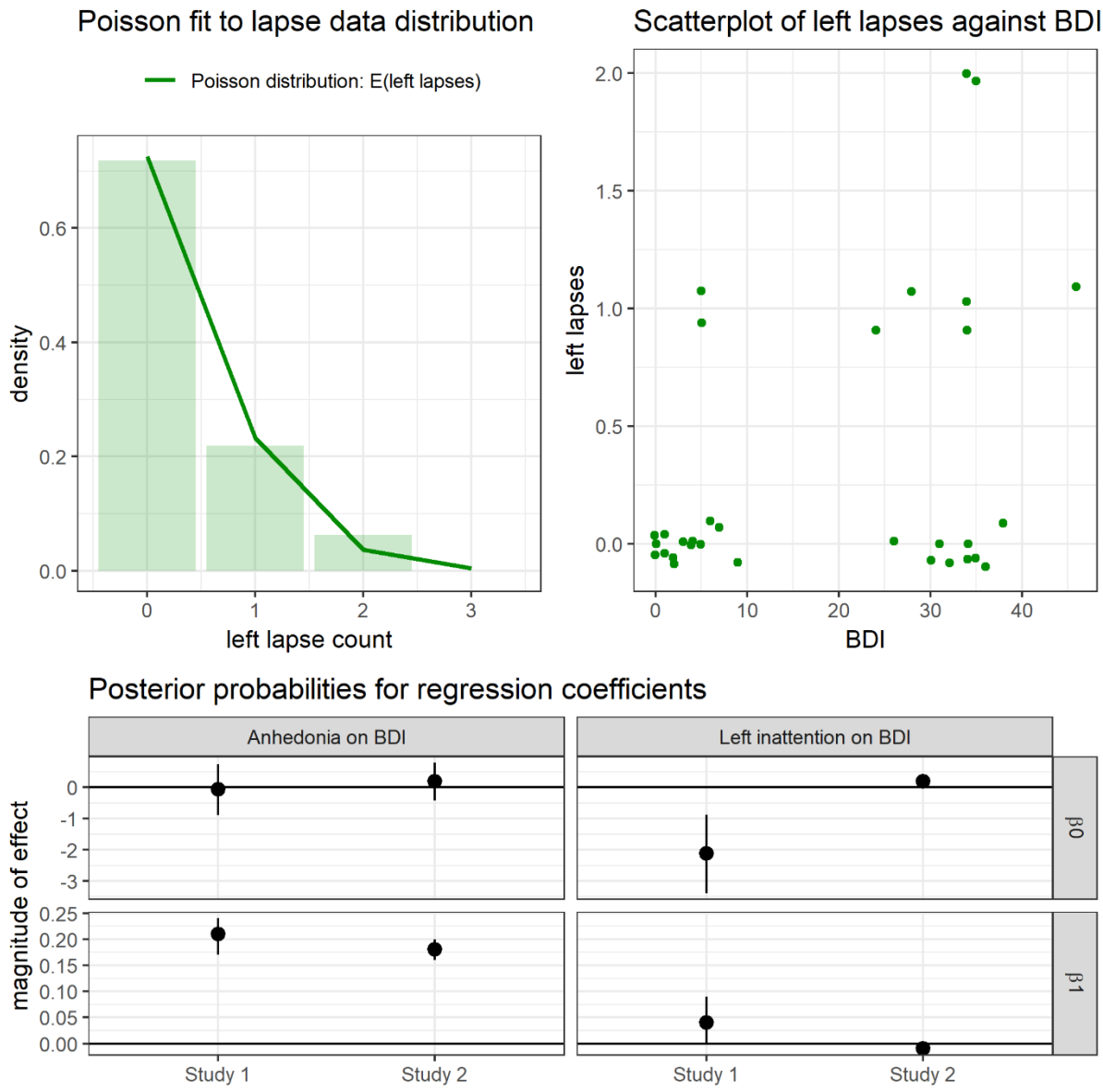


Figure G.1: Studies 1 and 2 linear and Poisson regression coefficients – anhedonia and indices of left-sided neglect on depression severity. Upper left panel: Study 1 Poisson distribution fit to left lapse count data. Upper right panel: Study 1 scatterplot of left lapses against total BDI score (jittered). Lower panels: posterior probabilities for the coefficients for intercept (β0) and slope (β1) for each regression. There was a credible association between anhedonia and BDI score in both studies. In both studies there was a trend towards a relationship between total BDI score and study-specific indices of lateralised attentional bias, but in neither study was it credibly different from zero.

G.1.2. Poisson regression

Given that the left-sided lapse variable is a count variable, the data was informally examined for fit to a Poisson distribution. A single outlier was 6.14 standards deviations from the mean of the distribution of all other counts, and 5.61 standard deviations from its predicted value given the regression model.

The remaining data showed little evidence of over-dispersion (Figure G.1, upper panels). The source of the outlier was examined, and it was found to arise from a series of 3 errors in 4 consecutive trials within the first 6 trials of a block. Specifically, the errors were made on each of the first 3 trials in the block in which a right-sided response was the correct one (counterintuitively given that all stimuli in the block occurred on the left). This pattern of errors is reflective of a brief confusion about the task instructions rather than canonical lapses, and so the decision was made on theoretical as well as distributional grounds to remove them from the data and to proceed with a Poisson regression.

The left-sided lapses were modelled as draws from a Poisson distribution

$$y_i \sim Poisson(\lambda_i) \tag{115}$$

where y_i denotes the outcome for the i^{th} participant and where

$$\log(\lambda_i) = \beta 0 + \beta 1 x_i \tag{116}$$

$$\beta 0 \sim N(0, \sigma^{\beta 0^2}) \tag{117}$$

$$\beta 1 \sim N(0, \sigma^{\beta 1^2}) \tag{118}$$

$$\sigma^{\beta 0} = \sigma^{\beta 1} = 2 \tag{119}$$

There was a trend towards an association between left-sided lapses and depression severity (Figure G.1, lower right panel). As before, residuals were calculated for the regression and a point estimate for each residual derived from the mean of the posterior distribution for that residual.

G.1.3. Partial correlations

A coefficient indexing the partial correlation between anhedonia and attentional bias, controlling for depression severity, was then estimated for each study. For each study, the residuals were modelled as draws from a multivariate normal distribution as follows (adapted from Lee & Wagenmakers, 2013)

$$\boldsymbol{Residuals}_i \sim N([\mu_1, \mu_2], \begin{bmatrix} \sigma_1^2 & r\sigma_1\sigma_2 \\ r\sigma_1\sigma_2 & \sigma_2^2 \end{bmatrix}) \tag{120}$$

where

$$\mu_1, \mu_2 \sim N(0,100) \tag{121}$$

$$r \sim Uniform(0,1) \tag{122}$$

$$\sigma_1, \sigma_2 \sim Cauchy(0,5), \sigma \geq 0 \quad (123)$$

G.2. Anhedonia results

As can be seen in Figure G.2, in both studies there is a credible correlation between indices of left-sided attentional disruption and anhedonia, over and above any contribution of depression severity. In Study 1 the correlation coefficient had a mean magnitude of 0.40 and lower and upper HDI limits of 0.11 and 0.66; while in Study 2 the coefficient had a mean magnitude of -.57 and lower and upper HDI limits of -0.29 and -0.82. Note that this correlation is negative because left-sided bias was denoted by negative values for c: in both studies these outcomes demonstrate that a higher anhedonia score is credibly related to more evidence of left-sided attentional bias.

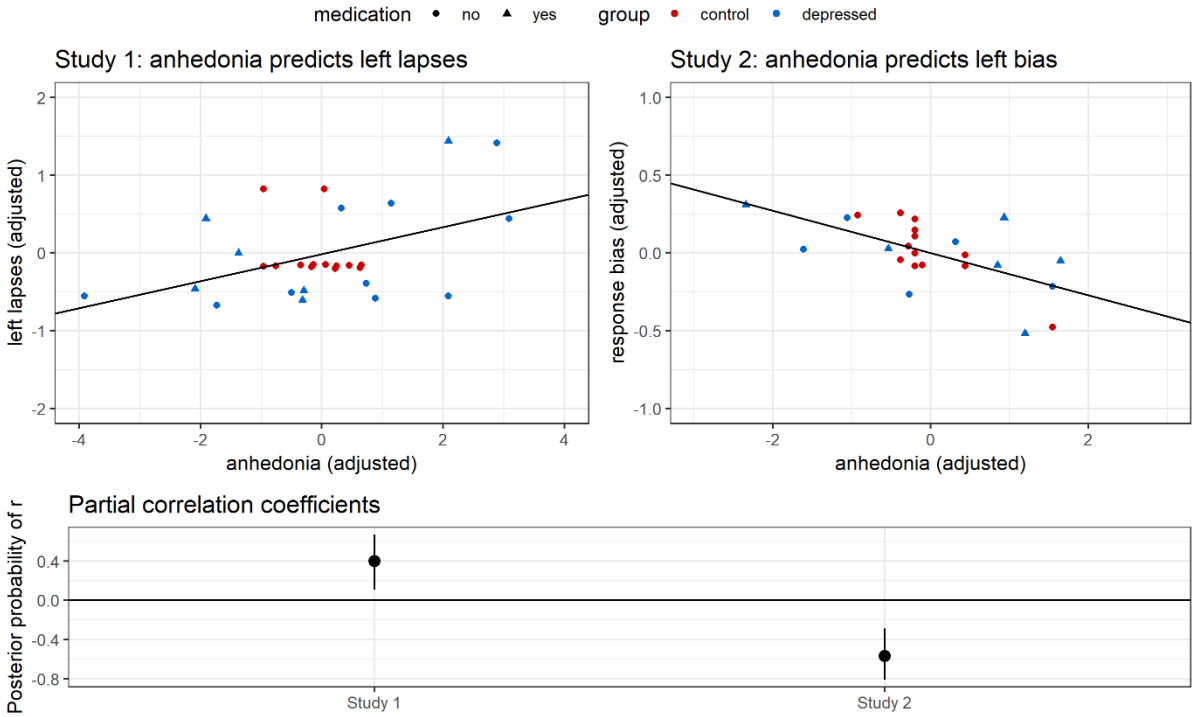


Figure G.2: Studies 1 and 2 anhedonia analyses: partial correlations between anhedonia and indices of left-sided neglect, adjusted for depression severity. Top left: in Study 1, after adjusting for overall depression severity, a higher score for anhedonia was predictive of a higher rate of left-sided asymptotic lapses. Top right: in Study 2, after adjusting for depression severity, a higher anhedonia score was predictive of an increase in left-sided response bias. Bottom panel: the most probable magnitudes of the two partial correlations are in the region of 0.4 – 0.6, while both correlations are credibly different from zero.

Appendix H: Study 6 handedness analysis

A non-significant trend towards a group difference in handedness in Study 6 motivated an additional analysis to assess any influence of handedness on the results of the Study 6 ANOVA. The data were subjected to a mixed ANCOVA with a between-participants factor of Group and within-participants factors of Cue Modality, Cue Validity, SOA and Target Laterality. Handedness (EHI score) was entered as a covariate. A Greenhouse-Geisser correction was employed where the assumption of sphericity was not met.

H.1. Effects of handedness

There was no main effect of handedness ($p > 0.6$) and no significant interactions between handedness and any other factor (ps > 0.09).

H.2. Influence of handedness on within-participants effects

The interaction observed in the ANOVA between validity and laterality no longer met statistical significance ($p > 0.7$). All other statistically-significant within-participants effects observed in the ANOVA were also present in the ANCOVA, including effects of cue validity ($F(1.51, 43.81) = 17.63$, $p < 0.001$, $\eta_p^2 = 0.38$); SOA ($F(2, 58) = 91.85$, $p < 0.001$, $\eta_p^2 = 0.76$); cue modality and SOA ($F(2, 58) = 7.13$, $p = 0.002$, $\eta_p^2 = 0.20$); validity and SOA ($F(4, 116) = 2.60$, $p < 0.04$, $\eta_p^2 = 0.08$); and SOA and laterality ($F(1.57, 45.60) = 5.90$, $p = 0.009$, $\eta_p^2 = 0.17$). As in the original ANOVA, there were no other significant main effects or interactions (all ps>0.1).

H.3. Influence of handedness on group effects

The key interaction between group and cue validity was unaffected by the inclusion of handedness as a covariate ($F(1.51, 43.81) = 4.74$, $p = 0.021$, $\eta_p^2 = 0.14$).

An interaction emerged between modality, laterality and group ($F(1,29) = 4.29$, $p = 0.047$, $\eta_p^2 = 0.13$), not present in the original ANOVA, which suggested that when the influence of handedness was covaried, depressed participants responded somewhat more quickly to somatic stimuli on the left, while controls responded somewhat more quickly to somatic stimuli on the right, relative to auditory stimuli.

As before, there was no main effect of group ($p > 0.6$), and no other significant interactions between group and any other factors (all ps>0.08).

H.4. Summary

In summary, there was no influence of handedness on any key outcomes of interest, although handedness did influence two interactions involving the factor of laterality. Given that the data were averaged across laterality before being used to optimize the predictive processing model, the decision was made to proceed without making any further adjustments for handedness.

Appendix I: Non-significant results

Non-significant results from the three classical analyses (reported in Chapters 6-8) are described here.

I.1. Study 4

I.1.1. Study 4 RT analysis

A repeated-measures ANOVA with a between-participants factor of group and within-participants factors of cue modality, block, cue validity, and target laterality was carried out on the RT data.

Within-participant effects

The ANOVA revealed that there was no main effect of modality ($F(1, 30) = 0.02$, $p = 0.89$, $\eta_p^2 < 0.01$), indicating that on average participants responded with comparable speed during somatic and auditory blocks.

There were no interactions between modality and block ($F(1, 30) < 0.01$, $p = 0.96$, $\eta_p^2 < 0.01$), modality and validity ($F(1, 30) = 1.29$, $p = 0.27$, $\eta_p^2 = 0.04$), block and validity ($F(1, 30) = 0.12$, $p = 0.73$, $\eta_p^2 < 0.01$), modality, block and validity ($F(1, 30) = 0.53$, $p = 0.47$, $\eta_p^2 = 0.02$), modality and laterality ($F(1, 30) = 1.20$, $p = 0.28$, $\eta_p^2 = 0.04$), block and laterality ($F(1, 30) = 0.11$, $p = 0.75$, $\eta_p^2 < 0.01$), modality, block and laterality ($F(1, 30) = 1.86$, $p = 0.18$, $\eta_p^2 = 0.06$), validity and laterality ($F(1, 30) = 0.01$, $p = 0.92$, $\eta_p^2 < 0.01$), modality, validity and laterality ($F(1, 30) = 0.05$, $p = 0.82$, $\eta_p^2 < 0.01$), block, validity and laterality ($F(1, 30) = 0.13$, $p = 0.72$, $\eta_p^2 < 0.01$), or modality, block, validity and laterality ($F(1, 30) = 0.17$, $p = 0.68$, $\eta_p^2 < 0.01$).

Group effects

Group did not interact with block ($F(1, 30) = 0.003$, $p = 0.95$, $\eta_p^2 < 0.01$), validity ($F(1, 30) = 1.93$, $p = 0.18$, $\eta_p^2 = 0.06$), laterality ($F(1, 30) = 0.09$, $p = 0.77$, $\eta_p^2 < 0.01$), modality x block ($F(1, 30) = 0.50$, $p = 0.49$, $\eta_p^2 = 0.02$), modality x validity ($F(1, 30) < 0.01$, $p = 0.96$, $\eta_p^2 < 0.01$), modality x block x validity ($F(1, 30) = 0.30$, $p = 0.59$, $\eta_p^2 = 0.01$), modality x laterality ($F(1, 30) = 0.16$, $p = 0.70$, $\eta_p^2 = 0.01$), block x laterality ($F(1, 30) = 1.42$, $p = 0.24$, $\eta_p^2 = 0.05$), modality x block x laterality ($F(1, 30) = 0.48$, $p = 0.49$, $\eta_p^2 = 0.02$), validity x laterality ($F(1, 30) = 0.95$, $p = 0.34$, $\eta_p^2 = 0.03$), modality x validity x laterality ($F(1, 30) = 0.38$, $p = 0.54$, $\eta_p^2 = 0.01$), block x validity x laterality ($F(1, 30) = 0.28, 0.60$, $\eta_p^2 = 0.01$), or modality x block x validity x laterality ($F(1, 30) < 0.01$, $p = 0.96$, $\eta_p^2 < 0.01$).

I.1.2. Study 4 error analysis

A cue modality by group ANOVA was conducted on the error scores. There was no main effect of modality ($F(1, 30) = 1.58$, $p = 0.22$, $\eta_p^2 = 0.05$) and no main effect of group ($F(1, 30) = 2.67$, $p = 0.11$, $\eta_p^2 = 0.08$).

I.1.3. Study 4 IIV analysis

A modality by group ANOVA found no main effect of modality ($F(1, 30) = 1.48$, $p = 0.23$, $\eta_p^2 = 0.05$).

I.2. Study 5

I.2.1. Study 5 RT analysis

A repeated-measures ANOVA with a between-participants factor of group and within-participants factors of cue relevance, cue modality, cue validity and target laterality was carried out on the RT data.

Within-participant effects

A non-significant trend towards a main effect of cue relevance ($F(1, 30) = 3.26$, $p = 0.081$, $\eta_p^2 = 0.10$) is explained by the relevance by validity interaction described in the main thesis: i.e., by a systematic disadvantage for the invalid minority, but not the valid majority, of relevant cues. There were also non-significant trends towards a main effect of modality ($F(1, 30) = 3.50$, $p = 0.071$, $\eta_p^2 = 0.10$), an interaction between modality and validity ($F(1, 30) = 3.36$, $p = 0.077$, $\eta_p^2 = 0.10$) and a 3-way interaction between modality, validity and laterality ($F(1, 30) = 3.57$, $p = 0.069$, $\eta_p^2 = 0.11$).

There was no evidence of a main effect of laterality ($F(1, 30) = 2.89$, $p = 0.10$, $\eta_p^2 = 0.09$), or of any interactions between relevance and modality ($F(1, 30) = 2.31$, $p = 0.14$, $\eta_p^2 = 0.07$), relevance, modality and validity ($F(1, 30) = 0.38$, $p = 0.54$, $\eta_p^2 = 0.01$), relevance and laterality ($F(1, 30) = 0.05$, $p = 0.83$, $\eta_p^2 = 0.002$), modality and laterality ($F(1, 30) = 0.14$, $p = 0.71$, $\eta_p^2 = 0.005$), relevance, modality and laterality ($F(1, 30) = 2.36$, $p = 0.14$, $\eta_p^2 = 0.07$), validity and laterality ($F(1, 30)$ 0.001, $p = 0.98$, $\eta_p^2 < 0.001$), or relevance, validity and laterality ($F(1, 30) = 0.02$, $p = 0.90$, $\eta_p^2 = 0.001$).

Group effects

There was no evidence that group interacted with relevance ($F(1, 30) = 1.93$, $p = 0.18$, $\eta_p^2 = 0.06$), modality ($F(1, 30) = 0.59$, $p = 0.45$, $\eta_p^2 = 0.02$), validity ($F(1, 30) = 2.70$, $p = 0.11$, $\eta_p^2 = 0.08$), relevance and modality ($F(1, 30) = 0.27$, $p = 0.61$, $\eta_p^2 = 0.009$), relevance and validity ($F(1, 30) = 1.71$, $p = 0.20$, $\eta_p^2 = 0.05$), relevance, modality and validity ($F(1, 30) = 0.08$, $p = 0.78$, $\eta_p^2 = 0.003$), relevance and laterality ($F(1, 30) = 0.033$, $p = 0.86$, $\eta_p^2 = 0.001$), modality and laterality ($F(1, 30) = 1.64$, $p = 0.21$, $\eta_p^2 = 0.05$), relevance, modality and laterality ($F(1, 30) = 0.67$, $p = 0.42$, $\eta_p^2 = 0.02$), validity and laterality ($F(1, 30) = 1.84$, $p = 0.19$, $\eta_p^2 = 0.06$), relevance, validity and laterality ($F(1, 30) = 1.39$, $p = 0.25$, $\eta_p^2 =$

0.04), modality, validity and laterality (F(1, 30) = 0.54, p = 0.47, η_p^2 = 0.02), or relevance, modality, validity and laterality (F(1, 30) = 0.05, p = 0.83, η_p^2 = 0.002). There was a non-significant trend towards a main effect of group (F(1, 30) = 3.56, p = 0.069, η_p^2 = 0.11) suggesting somewhat slowed responses in the depressed group relative to healthy controls; and a similarly non-significant trend towards an interaction between group and laterality (F(1, 30) = 3.87, p = 0.058, η_p^2 = 0.11) suggesting that control participants showed a tendency to respond more slowly to left-sided targets, whereas depressed participants showed no such effect.

I.2.2. Study 5 error analysis

An ANOVA with the factors of modality, validity and group was performed on the error scores. The ANOVA revealed no main effect of modality (F(1, 30) = 0.46, p = 0.51, η_p^2 = 0.02), no main effect of group (F(1, 30) < 0.01, p = 0.96, η_p^2 < 0.01), no interaction between modality and group (F(1, 30) = 0.23, p = 0.63, η_p^2 = 0.01), no interaction between validity and group (F(1, 30) < 0.01, p = 0.96, η_p^2 < 0.01), and no interaction between modality and validity (F(1, 30) = 0.11, p = 0.74, η_p^2 < 0.01).

I.2.3. Study 5 IIV analysis

A group by modality by validity ANOVA was conducted on IIV scores. There was no main effect of validity (F(1, 30) = 0.14, p = 0.72, η_p^2 < 0.01), no main effect of group (F(1, 30) = 2.24, p = 0.15, η_p^2 = 0.07), no interaction between modality and group (F(1, 30) = 0.10, p = 0.75, η_p^2 < 0.01), no interaction between validity and group (F(1, 30) = 2.01, p = 0.17, η_p^2 = 0.06) and no interaction between modality, validity and group (F(1, 30) = 0.75, p = 0.39, η_p^2 = 0.03).

I.3. Study 6

I.3.1. Study 6 RT analysis

The data were subjected to a repeated-measures ANOVA with a between-participants factor of group and within-participants factors of cue modality, cue validity, SOA and target laterality.

Within-participants effects

The ANOVA revealed a non-significant trend in the direction of a main effect of modality (F(1, 30) = 3.96, p = 0.06, η_p^2 = 0.12). There was no main effect of laterality (F(1, 30) = 0.16, p = 0.69, η_p^2 < 0.01) and no interactions between modality and validity (F(2, 60) = 0.97, p = 0.39, η_p^2 = 0.03), modality, validity and SOA (F(4, 120) = 1.69, p = 0.16, η_p^2 = 0.05), modality and laterality F(1, 30) = 0.05, p = 0.83, η_p^2 < 0.01), modality, validity and laterality (F(2, 60) = 0.09, p = 0.92, η_p^2 < 0.01), modality, SOA and laterality (F(1.67, 50.10) = 1.45, p = 0.24, η_p^2 = 0.05) or modality, validity, SOA and laterality (F(4, 120) = 0.54, p = 0.70, η_p^2 = 0.02).

Group effects

There was no main effect of group ($F(1, 30) < 0.01$, $p = 0.96$, $\eta_p^2 < 0.01$), and no interactions between modality and group ($F(1, 30) = 0.86$, $p = 0.32$, $\eta_p^2 = 0.03$), laterality and group ($F(1, 30) = 0.17$, $p = 069$, $\eta_p^2 < 0.01$), modality, validity and group ($F(2, 60) = 0.06$, $p = 0.94$, $\eta_p^2 < 0.01$), modality, SOA and group ($F(2, 60) = 0.05$, $p = 0.95$, $\eta_p^2 < 0.01$), validity, SOA and group ($F(4, 120) = 1.27$, $p = 0.29$, $\eta_p^2 = 0.04$), modality, validity, SOA and group $F(4, 120) = 0.70$, $p = 0.59$, $\eta_p^2 = 0.02$), validity, laterality and group ($F(2, 60) = 2.19$, $p = 0.12$, $\eta_p^2 = 0.07$), modality, validity, laterality and group ($F(2, 60) = 0.18$, $p = 0.83$, $\eta_p^2 = 0.01$), SOA, laterality and group ($F(2, 60) = 1.31$, $p = 0.28$, $\eta_p^2 = 0.04$), modality, SOA, laterality and group ($F(1.67, 50.10) = 0.54$, $p = 0.58$, $\eta_p^2 = 0.02$), validity, SOA, laterality and group ($F(4, 120) = 0.18$, $p = 0.95$, $\eta_p^2 = 0.01$), or modality, validity, SOA, laterality and group ($F(4, 120) = 1.45$, $p = 0.22$, $\eta_p^2 = 0.05$). There were non-significant trends in the direction of interactions between SOA and group ($F(1.68, 50.31) = 2.78$, $p = 0.08$, $\eta_p^2 = 0.09$), and modality, laterality and group $F(1, 30) = 3.06$, $p = 0.09$, $\eta_p^2 = 0.09$).

Appendix J: Interview and self-report measures

J.1. SCID-1 (First et al., 1996: example questions)

A. MOOD EPISODES

A1 – A15: MAJOR DEPRESSIVE EPISODE CRITERIA

"Now I am going to ask you some more questions about your mood ..."

NOTE: Criterion B (i.e., does not meet criteria for a Mixed Episode) has been omitted from the SCID.

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) or (2)
In the past month...

A1 ...has there been a period of time when you were feeling depressed or down most of the day, nearly every day? (What was that like?) IF YES: How long did it last? (As long as 2 weeks?) ? - +

(1) Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). **Note**: In children and adolescents, can be irritable mood.

A2 ... What about losing interest or pleasure in things you usually enjoyed? IF YES: Was it nearly every day? How long did it last? (As long as 2 weeks?) ? - +

(2) Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)

If neither **A1** nor **A2** is "+" during the current month, check for past Major Depressive Episodes by asking questions **A1** and **A2** again looking for lifetime episodes, beginning with "Has there EVER..."

IF AT LEAST ONE PAST DEPRESSED PERIOD: Have you had more than one time like that? Which one was the worst?

FOR THE FOLLOWING QUESTIONS, FOCUS ON THE WORST 2-WEEK PERIOD:

A3 How was your appetite? (Weight loss/gain, increased/decreased appetite?) ? - +

(3) Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. **Note**: In children, consider failure to make expected weight gains.

A4 How were you sleeping? (insomnia/hypersomnia, trouble falling asleep, waking frequently, waking too early) How many hours a night compared to usual? Was that nearly every night? ? - +

(4) Insomnia or hypersomnia nearly every day.

A5 Were you so fidgety or restless that you were unable to sit still? (was it so bad that other people noticed? What did they notice? Was it nearly every day?) *IF NO* what about the opposite? ? - +

(5)psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)

A6 What was your energy like? Fatigue/loss of energy, nearly every day ? - +

(6). Fatigue or loss of energy nearly every day

A7 How did you feel about yourself? (Worthless, guilty), nearly every day. ? - +

(7). Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
NOTE: CODE "-" IF ONLY LOW SELF ESTEEM

A8 Did you have trouble thinking or concentrating? (Indecisiveness) what kind of things did it interfere ? - +

with? IF NO: Was it hard to make decisions about everyday things?

(8). Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by objective account or as observed by others).

A9 Were things so bad that you were thinking a lot about death or that you would be better off dead? ? - +

What about thinking of hurting yourself? IF YES: Did you do anything to hurt yourself?

(9). Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan or committing suicide.

A10 **AT LEAST FIVE OF A(1) – A(9) ARE "+" AND AT LEAST ONE OF THESE IS ITEM A(1) OR A(2).** ? - +

If **A10** is "-" (i.e., fewer than five are "+"), ask the following if unknown:
Have there been any other times when you've been depressed and had even more of the symptoms that we've just talked about?
If "yes", go back to **A1** and ask about that episode.
If "no", go to **A16** (*Manic Episode*).

A11 IF UNCLEAR: has [the depression/OWN WORDS] made it hard for you to do your work, take care of things at time or get along with other people? ? - +

C._ The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

If **A11** is "-" (i.e. not clinically significant), ask the following if unknown:

Have there been any other times when you've been depressed and it had more of an effect on your life? If
"yes", go back to **A1**, and ask about that episode If

A12 Just before this began, were you physically ill? Taking any medications/change in amount of medications? ? - +

Just before this began, were you drinking or using any street drugs?

D. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug abuse, medication) or a general medical condition.

Etiological general medical conditions include degenerative neurological illnesses (e.g., Parkinson's disease)(, cerebrovascular disease (e.g., stroke), metabolic conditions (e.g., vitamin B12 deficiency), endocrine conditions (e.g., hyper- and hypothyroidism, hyper- and hypoadrenocorticism), viral or other infections (e.g., hepatitis, mononucleosis, HIV), and certain cancers (e.g., carcinoma of the pancreas).

Etiological substances include alcohol, amphetamines, cocaine, hallucinogens, inhalants, opiods, phencyclidine, sedatives, hypnotics, anxiolytics. Medications include antihypertensives, oral contraceptives, corticosteroids, anabolic steroids, anticancer agents, analgesics, anticholinergics, cardiac medication.

If there is any indication that the depression may be secondary (i.e., a direct physiological consequence of a general medical condition or substance), go to **A61** and return here to make a rating of "+" or "-".

If **A12** is "-" (i.e. mood is due to a substance or general medical condition), ask the following:

Have there been any other times when you've been depressed and it was not because of [GENERAL MEDICAL CONDITION/SUBSTANCE USE]?

If "yes", go back to **A1**, and ask about that episode

If "no", go to **A16** (*Manic episode*)

A13 IF UNKNOWN: did this begin soon after someone close to you died? ? - +

Have there been any other times when you've been depressed and it was not because of the loss of a loved one?

E. The symptoms are not better accounted for by Bereavement, i.e., after the loss [death] of a loved one, the symptoms persist for longer than 2 months or are characterised by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

If **A13** is "-" (i.e., the depressed mood is better accounted for by Bereavement), ask the following:

Have there been any other times when you've been depressed and it was not because of the loss of a loved one?

If "yes", go back to **A1**, and ask about that episode

If "no", go to **A16** (*Manic episode*)

A14 IF UNKNOWN: have you had (SYMOTOMS RATED "+" ABOVE) in the past month? ? - +

CRITERIA A, C, D AND E ARE "+" (MAKE A DIAGNOSIS OF MAJOR DEPRESSIVE EPISODE)

A15 How many separate times have you been [depressed/OWN WORDS] nearly every day for at least 2 weeks and had several of the symptoms you just described, such as [SYMPTOMS OF THE WORST EPISODE]

_____

Total number of Major Depressive Episodes, including current (CODE 99 if too numerous or indistinct to count)

J.2. BDI-II (Beck et al., 1996)

Please read each group of statements carefully, then pick out the **one statement** in each group which best describes the way you have been feeling during the **past 2 weeks, including today.** Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, simply circle the statement which has the largest number. Be sure that you do **not** circle more than one statement for Item 16 (change in sleeping pattern) and Item 18 (change in appetite).

1
0 I do not feel sad.
1 I feel sad.
2 I am sad all the time and I can't snap out of it.
3 I am so sad or unhappy I can't stand it.

2
0 I am not particularly discouraged about the future.
1 I feel discouraged about the future.
2 I feel I have nothing to look forward to.
3 I feel that the future is hopeless and that things cannot improve.

3
0 I do not feel like a failure.
1 I feel I have failed more than the average person.
2 As I look back on my life, all I can see is a lot of failures.
3 I feel I am a complete failure as a person.

4
0 I get as much satisfaction out of things as I used to.
1 I don't enjoy things the way I used to.
2 I don't get real satisfaction out of anything anymore.
3 I am dissatisfied or bored with everything.

5
0 I don't feel particularly guilty.
1 I feel guilty a good part of the time.
2 I feel quite guilty most of the time.
3 I feel guilty all of the time.

6
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
0 I don't feel disappointed in myself.
1 I am disappointed in myself.
2 I am disgusted with myself.
3 I hate myself.

8
0 I don't feel I am any worse than anybody else.
1 I am critical of myself for my weaknesses or mistakes.
2 I blame myself all the time for my faults.
3 I blame myself for everything bad that happens.

9
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
0 I don't cry any more than usual.
1 I cry more now than I used to.
2 I cry all the time now.
3 I used to be able to cry, but now I can't cry even though I want to.

11
0 I am no more irritated now than I ever am.
1 I get annoyed or irritated more easily than I used to.
2 I feel irritated all the time now.

12
0 I have not lost interest in other people.
1 I am less interested in other people than I used to be.
2 I have lost most of my interest in other people.
3 I have lost all of my interest in other people.

13
0 I make decisions about as well as I ever could.
1 I put off making decisions more than I used to.
2 I have greater difficulty in making decisions than before.
3 I can't make decisions at all anymore.

14
0 I don't feel I look any worse than I used to.
1 I am worried that I am looking old or unattractive.
2 I feel that there are permanent changes in my appearance that make me look unattractive.
3 I believe that I look ugly.

15
0 I can work about as well as before.
1 It takes an extra effort to get started at doing something.
2 I have to push myself very hard to do anything.
3 I can't do any work at all.

16
0 I can sleep as well as usual.
1 I don't sleep as well as I used to.
2 I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
3 I wake up several hours earlier than I used to and cannot get back to sleep.

17
0 I don't get more tired than usual.
1 I get tired more easily than I used to.
2 I get tired from doing almost anything.
3 I am too tired to do anything.

18
0 My appetite is no worse than usual.
1 My appetite is not as good as it used to be.
2 My appetite is much worse now.
3 I have no appetite at all anymore.

19
0 I haven't lost much weight, if any, lately.
1 I have lost more than 5 pounds. I am purposely trying to lose
2 I have lost more than 10 pounds. weight by eating less. Yes__ No___
3 I have lost more than 15 pounds.

20
0 I am no more worried about my health than usual.
1 I am worried about physical problems such as aches and pains; or upset stomach; or constipation.
2 I am very worried about physical problems and it's hard to think of much else.
3 I am so worried about my physical problems that I cannot think about anything else.

21
0 I have not noticed any recent changes 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.

3 I don’t get irritated at all by the things that used to irritate me.

J.3. BAI (Beck et al., 1988)

Below is a list of common symptoms of anxiety. Please carefully read each item in the list. Indicate how much you have been bothered by each symptom during the PAST WEEK, INCLUDING TODAY, by placing an X in the corresponding space in the column next to each symptom.

	NOT AT ALL	**MILDLY** It did not bother me much.	**MODERATELY** It was very unpleasant, but I could stand it.	**SEVERELY** I could barely stand it.
1. Numbness or tingling.				
2. Feeling hot.				
3. Wobbliness in legs.				
4. Unable to relax.				
5. Fear of the worst happening.				
6. Dizzy or lightheaded.				
7. Heart pounding or racing.				
8. Unsteady.				
9. Terrified.				
10. Nervous.				
11. Feelings of choking.				
12. Hands trembling.				
13. Shaky.				
14. Fear of losing control.				
15. Difficulty breathing.				
16. Fear of dying.				
17. Scared.				
18. Indigestion or discomfort in abdomen.				
19. Faint.				
20. Face flushed.				
21. Sweating (not due to heat)				

J.4. EHI (Oldfield, 1971)

Edinburgh Handedness Inventory

Please indicate with a check (✓) your preference in using your left or right hand in the following tasks.

Where the preference is so strong you would never use the other hand, unless absolutely forced to, put two checks (✓✓).

If you are indifferent, put one check in each column (✓ | ✓).

Some of the activities require both hands. In these cases, the part of the task or object for which hand preference is wanted is indicated in parentheses.

Task / Object	Left Hand	Right Hand
1. Writing		
2. Drawing		
3. Throwing		
4. Scissors		
5. Toothbrush		
6. Knife (without fork)		
7. Spoon		
8. Broom (upper hand)		
9. Striking a Match (match)		
10. Opening a Box (lid)		
Total checks:	LH =	RH =
Cumulative Total	CT = LH + RH =	
Difference	D = RH – LH =	
Result	R = (D / CT) × 100 =	
Interpretation: (Left Handed: R < -40) (Ambidextrous: -40 ≤ R ≤ +40) (Right Handed: R > +40)		

J.5. MAIA (Mehling et al., 2012)

Below you will find a list of statements. Please indicate how often each statement applies to you generally in daily life.

	Circle one number on each line					
	Never					**Always**
1. When I am tense I notice where the tension is located in my body.	0	1	2	3	4	5
2. I notice when I am uncomfortable in my body.	0	1	2	3	4	5
3. I notice where in my body I am comfortable.	0	1	2	3	4	5
4. I notice changes in my breathing, such as whether it slows down or speeds up.	0	1	2	3	4	5
5. I do not notice (I ignore) physical tension or discomfort until they become more severe.	0	1	2	3	4	5
6. I distract myself from sensations of discomfort.	0	1	2	3	4	5
7. When I feel pain or discomfort, I try to power through it.	0	1	2	3	4	5
8. When I feel physical pain, I become upset.	0	1	2	3	4	5
9. I start to worry that something is wrong if I feel any discomfort.	0	1	2	3	4	5
10. I can notice an unpleasant body sensation without worrying about it.	0	1	2	3	4	5
11. I can pay attention to my breath without being distracted by things happening around me.	0	1	2	3	4	5
12. I can maintain awareness of my inner bodily sensations even when there is a lot going on around me.	0	1	2	3	4	5
13. When I am in conversation with someone, I can pay attention to my posture.	0	1	2	3	4	5
14. I can return awareness to my body if I am distracted.	0	1	2	3	4	5
15. I can refocus my attention from thinking to sensing my body.	0	1	2	3	4	5
16. I can maintain awareness of my whole body even when a part of me is in pain or discomfort.	0	1	2	3	4	5

	Circle one number on each line					
	Never					Always
17. I am able to consciously focus on my body as a whole.	0	1	2	3	4	5
18. I notice how my body changes when I am angry.	0	1	2	3	4	5
19. When something is wrong in my life I can feel it in my body.	0	1	2	3	4	5
20. I notice that my body feels different after a peaceful experience.	0	1	2	3	4	5
21. I notice that my breathing becomes free and easy when I feel comfortable.	0	1	2	3	4	5
22. I notice how my body changes when I feel happy / joyful.	0	1	2	3	4	5
23. When I feel overwhelmed I can find a calm place inside.	0	1	2	3	4	5
24. When I bring awareness to my body I feel a sense of calm.	0	1	2	3	4	5
25. I can use my breath to reduce tension.	0	1	2	3	4	5
26. When I am caught up in thoughts, I can calm my mind by focusing on my body/breathing.	0	1	2	3	4	5
27. I listen for information from my body about my emotional state.	0	1	2	3	4	5
28. When I am upset, I take time to explore how my body feels.	0	1	2	3	4	5
29. I listen to my body to inform me about what to do.	0	1	2	3	4	5
30. I am at home in my body.	0	1	2	3	4	5
31. I feel my body is a safe place.	0	1	2	3	4	5
32. I trust my body sensations.	0	1	2	3	4	5

Appendix K: Ethics approval, consent form and information sheets

K.1. Ethics approval letter

Karen Douglas
Secretary

Dr T Dalgleish
MRC Cognition and Brain Sciences Unit
15 Chaucer Road
Cambridge
CB22EF

UNIVERSITY OF CAMBRIDGE

CAMBRIDGE
PSYCHOLOGY RESEARCH ETHICS
COMMITTEE

5 August 2013

Application No: Pre.2013.72

Dear Dr Dalgleish

Perceptual and Attentional Processes in Mood Regulation

The Cambridge Psychology Research Ethics Committee has given ethical approval to your research project: Perceptual and Attentional Processes in Mood Regulation, as set out in your application dated 29 July 2013.

The Committee attaches certain standard conditions to all ethical approvals. These are:

(a) that if the staff conducting the research should change, any new staff should read the application submitted to the Committee for ethical approval and this letter (and any subsequent letter concerning this application for ethical approval);

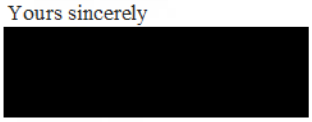
(b) that if the procedures used in the research project should change or the project itself should be changed you should consider whether it is necessary to submit a further application for any modified or additional procedures to be approved;

(c) that if the employment or departmental affiliation of the staff should change you should notify us of that fact.

Members of the Committee also ask that you inform them should you encounter any unexpected ethical issues.

If you would let us know that you that you are able to accept these conditions, I will record that you have been given ethical approval.

Yours sincerely



K S Douglas

cc: Dr A Bevan

17 Mill Lane Cambridge CB2
1RX Telephone: 01223 766894
Fax: 01223 332355 E-mail:
mb422@admin.cam.ac.uk

K.2. CBU adult volunteer panel consent form

Ethics Title:
Study Title:
Principal Investigator: **PRE/NRES Code**
Researcher(s): **Study/Project**

Agreement to continued membership of the CBU Adult Volunteer Panel

The MRC Cognition and Brain Sciences Unit (CBU) is part of the University of Cambridge (from July 1st 2017). The University of Cambridge have the responsibility for safeguarding research data and personal information.

Please initial to indicate that you have read each point

1. I agree to my continued membership of the CBU Adult Volunteer Panel and understand that this means the University of Cambridge holding my personally identifiable information (e.g. my name and address) that I provided when I registered as a volunteer with the MRC Cognition and Brain Sciences Unit Adult Volunteer Panel. This includes information given before the CBU became part of the University of Cambridge.	
2. I understand that the CBU Volunteer Panel uses a commercial web interface (sona-systems.com) to communicate with volunteers and that, whilst I remain a member of the Panel, my personal information is therefore held on computer servers belonging to this company in Canada and the Netherlands. These are compliant with EU law on data protection. I agree to this.	
3. I understand that, should I no longer wish to be a member of the Panel, or I cannot be contacted 5 years after my last participation, all personally identifiable information held about me will be deleted from the Panel and the Sona-sytems website.	
4. I confirm that I have had an opportunity to read the CBU Adult Volunteer Panel Information sheet and the CBU Human Subject Privacy Policy, had the opportunity to consider this information, ask any questions and had these questions answered satisfactorily.	

Agreement to participate in this study:

5. I confirm that the nature of the above named study has been explained to me and that I have agreed to take part.	
6. I confirm that I have read the participant information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
7. I understand that my participation in the above study is voluntary and that I am free to withdraw at any time without giving a reason.	
8. I understand that my personally identifiable information, such as my name, address and date of birth are treated as highly confidential by the research team and kept in a secure computing area and/or in a locked filing cabinet. I have read and understood for how long these details will be kept by the researchers running this study.	
9. [IF RELEVANT] I understand that MRI radiographers will complete a safety screening sheet that will include my name, address and date of birth. I understand that this is retained by the radiographers separately from my research data for 10 years in case of safety audit. I agree to this.	
10. [IF RELEVANT] I understand that the CBU has a duty of care to volunteers and the general public that, in exceptional circumstances, places limits on its duty of confidentiality to research participants. I understand and agree to this.	
11. I agree that my *anonymised* research data from this study will be kept in the long-term, may be combined with data from other CBU studies to answer new research questions, may be shared with other researchers or may be made 'Open' without new consent being sought from me.	
12. I agree to the CBU panel manager receiving the scores from measures I have completed in this study and making these available to other researchers within the CBU for the purposes of inviting particular participants (e.g. fluent French speakers) to take part in specific studies.	

To indicate your agreement with points 1-12 above, please sign below.

Panel id: Name of Participant:

Signature: …… Date: ……

K.3. Participant Information Sheets

K.3.1. Studies 1 and 4

Study Title: Attentional Orienting and Mood

Thank you for your interest in our project. We are doing a series of studies examining interactions between mood, attention and perception and we would like to invite you to participate in one of these studies. This information sheet provides some details about what you can expect if you decide to take part. If you would like to discuss the study further or ask any questions about it, please feel free to get in touch with us for an informal chat. Our contact details are provided at the bottom of the sheet.

What is the purpose of the project?

Although periods of low mood or anxiety can be a normal part of life, these feelings can become problematic if they persist for too long or become too easily triggered. We are interested in learning more about the reasons why some people become caught in ongoing low mood or anxiety, because a clearer understanding of these maintaining factors will help us to develop more specific and targeted treatments. We believe that interactions between mood and attention may be important in explaining why some people remain vulnerable to ongoing low mood or anxiety, and therefore the aim of this project is to find out more about how basic attentional mechanisms work at different levels of mood. In order to develop as full a picture of these issues as possible, we are interested in recruiting participants who have current or past experience of low mood or anxiety, but also in recruiting participants with no such experience.

What will the study involve?

If you decide to take part, we will ask you to come to the Cognition and Brain Sciences Unit on 2 separate occasions.

On the first occasion you will be asked to take part in an interview about experiences such as depression or anxiety which you may or may not have experienced. We will also ask you to fill out some questionnaires about various aspects of your mood.

On the second occasion, you will be asked to take part in some experimental tasks measuring aspects of perception and attention. The first task will involve identifying your perceptual threshold for auditory and tactile information. In the auditory condition, we will ask you to listen for a faint sound occurring in one of two intervals, and to tell us in which interval you think it occurred. The tactile condition is similar, except that we will ask you to try to detect a faint vibration from a small tactor placed against your skin. The tactors are designed to vibrate gently like a mobile phone or pager, and will not be painful or harm your skin in any way. The strength of the sound or vibration will be adjusted until we are able to identify your perceptual threshold (the point where you can detect the sound or vibration for a set proportion of the time). This should take 20 - 30 minutes in total. The second task focuses on attention. We will ask you to sit in a comfortable position at a desk holding 2 audio speakers to your left and to your right. We will also ask for permission to strap 2 small tactors to your left and right wrists. A light

from a small LED will flash either on your left or your right, and you will be asked to indicate on which side it occurred as quickly and accurately as you can, using left and right foot-pedals. Sometimes you will notice a sound from one of the speakers or a vibration from one of the tactors, but you do not have to respond in any way to these. This task will last for about 40 minutes, with a break every 10 minutes for you to rest or stretch your legs.

How long will it take?
We expect each session to take between 90 minutes and 2 hours, including plenty of time to allow for rests between tasks. We will be very happy to ensure that appointment times suit your convenience.

Will I find the study upsetting?
Some of the interview and questionnaire items will ask you about issues to do with mood and anxiety, including any past episodes of depression or times when you have been very anxious. If thinking or talking about these topics causes you to feel any distress, the study can be stopped or paused to allow you to take whatever time you need to recover. If helpful, we will provide you with a quiet room where you can be private, a hot drink, an opportunity to engage in a positive mood induction procedure, and an opportunity for a confidential chat with a registered clinical psychologist if you would like one. We can also provide general advice about ways of accessing further help or support if you would find this useful. When you are ready to leave, we will make whatever efforts are necessary to ensure that you are able to get home safely.

Will I be reimbursed for my time?
Yes: we will compensate you for your time at the rate of £6 per hour, and we will also contribute to your travel expenses (£2.50 for participants coming from within Cambridge and £3 for those coming from outside). These are the standard MRC CBU rates.

Do I have to take part?
No. It is completely up to you to decide whether or not you want to take part in the study. You can take as long as you want to decide and can ask any questions you like before deciding. If you do decide to take part you will still be free to change your mind at any time during the study, and you can withdraw at any point without giving a reason.

Will my data be kept confidential?
Yes: all the information that you provide throughout the study will be kept completely confidential and processed anonymously. We will allocate you a random identifier which will be kept with your data instead of your name, and we will make sure that no information that could personally identify you will be kept with your data. Any findings from the study that are published in academic journals or presented at conferences will be presented at the group level and will be completely anonymous.

Will I be given feedback about my data?
We will not be able to provide any specific feedback about your data from the perceptual and attention tasks because we will be analysing this data on a group level only. We will also not be making any formal

diagnoses on the basis of the interview or questionnaires about your mood. However, if you would like to have a chance to discuss issues around mood we will be happy to provide general advice about how to go about accessing services that may be beneficial for you.

Further information
If you would like any further information about the study, an opportunity to discuss it with a researcher or a chance to have your questions answered, please get in touch with us! You can talk it over with us or spend as much time as you like deciding whether or not to take part without in any way committing yourself.

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Thank you!

This project has received ethical approval from the Psychology Research Ethics Committee of the University of Cambridge

K.3.2. Study 2

Study Title: Mood, Perception and Context
Thank you for your interest in our project. We are doing a series of studies examining interactions between mood, attention and perception and we would like to invite you to participate in one of these studies. This information sheet provides some details about what you can expect if you decide to take part. If you would like to discuss the study further or ask any questions about it, please feel free to get in touch with us for an informal chat. Our contact details are provided at the bottom of the sheet.

What is the purpose of the project?
Although periods of low mood or anxiety can be a normal part of life, these feelings can become problematic if they persist for too long or become too easily triggered. We are interested in learning more about the reasons why some people become caught in ongoing low mood or anxiety, because a clearer understanding of these maintaining factors will help us to develop more specific and targeted treatments. We believe that interactions between mood and attention may be important in explaining why some people remain vulnerable to ongoing low mood or anxiety, and therefore the aim of this project is to find out more about how basic attentional mechanisms work at different levels of mood. In order to develop as full a picture of these issues as possible, we are interested in recruiting participants who have current or past experience of low mood or anxiety, but also in recruiting participants with no such experience.

What will the study involve?

You will be asked to take part in some experimental tasks measuring aspects of perception and attention. The tasks will involve identifying your perceptual threshold for auditory and tactile information. In the auditory condition, we will ask you to listen for a faint sound occurring either to your left or your right, and to tell us which side you think it occurred. The tactile condition is similar, except that we will ask you to try to detect faint vibrations from small tactors placed against the skin of your left and right wrists. The tactors are designed to vibrate gently like a mobile phone or pager, and will not be painful or harm your skin in any way. While you are doing this task, we will ask you to keep your eyes fixed on a computer monitor in front of you. The monitor will display a word (positive, negative or neutral) during each interval, but you do not have to respond in any way to these. The strength of the sound or vibration will be adjusted until we are able to identify your perceptual threshold (the point where you can detect the sound or vibration for a set proportion of the time). Opportunities to rest will be provided between tasks. We will also ask you to answer some interview questions and to fill out some questionnaires about various aspects of your mood.

How long will it take?
We expect the session to take about 2 hours, including plenty of time to allow for rests between tasks. We will be very happy to ensure that appointment times suit your convenience.

Will I find the study upsetting?
Some of the interview and questionnaire items will ask you about issues to do with mood and anxiety, including current episodes of depression or times when you have been very anxious. If thinking or talking about these topics causes you to feel any distress, the study can be stopped or paused to allow you to take whatever time you need to recover. If helpful, we will provide you with a quiet room where you can be private, a hot drink, an opportunity to engage in a positive mood induction procedure, and an opportunity for a confidential chat with a registered clinical psychologist if you would like one. We can also provide general advice about ways of accessing further help or support if you would find this useful. When you are ready to leave, we will make whatever efforts are necessary to ensure that you are able to get home safely.

Will I be reimbursed for my time?
Yes: we will compensate you for your time at the rate of £6 per hour, and we will also contribute to your travel expenses (£2.50 for participants coming from within Cambridge and £3 for those coming from outside). These are the standard MRC CBU rates.

Do I have to take part?
No. It is completely up to you to decide whether or not you want to take part in the study. You can take as long as you want to decide and can ask any questions you like before deciding. If you do decide to take part you will still be free to change your mind at any time during the study, and you can withdraw at any point without giving a reason.

Will my data be kept confidential?
Yes: all the information that you provide throughout the study will be kept completely confidential and processed anonymously. We will allocate you a random identifier which will be kept with your data instead of your name, and we will make sure that no information that could personally identify you will be kept with your data. Any findings from the study that are published in academic journals or presented at conferences will be presented at the group level and will be completely anonymous.

Will I be given feedback about my data?
We will not be able to provide any specific feedback about your data from the perceptual and attention tasks because we will be analysing this data on a group level only. We will also not be making any formal diagnoses on the basis of the interview or questionnaires about your mood. However, if you would like to have a chance to discuss issues around mood we will be happy to provide general advice about how to go about accessing services that may be beneficial for you.

Further information
If you would like any further information about the study, an opportunity to discuss it with a researcher or a chance to have your questions answered, please get in touch with us! You can talk it over with us or spend as much time as you like deciding whether or not to take part without in any way committing yourself.

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Thank you!

This project has received ethical approval from the Psychology Research Ethics Committee of the University of Cambridge

K.3.3. Study 5

Study Title: Attentional Flexibility and Mood
Thank you for your interest in our project. We are doing a series of studies examining interactions between mood, attention and perception and we would like to invite you to participate in one of these studies. This information sheet provides some details about what you can expect if you decide to take part. If you would like to discuss the study further or ask any questions about it, please feel free to get in touch with us for an informal chat. Our contact details are provided at the bottom of the sheet.

What is the purpose of the project?
Although periods of low mood or anxiety can be a normal part of life, these feelings can become problematic if they persist for too long or become too easily triggered. We are interested in learning more about the reasons why some people become caught in ongoing low mood or anxiety, because a clearer understanding of these maintaining factors will help us to develop more specific and targeted treatments. We believe that interactions between mood and attention may be important in explaining why some people remain vulnerable to ongoing low mood or anxiety, and therefore the aim of this project is to find out more about how basic attentional mechanisms work at different levels of mood. In order to develop as full a picture of these issues as possible, we are interested in recruiting

participants who have current or past experience of low mood or anxiety, but also in recruiting participants with no such experience.

What will the study involve?
If you decide to take part, we will ask you to come to the Cognition and Brain Sciences Unit to take part in some experimental tasks measuring aspects of attention. We will ask you to sit in a comfortable position at a desk holding 2 audio speakers to your left and to your right. We will also ask for permission to strap 2 small tactors to your left and right wrists. The tactors are designed to vibrate gently like a mobile phone or pager, and will not be painful or harm your skin in any way. A light from a small LED will flash either on your left or your right, and you will be asked to indicate on which side it occurred as quickly and accurately as you can, using left and right foot-pedals. Sometimes you will notice a sound from one of the speakers or a vibration from one of the tactors, but you do not have to respond in any way to these. There will be a break every 10 minutes for you to rest or stretch your legs. We will also ask you to answer some interview questions and fill out some questionnaires about various aspects of your mood.

How long will it take?
We expect the session to take about 90 minutes, including plenty of time to allow for rests between tasks. We will be very happy to ensure that appointment times suit your convenience.

Will I find the study upsetting?
Some of the interview and questionnaire items will ask you about issues to do with mood and anxiety, including any past episodes of depression or times when you have been very anxious. If thinking or talking about these topics causes you to feel any distress, the study can be stopped or paused to allow you to take whatever time you need to recover. If helpful, we will provide you with a quiet room where you can be private, a hot drink, an opportunity to engage in a positive mood induction procedure, and an opportunity for a confidential chat with a registered clinical psychologist if you would like one. We can also provide general advice about ways of accessing further help or support if you would find this useful. When you are ready to leave, we will make whatever efforts are necessary to ensure that you are able to get home safely.

Will I be reimbursed for my time?
Yes: we will compensate you for your time at the rate of £6 per hour, and we will also contribute to your travel expenses (£2.50 for participants coming from within Cambridge and £3 for those coming from outside). These are the standard MRC CBU rates.

Do I have to take part?
No. It is completely up to you to decide whether or not you want to take part in the study. You can take as long as you want to decide and can ask any questions you like before deciding. If you do decide to take part you will still be free to change your mind at any time during the study, and you can withdraw at any point without giving a reason.

Will my data be kept confidential?
Yes: all the information that you provide throughout the study will be kept completely confidential and processed anonymously. We will allocate you a random identifier which will be kept with your data instead of your name, and we will make sure that no information that could personally identify you will be kept with your data. Any findings from the study that are published in academic journals or presented at conferences will be presented at the group level and will be completely anonymous.

Will I be given feedback about my data?
We will not be able to provide any specific feedback about your data from the perceptual and attention tasks because we will be analysing this data on a group level only. We will also not be making any formal diagnoses on the basis of the interview or questionnaires about your mood. However, if you would like to have a chance to discuss issues around mood we will be happy to provide general advice about how to go about accessing services that may be beneficial for you.

Further information
If you would like any further information about the study, an opportunity to discuss it with a researcher or a chance to have your questions answered, please get in touch with us! You can talk it over with us or spend as much time as you like deciding whether or not to take part without in any way committing yourself.

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Thank you!

This project has received ethical approval from the Psychology Research Ethics Committee of the University of Cambridge

K.3.4. Study 6

Study Title: Attentional Orienting and Mood
Thank you for your interest in our project. We are doing a series of studies examining interactions between mood, attention and perception and we would like to invite you to participate in one of these studies. This information sheet provides some details about what you can expect if you decide to take

part. If you would like to discuss the study further or ask any questions about it, please feel free to get in touch with us for an informal chat. Our contact details are provided at the bottom of the sheet.

What is the purpose of the project?

Although periods of low mood or anxiety can be a normal part of life, these feelings can become problematic if they persist for too long or become too easily triggered. We are interested in learning more about the reasons why some people become caught in ongoing low mood or anxiety, because a clearer understanding of these maintaining factors will help us to develop more specific and targeted treatments. We believe that interactions between mood and attention may be important in explaining why some people remain vulnerable to ongoing low mood or anxiety, and therefore the aim of this project is to find out more about how basic attentional mechanisms work at different levels of mood. In order to develop as full a picture of these issues as possible, we are interested in recruiting participants who have current or past experience of low mood or anxiety, but also in recruiting participants with no such experience.

What will the study involve?

If you decide to take part, we will ask you to come to the Cognition and Brain Sciences Unit to take part in some experimental tasks measuring aspects of attention. We will ask you to sit in a comfortable position at a desk holding 2 audio speakers and 2 small LEDs (light-emitting diodes) to your left and to your right. We will also ask for permission to strap 2 small tactors to your left and right wrists. The tactors are designed to vibrate gently like a mobile phone or pager, and will not be painful or harm your skin in any way. You will be asked to ignore some of these stimuli, and to respond to others using left and right footpedals. There will be a break every 10 minutes for you to rest or stretch your legs. We will also ask you to fill out some questionnaires about various aspects of your mood.

How long will it take?

We expect the session to take about 90 minutes, including plenty of time to allow for rests between tasks. We will be very happy to ensure that appointment times suit your convenience.

Will I find the study upsetting?

Some of the questionnaire items will ask you about issues to do with mood and anxiety, including any past episodes of depression or times when you have been very anxious. If thinking or talking about these topics causes you to feel any distress, the study can be stopped or paused to allow you to take whatever time you need to recover. If helpful, we will provide you with a quiet room where you can be private, a hot drink, an opportunity to engage in a positive mood induction procedure, and an opportunity for a confidential chat with a registered clinical psychologist if you would like one. We can also provide general advice about ways of accessing further help or support if you would find this useful. When you are ready to leave, we will make whatever efforts are necessary to ensure that you are able to get home safely.

Will I be reimbursed for my time?

Yes: we will compensate you for your time at the rate of £6 per hour, and we will also contribute to your travel expenses (£2.50 for participants coming from within Cambridge and £3 for those coming from outside). These are the standard MRC CBU rates.

Do I have to take part?
No. It is completely up to you to decide whether or not you want to take part in the study. You can take as long as you want to decide and can ask any questions you like before deciding. If you do decide to take part you will still be free to change your mind at any time during the study, and you can withdraw at any point without giving a reason.

Will my data be kept confidential?
Yes: all the information that you provide throughout the study will be kept completely confidential and processed anonymously. We will allocate you a random identifier which will be kept with your data instead of your name, and we will make sure that no information that could personally identify you will be kept with your data. Any findings from the study that are published in academic journals or presented at conferences will be presented at the group level and will be completely anonymous.

Will I be given feedback about my data?
We will not be able to provide any specific feedback about your data from the perceptual and attention tasks because we will be analysing this data on a group level only. We will also not be making any formal diagnoses on the basis of the interview or questionnaires about your mood. However, if you would like to have a chance to discuss issues around mood we will be happy to provide general advice about how to go about accessing services that may be beneficial for you.

Further information
If you would like any further information about the study, an opportunity to discuss it with a researcher or a chance to have your questions answered, please get in touch with us! You can talk it over with us or spend as much time as you like deciding whether or not to take part without in any way committing yourself.

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