Problematic attention processing and fear learning in adolescent anxiety: testing a

combined cognitive and learning process model

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Highlights

- Anxiety in adolescents was characterised by biases in attention.
- Anxiety in adolescents was characterised by over-generalisation of fear.
- Biases in attention and fear generalisation inter-related with each other.

Abstract

Background and Objectives: Anxiety in adolescence is characterised by disturbances in attentional processes and the overgeneralisation of fear, however, little is known about the combined and reciprocal effects of and between these factors on youth anxiety. The present study investigated whether attention (attention allocation and control) and fear generalisation processes together predict more variance on adolescent anxiety symptoms than each factor in isolation, and explored their interrelations.

Methods: 197 adolescents completed a novel conditioning task, which paired balloon cues with mildly aversive or neutral outcomes. A spatial cueing task, and self-report measures of emotional attentional control and anxiety, were also completed.

Results: Threat-avoidant attention allocation biases, impaired attention control, and exaggerated fear generalisation together predicted greater variance in anxiety symptoms (55.3%), than each set of fear and attention processes in isolation. Results also provided evidence of an interplay between these factors. Individual differences in threat-avoidant attention allocation biases predicted variability in the generalisation of fear, whilst the association between heightened anxiety and the overgeneralization of fear was moderated by poor attention control.

Conclusions: This study provides unique evidence of the combined effects of attention and fear generalisation mechanisms in explaining youth anxiety, and interrelations between these factors. Importantly, results suggested that deficiencies in attention control may bring out anxiety-associated impairments in fear generalisation.

Limitations: We relied on self-reported ratings of fear during generalization and also of

attention control. Thus demand effects cannot be discounted. Reaction-time measures of

attention focus are also indirect assessments of attention that may lack precision.

Keywords: adolescence, combined cognitive biases, selective attention bias, fear learning,

attention control

1. Introduction

Anxiety problems emerging during adolescence are common, disabling and predict risk for adult psychopathologies (Pine, Cohen, Gurley, Brook & Ma, 1998; Costello, Mustillo, Erkanli, Keeler, & Angold , 2003). Understanding the pathways by which heightened anxiety symptoms emerge at this developmental juncture can help identify new targets for early intervention. Problematic attentional processes and fear learning both play a critical role in the pathogenesis of anxiety in young people (Lau & Waters, 2016), but have largely been investigated separately. Few studies have assessed the combined effects of these cognitive-learning processes on adolescent anxiety despite adult data suggesting the contribution of multiple information-processing factors on common psychopathological conditions such as anxiety. This study addresses this gap by assessing whether problematic attention processes (preferential attention allocation to threats and attention control difficulties) and heightened fear generalisation predict more variance in anxiety together than in isolation and whether these biases influence one another (concurrently) during adolescence.

Accumulating data associates youth anxiety with the tendency to automatically allocate attention toward or away from threat-related stimuli. Experimental tasks which compare response times to probes replacing threatening versus non-threatening stimuli show anxious youth to be quicker in detecting (and sometimes avoiding) probes following threatening faces (Waters, Bradley, & Mogg, 2014; Dudeney, Sharpe, & Hunt, 2015; de Voogd, Wiers, Prins, & De Jong, 2016). Anxious youth also show general difficulties in the voluntary control of attention (Muris, van der Pennen, Sigmond, & Mayer, 2008; Susa, Pitica, Benga, & Miclea, 2012), which may further protect against the expression of anxiety-related cognitive impairments (Derryberry & Reed, 2002; Bardeen & Orcutt, 2011; Taylor, Cross, & Amir, 2016). Independently, youth anxiety has been characterized by exaggerated

fear learning (Lau & Waters, 2016). Notably, anxious, relative to non-anxious, youth show elevated fear to a stimulus that has been associated with an aversive outcome (a conditional stimulus; CS+) and heightened generalisation of this fear to safe stimuli that have never been paired with an aversive outcome (CS-) (Lau, et al., 2008; Waters, Henry, & Neumann,, 2009) and which are only perceptually similar to the CS+ (Schiele, et al., 2016). Such elevated responses to 'safe' stimuli may reflect difficulties discriminating threat from safety, possibly underpinned by difficulties in fear inhibition (Britton, et al., 2013; Jovanovic, et al., 2014; Haddad, Bilderbeck, James, & Lau , 2015). Yet, whilst studies have successfully demarcated abnormal attention and fear generalisation processes as vulnerability factors for youth anxiety (Lau & Waters, 2016), these have largely been considered separately.

Long-standing integrative models of psychopathology emphasise that maladaptive cognitive and/or learning factors likely co-exist in anxious individuals and, importantly, inter-relate to influence symptoms (Hirsch, Clark, & Mathews, 2006; Everaert, Koster, & Derakshan, 2012; Waters & Craske, 2016). The "combined cognitive bias" hypothesis suggests that these "cognitive processes are likely to work together in various ways serving to maintain specific emotional disorders" (Hirsch, et al., 2006), leading to some studies considering how attention, memory and/or interpretation biases explain common (but also distinct variance) on youth anxiety (Watts & Weems 2006; Klein et al., 2014; Klein, de Voogd, Wiers, & Salemink, 2017). However, a more important tenet of this hypothesis and a recent integrative youth anxiety model (Waters &Craske, 2016) is that certain cognitive factors inter-relate with other (Hirsch et al., 2006) and/or with learning factors (Waters & Craske, 2016). Specifically, dysfunctional cognitive processes of attention towards threat, and learning processes in the discrimination between threat and safety are thought to comprise different stages of the same system involved in coordinating the bodily (fear)

response towards threatening situations, and these may influence each other in pathological anxiety.

Indeed, some studies have shown preferential attention allocation in the presence of CS+s, relative to other stimuli, following conditioning procedures in youth (Pischek-Simpson, Boschen, Neumann, & Waters, 2009; Haddad, Lissek, Pine, & Lau,2011; Shechner, Pelc, Pine, Fox, & Bar-haim, 2012). However, it may also be the case that selective attention allocation biases towards threat can facilitate or attenuate aspects of fear learning. Attention towards threatening cues could enhance fear acquisition processes as well as fear inhibition processes such as extinction learning in youth, the process when a threat stimulus becomes safe as it no longer predicts an aversive outcome (Waters & Kershaw, 2015). Similarly, poor attention control could attenuate adaptive learning processes. For example, adult findings suggest that if attention is captured by perceived threat, individuals ignore aspects of the situation that confer safety thereby reducing the possibility of learning that the situation is, in fact, safe (Barry, Griffith, Vervliet, & Hermans, 2015; Barry, Vervliet, & Hermans, 2016).To date, research is yet to examine the association between these attention processes and the generalization of fear. Fear generalisation is posited to share common inhibitory mechanisms with fear extinction, as both involve responding to stimuli that should be considered safe (Lisseket al., 2014). As such, given that deficits in fear extinction relate to problems with the automatic allocation of attention to threat and in voluntarily controlling attention, it is expected that abnormalities in these attention processes would be similarly associated with heightened fear generalisation.

In the present study, we assessed two novel questions: a) do attention and learning factors together explain more variance on anxiety symptoms than each in isolation, and b) do attention factors (attention bias and control) influence learning processes during fear

generalisation? Given that attention control may protect against anxiety-related impairments (Derryberry & Reed, 2002), it may be that attention control and anxiety interact with one another in their relationship with fear generalisation, such that poor attention is only associated with increased fear generalization in youth with high levels of anxiety. Thus, we tested two sets of hypotheses. First, that individual differences in attention allocation biases (measured by a spatial cueing task), attention control (measured by self-report), and fear generalisation (indexed by learned fear to a CS- and other perceptually similar, novel cues) would predict greater variance in self-reported anxiety symptoms together than each bias in isolation. Second, that there would be an interdependent relationship between these processes, such that i) automatic attention allocation biases and ii) attention control, as well as its interaction with anxiety, would predict individual differences in the generalisation of fear.

2. Methods

2.1. Participants

197 adolescents, fluent in English, were recruited from mainstream secondary schools in the UK to take part (see Table 1 for participant characteristics). While all 197 participants provided data on the demographics and experimental tasks, only 175 participants completed the Screen for Anxiety Related Emotional Disorders (SCARED) questionnaire ahead of the study session online. The study was approved by the University Research Ethics Committee. All participants provided written consent. For those aged 16 years and under, parents provided consent.

2.2. Measures

2.2.1. The Screen for Child Anxiety Related Disorders (SCARED) (Birmaheret al., 1999). This is a self-report measure containing 41 items regarding the symptoms of anxiety

disorders. Participants rate each item on a 3-point Likert scale from 0 (*Not true*) to 2 (*very true*). High total scores represent high anxiety. Cronbach's alpha was .89 in this study.

2.2.2. The Emotional Attentional Control Scale (eACS) (Barry, Hermans, Lenaert, Debeer, & Griffith et al., 2013). This is a 14-item self-report measure of the ability to shift and focus attention during emotionally demanding or distracting situations (e.g. *'when I am in an unpleasant situation, I am still able to concentrate')*. Items are rated on a 4-point Likert-scale from 0 (*almost never*) to 4 (*always*). High total scores denote good attention control abilities. In this study, Cronbach's alpha was .96.

2.2.3. Balloon Fear Conditioning Task. This task comprised two phases: acquisition and generalisation. CSs were images of uninflated yellow balloons with a small (CS+) or a large (CS-) black circle presented at the centre of each balloon (Figure 1). We employed two novel UCSs to assess which was more salient in provoking fear in adolescents: the 'burst' UCS condition was a central image of a burst yellow balloon alongside two images of deflated balloons and a bursting sound (70dB), and the 'social' UCS comprised the same central image but alongside two images of angry faces (Tottenham et al.,2009) and a groaning noise signifying social disapproval (70dB) (Figure 1). During acquisition participants received 8 trials of each of the CS+ and CS-. On CS+ trials, a UCS immediately followed the key-press to inflate on 6 of 8 trials (75%), but none of the CS- trials were paired with the UCS. Four images of the same uninflated yellow balloon with black circles that were 20/40/60/80% larger than the circle shown on the CS+, served as the GS1/GS2/GS3/GS4 respectively (Figure 1). During generalisation, participants received 4 trials of each of the CS+/CS-/GS1/GS2/GS3/GS4. The CS+ was followed by the UCS on 50% of trials. The CS-/GS1/GS2/GS3/GS4 were never paired with the UCS. In both phases, the order of trials was

pseudo-random; thus, the same stimuli were not shown on more than two consecutive trials.

Participants were instructed to imagine they were attending a party, and had to inflate some balloons, taking care not to burst any. In each trial, a fixation cross was presented for 1000ms, followed by an image of a single uninflated CS balloon for 2000ms. Participants were instructed to press the spacebar to inflate the balloon. Immediately following pressing the spacebar to inflate, either an image of a correctly inflated yellow balloon or a UCS was displayed for 2000ms. On half of all trials, before making a key-press to inflate the balloon, participants rated on a 10-point Likert scale how fearful they were that the balloon would burst after inflation (1= not fearful at all, 10= very fearful).

2.2.4. Spatial Cueing Task. The task consisted of 200 randomly-ordered trials delivered in 5 blocks of 40 trials. In each trial a central fixation cross was presented for 500ms, followed by either a neutral or angry face cue (5.5 x 7.5cm) to the left or right of the central fixation cross position for 500ms (10 angry/10 neutral, 5 female/5 male) (Tottenham et al., 2009), which was then replaced by a target either on the same side of the screen (valid trials) or the opposite side (invalid). Participants were instructed to press one of two keys (z or m) to indicate the alignment of the target, two dots (1 cm) aligned vertically (:) or horizontally (..), as quickly and accurately as possible. The target was presented until the participant responded, or 1100ms had elapsed. After 1000ms the next trial began. The order and position of face cues and targets as well as the alignment of the target (resulting in 8 possible trial types for each face cue identity), were fully counterbalanced. Four trial categories were calculated across all trial types: valid angry and valid neutral and invalid angry and invalid neutral. Valid and invalid reaction time (RT) data were used as the dependent measures. Consistent with previous research using visual-probe identification

tasks (e.g. Gray et al., 2016; Pine et al., 2005;), incorrect trials or trials where no response was made, and trials with reaction times (RT) <200ms or ±2 standard deviations of each participants' mean reaction time were excluded in analyses (14.4% of trials).

2.3. General Procedure

A week after providing consent and completing the questionnaires, participants completed the SCT followed by the (balloon) fear conditioning task. Prior to task completion, participants were randomly allocated to receive either the 'burst' or 'social' UCS in the fear conditioning task. All participants were given £5 vouchers for their time.

2.4. Statistical Analysis

To examine whether differential learning occurred during acquisition, and whether there were differences between UCS conditions, a 2 (stimuli: fear to CS+/CS-) x 2 (condition: burst/social) repeated measures analysis of variance (ANOVA) was conducted on average self-reported fear to the CS+ and CS- across acquisition trials. To examine whether fear generalized from CS+ to the GSmid, a 3-way (stimuli: fear to CS+/GSmid/CS-) repeated-measures ANOVA was performed on average fear to the CS+ and CS- across trials, and to average fear ratings to the GS stimuli termed GSmid[1]. To assess whether threat-based attention allocation biases emerged, SCT reaction time data were analysed using a 2 (target position: valid/invalid) x 2 (face cue neutral/angry) repeated-measures ANOVA. In all ANOVAs, main and interaction effects were followed up. Consistent with prior studies (e.g. Mogg, Holmes, Garner & Bradley, 2008), a threat-based attention biases index was also calculated for subsequent analysis:

(invalid angry RT – valid RT angry) - (invalid neutral RT – valid RT neutral)

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[1] The GS2 and GS3 were used as they are the most ambiguous of all the GSs, and therefore expected to show the clearest association with anxiety symptoms, however, additional analyses were conducted using different pairings of GS, which garnered equivalent results.

Positive bias scores reflect threat-based attentional engagement, whereas negative scores denote threat-based attentional avoidance. As discussed by Mogg and colleagues (2008), this measure summarises the interaction effect of cue validity (valid and invalid) and cue valence (threat and neutral) on RTs, as it is the difference between the cueing effect of threat cues and the cueing effect of neutral cues. Furthermore, inclusion of RTs to neutral faces in the threat bias index accounts for any baseline differences in RTs to non-angry face stimuli across individuals/groups. Before conducting regression analysis to test our hypotheses we first examined gender and age effects and correlations with anxiety symptoms on these indices using t-tests and bivariate correlations.

To examine our first hypothesis that fear and attention indices predicted more variance on anxiety symptoms, we conducted a regression analysis with anxiety scores as the dependent variable. Age and gender were entered as predictors in Step 1. In Step 2, fear to the CS+ and CS- during acquisition, and fear to the GSmid during generalisation were entered into the model. In Step 3, attention control and threat-based attention allocation biases scores were then entered as predictors. At each step, the change in R^2 statistic was assessed. To test the second hypothesis of inter-relationships between anxiety-relevant biases we performed regression analyses for fear to CS- and fear to GSmid if they significantly predicted anxiety in the first regression. In Step 1 age and gender were entered, then attention control and attention control * anxiety, then in step 3 attention allocation biases was added. Key assumptions of linear regression were met (linear relationships between independent variables and dependent variable, multivariate normality, no or little multicollinearity, no auto-correlation and homoscedasticity.

3. Results

3.1. Participant characteristics

Means and SDs for anxiety symptoms, attention control, fear indices from the fear conditioning task, and the attention allocation bias score are presented in Table 1. Age and gender differences emerged with respect to anxiety symptoms and attention control (Tables 1 and 2). Also, females reported greater fear to the CS- during acquisition as compared to males (Table 1) but there were no age effects on CS+ and CS- during acquisition, nor fear to the GSmid during generalization (Table 2). No gender differences were found with respects to the attention bias index (Table 1 and 2). Greater anxiety was significantly positively correlated to each of the fear indices and to attention control, but no significant relationship was found with attention allocation bias scores (Table 2).

3.2. Fear acquisition and generalisation

The 2x2 mixed design ANOVA performed on fear ratings during acquisition revealed only a significant main effect of stimulus-type $F(1,195)=75.089$, p<0.001, whereby CS+ received significantly greater fear ratings than the CS- (MD= 1.467, SE= 0.170, p<0.001). The absence of main or interacting effects involving UCS condition (all p's>0.05), indicated comparable fear to each stimulus across the 'burst' and 'social' conditions. All further analyses were therefore conducted collapsed across UCS conditions. The second ANOVA performed on fear ratings to the CS+, CS- and GSmid revealed a significant main effect of stimulus-type during the generalisation phase $F(2,392) = 93.086$, $p < 0.001$, such that fear ratings for the CS+ were greater than the GSmid index (MD=1.939, SE=0.182, p<0.001), which was rated more fearfully than the CS- (MD=0.480, SE=0.136, p=0.001).

3.3. Attention allocation biases

RT data to neutral and angry valid and invalid cues are presented in Figure 2. The 2x2 mixed ANOVA on response times during the spatial cueing task showed a significant interaction between face cue and validity only $F(1,196)=4.698$, p=.031. Decomposing this

interaction, participants were quicker to detect the alignment of the target on valid trials than invalid trials, but only for targets replacing angry faces (MD= -8.240, SE= 3.725, p=.028). Participants also responded faster on valid angry than valid neutral trials (MD= 4.270, SE= 1.898, p=.026).

3.4. Regression analyses predicting anxiety symptoms

In Step 1 of the first regression (Table 3), the model was found to be significant (Adjusted R^2=0.161). At this step, age and gender were significant predictors. At Step 2, the model significantly improved (Adjusted R^2=0.223) and fear to the GSmid emerged as a significant predictor. After Step 3, the model was again significant (Adjusted R^2=0.553). At this step, attention control and attention allocation biases were significant predictors of anxiety, such that poor attention control and attention allocation biases reflecting attention avoidance, were both associated with greater anxiety.

3.5. Regression analyses predicting fear generalisation

In the next regression, fear to GSmid was used as the dependent measure (Table 4). At step 1, age but not gender was a significant predictor, with the model predicting a significant amount of variance in fear to the GSmid (Adjusted R^2=0.017). At step 2, the model was again significant (Adjusted R^2=0.128). At this step, the interaction between attention control and anxiety emerged as a significant predictor, such that higher anxiety was associated with higher fear ratings to the GSmid in participants with poor attention control (r=0.335, N=82, p=.002) but not those with good attention control (r=0.008, N=92, p=.937). At Step 3, the model was also significant, accounting for 15.1% of variance in fear to the GSmid (Adjusted R^2=0.151). At this step, attention allocation bias scores emerged as a significant predictor of variability in fear to the GSmid, such that greater attentional avoidance with threat predicted higher fear ratings to the GSmid.

4. Discussion

This study sought to draw on recent integrative models of adolescent anxiety (Waters & Craske, 2016), by addressing whether problematic attention allocation biases in the presence of threat, attention control difficulties and exaggerated fear generalisation predict greater variance in adolescent self-reported anxiety symptoms than each of these processes in isolation, and whether interdependent relationships exist between them. As hypothesised, threat-avoidant attention allocation biases, poor attention control, and greater fear responding to the GSmid, together predicted greater variance in anxiety symptoms, than each set of fear and attention processes separately. Also, as expected, we found evidence of an association between attention and fear learning processes; threat-avoidant attentional allocation predicted individual differences in fear responding to the generalisation stimulus, whilst attention control moderated anxiety differences in the generalisation of self-reported fear. Specifically, anxious adolescents with poor attention control showed greater generalised fear than adolescents with lower anxiety.

These results replicate and extend prior findings on fear learning in youth. Previous fear conditioning studies in youth have only looked at fear responses to CS+/CS. Here we showed that anxious adolescents displayed higher fear for a generalisation stimuli that was perceptually similar to the CS+ relative to adolescents with lower anxiety, which has been found consistently in adult anxiety (Lissek, et al., 2010; Haddad, Pritchett, Lissek, & Lau, 2012; Lissek et al., 2014). One surprising finding, however, was that when fear indices were explored collectively, fear to the GSmid was the strongest predictor of anxiety symptoms; neither fear to the CS+ or CS- continued to predict anxiety. This is despite individual significant correlations between each of the fear learning variables and anxiety, consistent with previous research (Britton, et al.,2013;Lau and Waters, 2016). It may be that the GSmid

fear index was perceived to be more ambiguous than either the CS+ or CS-, where contingencies with the aversive outcome were more clearly presented. Such ambiguity or 'uncertainty' is likely to produce greater variance between participants, which might then make it a better predictor of anxious symptoms than other indices with less between-participant variability (Dugas, Gagnon, Ladouceur, & Freeston, 1998).

Beyond these 'univariate' associations with anxiety, our data also suggest a possible additive effect of attention allocation biases, attention control and fear generalisation that combine to exacerbate anxious symptomology in youth. The fear learning and generalization indices explained 22.3% of variability in anxiety symptoms, but when the attention indices were added into the regression, the combined effect of all indices explained 55.3% of anxiety variance. This finding validates both theoretical accounts which postulate that the combined effect of multiple cognitive factors may explain psychopathology to a greater degree than individual biases separately (Hirsch, et al., 2006; Everaertet al., 2012) and with more recent models of adolescent anxiety, which integrate attention and learning processes (Waters & Craske, 2016).

The results also provided evidence of relationships between attention and learning processes. Our results show that an increased automatic attentional avoidance for threat related to heightened fear generalisation in youth. This finding adds to a growing literature suggesting a bidirectional interrelationship between attention allocation biases and threat-safety learning biases in youth (Haddad et al., 2011; Waters & Kershaw, 2015; Waters & Craske, 2016), and builds on previous research demonstrating interrelations among cognitive biases in adult anxiety and depression (Hirsch et al., 2006; Everaert et al., 2012). Our results also indicated that the interaction between attention control and anxiety, predicted individual differences in fear generalisation. This finding extends work

documenting a moderating role of attention control in the expression of anxiety-related deficits in cognitive processing (Derryberry & Reed, 2002; Bardeen and Orcutt, 2011). Here, high anxious adolescents with poor attention control showed greater fear to the generalization stimuli, suggesting it may be that strong attention control protects against anxiety-related problems associated with exaggerated fear generalisation. These results are consistent with research in adults suggesting a relationship between attention control problems and slowed fear extinction after conditioning (Barry et al., 2016).

There are several limitations of the current study and possible avenues for further research. Firstly, as our findings rely on self-reported attention control, experimental measures such as flanker tasks (Eriksen & Eriksen, 1974) or attentional network tasks (Fan, McCandliss, Sommer, Raz, & Posner, 2002) that measure individual differences in the ability to focus attention and inhibit distraction should be used to replicate our findings. Furthermore, while self-report fear data provide valid indices of fear learning (Boddez et al., 2013), replication of our findings with psychophysiological measures of fear would add support to our conclusions. This may be particularly important to establish that fear learning rather than simple associative learning had occurred. Although we sought to confirm that across all participants, there was greater self-reported fear to the CS+ versus CS- across acquisition trials – suggesting that discriminatory fear learning had occurred – we cannot be sure that these within-group stimulus differences only reflected simple associative learning. However, given the novelty of this paradigm, establishing self-reported fear differences to the CSs is a first step to assessing its potential to install fear acquisition. A similar issue concerns complementary measures of attention-orienting bias; incorporating eye-gaze data to provide more continuous assessments of attention-vigilance and avoidance across time-course would be helpful to further inform the nature of the attention-orienting bias. This is

particularly the case given some unexpected findings in this task. We did not observe a significant difference between valid and invalid trials that followed neutral faces (although there was a small difference in reaction times in the expected direction between these trials). This may be because unlike angry faces, there is more variability between people in the way that they respond to neutral faces, with some engaging and others avoid the face because they perceive it to be sufficiently aversive. This would serve to attenuate any main effect of cue validity. Alternatively, neutral faces may disengage attention in all individuals, again removing any difference between valid and invalid trials.

The current findings provide the first evidence of the unique and combined effects of problematic threat attention allocation biases, difficulties in attention control and heightened fear generalization in explaining elevated anxious symptoms in adolescents. These findings have significant implications for the treatment of pathological youth anxiety; as they suggest that interventions may need to target different biases simultaneously, and to reduce their effects on one another, and ultimately reduce symptoms (Platt, Waters, Schulte-Koerne, Engelmann, & Salemink,2017). Further research is needed to assess the direction of influence or causality of each bias on another (Everaert et al., 2012), for example through longitudinal designs or experimental manipulations. Investigating the combined effect of attention and fear generalisation processes, and their relationship in clinically anxious adolescents would also inform clinical relevance.

References

Bardeen, J. R., & Orcutt, H.K. (2011). "Attentional control as a moderator of the relationship between posttraumatic stress symptoms and attentional threat bias." *Journal of anxiety disorders*, 25(8), 1008-1018.

Barry, T.J.,Griffith,W., Vervliet,B. &Hermans,D. (2015). "The role of stimulus specificity and attention in the generalization of extinction." *Journal of Experimental Psychopathology,* 7(§), 143-152.

Barry, T.J., Vervliet,B. & Hermans,D. (2016). "Threat-related gaze fixation and its relationship with the speed and generalisability of extinction learning." *Aust J Psychol*, 68(3), 200–208.

Barry, T. J., Hermans,D., Lenaert,B. Debeer,E. & Griffith,J.W. (2013). "The eACS: Attentional control in the presence of emotion." *Personality and Individual Differences,* 55(7), 777-782.

Birmaher, B., Brent,D.A., Chiappetta,L.,Bridge,J., Monga,S., & Baugher,M. (1999). "Psychometric properties of the Screen for Child Anxiety Related Emotional Disorders (SCARED): a replication study." *J Am Acad Child Adolesc Psychiatry***, 38(10), 1230-1236.

Boddez, Y., Baeyens, F., Luyten,L., Vansteenwegen,D., Hermans,D., & Beckers,T. (2013). "Rating data are underrated: Validity of US expectancy in human fear conditioning." *Journal of Behavior Therapy and Experimental Psychiatry,* 44(2), 201-206.

Britton, J. C., Grillon,C., Lissek,S., Norcross,M.A., Szuhany,K.L.,Chen,G., Ernst,M., Nelson,E.E, Leibenluft,E., Shechner,T., & Pine,D.S. (2013). "Response to learned threat: An FMRI study in adolescent and adult anxiety." *Am J Psychiatry,* 170(10), 1195-1204.

Costello, E. J., Mustillo,S., Erkanli,A., Keeler,G., & Angold,A. (2003). "Prevalence and development of psychiatric disorders in childhood and adolescence." *Arch Gen Psychiatry,* 60(8), 837-844.

De Voogd, E. L., Wiers,R.W., Prins,P.J., de Jong,P.J., Boendermaker,W.J., Zwitser,R.J., &Salemink,E. (2016). "Online attentional bias modification training targeting anxiety and depression in unselected adolescents: Short- and long-term effects of a randomized controlled trial." *Behav Res Ther,* 87, 11-22.

Derryberry, D. &Reed, M.A. (2002). "Anxiety-related attentional biases and their regulation by attentional control." *J Abnorm Psychol,* 111(2),225-236.

Dudeney, J., Sharpe, L., & Hunt, C. (2015). "Attentional bias towards threatening stimuli in children with anxiety: A meta-analysis." *Clin Psychol Rev,* 40,66-75.

Dugas, M. J., Gagnon,F., Ladouceur, R. & Freeston, M.H. (1998). "Generalized anxiety disorder: A preliminary test of a conceptual model." *Behaviour research and therapy,* 36(2), 215-226.

Eriksen, B. A. & Eriksen, C.W. (1974). "Effects of noise letters upon the identification of a target letter in a nonsearch task." *Perception & Psychophysics,* 16(1), 143-149.

Everaert, J., Koster,E.H., andDerakshan, N. (2012). "The combined cognitive bias hypothesis in depression." *Clin Psychol Rev*, 32(5), 413-424.

Fan, J., McCandliss,B.D., Sommer,T., Raz,A., &Posner,M.I. (2002). "Testing the efficiency and independence of attentional networks." *J Cogn Neurosci*, 14(3), 340-347.

Gray, P., Baker, H. M., Scerif, G. & Lau, J. Y. (2016). Early maltreatment effects on adolescent attention control to non-emotional and emotional distractors. Australian journal of psychology 68, 143-153, doi:10.1111/ajpy.12139.

Haddad, A. D., Bilderbeck, A., James,A.C., and Lau,J.Y.(2015). "Fear responses to safety cues in anxious adolescents: Preliminary evidence for atypical age-associated trajectories of functional neural circuits." *J Psychiatr Res,* 68, 301-308.

Haddad, A. D. M., Lissek,S., Pine,D.S.,& Lau, J.Y. (2011). "How do social fears in adolescence develop? Fear conditioning shapes attention orienting to social threat cues." *Cognition & emotion*, 25(6), 1139-1147.

Haddad, A. D. M., Pritchett,D., Lissek,S.,& Lau,J.Y. (2012). "Trait Anxiety and Fear Responses to Safety Cues: Stimulus Generalization or Sensitization?" *Journal of Psychopathology and Behavioral Assessment,* 34(3), 323-331.

Hirsch, C. R., Clark,D.M., & Mathews,A. (2006). "Imagery and interpretations in social phobia: support for the combined cognitive biases hypothesis." *Behav Ther,* 37(3)223-236.

Jovanovic, T., Nylocks,K.M., Gamwell,K.L., Smith,A., Davis,T.A., Norrholm,S.D., & Bradley,B. (2014). "Development of fear acquisition and extinction in children: effects of age and anxiety." *Neurobiol Learn Mem*, 113, 135-142.

Klein, A. M., de Voogd,L., Wiers,R.W., & Salemink,E. (2017). "Biases in attention and interpretation in adolescents with varying levels of anxiety and depression." *Cogn Emot*, 1-9.

Klein, A. M., Titulaer,G., Simons,C., Allart,E., de Gier,E., Bogels,S.M., Becker,E.S., &Rinck,M. (2014). "Biased interpretation and memory in children with varying levels of spider fear." *Cogn Emot,* 28(1), 182-192.

Lau, J. Y., Lissek,S., Nelson,E.E., Lee,Y., Roberson-Nay,R., Poeth,K., Jenness,J., Ernst,M., Grillon,C. & Pine,D.S. (2008). "Fear conditioning in adolescents with anxiety disorders: results from a novel experimental paradigm." J Am Acad *Child Adolesc Psychiatry,* 47(1), 94-102.

Lau, J. Y. & Waters,A.M. (2016). "Annual Research Review: An expanded account of information-processing mechanisms in risk for child and adolescent anxiety and depression." *J Child Psychol Psychiatry*.

Lissek, S., Kaczkurkin,A.N., Rabin,S., Geraci,M., Pine,D.S., & Grillon,C. (2014). "Generalized anxiety disorder is associated with overgeneralization of classically conditioned fear." *Biol Psychiatry*, 75(11), 909-915.

Lissek, S., Rabin,S., Heller,R.E., Lukenbaugh,D., Geraci,M. Pine,D.S., & Grillon,C. (2010). "Overgeneralization of conditioned fear as a pathogenic marker of panic disorder." *Am J Psychiatry,* 167(1), 47-55.

Mogg, K., Holmes, A., Garner, M., & Bradley, B.P. (2008). Effects of threat cues on attentional shifting, disengagement and response slowing in anxious individuals. *Beh Res Ther*, 46, 656–667.

Muris, P., Van Der Pennen,E., Sigmond,R. & Mayer,E. (2008). "Symptoms of anxiety, depression, and aggression in non-clinical children: relationships with self-report and performance-based measures of attention and effortful control." *Child Psychiatry Hum Dev,* 39(4), 455-467.

Pine, D. S., Cohen,P., Gurley,D., Brook J,.& Ma, Y. (1998). "The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders." *Arch Gen Psychiatry,* 55(1), 56-64.

Pine, D.S., Mogg, K., Bradley, B.P., Montgomery, L., Monk, C., McClure, E., et al., (2005). Attentional bias to threat in maltreated children: implications for vulnerability to stress-related psychopathology. *Am J Psychiatry*, 162 (2), 291-296. doi:10.1176/appi.ajp.162.2.291.

Pischek-Simpson, L. K., Boschen,M.J., Neumann D.L., & Waters,A.M. (2009). "The development of an attentional bias for angry faces following Pavlovian fear conditioning." *Behav Res Ther,* 47(4), 322-330.

Platt, B., Waters,A.M., Schulte-Koerne,G., Engelmann, L. & Salemink,E. (2017). "A review of cognitive biases in youth depression: attention, interpretation and memory." *Cogn Emot,* 31(3), 462-483.

Schiele, M. A., Reinhard,J., Reif,A., Domschke,K., Romanos,M., Deckert, J., & Pauli,P. (2016). "Developmental aspects of fear: Comparing the acquisition and generalization of conditioned fear in children and adults." *Dev Psychobiol,* 58(4), 471-481.

Shechner, T., Pelc,T., Pine,D.S., Fox,N.A. &Y. Bar-Haim (2012). "Flexible attention deployment in threatening contexts: an instructed fear conditioning study." *Emotion,* **12**(5), 1041-1049.

Susa, G., Pitica,I., Benga, O., & Miclea,M. (2012). "The self regulatory effect of attentional control in modulating the relationship between attentional biases toward threat and anxiety symptoms in children." *Cogn Emot,* **26**(6), 1069-1083.

Taylor, C. T., Cross, K., &Amir,N. (2016). "Attentional control moderates the relationship between social anxiety symptoms and attentional disengagement from threatening information." *J Behav Ther Exp Psychiatry,* 50, 68-76.

Tottenham, N., Tanaka,J.W., Leon,A.C., McCarry,T., Nurse,M., Hare,T.A., Marcus,D.J., Westerlund,A., Casey,B.J., & Nelson,C. (2009). "The NimStim set of facial expressions: judgments from untrained research participants." *Psychiatry Res,* 168(3), 242-249.

Waters, A. M., Bradley,B.P., & Mogg,K. (2014). "Biased attention to threat in paediatric anxiety disorders (generalized anxiety disorder, social phobia, specific phobia, separation anxiety disorder) as a function of 'distress' versus 'fear' diagnostic categorization." *Psychol Med,* 44(3), 607-616.

Waters, A. M. & Craske,M.G. (2016). "Towards a cognitive-learning formulation of youth anxiety: A narrative review of theory and evidence and implications for treatment." *Clin Psychol Rev*, 50, 50-66.

Waters, A. M., Henry,J., & Neumann,D.L. (2009). "Aversive Pavlovian conditioning in childhood anxiety disorders: impaired response inhibition and resistance to extinction." *J Abnorm Psychol,* 118(2), 311-321.

Waters, A. M., & Kershaw,R. (2015). "Direction of attention bias to threat relates to differences in fear acquisition and extinction in anxious children." *Behav Res Ther,* 64, 56-65.

Watts, S. E., & Weems,C.F. (2006). "Associations among selective attention, memory bias, cognitive errors and symptoms of anxiety in youth." *Journal of abnormal child psychology,* 34(6), 838-849.

TABLE 1.

Sample characteristics

	Total Sample Mean (SD)	Males Mean (SD)	Females Mean (SD)	Gender Differences	
				Test statistic (df)	Cohen's d
Age	13.66 (1.64)	13.66 (1.53)	13.67 (1.73)	-0.75 (195)	-
% Caucasian	93.40%	95.40%	91.82%	χ^2 (9,197)=7.511, p=.584)	-
SCARED total score	23.26 (16.14)	17.05 (13.17)	28.25 (16.63)	-4.971 (172.97) ***	0.74
Emotional Attention Control Scale total score	34.65 (8.43)	37.57 (8.01)	32.40 (8.08)	4.421 (191) ***	0.64
CS+ fear acquisition	5.43 (2.39)	5.22 (2.53)	5.60 (2.28)	-1.096 (195)	-
CS- fear acquisition	3.95 (2.08)	3.51 (1.98)	4.30 (2.10)	-2.683 (195) **	0.3
GSmid fear generalisation	3.41 (2.00)	3.15 (1.78)	3.61 (2.14)	-1.609 (195)	-
Threat-based attention biases	6.40 (41.46)	2.07 (38.62)	9.83 (43.42)	-1.307 (195)	-

*p<.05, **p<.01, ***p<.001

TABLE 2.

Sample-wide correlations

	Threat-based attention bias *(r)*	Age *(r)*	Total SCARED score *(r)*	Total eACS score *(r)*
Age	-.087			
SCARED total score	-.089	.208**		
eACS total score	.008	-.069	-.708***	
CS+ fear acquisition	.020	.028	.243**	-.261***
CS- fear acquisition	.008	-.038	.223**	-.284***
GSmid fear generalisation	.135	-.127	.251**	-.256***

*p<.05, **p<.01, ***p<.001

TABLE 3. Hierarchical regression predicting self-reported anxiety

	SCARED total score				
Predictor	B	SE	β	t statistic, p value	Variance inflation factor
Step 1					
Age	2.081	.669	.217	t = 3.11, p < 0.001	1.000
Gender	11.437	2.260	.352	t = 5.06, p < 0.001	1.000
F(2, 171) = 17.60, p < .001					
Step 2					
Age	2.37	.654	.247	t = 3.62, p < 0.001	1.057
Gender	10.473	2.218	.323	t = 4.72, p < 0.001	1.029
CS+ fear acquisition	.685	.543	.101	t = 1.26, p = ns	1.350
CS- fear acquisition	.180	.657	.023	t = 0.27, p=ns	1.750
GS fear generalisation	1.594	.680	.198	t = 2.38, p < 0.05	2.158
F(3, 168) = 5.569, p = .001					
Step 3					
Age	1.749	.499	.182	t = 3.48, p < 0.001	1.071
Gender	5.204	1.765	.160	t = 2.83, p < 0.001	1.146
CS+ fear acquisition	-.004	.417	-.001	t = -0.04, p = ns	1.359
CS- fear acquisition	-.552	.503	-0.70	t = -1.10, p=ns	1.823
GS fear generalisation	1.258	.524	.157	t = 2.38, p < 0.05	2.177
eACS	-1.179	.108	-.625	t = 10.82, p < 0.001	1.259
Threat-based attention bias	-.041	.020	-.107	t = -2.27, p < 0.05	1.093
F(2, 166) = 63.075, p < .001					

*p<.05, **p<.01, ***p<.001

TABLE 4. Hierarchical regression predicting self-reported fear to the GSmid

Predictor	B	SE B	β	t statistic, p value	Variance inflation factor
				Fear to the GSmid	
Step 1					
Age	-.179	.090	-.150	t = -1.99, p < 0.05	1.000
Gender	.320	.304	.079	t = 1.05, p = ns	1.000
F(2, 171) = 2.532, p = .082					
Step 2					
Age	-.242	.088	-.202	t = -2.76, p < 0.01	1.070
Gender	-.041	.312	-.010	t = -0.13, p = ns	1.182
SCARED	.013	.014	.101	t = 0.89, p = ns	2.557
eACS	-.033	.024	-.139	t = -1.36, p = ns	2.062
SCARED*eACS	-.003	.001	-.222**	t = -2.79, p < 0.01	1.259
F(3, 168) = 8.217, p < .001					
Step 3					
Age	-.233	.087	-.195	t = -2.68, p < 0.01	1.072
Gender	-.109	.309	-.027	t = -0.37, p = ns	1.199
SCARED	.015	.014	.121	t = 1.06, p = ns	2.586
eACS	-.029	.024	-.124	t = -1.22, p = ns	2.071
SCARED*eACS	-.003	.001	-.245	t = -3.07, p < 0.01	1.280
Threat-based attention bias	.008	.003	-.168	t = 2.22, p < 0.05	1.106
F(1, 167) = 5.512, p = .020.					

*p<.05, **p<.01, ***p<.001

Figure 1

CS+ GS1 GS2 GS3 GS4 CS-

Burst UCS   Social UCS

Figure 2