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Neural and Behavioral Correlates of Visual Attention to Emotion Predicts Anxiety in Children

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Abstract

Cognitive theories propose that selective attention is essential to extracting relevant emotional information from the environment and guiding subsequent behavior (Atkinson & Braddick, 2012; Carrasco, 2011; Wieser & Keil, 2020). Excessive selective attention to threat-related information (i.e., attention bias for threat) is associated with heightened anxiety in both children and adults (Bar-Haim et al., 2007; Cisler & Koster, 2010). However, the underlying mechanisms and how they unfold over the course of development to influence anxiety outcomes are still poorly understood. Through the investigation of age-related changes in attention bias to threat and anxiety outcomes, we can begin to characterize developmental pathways for anxiety, and address outstanding questions in the literature regarding the neural and behavioral time course of selective attention to emotional information predictive of anxiety.

The current study examines the role of attention to emotion and anxiety outcomes by addressing methodological limitations of the extant literature and empirically testing theoretical developmental models of attention bias and anxiety. This study is one of the first of its kind to use a longitudinal and multi-method approach to characterize developmental changes in attention bias and anxiety symptoms using converging evidence from behavioral, eye-tracking, and neural correlates of the brain.

Overall, this research suggests that across multiple measures of attention bias for threat, the presence of threat bias early in development is a risk factor for anxiety outcomes. Findings from this study reveal that behavioral measures of attention bias early in childhood are predictive of anxiety symptoms, and initial attention allocation as well as attentional control are key features of selective attention that are predictive of anxiety outcomes.

CHAPTER 1

Introduction

Selective attention is essential for allocating cognitive resources to emotional information, as well as for perceiving the salience of that information (Atkinson & Braddick, 2012; Carrasco, 2011; Wieser & Keil, 2020). Importantly, preferential attention (biases) for threat-related information is present early in infancy (Hoehl & Striano, 2010; Safar & Moulson, 2020; Yrttiaho et al., 2014) and the underlying neural systems reflecting facilitated threat detection are subject to developmental changes in prefrontal cortex-amygdala connectivity (Atkinson & Braddick, 2012; Wu et al., 2016). While these attention biases can optimize behavioral responses to minimize harm and advance social goals, a large body of literature suggests that enhanced attention to threat-related information is associated with heightened anxiety in both children and adults (Bar-Haim et al., 2007; Cisler & Koster, 2010). Specific components of selective attention linked with anxiety include vigilance (initial and rapid attention allocation), avoidance (attention allocation away), and difficulty in disengagement from threat (inability to shift attention) (Cisler & Koster, 2010; Gupta et al., 2019).

Anxiety disorders may present as involuntary feelings of worry and fear, can appear in children as young as 2 years old, and are highly common across the lifespan (Bandelow & Michaelis, 2015; Cho et al., 2019; Kessler et al., 2005). Despite research efforts to characterize the etiology of anxiety, the mechanisms underlying selective attention and anxiety remain poorly understood. Behavioral measures of selective attention in anxiety, commonly measured by the Dot Probe Task (DPT), report vigilant and avoidant patterns of attention to threat in anxious adults and youth (Abend et al., 2018; Koster et al., 2006; Morales et al., 2015). During the DPT, children view angry-neutral and happy-neutral face pairs (one face on each side of screen) followed by an asterisk probe appearing on one side. Shorter reaction times or latency to fixate probes appearing on the side of where an angry face appeared indicates biased attention towards the angry face (i.e., vigilance or bias towards threat), whereas shorter latencies to fixate probes on the opposite side of the angry face indicates a biased attention away from the angry face (i.e., avoidance or biased away from threat; Burris et al., 2017). At the neural level, attention- and emotion-related processes can be measured with event-related potentials (ERPs), which are temporally sensitive measure of the brain derived from event related changes in the scalp recorded electrical signals generated by neuronal activity (Hajcak et al., 2010; Kappenman & Luck, 2012). Several ERP components reflecting attention and emotion-related processing have been extensively studied in the selective attention and anxiety literature. Specifically, the enhanced neural response of the P100 (an index of initial attention allocation), N170 (an index of face processing), Negative Central (Nc; an index of attention to salient information), and Late Positive Potential (LPP; an index of sustained attention and appraisal) have all been linked with emotional processing and anxiety (Gupta et al., 2019). Further, neuroimaging studies report enhanced activity in the dorsolateral and ventrolateral prefrontal cortex (dlPFC, vlPFC) and amygdala activity in anxious youth (Britton et al., 2012; Fu et al., 2017; Monk et al., 2008). Overall, behavioral and neural evidence suggests that the attention system is adaptively tuned for identifying threat-relevant information in the environment, but for some individuals the enhanced processing of perceived threat is linked to heightened anxiety symptoms (Bar-Haim et al., 2007; Gupta et al., 2019).

Although the literature independently links behavioral and neural correlates of attention to threat with anxiety, it currently lacks a framework for brain-behavior interactions of attention bias, as well as a trajectory for how selective attention changes and influences anxiety across development. The role of attention to threat in anxiety is difficult to unpack because our behavioral measures do not clearly correspond to neural measures due to temporal limitations of traditional behavioral assessments of attention bias (i.e., reaction time). Further, methodological constraints including challenges associated with investigating infants and young children, the wide variation in study designs and task parameters, and the lack of temporally precise implicit measures have all contributed to inconsistent empirical support for developmental models of attention and anxiety. As such, further research is needed to establish convergence between behavioral and neural measures of selective attention to threat by combining behavioral and neural assessments of attention bias and anxiety outcomes in a longitudinal study design.

This dissertation will address these limitations through two primary goals. First, the present study uses temporally sensitive and implicit measures of selective attention and emotion processing--namely eye tracking and ERP—in a longitudinal design spanning infancy to middle childhood. In doing so, the present study can better characterize developmental mechanisms of attention bias spanning infancy to middle childhood, as well as the neural time course of selective attention to emotional information predictive of anxiety outcomes. To date, studies of pediatric populations have yielded mixed findings (Dudeney et al., 2015; Fu & Perez-Edgar, 2019), contributing to inconclusive results on developmental patterns of attention to threat and mechanisms of anxiety. A major source of inconsistency in the literature stems from a reliance on behavioral reaction time and self-report questionnaires of selective attention that are both temporally imprecise measures of attention and developmentally inappropriate for infants and young children. Thus, to date, much of our understanding of attention bias in anxiety comes from older children, and may reflect the behavioral component of attention, rather than the visual processes themselves.

Longitudinal study designs with an emphasis on how individual differences in behavioral and neural correlates of selective attention to emotion predict anxiety outcomes are necessary to reveal and clarify the complex relations between attention processes and the emergence of anxiety in development. Through the investigation of age-related changes in attention bias to threat and anxiety outcomes, we can begin to characterize developmental pathways for anxiety, and tease apart how components of selective attention (i.e., vigilance, avoidance, difficulty in disengaging attention) persist or change across development to predict anxiety. Further, the inclusion of temporally sensitive measurements like eye tracking and ERPs can address outstanding questions in the literature regarding the time course and components of selective attention in anxiety, specifically questions regarding *when* and *how* emotional visual information is encoded (i.e., initial attention allocations relative to sustained attention and appraisal), and *which* underlying patterns of attention to threat (i.e., vigilance, avoidance, disengagement) are predictive of anxiety (Dustman et al., 1999; Gupta et al., 2019; Marandi & Gazerani, 2019). Characterizing the neural chronometry of attention bias and the types of attention patterns associated with anxiety symptoms of young children is a critical step in rectifying inconsistencies of the attention bias literature. Thus, the present study uses eye-tracking and ERP methods in a longitudinal design to characterize developmental mechanisms of attention bias, specifically the stability of attention components (i.e., vigilance, avoidance) spanning infancy to middle childhood, as well as the neural time course of selective attention to emotional information predictive of anxiety outcomes.

The second goal of this dissertation is to empirically test theoretical developmental models of attention bias and anxiety (Field & Lester, 2010). Dominant theories of attention and anxiety are largely based on empirical evidence from adults and are therefore not applicable to pediatric populations. The present study empirically tests two theoretical models proposed by Field and Lester (2010) to disambiguate individual differences in the *development* of anxiety: (1) the *Integral Bias Model* which suggests that development does not influence attention bias such that those born with an attention bias for threat will maintain an attention bias throughout the lifespan, and (2) the *Moderation Model* which suggests that development moderates attention bias to threat such that all infants have a normative bias towards threat that disappears across development, but individual developmental factors (i.e., environmental, biological, social-emotional) can maintain or increase this bias resulting in anxiety disorders (Field & Lester, 2010). Specifically, the present study examines these two theories by using a longitudinal eye tracking measure of attention bias to investigate how early developmental time points of attention bias, as well as the continued persistence of a threat bias across development (9 months to 8 years of age) is predictive of anxiety symptoms. Support for the *Integral Bias Model* would come from results in which measures of attention bias at any time point predict anxiety, and attention bias is stable and highly related across development. In contrast, support for the *Moderation Model* would come from results in which the relation between early occurring attention bias and later anxiety is moderated by additional individual-level characteristics (such as those indexed by neural responses to attention-emotional information) measured at other points in development, indicating that early occurring attention bias alone is not enough to explain anxiety development, and measures at other points in development interact with earlier measures to predict emergence of anxiety symptoms. Additional support for the moderation model could come from results showing that measures of attention bias at some points in development—but not all points in development—predict anxiety, indicating that other factors are interacting with attention bias over development such that attention bias measured at only certain developmental timepoints predict emergence of anxiety symptoms.

Additionally, the current study includes neural measures of selective attention to emotion and anxiety symptoms in middle childhood, which allows us to empirically test the notion that earlier developmental time points of attention bias to threat may be biologically embedded in the neural system for attention and emotion, conferring even greater risk for development of anxiety (Mogg & Bradley, 2016; O'Toole et al., 2013). There is some preliminary evidence to indicate that enhanced threat processing measured by neural correlates of the brain are longitudinally predictive of childhood anxiety measured two years later (O'Toole et al., 2013), suggesting that early onset of attention bias for threat may have a casual role in shaping the attention system to be predictive of anxiety. However, the extant literature is limited to a focus on older children (5- to 9-years-old) and therefore it remains unknown how attention bias for threat present earlier in development impacts ongoing brain maturation and subsequent attention mechanisms. While the scope of the current study does not evaluate brain maturation directly, our ERP measures index neural correlates of brain activity reflecting attention-emotion processes that may be influenced by the developmental persistence of attention for threat and subsequently, may predict anxiety. Specifically, the evidence in the literature showing enhanced ERPs indexing attention for threat related to anxiety (predominantly measured in older children and adults; (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & Van Ijzendoorn, 2007b; Bechor et al., 2019; DeCicco et al., 2012; Kujawa et al., 2016; MacNamara & Hajcak, 2009; Mueller et al., 2009; O'Toole et al., 2013; Wauthia & Rossignol, 2016; Zhang et al., 2018)), may in fact, be reflective of an overall attention system that has been tuned for identifying threat across development, but this effect has not been clearly documented due to a lack of longitudinal investigation. To our knowledge, this is the first study of its kind to longitudinally evaluate how attention bias measured in infancy and early childhood predicts neural correlates of the brain, and how both behavior and neural measures of attention separately and in combination predict anxiety as it first emerges in middle childhood.

Current Study

This dissertation investigates attention patterns to threat in a longitudinal community sample of children that may or may not be at risk for anxiety disorders. Specifically, this study uses eye tracking to assess attention biases to threat longitudinally over infancy to middle childhood and capitalizes on the high temporal resolution of ERP to examine the neural time course of children's selective attention to emotional faces and scenes. We examine the relations among these assessments of attention bias and emerging anxiety symptoms. This approach facilitates the two goals outlined above: (1) to address methodological limitations of extant literature and better characterize the development of attention bias and its role in anxiety by examining the relation between neural correlates of attention to emotion and behavioral correlates of attention, and how the combination of these measures can help predict individual differences in anxiety outcomes of young children; and (2) to test developmental models of attention bias and anxiety proposed (Field & Lester, 2010).

Data was collected across three time points, spanning approximately 7 years. Eye tracking data (DPT task) was collected at Time 1 from 2013 to 2015 when participants were 9 months- 4 years old and at Time 2 from 2016 to 2017 when participants were 2.6-6 years old. Time 3 data collection occurred from June 2018 to March 2020 when participants were 6- 8 years old and includes both eye tracking and EEG data collection. The current study examines relations among eye tracking data from Time 1 and Time 2 predicting eye tracking, ERP, and anxiety symptom data at Time 3, as well as concurrent relations among eye tracking, ERP, and anxiety data at Time 3.

Hypotheses

Hypothesis 1. Children's behavioral assessment of attention bias to threat (assessed with eye tracking) will longitudinally predict their neural correlates of attention to emotional stimuli (assessed with ERPs).

To date, the attention bias literature has predominately relied on behavioral measures (DPT reaction time measures, questionnaires), eye tracking measures (DPT measures latency or proportion of looking time, overlap task measuring latency to fixate), or separately, ERPs (measuring mean amplitude or latency in response to emotional facial expressions). Given that few studies have combined across measures, the role of attention to threat in anxiety is difficult to discern because behavioral measures do not clearly correspond to neural measures. The lack of evidence of a clear relationship between attention to threat and anxiety may be due to the reliance on behavioral reaction time measures of attention which are temporally imprecise measurements of attention. It is possible that eye tracking, which can measure quick shifts of attention, may reveal relations with neural measures, but no study has longitudinally tested this to date.

Prior research has concurrently examined attention to threat using the DPT with combined behavioral reaction time (non-eye tracking) and ERP measures in adults and children (Bechor et al., 2019; Kappenman et al., 2014, 2015; Thai et al., 2016). In addition to poor test-retest reliability on the behavioral DPT, studies report that behavioral reaction times are not significantly correlated with ERP measures of attention to threat, indicating that these measures are indexing different processes (Kappenman et al., 2014, 2015; Thai et al., 2016). Given the rate at which attention is deployed, behavioral reaction time measures are only able to capture the end-result of a complex cascade of neural and cognitive processes, while ERP correlates can provide a continuous neural index of attention of initial allocation and sustained attention (Shechner et al., 2012). Eye tracking can provide a similar, though behavioral, index of attention allocation and maintenance. Modified eye tracking versions of the DPT that measure fixation latency rather than behavioral reaction time have reported good internal reliability in adults (Armstrong & Olatunji, 2012) and young children (Burris et al., 2017). However, it remains unclear how eye tracking, a temporally sensitive measure of attention, corresponds to neural indices of attention. To date, no prior research has evaluated how an eye tracking DPT measure of attention to threat corresponds to neural correlates of attention to emotional faces and scenes. Characterizing relations between the DPT eye tracking and ERPs is essential in the investigation of attention to threat and anxiety outcomes in childhood.

The present study used an eye tracking version of the DPT, which makes it a temporally sensitive measure of selective attention that may thus be better able to capture variance related to children's neural correlates of attention assessed with another temporally sensitive measure of ERPs. We hypothesized there would be consistencies in attention bias across development as revealed in early attention biases predicting later neural correlates of selective attention to emotional information. Specifically, DPT and early ERPs (P1: 100-150ms, N170: 160-250ms) would be related, given that both DPT and early peaking ERPs are thought to reflect initial attention allocation, and vigilance or avoidance of initial attention (Cisler & Koster, 2010; Gupta et al., 2019; Mogg et al., 2004). We expected to see no relation between DPT and later time course peaking ERPs (Nc: 275-500ms, LPP middle: 600-1100ms, LPP late: 1100-2000ms), given that DPT might reflect more initial attention allocation processes whereas later peaking

ERP components reflect more sustained attention to salient stimuli and appraisal processes (Dennis et al., 2009; Hajcak et al., 2010). The test of this hypothesis will address both goals of the current study: 1) the use of temporally sensitive eye tracking and ERPs to measure selective attention for threat will address existent methodological limitations of the literature by establishing consistencies in brain-behavior relation of attention bias, and 2) this analysis will address theoretical assumptions about the causal role of behavioral attention bias for threat present early in development as predictive of enhanced neural brain response for threat, suggesting that early behavior is influencing organization of attention networks.

Hypothesis 2. Behavioral and neural measures of children's attention bias to threat will be related to anxiety symptoms.

A large corpus of literature demonstrates connections between attention bias and anxiety (Bar-Haim et al., 2007; Cisler & Koster, 2010; Dudeney et al., 2015; Fu & Perez-Edgar, 2019; Mogg & Bradley, 2016). We thus hypothesized that similar relations would be evident in our data.

Hypothesis 2a. Children's behavioral assessment of attention bias to threat (eye tracking) will longitudinally predict anxiety symptoms. Using an eye tracking DPT, Burris and colleagues (2017) found that some level of vigilance may be normative in infancy and early childhood. They reported that infants and young children ranging 9 to 48 months of age show group level vigilance for both threatening and happy emotional faces (Burris et al., 2017).

In a recent two-year follow up longitudinal analysis of the same sample, the authors reported that group level analyses showed that attention bias was consistent across Time 1 and Time 2, providing preliminary support for the *Integral Bias Model*. However, analyses of within-subject variability revealed Time 1 Angry Bias scores were not predictive of Time 2, providing preliminary empirical support for the *Moderation Model* (Burris & Rivera, *under review*). Interestingly, when participants were segmented according to those who have an angry bias at both time points (i.e., persistent vigilance for threat) relative to those who did not (i.e., variable bias for threat), those with a developmental persistence of vigilance for threat exhibited heightened symptoms of anxiety. This longitudinal study is one of the first to use the DPT spanning infancy into early childhood to investigate how attention, particularly vigilance, may interact with anxiety across development (Burris & Rivera, *under review*). Extending these findings, the current study will measure attention to threat using the DPT at a third time point in this longitudinal sample. Similarly, we hypothesized if our data reveals a consistent attention bias for threat across developmental time points, this will show support for the *Integral Bias Model* suggesting that attention bias for threat remains stable across development. However, if we find a lack of stability in individual variability of Angry Bias scores, this will provide preliminary support for the *Moderation Model* suggesting that developmental factors can maintain or increase threat bias throughout development. Further, we examined how a combination of two developmental time points of Angry Bias scores measured by the Dot Probe Task (DPT 1 and 2, DPT 2 and 3, DPT 1 and 3) would be predictive of anxiety symptoms at Time 3. In line with Burris & Rivera, *under review*, we expected that individuals with larger Angry Bias scores at both developmental time points would show higher levels of anxiety symptoms at Time 3, suggesting heightened anxiety in individuals who have a developmentally persistent threat bias.

Hypothesis 2b. Neural correlates of the brain (ERPs) indexing early and later temporal indices of selective attention to emotional stimuli will predict children's anxiety symptoms. Given that ERPs may reflect a biological embedding of attention bias (i.e., changes in the brain reflecting vigilance for threat) across the first few years of life, we wanted to know how changes in the brain correspond to concurrent measures of anxiety. Specifically, how do neural measures of visual selective attention to emotional faces and scenes correspond to parent report of child anxiety? Given that prior research reports a link between ERPs and anxiety, we expected to see similar patterns, particularly for P1, N170, and LPP, such that enhanced ERPs are associated with enhanced anxiety symptoms.

Further, the high temporal resolution of ERP makes it an especially powerful tool for indexing components of selective attention such as initial attention allocation (reflected in early ERP components of P1 and N170) and sustained attention to salient information (reflected in later components of Nc and LPP). We did not have specific hypotheses about whether early or later components would differentially predict anxiety, but such differential relations would be informative for the field. Charting the temporal dynamics of attention bias to threat associated with enhanced anxiety can build knowledge regarding mechanisms of how changes in attention across development may predict anxiety outcomes. Moreover, characterizing the specific aspects of attention for threat most predictive of anxiety is highly relevant for clinical diagnosis and intervention.

Overall, the tests for hypotheses 2a and b will address both goals of the current study: 1) evaluation of temporally sensitive ERP and longitudinal eye tracking measures of attention to threat in predicting anxiety symptoms will address prior methodological limitations of studying young children, and 2) this analysis will evaluate the empirical support for *Integral Bias Model* vs *Moderation Model* present in our longitudinal eye tracking measure of attention to threat. We may draw preliminary support for the *Integral Bias Model* if our longitudinal DPT data reveals consistency across developmental time points, suggesting that attention bias for threat remains stable across development. Alternatively, we may draw preliminary support for the *Moderation Model* if our longitudinal DPT data shows a lack of stability in attention bias for threat, suggesting that individual- level factors can change threat bias throughout development.

Hypothesis 3. A combined effect of neural correlates of the brain (ERPs) and temporally sensitive behavioral indices (eye tracking) will predict children's anxiety symptoms.

Finally, the *Moderation Model* proposed by Field & Lester (2010) posits that the developmental persistence of attention bias predicts anxiety, and so the addition of neural measures of attention to emotion may offer a more sensitive index that reflects development tuning of attention bias. Thus, we examined if neural correlates of the brain help explain the relation between longitudinal DPT and child anxiety symptoms at Time 3. Further, we aimed to establish how longitudinal eye tracking DPT combined with neural measures of visual selective attention to emotional faces and scenes predict anxiety. We expected that the combined effect of DPT and ERPs will serve as a better predictor of anxiety outcomes than either measure alone. Given the literature reports that both early and later peaking ERPs are predictive of anxiety (Bechor et al., 2019; Mueller et al., 2009; Wauthia & Rossignol, 2016), we expected to see that both types of ERPs would moderate the relation between DPT and anxiety. As previously highlighted in Hypothesis 1 and 2b, we expected that enhanced early peaking ERPs (P1, N170) would reveal a relation between anxiety and initial attention allocation, whereas later peaking ERPs (Nc, LPP) would reveal a relation between anxiety and prolonged attention to threat reflecting sustained processing of salient information. In line with the *Moderation Model*, we predicted that DPT 1 or 2, in combination with ERP brain measures at Time 3, would predict anxiety symptoms at Time 3. However, if we found that any DPT time point predicts anxiety, and DPT attention bias remains consistent across all 3 developmental time points (i.e., DPT

Time 1 predicts Time 2 and 3), this would be empirical support for the *Integral Bias Model*, suggesting that development does not impact attention bias. In sum, the tests of hypothesis 3 will also address both goals of the current study: 1) assess how the combination of longitudinal eye tracking measures of attention bias combined with neural correlates of attention bias to predict anxiety outcomes may help overcome methodological limitations, and 2) this analysis will provide an additional evaluation of the *Integral Bias Model* vs *Moderation Model*.

CHAPTER 2

Review of Literature

Role of Visual Attention to Emotion

Visual attention to emotion-related information is essential to how we learn and interact with our environment. Selective attention—the preferential processing of high-priority stimuli—is particularly evident in the enhanced processing of threatening stimuli (Atkinson & Braddick, 2012; Carrasco, 2011; Wieser & Keil, 2020). From an evolutionary perspective, this process is essential to adaptive behavioral responses that can both minimize potential harm and advance social-emotional goals (Ohman & Wiens, 2004; Pourtois et al., 2013). Research suggests that threat-related cues are prioritized at several levels of processing, exhibiting rapid and more accurate detection and longer duration of attention relative to neutral, non-emotional stimuli (Barbot & Carrasco, 2018; Goodwin et al., 2017).

Importantly, research findings suggest that these abilities come on-line very early in development. For example, young infants orient faster to snake versus flower stimuli, and to angry versus happy faces (LoBue et al., 2017). While a snake may connote physical threat, emotional facial expressions provide essential social-emotional communication, and serve as indicators of social threat. Infant behavioral research suggests enhanced processing of threatening faces by 3-4 months (Bayet et al, 2017), while neural evidence suggests this enhanced processing emerges by 5-7 months (Hoehl & Striano, 2010; Safar & Moulson, 2020; Yrttiaho et al., 2014). These findings highlight the possibility that empirical differences in attention to social threat between 3–4-month-olds and 5-7-months-olds may reflect differential development of attentional mechanisms. Further support for age-related changes in attention to emotion processing come from findings that amygdala responses to emotional information hinge on attention allocation supported by the prefrontal cortex (PFC) (Cisler & Koster, 2010; Monk et al., 2008), and this system undergoes significant developmental changes (Atkinson & Braddick, 2012).

In sum, research on selective attention suggests visual attention mechanisms interact with emotional cues to facilitate detection and processing of salient environmental information, and that these processes are subject to developmental changes. While these perceptual biases can be adaptive, a parallel line of research suggests that these processes may become exaggerated in some individuals and have implications for anxiety disorders.

Role of Attention in Anxiety

To date, the underlying mechanisms involved in threat detection and anxiety, as well as how selective attention patterns interact with other risk factors (i.e., biological, environmental) in the development of anxiety remain unclear. Anxiety disorders are marked by persistent and involuntary feelings of worry and fear that can be severely debilitating. They are highly common in individuals across the lifespan, with an estimated lifetime prevalence of 29%–33.7% (Bandelow & Michaelis, 2015; Kessler et al., 2005), and can appear in children as young as 2 years of age (Cho et al., 2019; Costello et al., 2011; Kessler et al., 2005). The presence of anxiety in childhood and adolescence has been associated with greater risk of long-term negative outcomes, such as depression, suicidal ideation, academic underachievement, and substance abuse (Beesdo-Baum & Knappe, 2012; Woodward & Fergusson, 2001). Given the high prevalence and negative impact on quality of life, much research has focused on the etiology of anxiety disorders to identify potential risk factors. In particular, research suggests that selective attention to threatening information likely interacts with several biological (i.e., EEG frontal asymmetry, RSA), temperamental (i.e., behavioral inhibition), and environmental risk factors for anxiety (i.e., maternal anxiety) (Bosquet & Egeland, 2006; Morales et al., 2017; Pérez-Edgar et al., 2013; Pérez-Edgar & Guyer, 2014; Waters et al., 2008). Yet, the mechanisms driving these processes and how patterns of attention to threat unfold over the course of development to influence anxiety outcomes have not been well studied.

A growing body of literature suggests that biased selective attention to threat, characterized as differential attention allocation for threat-related information, is associated with heightened anxiety in both children and adults (Bar-Haim et al., 2007; Cisler & Koster, 2010; Dudeney et al., 2015; Fu & Perez-Edgar, 2019; Mogg & Bradley, 2016). In particular, benign or ambiguous emotional cues are perceived negatively or as threatening in adult individuals with anxiety disorder (Azoulay et al., 2020; Lau & Waters, 2017). Moreover, behavioral studies of briefly-presented threat cues (i.e., 17ms) suggest that adults with anxiety can perceive threatening information without conscious awareness of the threat (Mogg & Bradley, 2002), and neuroimaging findings implicate altered amygdala-prefrontal cortex connectivity during subliminal processing of threat in adult and pediatric populations (Hur et al., 2019; Monk et al., 2008). These findings suggest that the attention system is tuned to detect threat-related information in the environment, a process that could be especially exaggerated in those with anxiety.

Several components of selective attention have been documented in anxious individuals, including vigilance, avoidance, and difficulty disengaging attention from threat (Cisler & Koster, 2010; Gupta et al., 2019). *Vigilant* attention patterns are defined by facilitated attention to threat, marked by unconscious and rapid attention allocation towards threatening information. *Avoidant* attention patterns are characterized by attention allocation away from threatening information. *Difficulty in disengaging* from threat is defined as the inability to shift attention away from threatening information (Cisler & Koster, 2010; Gupta et al., 2019). Despite the established relationship between patterns of attention and the presence of anxiety, the literature currently lacks a clear framework for how these attention patterns develop and change with age, and how their respective temporal time course is associated with anxiety. Methodological inconsistencies/limitations such as varying study designs, reliance on temporally limited indices of attention (i.e., motor reaction time tasks), and longitudinal constraints associated with data collection from young children, have all contributed to inconsistent findings.

Behavioral Measures of Attention in Anxiety

While several experimental paradigms have been used to assess patterns of attention, the dot probe task (DPT) has been considered the gold-standard assessment of attention to threat (also referred to as threat bias) (Gupta et al., 2019; MacLeod et al., 1986). In the classic version of this task, two stimuli (often neutral and fearful faces) are briefly presented on opposing sides of the monitor (either vertically or horizontally). The stimuli quickly disappear and are followed by a visual probe (e.g., an asterisk or crosshair) in the location of one of the images. Participants push a button to indicate the location on the screen at which the probe appeared. Probes appearing in the same spatial location as the salient stimuli (i.e., fearful face) are considered congruent trials, whereas probes presented on the opposite side of the salient stimuli (i.e., neutral face side) are considered incongruent trials. In the traditional version of the task, button press reaction times between congruent and incongruent trials are compared. Shorter reaction times on congruent versus incongruent trials indicates attentional vigilance towards the salient stimuli, whereas shorter reaction times on incongruent versus congruent trials indicate attentional avoidance (Bantin et al., 2016; Bar-Haim et al., 2007). Variations of this task include differences in timing of presentation (ranging from 500ms–1500ms), stimuli (i.e., words, emotional faces, images), and motor versus eye fixation reaction time measurements.

The DPT has been extensively used in adult and pediatric research to measure vigilance and avoidance of attention to emotional information, and to probe theoretical questions regarding the nature of attention in anxiety. The flexibility of the DPT design, including variations in the type of stimulus (i.e., faces, emotional scenes, words), duration of stimuli presentation (i.e., 500ms–1500ms), and mode (behavioral, eye tracking, neural) have made the use of this task highly prevalent across multiple fields of research. Over the years, the reliability of the traditional reaction time DPT has come into question, with some studies reporting low internal consistency and poor test-retest reliability (Kappenman et al., 2014; Schmukle, 2005), while other studies report good internal consistency (Bar-Haim et al., 2007, 2010). Given the rate at which attention is deployed, behavioral reaction time measures are only able to capture the end-result of a complex cascade of neural and cognitive processes (Shechner et al., 2012). Yet, a considerable amount of research investigating patterns of attention to threat and anxiety (i.e., those using DPT, spatial cuing paradigms) relies on motor-based reaction time and self-report measures of attention (Shi et al., 2019). Electrophysiological research on the visual system suggests that attention orienting can occur on the order of 100ms shifts from object to object (Luck et al., 2000), a time-course considerably faster than a motor response (Cross-Villasana et al., 2015; Töllner et al., 2012). As such, much of our understanding of attention bias to threat may reflect the consequential behavioral component of attention, rather than the visual process itself. While data on button presses can provide one kind of valuable information, understanding the processes prior to such behavioral output can inform us about the mechanisms underlying selective attention to threat (i.e., *when* in the visual processing stream salient features are encoded and *how* the brain allocates attention to and processes this information).

In recent years, the use of eye tracking to index attention rather than button-press responses has shown good internal reliability, as well as applicability to a wider developmental range of ages (Armstrong & Olatunji, 2012; Burris et al., 2017). Still, there remains a lack of convergence between behavioral and neural measures of attention to emotion and anxiety outcomes. To address this, a developmental cognitive neuroscience approach; specifically, the use of temporally sensitive behavioral measurements (i.e., eye tracking) and neural measures (i.e., EEG), is necessary.

Neural Correlates of Attention to Emotion

A well-suited method to study attention to emotion is event-related potentials (ERPs). ERPs are derived from event-related changes in the scalp recorded electrical signals generated by neuronal activity, are non-invasive, and provide excellent temporal resolution (in milliseconds) allowing for the indexing of quick attentional processes. Most notably, ERPs do not require an overt motor or verbal response, making this technology suitable for the study of neural activity in young children. They have been extensively used in the literature to investigate attention to and processing of emotional facial expressions and emotion-eliciting images (Hajcak et al., 2010; Kappenman & Luck, 2012). Patterns of brain activity, typically seen as fluctuations in amplitude and latency of scalp recorded voltage, change in response to cognitive and emotional processes, and consistent patterns of brain activity are typically named as *components* (Kappenman & Luck, 2012). Age-related changes in cognition are reflected by changes in morphology, timing, scalp topography and lateralization of these components (Reuter et al., 2019; Segalowitz et al., 2010). While many ERP components reflecting attention and emotion processing have been identified, the present study will evaluate four (P100, N170, Nc, LPP) which are commonly documented in the developmental literature (Nelson & McCleery, 2008).

P100 (P1)

The P1 component is characterized as a positive deflection roughly 100 ms post-stimulus onset over occipital sites, reflecting initial visual attention allocation and localized to the visual cortex in adults (Di Russo et al., 2002; Kappenman & Luck, 2012). Developmental research on the P1 has documented event-related decreases in latency from 250–300 ms in newborns to 100 ms by 6 months of age (Coch & Gullick, 2012; Nelson & McCleery, 2008; Taylor et al., 2004). Further, attention modulates the magnitude of the P1 such that larger amplitudes are seen during sustained attention (Conte et al., 2020). The P1 is also sensitive to emotional facial expressions in infants and children (Batty & Taylor, 2006; Dennis et al., 2009). Finally, there is some evidence to suggest that anxious adults (Mueller et al., 2009) and youth (8–15 years old; Bechor et al., 2019) exhibit an enhanced P1 raw mean amplitude for threatening relative to neutral stimuli, suggesting vigilance for threat (Wauthia & Rossignol, 2016).

N170

The N170 is recognized in adults as a negative deflection over lateral posterior electrodes peaking between 130–200 ms after stimulus onset and is believed to reflect the perceptual encoding of faces (Bentin et al., 1996). In healthy controls, it is right-lateralized, emerges as an increase of amplitude to faces relative to non-face objects (i.e. houses) and is sensitive to face inversion (Rossion & Jacques, 2012). The N170 is considered a neural marker of cortical specialization for face processing and developmental research has documented a protracted development that is thought to reflect gaining expertise with faces. The infant N290 and P400 components are considered the developmental precursors to the face-specific adult N170 component (Halit et al., 2003). By 4 years of age, the N170 morphology begins to look more adult-like (Batty & Taylor, 2006). Further, in adults, the N170 is sensitive to facial expressions, such that emotional facial expressions (anger, fear, happiness) elicit larger raw mean amplitudes relative to neutral expressions (Hinojosa et al., 2015). This sensitivity for emotional faces is not present in childhood but appears sometime around adolescence (~14 years), possibly due to the ongoing maturation of brain regions involved in face processing (Batty & Taylor, 2006; O'Toole et al., 2013). Finally, enhanced threat processing indexed by the N170 has been documented in adults with social anxiety (Zhang et al., 2018), youth with anxiety disorder (Bechor et al., 2019), and is predictive of childhood anxiety symptoms (O'Toole et al., 2013).

Negative Central (Nc)

The Nc component is a negative peak appearing approximately 300-800 ms after stimulus onset in infants and children over frontal and central midline electrodes. The Nc reflects attention control to salient stimuli, is larger during periods of attention compared to inattention, modulated by facial familiarity, and localized to the posterior cingulate cortex and regions within the prefrontal cortex (Guy et al., 2016; Hoehl et al., 2008; Reynolds & Richards, 2010; Robey & Riggins, 2016; Xie et al., 2018). Nc can be computed as either raw mean amplitude or difference waves to isolate attention effects (Richards et al., 2003; Luck, 2014). In young children, the Nc has also shown sensitivity to emotional facial expressions with a larger amplitude and quicker latency to threatening faces relative to happy faces, an effect that has also been associated with more effective emotion regulation (Dennis et al., 2009; Todd et al., 2008). Given the time-course, the Nc may be less sensitive to low-level characteristics of stimuli than the preceding P1, making it a useful index of attention to threatening faces (i.e., vigilance).

Late Positive Potential (LPP)

The LPP component is a positive deflection peaking approximately 300 ms after stimulus onset in adults, by 500 ms post stimulus in children, and can be sustained for several seconds over posterior inferior and superior recording sites (Hajcak et al., 2010). The LPP reflects sustained attention to and processing of emotionally salient information and appears larger in amplitude for emotional (both pleasant and unpleasant) relative to neutral stimuli (often computed as either raw mean amplitude or difference waves to isolate emotion effects; Moran et al., 2013; Wieser & Moscovitch, 2015). Simultaneous fMRI and ERP recordings have linked the LPP to activation in the visual cortex and emotion-processing regions such as the amygdala and prefrontal cortex (Liu et al., 2012; Sabatinelli et al., 2013). Scalp distribution of the LPP in adults and children suggests that the LPP is maximal at parietal-occipital sites approximately 300–800ms post stimulus onset (Decicco et al., 2014; Hajcak & Dennis, 2009). Finally, the LPP has been established as a reliable measure of attention to emotion across childhood and adolescence (Kujawa et al., 2013) and in adulthood (Huffmeijer et al., 2014).

In adults the LPP has been used as a neural marker of cognitive reappraisal, a form of emotion regulation during which individuals cognitively reassign the meaning of a stimulus to decrease emotional impact (Hajcak & Nieuwenhuis, 2006; Ochsner & Gross, 2005; Rehmert, A.E. , Kisley, 2008; Wood & Kisley, 2006). In children, the evidence remains mixed, with some studies reporting that reappraisal does modulate the LPP in 4–10 year old children (Dennis & Hajcak, 2009; Hua et al., 2015), while other studies find no group-level modulation of the LPP in children 5–9 years old (Decicco et al., 2014; DeCicco et al., 2012). Importantly, DeCicco and colleagues (2014) reported age-related changes such that older but not younger children showed LPPs sensitive to reappraisal, potentially due to the ongoing maturation of the prefrontal cortex. Given that reappraisal recruits prefrontal cognitive resources to regulate emotional responses, particularly working memory to modify or update new information, developmental changes in cognition should be properly accounted for in studies of cognitive reappraisal in children (Pe et al., 2013). As such, it remains unclear at what age the LPP can be considered a reliable index of cognitive reappraisal. Regardless, these findings demonstrate that LPP indexes aspects of attention, and potentially attention modulation (through reappraisal) at least in adults and older children.

More relevant to the present study, several studies report that adults with anxiety disorder exhibit enhanced LPP amplitude to threatening images, reflecting vigilant attention for threat that is characteristic of anxiety disorders (Bar-Haim et al., 2007; MacNamara & Hajcak, 2009, 2010). In children and adolescents, LPP amplitudes for threatening stimuli are associated with greater observed fear (Solomon et al., 2012) and anxiety symptoms (DeCicco et al., 2012; Dennis et al., 2009; Kujawa et al., 2015). Further, using the LPP as an index, Weinberg and Hajcak (2011) examined early and late stages of attention allocation to emotional stimuli in adults with generalized anxiety disorder. Taken together, the LPP is considered a reliable measure of sustained attention to and processing of emotionally salient information, and a useful index of individual differences in emotion regulation and anxiety across development.

In sum, with the high temporal resolution of ERPs, researchers can chart the neural chronometry of attention to emotional stimuli across development. The early peaking components, specifically the P1 and N170, reflect automatic attention allocation to emotional information (both emotional faces and complex scenes). The later peaking components, such as the Nc and LPP, reflect sustained attention to and more strategic processing of emotional information. Given that sensitivity for threatening information is characteristic of anxiety disorders, ERPs are especially useful for charting meaningful individual differences in attention and emotion processes that could serve as neural signatures of risk for anxiety. Finally, this information is most valuable when paired with complementary behavioral data to clarify the significance of ERP measured differences in attention and emotion.

Role of Development in Attention and Anxiety

While the adult literature has established that attention plays a pivotal role in processing emotional information, and likely interacts with other risk factors for anxiety, the underlying mechanisms and how they unfold over the course of development to influence anxiety outcomes are still poorly understood. Characterizing the developmental progression of attention and anxiety affords a unique opportunity to identify sensitive periods in development that serve as pivotal points of entry for intervention. Unfortunately, studies of attention and anxiety in youth have yielded mixed findings, contributing to an inconclusive theoretical framework for how these attention patterns develop and change with age.

One source of inconsistency comes from methodological limitations which include varying study designs, reliance on temporally limited indices of attention (i.e., motor reaction time tasks, questionnaires) and lack of longitudinal data collection from young children. The ability to examine longitudinal patterns over early childhood offers a unique opportunity to investigate antecedents to the early emergence of anxiety. In particular, eye tracking and EEG/ERP are powerful tools that can offer temporally sensitive measurements of attention and emotion-related processes across the lifespan (Dustman et al., 1999; Marandi & Gazerani, 2019). Using eye tracking, researchers have documented developmental changes in attention and oculomotor control (Kramer et al., 2005), noting increased efficiency in pro-saccades and anti-saccades, smooth-pursuit eye movement involved in tracking, and face perception (Gredebäck et al., 2010; Karatekin, 2007; Katsanis et al., 1998). At the neural level, developmental changes in cognition are reflected by changes in morphology, timing, scalp topography and lateralization of EEG/ERP correlates (Johnstone et al., 1996; Reuter et al., 2019; Segalowitz et al., 2010). Thus, using temporally sensitive measurements of attention and longitudinal experimental designs, researchers can bridge the empirical gap and build a theoretical framework to explain the progression of attention and anxiety. Finally, ERPs can help characterize the neural time course of selective attention to delineate earlier versus later attentional processes predictive of anxiety outcomes.

Another source of inconsistency in the literature stems from contradictory empirical evidence and limited consideration for the role of development in theoretical models of anxiety. From infancy to emerging adulthood, the brain undergoes significant structural and functional changes that parallel advances in cognition (Amso et al., 2016; Blakemore & Choudhury, 2006; Fiske & Holmboe, 2019). Yet, dominant theories of attention and anxiety are largely based on empirical evidence from adult populations and are not necessarily applicable when applied to developmental populations. To address these limitations, Field and Lester (2010) put forth three theoretical models in an attempt to characterize the developmental trajectory of attention to threat and anxiety. The most relevant to the present study are the *Moderation Model* and *Integral Bias Model*. The *Integral Bias Model* posits that attention bias for threat is innate, so individuals born with it maintain it throughout development and development does not influence the attention bias. In the context of the present study and in support of this model, we would expect attention bias for threat to be consistent across all developmental time points. Any developmental time point would be predictive of anxiety outcomes and earlier developmental time points of attention bias would be predictive of later time points (Field & Lester, 2010).

The *Moderation Model* posits that individuals are born with an attention bias for threat that diminishes over the course of development, but for those who maintain it go on to develop anxiety disorders (Field & Lester, 2010). In support of this model, we would expect that any developmental time point of attention bias would predict anxiety. Further, given that this model proposes the presence of an attention bias at birth, that diminishes for most people, but is maintained for those at higher risk for anxiety, we would expect to see changes in the brain reflecting the persistent presence of this bias across development. Therefore, measures of the brain may provide a more sensitive index of attention bias that has been embedded into the biology, reflecting a developmental tuning of the brain for preferentially identifying threat in the environment. As such, empirical models that combine both developmental measures of attention bias as well as measures of brain activity may be most likely to reveal support for the *Moderation Model*, as the combination of these measures can tap into the sensitive embedding of attention bias.

Further, Burris & Rivera (*under review*) present longitudinal evidence that suggests attention bias for threat is present in infancy and persists for some infants across a two-year time span to predict anxiety symptoms. These findings show preliminary support for the *Moderation Model*, suggesting that individuals are born with an attentional bias for emotion that diminishes for most individuals, but parents report heightened anxiety symptoms for those who continue to show a persistent attention bias for threat-specific stimuli in a two-year follow up. The addition of a neural measure will further characterize the cascading effect of having an attention system that is highly tuned for threat in early development.

CHAPTER 3

Methods

Participants

Participants were recruited as part of a larger longitudinal study investigating attention and emotion processing in young children. The present study included a total of 50 children (23 female) who previously participated at Time 1 (*M* = 23.8 months, *SD* = 11.5, range = 9.13-48.09 months),Time 2 (*M* = 48.21.14 months, *SD* = 9.96, range = 32.27-72.05 months), and Time 3 (*M* = 80.28 months, *SD* = 6.02, range = 73.30-100.23 months). Parent report of child ethnicity was 60% White, 18% Hispanic, 12% Multiethnic, 8% Asian, and 2% Native Hawaiian/Pacific Islander. Parents were well-educated: 38% had a 4-year degree from a college or university, 26% had a doctoral degree (Ph.D., M.D.), 22% had a Master's degree, 10% had a 2-year degree from a college or trade school, and 4% had "some college". All participants had normal or corrected to normal vision and were described as healthy. Two children were excluded from the final sample: one participant refused to wear the EEG cap and one participant was diagnosed with Autism Spectrum Disorder. The final sample consisted of 48 children (22 females; Time 1 (*M* = 21.24 months, *SD* = 10.14, range = 9.13-48.09 months), Time 2 (*M* = 47.14 months, *SD* = 9.18, range = 32.27-72.05 months), and Time 3 (*M* = 80.19 months, *SD* = 6.12, range = 73.3-100.23 months). Included and excluded participants did not differ on demographic variables (*p*s > 0.05). Additionally, we examined the potential effect of child anxiety on attrition between Time 2 and Time 3 (anxiety was not measured at Time 1). There was no significant difference in reported child anxiety at Time 2 (n=84) relative to the children who returned approximately two years later to participate at Time 3 (n=50; p= .9). Finally, we examined the potential effect of child anxiety on EEG data quality inclusion and exclusion for both ERP tasks and found no significant differences for any ERP component (*ps*> .31). Institutional Review Board of the University of California, Davis, approved the experimental protocol, and informed consent was obtained from a parent or caregiver of each participant. Participants were compensated with a small toy and a gift card.

Measures

Child Anxiety Symptom Report

Modified Spence Children's Anxiety Scale-Parent. (MSCAS-Parent; Lagattuta et al., 2012) is a parent report of child worry and anxiety, created and modified from The Spence Children's Anxiety Scale (Spence, 1998) and The Spence Preschool Anxiety Scale (Spence et al., 2001). The short form version includes 18 items, reported using a 5-point Likert scale ranging from "never true at all" to "very often true", which measure child separation anxiety, physical injury fears, social phobia, panic attack, agoraphobia, and generalized anxiety disorder.

Dot Prob Task (DPT) Behavioral Measure of Child Attention Bias

DPT Task Design. The current study used a modified eye tracking version of the DPT. Pairs of faces were presented across two blocks with a total of 80 trials: 31 Angry- Neutral, 32 Happy-Neutral, and 17 Neutral-Neutral faces. Face- pairs were presented for 500ms, followed by a presentation of an asterisk probe for 1500ms (Figure 1). There were two trials types: congruent and incongruent. During congruent trials, the probe was presented in the same spatial location as an emotional face, either happy or angry. For incongruent trials, the probe was presented in same spatial location following a neutral face. Trial congruency was counterbalanced and randomized. Close-mouth face images of 28 adult actors (14 female) were selected from the NimStim stimulus set (Tottenham et al. 2009). Faces were cropped to the oval image of only the face, with little to no hair visible. Images were then randomized by identity, emotion (happy, angry, neutral), sex (male, female) and race (Caucasian, African American, Asian). Refer to Burris et al., 2017; *under review* for additional task design specifics. See Figure 1.

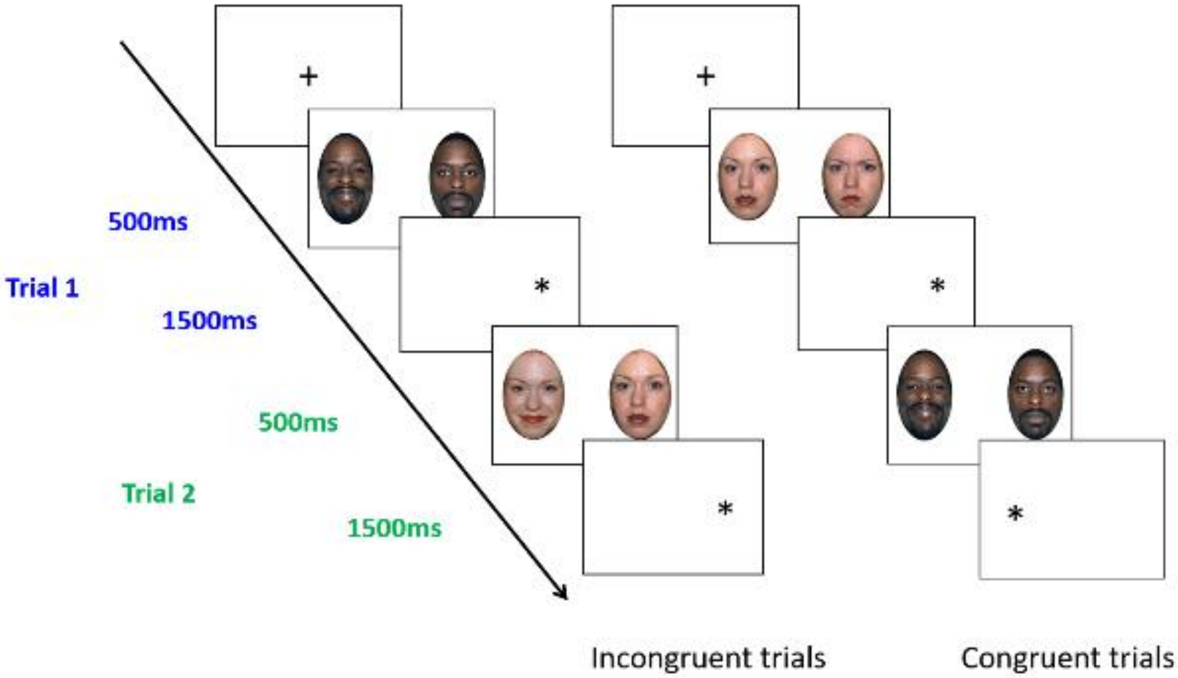


Figure 1. Dot Probe Task

Eye Tracking Procedure. At Time 1 and Time 2, stimuli were presented on a 17-inch Tobii 1750 LCD binocular eye tracker (1280 x 1024 pixels resolution) with a sampling rate of 50 Hz (Tobii Technology, Sweden). Tobii ClearView software was used to display stimuli and record gaze data, including a five-point calibration procedure. At Time 3, stimuli were presented on a 24-inch monitor with a Tobii X60 Studio binocular eye tracker (1280 x 1024 pixels resolution), sampling rate of 60 Hz. Tobii Pro Lab software was used to display and record data, including calibration. Missing data due to blinks was interpolated, and gaze from at least one eye was used to determine gaze coordinates.

Children were seated approximately 60 cm from the eye tracker monitor in a dimly lit and quiet room. At Time 1 and 2, children were seated in their caregiver's lap, but at Time 3 children were old enough to sit independently. Caregivers were asked to not interact with their children during the task presentation. The experiment began with a five-point calibration procedure, during which caregivers were asked to close their eye to verify gaze data collected was from the child. The calibration routine was repeated until all five points were captured. There was then a continuous presentation of 80 trials, for a total presentation time of 3 minutes.

DPT Data Preparation and Analysis. Using Tobii Pro Lab analysis software, eye tracking data was analyzed with the Area-of-Interest (AOI) tool (Tobii Technologies, Sweden). AOIs were created separately by defining an area around the face and the probe. The measure of interest was latency to first fixate to the asterisk probe. Visual attention to emotional faces (happy, angry) were calculated independently by subtracting the average latency to fixate to the asterisk probe on congruent trials from the average latency to fixate to the asterisk probe on incongruent trials. Positive values represent a vigilance for emotional faces, a score around zero indicates no bias towards emotional faces, and a negative value indicates bias away, or avoidance of emotional faces. Neutral-neutral trials serve as filler conditions and were not included in the analysis. Thus, the final DPT variable of behavioral attention bias consisted of Angry Bias scores and Happy Bias scores, reflecting the average latency to fixate to an asterisk probe on incongruent relative to congruent trials, wherein higher positive scores indicate greater attention bias to emotions (vigilance), and higher negative scores indicate greater attention bias away from emotions (avoidance).

ERP Measures of Child Neural Correlates of Attention to Emotional Stimuli

Children participated in two separate ERP tasks that measured their neural correlates of attention to emotional faces (Emotional Faces Task) and emotional objects and scenes (International Affective Picture System Task).

Emotional Faces Task. Children passively viewed 300 emotional facial expressions from the NimStim Face Stimulus Set (Tottenham et al., 2009). Facial expressions consisted of 6 emotion categories, each presented for 50 trials which included fearful faces, angry faces, happy faces, neutral faces, fearful faces at 40% intensity, and angry faces at 40% intensity. Reduced intensity of angry and fearful faces was created by morphing the actor's neutral expression with the full emotional expression. For the purposes of the present study, data collected for the reduced intensity emotions were not analyzed, only full intensity (100%) emotions. All images were 400 x 500 pixels in size and centrally presented on a grey background in fixed random order. Each image was presented for 1000ms and preceded by a fixation cross for a random duration between 800-1400ms. See Figure 2 for schematic of task.

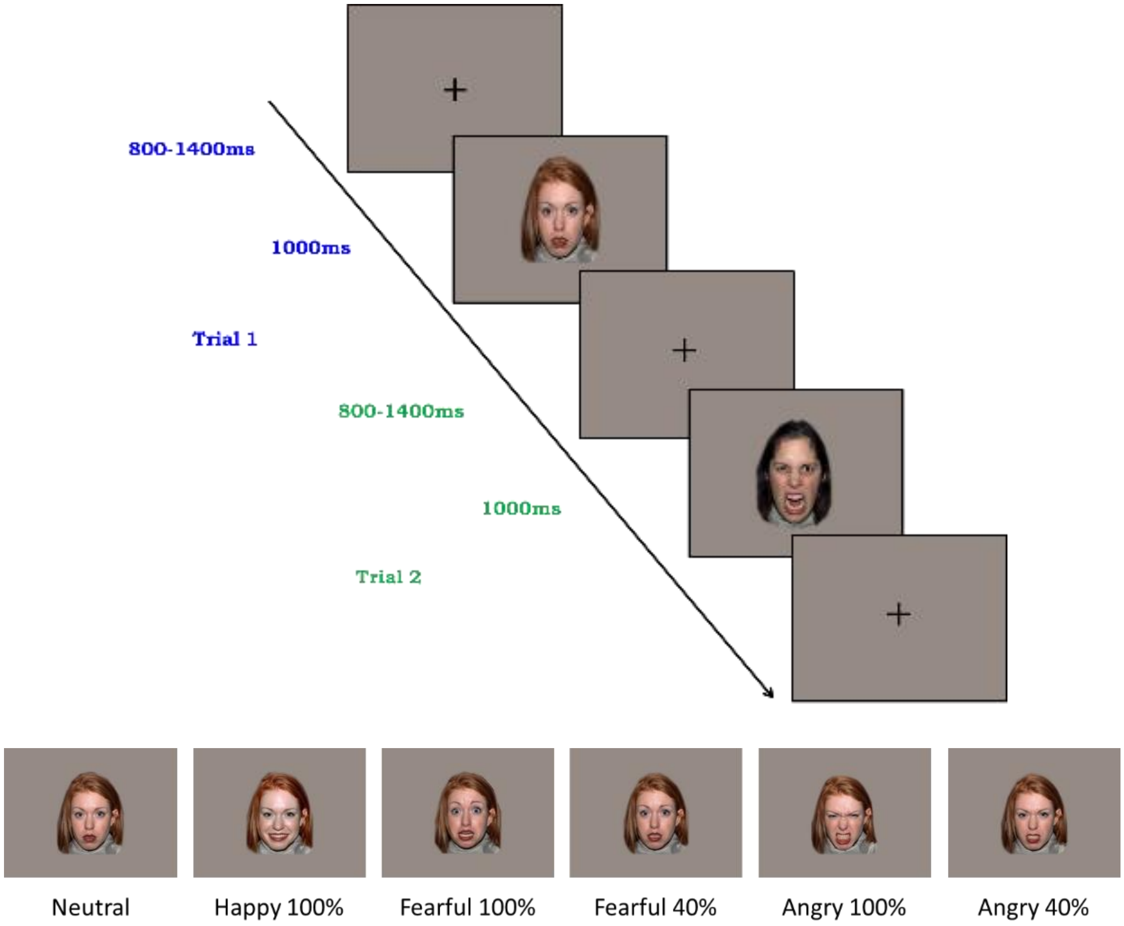


Figure 2. Emotional Faces ERP Task

International Affective Picture System (IAPS) Task. Children passively viewed 90 developmentally appropriate pictures selected from the International Affective Picture System (IAPS) and previously used with this age group (Dennis, 2009; Hajcak & Dennis, 2009). IAPS images consisted of 30 pleasant images designed to evoke positive emotions (i.e., kittens), 30 unpleasant images to evoke negative emotions (i.e., shark bearing teeth), and 30 neutral images depicting mundane and non-emotional scenes (i.e., chair). All images were centrally presented on a grey background, 729 x 602 pixels in size, and matched for luminance. Across six blocks, 30 images were presented, where 10 images per emotion category were randomly selected without replacement. Each image was presented twice for 2000 ms (total 180 trials, 60 per emotion category), and preceded by a fixation cross for a random duration between 500-1000ms. Stimuli were presented using Presentation (version 19.0 build 02.27.17) from Neurobehavioral Systems, Inc. (http://www.neurobs.com). See Figure 3 for schematic of task.

Given the aversive nature of the ‘unpleasant’ images, we confirmed that children’s looking did not differ across the unpleasant, pleasant, and neutral conditions in this task. Data from the monitor mounted camera that recorded children’s face and eyes during ERP data collection were coded off-line to verify that children were attending to all images during IAPS task, and to denote which children were moving or not attending to the images. Coding was completed by trained research assistants with high inter-rater reliability (ICC= .885, range= .809-.931, p = .000). Coders inspected each subject’s video recording frame by frame to log duration of looking time on a trial-by-trial basis. From the entire sample, 2 subjects were removed from this analysis: 1 for not completing the task and 1 did not have an available video due to technical difficulties with the recording. Importantly, there were no significant condition differences in duration of looking time in the whole sample (n = 48; *ps* > .56), sample sized based on LPP data quality (n = 42, *ps* > .58), or sample size based on P1 data quality n = 44, *ps* > .57), confirming that differences in ERP components across conditions could not be attributable simply to condition differences in looking duration.

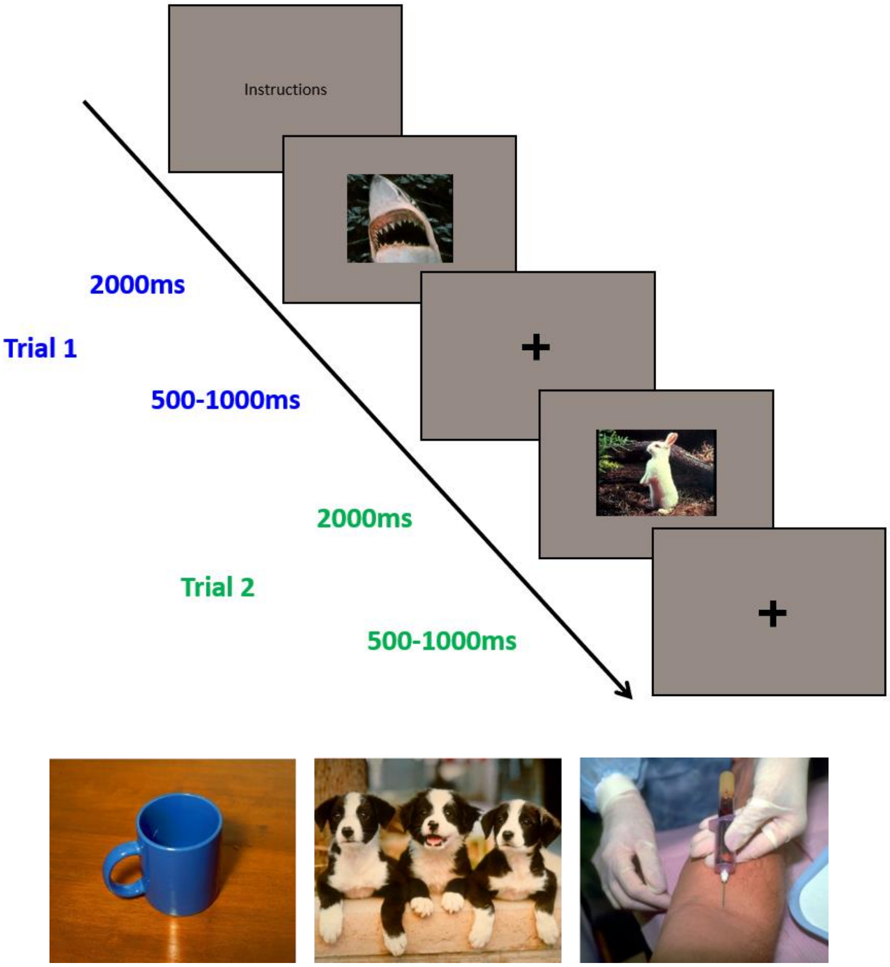


Figure 3. IAPS ERP Task

ERP Data Collection Procedure. Children participated first in the Emotional Faces ERP Task, followed by the IAPS ERP Task. Prior to both tasks, the child’s head circumference was measured to fit a soft cloth EASYCAP. Once the appropriate cap was fitted, electrode sites on the scalp were gently abraded with rubbing alcohol and electrolyte gel was used to keep impedances below 50 KΩ. Children were seated approximately 89 cm from the monitor in a dimly lit and electrically shielded room. A small camera was mounted at the top of the monitor and children’s eye movements were recorded throughout the experiment with the camera to ensure participants were attending to the stimuli.

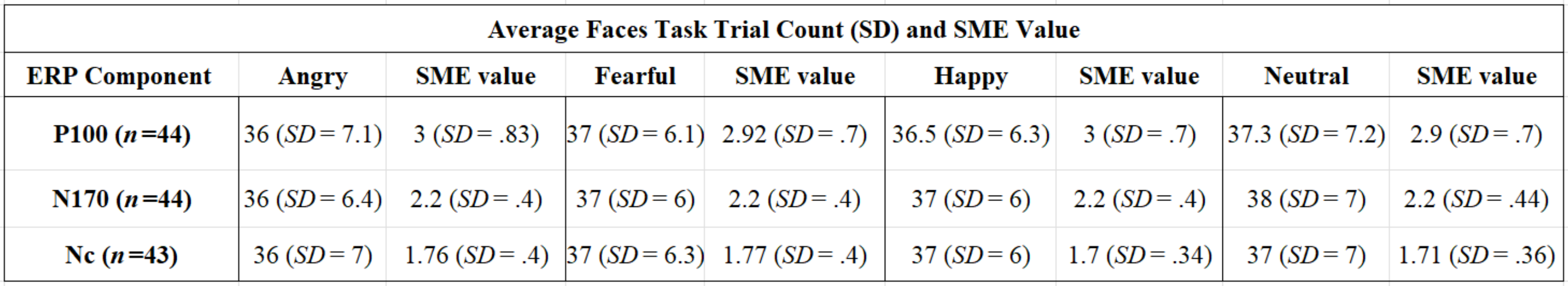
During EEG recording, an experimenter sat in the testing room next to the child to direct their attention to the screen and provide breaks as needed. Participants were instructed to sit still and attend to images. To prevent fatigue, after 1-2 blocks of testing, children were given a quick break during which they received stickers to put onto a sticker sheet. During ERP data collection, parents were seated in a separate room where they were able to watch video feed of their child in testing booth. Total ERP data collection took approximately 1.5- 2 hours to complete, with 30-45 minutes for EEG cap and scalp preparation, 45 minutes to complete the Emotional Faces task, and 20 minutes to complete the IAPS task, breaks included.

EEG Recording, Processing, and Analysis. For both ERP tasks, EEG data were collected using Ag-AgCl electrodes in a 64-channel EASYCAP with a Compumedics Neuroscan Synamp II amplifier (Neuroscan, 2011). Data were sampled at a rate of 1000 Hz. Four face electrodes were not used during data acquisition and an average reference channel was added to total 61 active electrodes. For each electrode, impedances were kept under 50 KΩ and all recordings were referenced to the vertex (Cz).

EEG recordings were processed with EEGLAB (version 14.1.2) (Delorme & Makeig, 2004) and ERPLAB (version 7.0.0) (Lopez-Calderon & Luck, 2014) toolboxes within MATLAB R2019a. To account for any lag between when the Presentation software sent a stimulus to the participant monitor and when the stimulus was displayed on screen, photosensor timing tests were conducted. Tests revealed an average timing delay of 26.21 ms, *SD*= 4.81, thus, prior to further data analysis event codes were shifted 26 ms to reflect the timing delay. Continuous EEG data was bandpass filtered at 0.1-30 Hz, followed by visual inspection and manual rejection of contaminated data, bad channel detection and replacement using spherical interpolation. Eye movement artifacts were identified and removed from the data using independent component analysis (ICA). After ICA decomposition, data were re-referenced using an average reference, baseline corrected, segmented into epochs with a pre-stimulus baseline of -200ms to 2000ms post-stimulus onset for the IAPS task, baseline of -100ms to 2000ms post-stimulus onset for the Faces task. Given the long time course of the LPP (2000ms), a linear detrend was applied to account for strong DC drifts in the IAPS Task data, which could disproportionally affect later-peaking components. Next, a sample-to-sample threshold function was applied to identify and remove epochs in which shifts in voltage were greater than 100 µV, and a simple voltage threshold function to flag and remove epochs in which voltage shifts were less than or greater than 120 µV (-/+ 120 µV).

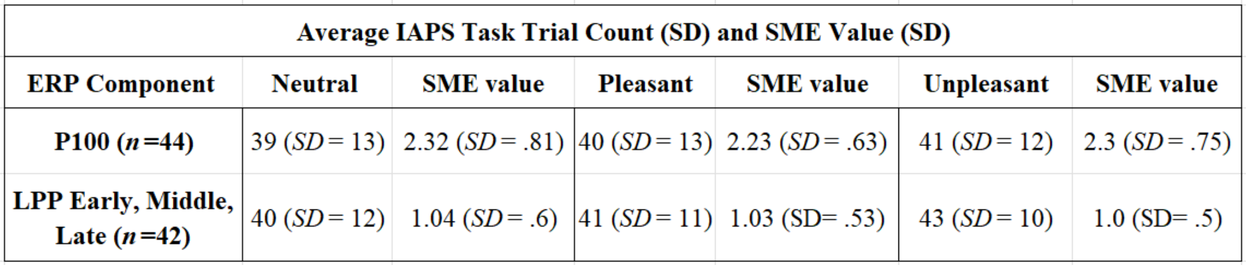
Average subject ERPs were computed for an objective measure of data quality of single-subject ERPs was calculated using the standardized measurement error (SME) of individual subject P1, N170, Nc, and LPP mean amplitude to determine subject exclusion (Luck et al., 2020). SME values for each condition (Faces Task: Neutral, Happy, Fearful, Angry; IAPS Task: Neutral, Pleasant, Unpleasant) in each ERP component were calculated, and outliers were identified as values greater than Q3 + 1.5(IQR) (interquartile range). Subjects were excluded if their SME was an outlier in any condition in any of the ERP components (P1, N170, Nc, LPP early, middle, late) (see *Table 1* for sample size summary). To determine if trial count varied across conditions, a repeated measures ANOVA was conducted. In each component, the number of trials did not significantly differ across conditions (*p*s > 0.05). Trial count was negatively correlated with SME values in each condition and ERP component, such that higher trial counts were associated with lower SME values (*p*s < 0.001). See Table 1 and Table 2 for summary.

Table 1. Emotional faces task summary of data quality and trial count per ERP component



Average Faces Task Trial Count (SD) and SME Value								
ERP Component	**Angry**	**SME value**	**Fearful**	**SME value**	**Happy**	**SME value**	**Neutral**	**SME value**
P100 (*n* =44)	36 (*SD* = 7.1)	3 (*SD* = .83)	37 (*SD* = 6.1)	2.92 (*SD* = .7)	36.5 (*SD* = 6.3)	3 (*SD* = .7)	37.3 (*SD* = 7.2)	2.9 (*SD* = .7)
N170 (*n* =44)	36 (*SD* = 6.4)	2.2 (*SD* = .4)	37 (*SD* = 6)	2.2 (*SD* = .4)	37 (*SD* = 6)	2.2 (*SD* = .4)	38 (*SD* = 7)	2.2 (*SD* = .44)
Nc (*n* =43)	36 (*SD* = 7)	1.76 (*SD* = .4)	37 (*SD* = 6.3)	1.77 (*SD* = .4)	37 (*SD* = 6)	1.7 (*SD* = .34)	37 (*SD* = 7)	1.71 (*SD* = .36)

Table 2. IAPS task summary of data quality and trial count per ERP component



Average IAPS Task Trial Count (SD) and SME Value (SD)						
ERP Component	**Neutral**	**SME value**	**Pleasant**	**SME value**	**Unpleasant**	**SME value**
P100 (*n* =44)	39 (*SD* = 13)	2.32 (*SD* = .81)	40 (*SD* = 13)	2.23 (*SD* = .63)	41 (*SD* = 12)	2.3 (*SD* = .75)
LPP Early, Middle, Late (*n* =42)	40 (*SD* = 12)	1.04 (*SD* = .6)	41 (*SD* = 11)	1.03 (SD= .53)	43 (*SD* = 10)	1.0 (SD= .5)

ERP Components for Analysis. Mean amplitude was computed separately for each subject, component of interest (P1, N170, Nc, and LPP), channel cluster (see details below), as well as a grand averaged across all subjects. All channel clusters and component epochs were based on prior research, and final epochs were determined by visual inspection of the grand average waveform, collapsed across all conditions to avoid bias due to visible condition effects.

For the P1 component, mean amplitude was measured at 100-150 ms for the Faces Task and 115-190 ms for the IAPS Task in occipital channels at O1, O2, and Oz (Bechor et al., 2019; Meaux et al., 2014; Wauthia & Rossignol, 2016). For the N170 component, mean amplitude was measured at 160-250 ms in posterior inferior channels (right: PO8, PO10; left: PO7, PO9) (Hinojosa et al., 2015). In line with prior research, P1 and N170 raw mean amplitude was computed for each emotional face and IAPS image (Hinojosa et al., 2015; Wauthia & Rossignol, 2016).

For the Nc component, mean amplitude was measured at 275-500 ms in central channels at C1, C2 (Dennis et al., 2009; Peltola et al., 2009). For the LPP component, mean amplitude was measured at three different time windows corresponding to early (300-600ms), middle (600-1000ms), and late (1000-2000ms) segments of the LPP (Dennis, 2009). LPP channel locations included O1, Oz and O2 in central channel regions, and posterior-inferior channels (right: PO8, PO10; left: PO7, PO9) (Hajcak & Dennis, 2009; Kujawa et al., 2013; Wauthia & Rossignol, 2016). See Figure 4. For the Nc and LPP ERP components, given that we were specifically interested in how sustained attention allocation to emotionally salient faces/scenes may moderate this relation, difference waves were computed to isolate the neural activity for affect (Moran et al., 2013; Richards et al., 2003; Luck, 2014; Wieser & Moscovitch, 2015).

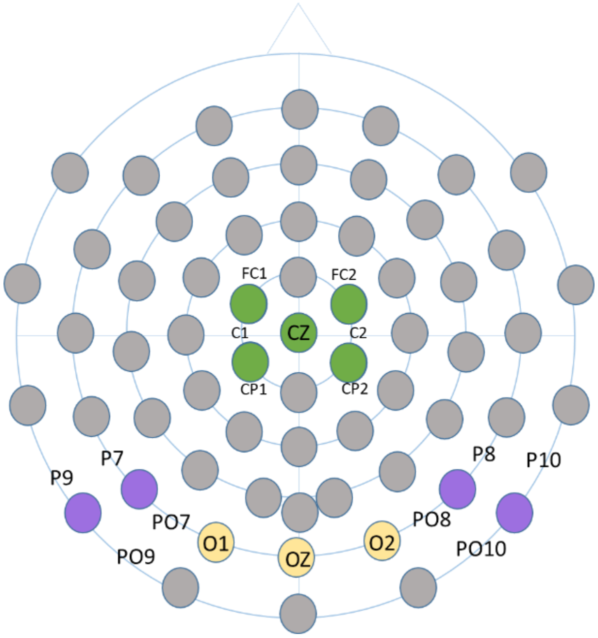


Figure 4. Channel clusters for analyzing the P1, N170, Nc, and LPP. Purple represents left and right posterior-inferior clusters (used for N170 and LPP left, right clusters), yellow represents central posterior-superior clusters (used for P1 and LPP midline cluster), green

represents central channels cluster (used for Nc). Labels indicate the international 10-10 electrode positions with respect to electrode montage used in the present study.

Overall Procedure

All visits began with an informed consent protocol and parents completed a demographic questionnaire form. At Time 1 and Time 2, children completed the DPT eye tracking task. Approximately 2 years (*M*= 26 months, *SD*= 3.2) from their Time 1 visit, children were brought back to the lab at Time 2 to complete the DPT eye tracking task while parents completed the MSCAS-Parent report of child anxiety. During the first session of Time 3 (approximately 2.5 years after Time 2; *M*= 31 months, *SD*= 8.3), children completed both ERP tasks while parents completed a battery of questionnaires assessing children's social-emotional wellbeing, including the MSCAS-Parent. Children came back into the lab for a second session within 2 weeks of the first (*M*= 8 days, *SD*=9.7) during which, children completed the DPT eye tracking task and a self-report measure of worry and anxiety (MSCAS-Child), while parents completed additional questionnaires assessing parent and child social-emotional wellbeing.

Data Analysis Plan

Preliminary Analyses

Determining Covariates. To account for sociodemographic differences in neural responses and child anxiety, we assessed age and sex as possible covariates in analyses. Prior research has documented age (Gold et al., 2020) and sex (Jalnapurkar et al., 2018) effects on anxiety, as well as age related changes in P1, N170, and LPP mean amplitude (MacNamara et al., 2016; Meaux et al., 2014), and sex related changes in LPP (Dennis & Hajcak, 2009). One-way RM ANOVAs and bivariate correlations were conducted to evaluate differences in age and sex among child anxiety, P1, N170, Nc, and LPP mean amplitude.

Preliminary Dot Probe Task Analyses. A repeated measures ANOVA was used to evaluate change in DPT Angry and Happy Bias scores across three time points. Further, bivariate correlations were conducted to evaluate the stability of Angry Bias and Happy Bias scores across the three time points.

Preliminary ERP Task Analyses. Repeated measures ANOVAs were conducted separately for each component (P1, N170, Nc, LPP early, middle, late) to examine group-level condition (Faces Task: Angry, Fear, Happy, Neutral; IAPS Task: Unpleasant, Pleasant, Neutral) effects. Greenhouse-Geisser correction was used to adjust degrees of freedom for ANOVAs that did not meet the assumption of sphericity. Corrections for multiple comparisons across condition and electrode cluster were performed using a false discovery rate (FDR) threshold of $p < 0.05$.

Focal Analyses

To address each of the 3 hypotheses, bivariate correlations calculated using Pearson's R were used to examine the relations among P1, N170, Nc, LPP early, middle, and late mean amplitudes, child anxiety, and DPT Angry Bias and Happy Bias Scores. To examine the combined effect of DPT (modeled separately per DPT time point and Angry/Happy bias scores) and ERPs (modeled separately per ERP component) in predicting child anxiety, moderation analyses were conducted using the PROCESS macro in SPSS (Hayes, 2018). Further, moderation analysis was also used to examine the longitudinal effect of DPT time points in predicting anxiety symptoms. Variables were mean centered and significant effects were determined using 95% confidence intervals based on 5000 bootstrap samples. Corrections for multiple comparisons across condition, electrode cluster, time window (LPP only) were performed using a false discovery rate (FDR) threshold of $p < 0.05$.

CHAPTER 4

Results

Preliminary Analyses

Determining Covariates. Prior to conducting higher level analyses, we examined sociodemographic differences in child anxiety as possible covariates. Child age was not associated with parent reported child anxiety (MSCAS-Parent) at Time 2 (r =.114, p =.442) or Time 3 (r =-.229, p =.13). Child sex did not significantly interact with child anxiety at Time 2 (p =.114) or Time 3 (p = .080). Given that age and sex were not significantly related to child anxiety, no covariates were used in subsequent analyses.

Dot Probe Task Analyses

To evaluate change in DPT Angry and Happy Bias scores across three time points in the participants who completed DPT at all timepoints, we conducted a 3 (Time Point: Time 1, Time 2, Time 3) by 2 (Emotion Bias: Angry Bias, Happy Bias) repeated measures ANOVA. Importantly, findings were the same as previously reported in the larger sample across Time 1 and Time 2 (Burris & Rivera, *in press*). There was a significant main effect of Emotion Bias, F (1, 44) = 7.37, p = .01. Post-hoc analyses revealed that Angry Bias scores (M= 67.62, SD= 11.6) were significantly greater than Happy Bias scores (M= 28.11, SD= 9.7): *mean difference* = 39.51, *S.E* = 14.56, p = .01, [10.12, 68.85]. There was no significant main effect of Time Point, F (2, 88) = .5, p = .61 (Time 1 (M= 43.6, SD= 10.9), Time 2 (M= 43.3, SD= 10.75), Time 3 (M= 56.74, SD= 13.7)). No significant interactions emerged, F (2, 88) = .43, p = .66. Further, bivariate correlations were conducted to evaluate the stability of Angry Bias and Happy Bias scores across the three time points. Analyses revealed that Angry Bias scores and separately, Happy Bias scores, were not significantly correlated across Time points 1, 2, or 3 (ps >.13) suggesting that individual time points of attention bias are not predictive of future time points and therefore do not support the *Integral Bias Model*. See Table 3 for summary.

Table 3. Summary of Age, DPT Bias Scores, and Anxiety Scores

	Age (months. Days)		**Angry bias**		**Happy bias**		**MSCAS-Parent Total**	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
Time 1 (*N*=48)	21.24 (10.14)	9.13-48.09	56.14 (112.4)	-241.05-258.02	32.87 (110)	-205.4-253.34	*N/A*	*N/A*
Time 2 (*N*=48)	47.14 (9.18)	32.27-72.05	72.25 (132.32)	-319.30-320.10	17.84 (85.04)	-152.04-213.52	28.38	1-85
Time 3 (*N*=48)	80.19 (6.12)	73.30-100.23	78.52 (128.42)	-213.7-498.92	34.95 (109.03)	-307.4-233.1	24.13 (*N*=45)	10-45

Emotional Faces Task Analyses

P1. Based on prior literature, P1 mean amplitude was evaluated in 100-150ms post-stimulus onset in occipital channels at O1, O2, and Oz. To evaluate P1 mean amplitude differences conditions, we conducted a one-way repeated measures ANOVA. In line with prior research showing no emotion modulation of P1 (Coch & Gullick, 2012; Kulke, 2019) , our data showed no significant differences in mean amplitude between conditions, at the group level, *F* (3, 129) = .198, *p* = .9 (Angry (*M*= 33.2, *SD*= 8.2), Fear (*M*= 32.8, *SD*= 8.95), Happy (*M*= 33.2, *SD*= 8.82), and Neutral (*M*= 32.9, *SD*= 9)). See Figure 5.

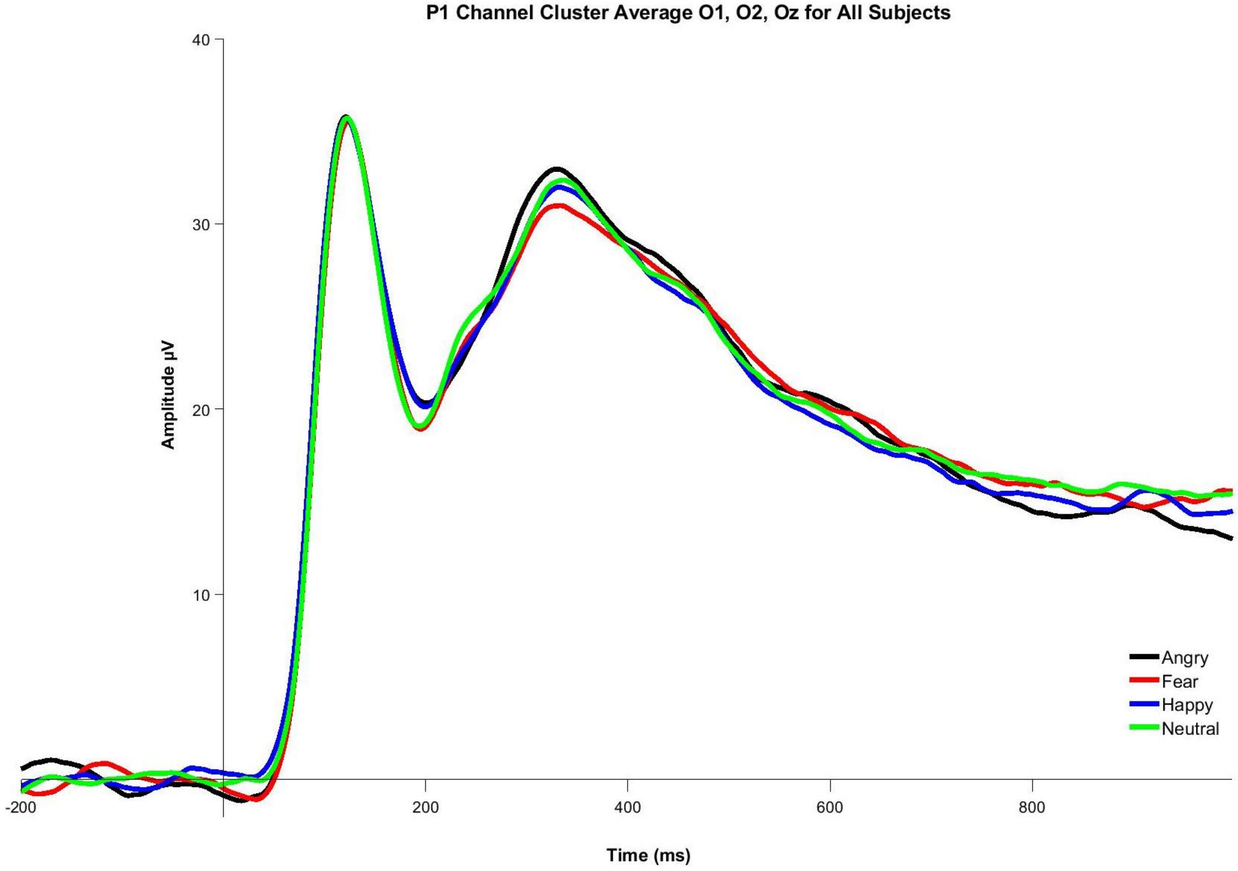


Figure 5. Emotional Faces Task Grand Averaged ERP waveforms for P100 (100-150ms)

N170. Based on prior literature, N170 mean amplitude was evaluated in 160-250 ms post-stimulus onset in posterior inferior channels (right: PO8, PO10; left: PO7, PO9) (Hinojosa et al., 2015). Importantly, to account for age-related differences of the P1 amplitude which precedes the N170 and can influence the magnitude of response, we corrected for the P1 by subtracting the mean amplitude of P1 from mean amplitude of N170 for each condition (Kuefner et al., 2010; Tian et al., 2015). To evaluate N170 mean amplitude differences conditions and channel clusters, we conducted a 4 (Condition: Angry, Fear, Happy, Neutral) by 2 (Cluster: Left, Right) repeated measures ANOVA. There were no significant differences in mean amplitude between conditions, *F* (3, 126) = .082, *p* = .97 (Angry (*M*= -29.16, *SD*= 1.32), Fear (*M*= -29.1, *SD*= 1.4), Happy (*M*= -28.9, *SD*= 1.4), and Neutral (*M*= -28.9, *SD*= 1.4)). There were no significant differences in mean amplitude between channel cluster, *F* (1, 42) = 1.4, *p* = .25 (Left Cluster (*M*= -29.6, *SD*= 1.5), Right Cluster (*M*= -28.4, *SD*= 1.4)). No significant interactions emerged, *F* (3, 126) = .244, *p* = .87. Given there were no main effects or interactions with channel cluster, N170 mean amplitude was collapsed across Left and Right channel clusters in subsequent analyses. See Figure 6.

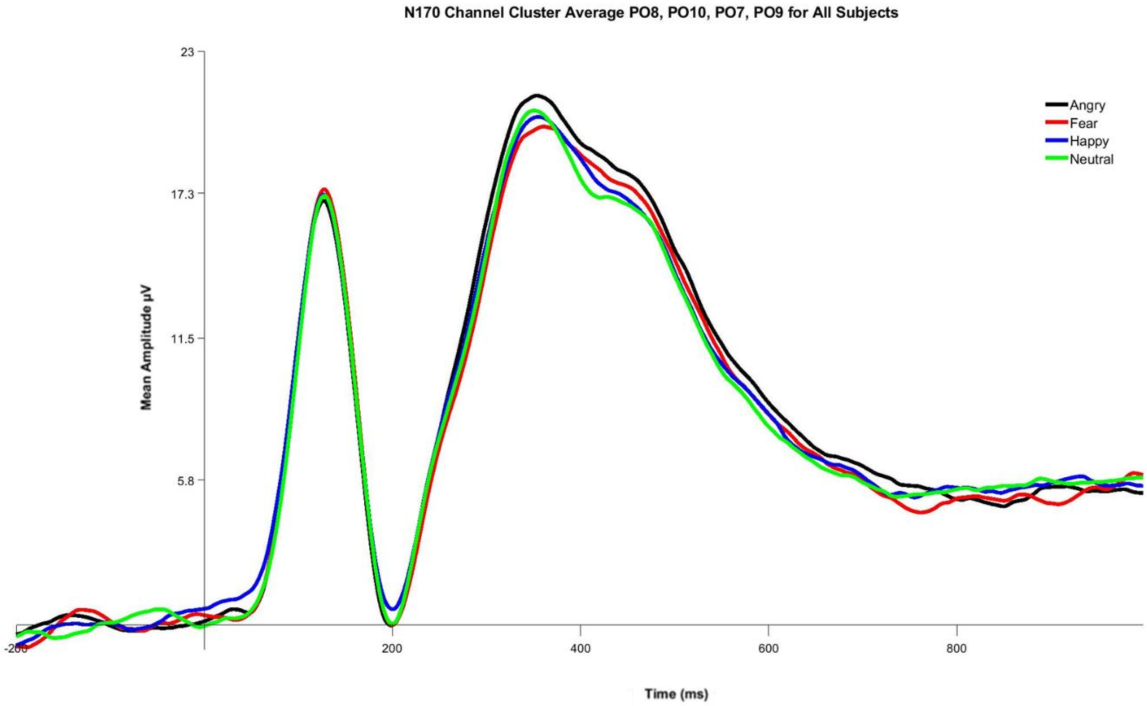


Figure 6. Emotional Faces Task Grand Averaged ERP waveforms for N170 (160-250ms)

Negative Central (Nc). Based on prior literature, Nc mean amplitude was evaluated in 275-500ms post-stimulus onset in central channels at C1, C2. To evaluate Nc mean amplitude differences across conditions, we conducted a one-way repeated measures ANOVA. There was a significant main effect of condition, *F* (3, 129) = 3.34, *p* = .021 (Angry (*M*= -10.13, *SD*= 3.4), Fear (*M*= -9.22, *SD*= 3.3), Happy (*M*= -9.35, *SD*= 2.8), and Neutral (*M*= -9.04, *SD*= 2.81)).

However, post-hoc analyses revealed that mean amplitude comparisons for all conditions were non-significant (*p*s >.25), and Angry relative to Neutral revealed a non-significant trend: *mean difference* = -1.09, *S.E* = .403, *p* = .059, [-2.2, .026]. See Figure 7.

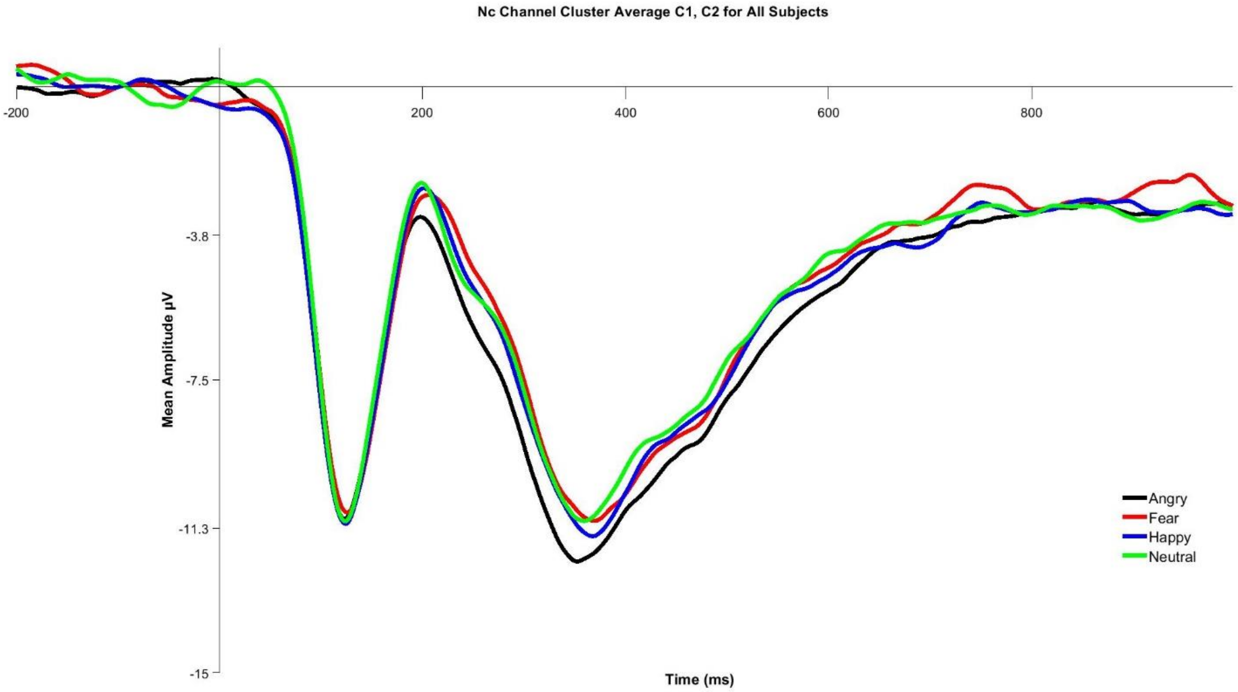


Figure 7. Emotional Faces Task Grand Averaged ERP waveforms for Nc (275-500ms)

IAPS Task Analyses

P1. Based on prior literature, P1 mean amplitude was evaluated in 115-190ms post-stimulus onset in occipital channels at O1, O2, and Oz. To evaluate P1 mean amplitude differences between neutral, pleasant, and unpleasant conditions, we conducted a one-way repeated measures ANOVA. There were no significant differences in mean amplitude between conditions, *F* (1.62, 76.2) = 1.68, *p* = .2 (Unpleasant (*M*= 35.4, *SD*= 12.05), Pleasant (*M*= 36.7, *SD*= 12.33), and Neutral (*M*= 35.3, *SD*= 14). See Figure 8.

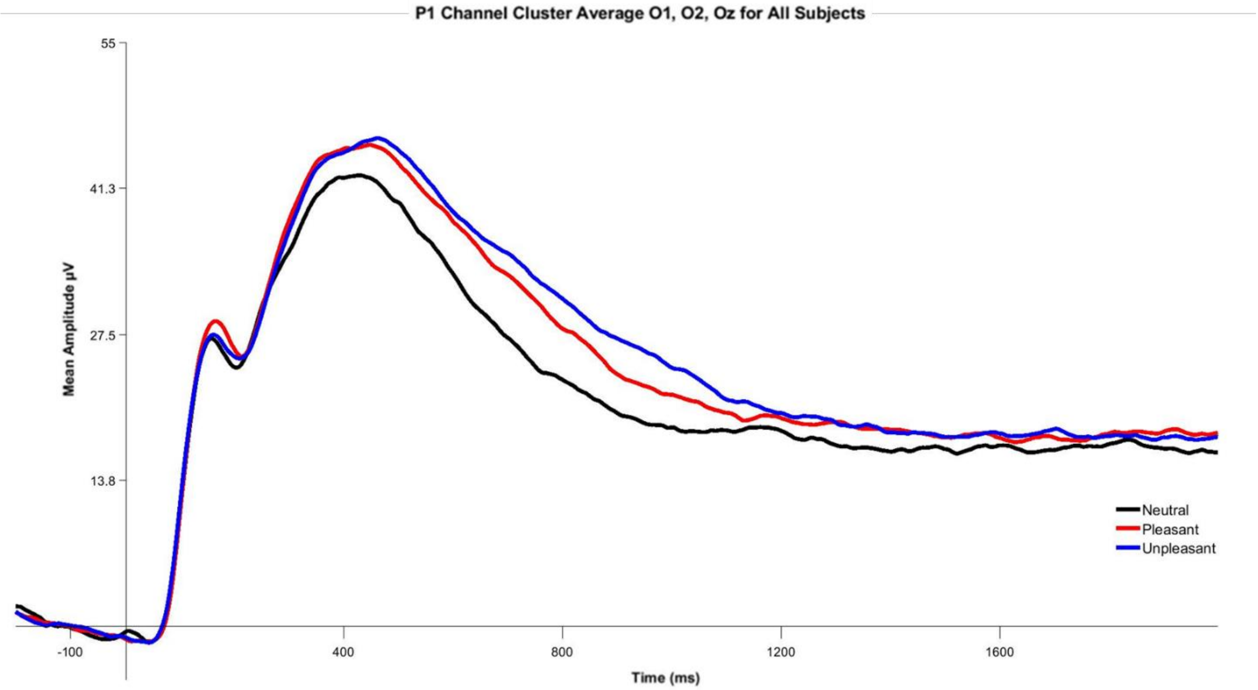


Figure 8. IAPS Task Grand Averaged ERP waveforms for P100 (115-190ms)

LPP. Based on prior literature, LPP mean amplitude was evaluated in the left (PO7, PO9) and right (PO8, PO10) posterior-inferior and central (O1, Oz, O2) posterior-superior channels across three different time windows: early 300-600ms, middle 600-1100ms, late 1100-2000ms. Repeated measures of analyses of variance (ANOVAs) were run to evaluate condition and channel cluster differences in LPP mean amplitude. Specifically, we ran 3 (condition: neutral, pleasant, unpleasant) by 3 (cluster: left, central, right) repeated measures ANOVAs for each LPP time window. Significant interaction effects were followed by paired-sample t-tests.

In the LPP early time window (300-600ms) there was a significant main effect of condition, *F* (1.53, 62.9) = 36.4, *p* = .000. Post-hoc analyses revealed that mean amplitude for Unpleasant (*M*= 43.1, *SD*= 1.5) and Pleasant (*M*= 42.4, *SD*= 1.5) were significantly greater than Neutral (*M*= 38.7, *SD*= 1.4): *mean difference* = 4.34, *S.E* = .64, *p* = .000, [2.73, 5.94] and *mean difference* = 3.7, *S.E* = .59, *p* = .001, [2.2, 5.18], respectively. There was also a main effect of channel cluster, *F* (2, 82) = 33.6, *p* = .000. Post-hoc analyses revealed that mean amplitude was significant different in all three clusters: left channel cluster (*M*= 34.8, *SD*= 1.5), center channel cluster (M= 47.1, SD=1.9), and right channel cluster (*M*= 42.3, *SD*= 1.5). Center cluster was greater than left cluster: *mean difference* = 12.4, *S.E* = 1.7, *p* = .000, [8.0, 16.7] and right cluster: *mean difference* = 4.8, *S.E* = 1.4, p = .006, [1.21, 8.4]; right cluster was greater than left cluster: *mean difference* = 7.5, *S.E* = 1.4, p = .000, [4.2, 10.9]. No significant interactions emerged, *F* (3.3, 135.13) = .533, *p* = .68.

In the LPP middle time window (600-1100ms) there was a significant main effect of condition, *F* (1.7, 68.6) = 74.6, *p* = .000. Post-hoc analyses revealed significant differences in mean amplitude for all conditions: Unpleasant (*M*= 29.5, *SD*= 1.05), Pleasant (*M*= 27, *SD*= .96), and Neutral (*M*= 23, *SD*= 1.1). Unpleasant was greater than Pleasant: *mean difference* = 2.5, *S.E* = .41, *p* = .000, [1.5, 3.5] and Neutral: *mean difference* = 6.61, *S.E* = .61, *p* = .000, [5.1, 8.1]; Pleasant was greater than Neutral: *mean difference* = 4.1, *S.E* = .6, *p* = .000, [2.7, 5.6]. There was also a main effect of channel cluster, *F* (1.7, 68.2) = 43.1, *p* = .000. Post-hoc analyses revealed that mean amplitude was significant different in all three clusters: left channel cluster (*M*= 22, *SD*= .97), center channel cluster (*M*= 31.1, *SD*=1.4), and right channel cluster (*M*= 26.5, *SD*= 1.1). Center cluster was greater than left cluster: *mean difference* = 9.3, *S.E* = 1.2, *p* = .000, [6.3, 12.2] and right cluster: *mean difference* =4.6, *S.E* = .99, p = .000, [2.1, 7.0]; right cluster was greater than left cluster: *mean difference* = 4.7, *S.E* = .8, p = .000, [2.8, 6.7]. There was a significant interaction of condition and cluster, *F* (3.3, 133.3) = 3.14, *p* = .024, such that mean amplitude of the LPP showed the same pattern (Unpleasant > Pleasant > Neutral) in each channel cluster but overall LPP amplitude varied by cluster channel location (Center > Right > Left).

In the LPP late time window (1100-2000ms) there was a significant main effect of condition, *F* (1.64, 67.2) = 20.4, *p* = .000. Post-hoc analyses revealed that mean amplitude for Unpleasant (*M*= 18.3, *SD*= .66) and Pleasant (*M*= 18.02, *SD*= .66) were significantly greater than Neutral (*M*= 16.6, *SD*= .66): *mean difference* = 1.7, *S.E* = .3, *p* = .000, [.94, 2.4] and *mean difference* = 1.41, *S.E* = .33, *p* = .000, [.59, 2.22], respectively. Mean amplitude for Pleasant and Unpleasant conditions did not differ: *mean difference* = .27, *S.E* = .21, *p* = .62, [-.25, .8]. There was also a main effect of channel cluster, *F* (2, 76.2) = 58.5, *p* = .000. Post-hoc analyses revealed that mean amplitude was significant different in all three clusters: left channel cluster (*M*= 13.9, *SD*= .66), center channel cluster (*M*= 21.9, *SD*= .96), and right channel cluster (*M*= 16.9, *SD*= .67). Center cluster was greater than left cluster: *mean difference* = 8.1, *S.E* = .84, *p* = .000, [5.9, 10.2] and right cluster: *mean difference* =4.9, *S.E* = .76, p = .000, [3.1, 6.9]; right cluster was greater than left cluster: *mean difference* = 3.1, *S.E* = .65, p = .000, [1.4, 4.7]. No significant interactions emerged, *F* (3.1, 126.3) = .24, *p* = .88. See Figure 9.

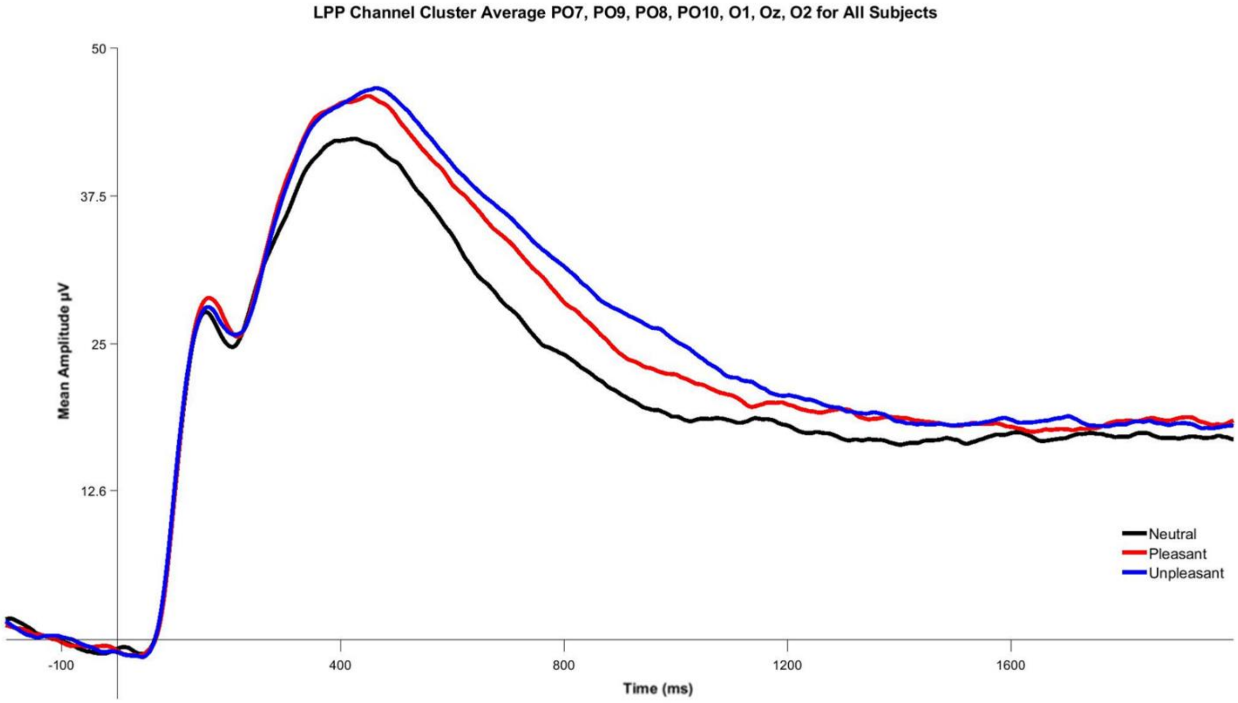


Figure 9. IAPS Task Grand Averaged ERP waveforms for LPP across left, midline, and right electrode clusters early 300-600ms, middle 600-1100ms, late 1100-2000ms.

Focal Analyses

Hypothesis 1. Children's behavioral assessment of attention bias to threat (assessed with eye tracking) will longitudinally predict their neural correlates of attention to emotional stimuli (assessed with ERPs).

To examine the relation between DPT and ERPs, bivariate correlations were conducted between DPT Angry Bias and Happy Bias scores measured at Time 1, 2, 3 and Faces Task P1/N170/Nc and separately, IAPS Task P1/ LPP early, middle, late measured at Time 3. FDR corrections were made for multiple comparisons (see data analysis plan above for details).

Faces Task P1 for Neutral (r= .374, p = .012, adjusted p =.048) condition was significantly correlated with DPT Angry Bias scores at Time 2, such that enhanced P1 for Neutral faces was associated with increased DPT Angry Bias scores. P100 for Angry faces (r= .307, p = .043, adjusted p =.086) showed a similar pattern of activity, though a non-significant trend following correction for multiple comparisons. No significant associations between Faces Task P1 for Happy/ Fearful, and DPT Angry/Happy Bias scores at Time 1, 2, 3 emerged (*ps* > .05). There was no significant association (*ps* > .05) between Faces Task N170 and DPT Angry Bias and Happy Bias scores at Time 1, 2, 3. See Figure 10.

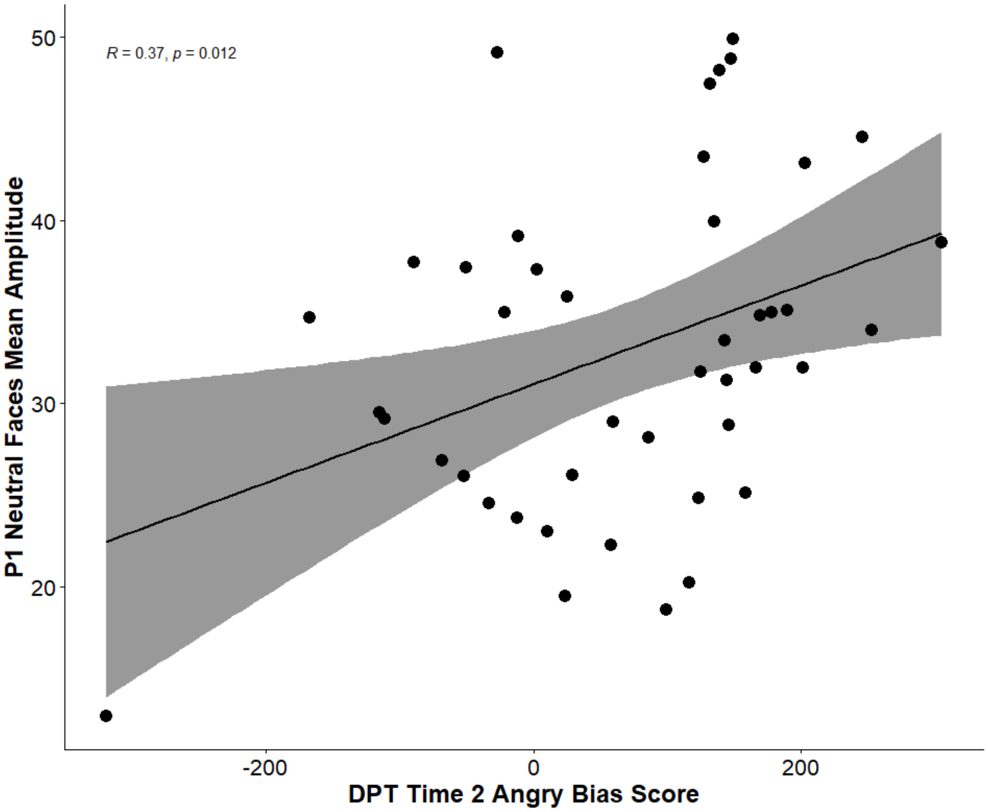


Figure 10. Scatterplot depicting the association between mean amplitude P1 for Neutral Emotional Faces at Time 3 and DPT Angry Bias scores at Time 2.

Faces Task Nc Fearful-Neutral differences waves and DPT Angry Bias score at Time 1 revealed a trend level correlation (*r*= .359, *p* = .017, adjusted *p* =.051), such that enhanced Nc for Fearful faces relative to Neutral faces was associated with increased Angry Bias scores.

IAPS Task for P1 Neutral (*r*= .410, *p* = .006, adjusted *p* =.018), Pleasant (*r*= .355, *p* = .018, adjusted *p* =.019), and Unpleasant (*r*= .371, *p* = .013, adjusted *p* =.018) conditions were significantly correlated with DPT Angry Bias scores at Time 2, such that enhanced P1 was associated with increased Angry Bias scores. See Figure 11.

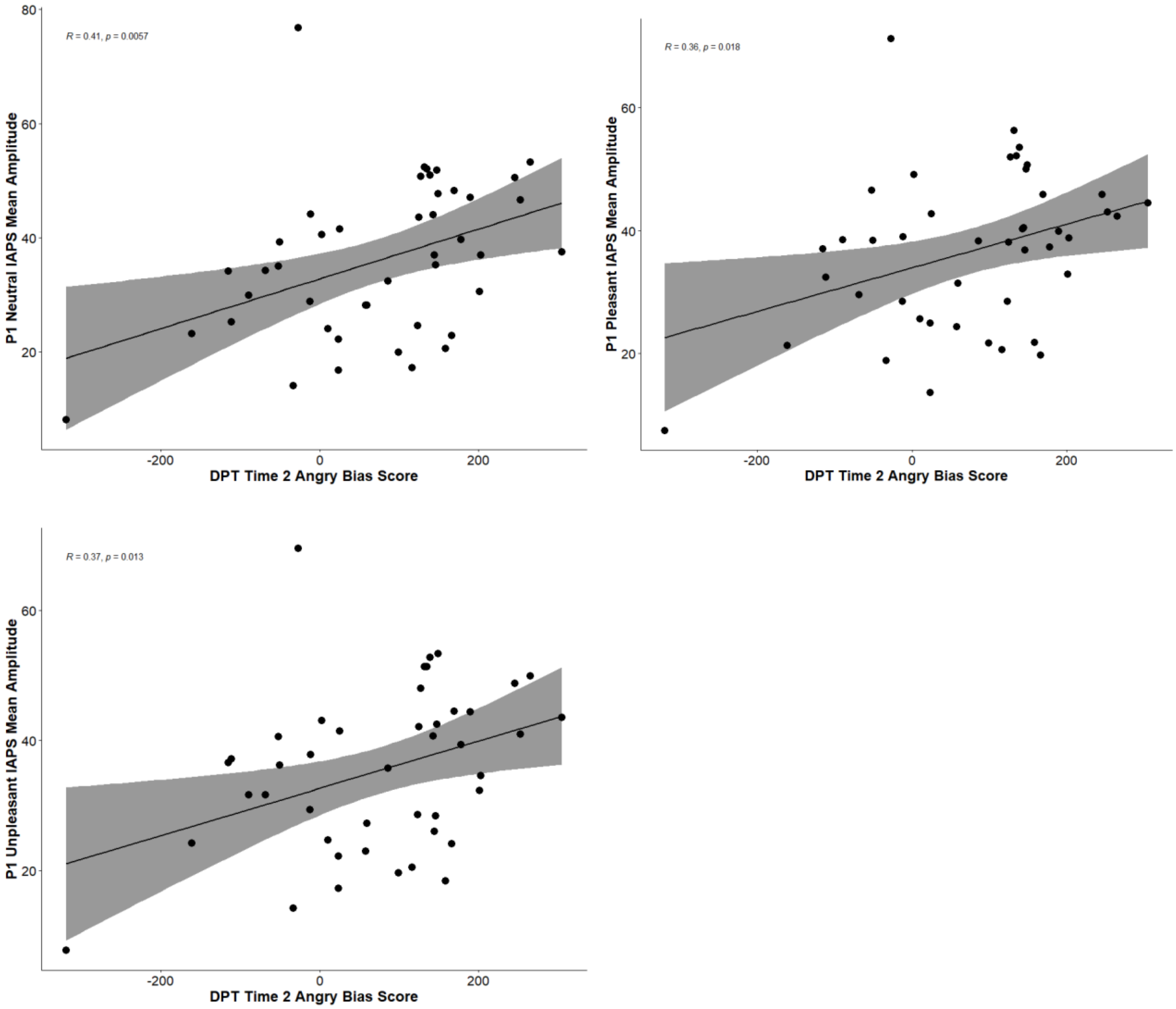


Figure 11. Scatterplots depicting the association between mean amplitude P1 for Neutral, Pleasant, and Unpleasant IAPS images IAPS Task at Time 3 and DPT Angry Bias Scores at Time 2.

IAPS Task for LPP early, middle, late time windows for Neutral, Pleasant, and Unpleasant difference waves were not significantly correlated with DPT Angry/Happy Bias scores at Time 1, 2, 3 (*ps* > .05).

Hypothesis 2a. Children's behavioral assessment of attention bias to threat (eye tracking) will longitudinally predict anxiety symptoms.

Paired sample t-tests revealed no significant differences in parent report of child anxiety (Parent-MSCAS total) at Time 2 (M= 28.3, SD= 20.3) relative to Time 3 (M= 24.13, SD= 9; t (44) = 1.83, p= .074).

To examine the relation between DPT and child anxiety, bivariate correlations were conducted between DPT Angry and Happy Bias scores measured at Time 1, Time 2, Time 3, and Parent-MSCAS at Time 2, and Time 3. DPT Angry Bias scores at Time 1 were not related to child anxiety at Time 2 (r= .16, p = .28) or Time 3 (r= .172, p = .26, adjusted p =.39). DPT Angry Bias scores at Time 2 were non-significantly related to child anxiety at Time 2 (r= .26, p = .07, adjusted p = .21), and significantly related at Time 3 (r= .41, p = .005, adjusted p =.015). See Figure 12. DPT Angry Bias scores at Time 3 were not related to child anxiety at Time 2 (r= -.06, p = .71) or Time 3 (r= .02, p = .89, adjusted p =.89). Happy Bias scores were not significantly related to child anxiety at Time 2 or Time 3 (p's >.16). These again fail to support the *Integral Bias Model*.

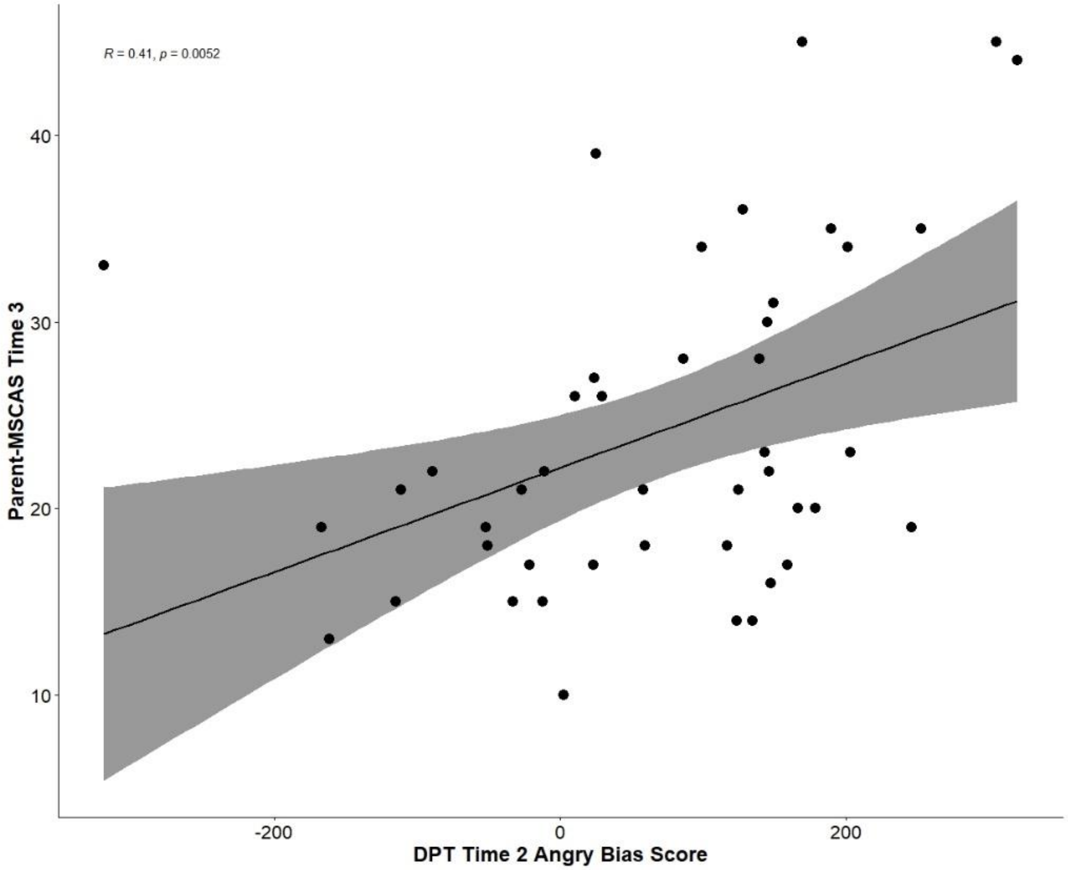


Figure 12. Scatterplot depicting the association between DPT Angry Bias Scores at Time 2 and child anxiety (Parent-MSCAS) at Time 3.

Further, to examine whether the persistence of attention bias for threat present earlier in development would predict anxiety symptoms, moderation analysis was used to examine the combined effect of DPT Angry Bias at Time 1 and 2, Time 2 and 3, and Time 1 and 3 in predicting anxiety symptoms at Time 3. Specifically, we conducted separate moderation models for each DPT Angry Bias time point as predictor, each DPT Angry Bias time point as moderator, with Time 3 parent- reported MSCAS as outcome. The combination of two developmental time points of attention bias for threat measured with the DPT Angry Bias scores was not predictive of child anxiety (*p*s > .16), suggesting that the addition of more than one behavioral measure of attention bias over time does not add to our understanding of the emergence of anxiety symptoms.

Hypothesis 2b. Neural correlates of the brain (ERPs) indexing early and later temporal indices of selective attention to emotional stimuli will predict children's anxiety symptoms.

To examine the relation between ERPs and child anxiety, bivariate correlations were conducted between Faces Task P1/N170/Nc and separately, IAPS Task P1/ LPP early, middle, late at Time 3, and Parent-MSCAS at Time 2 and Time 3. FDR corrections were made for multiple comparisons.

Faces Task P1 for Happy and Neutral conditions were not significantly related to child anxiety at Time 2, and P1 for Fearful (*r*= .286, *p* = .06, adjusted *p* =.06) and Angry (*r*= .291, *p* = .055, adjusted *p* =.07) conditions showed a nonsignificant trend with child anxiety. No significant associations between P1 conditions and child anxiety at Time 3 emerged (*ps* > .27).

Faces Task N170 revealed no significant associations between N170 for face conditions and child anxiety at Time 2 or 3 (*ps* > .47). There were also no significant associations between Nc for faces conditions and child anxiety at Time 2 or 3 (*ps* > .12).

IAPS Task for P1 Neutral (*r*= .376, *p* = .012, adjusted *p* =.036), Pleasant (*r*= .363, *p* = .015, adjusted *p* =.015), and Unpleasant (*r*= .372, *p* = .013, adjusted *p* =.019) conditions were significantly correlated with child anxiety at Time 2, such that enhanced P1 was associated with increased parental report of anxiety symptoms. No significant associations between LPP early, middle, late time window conditions and child anxiety at Time 3 emerged (*ps* > .31). No significant associations between LPP early, middle, late time windows for IAPS Neutral, Pleasant, Unpleasant conditions and child anxiety at Time 2 or 3 emerged (*ps* > .28). See Figure 13.

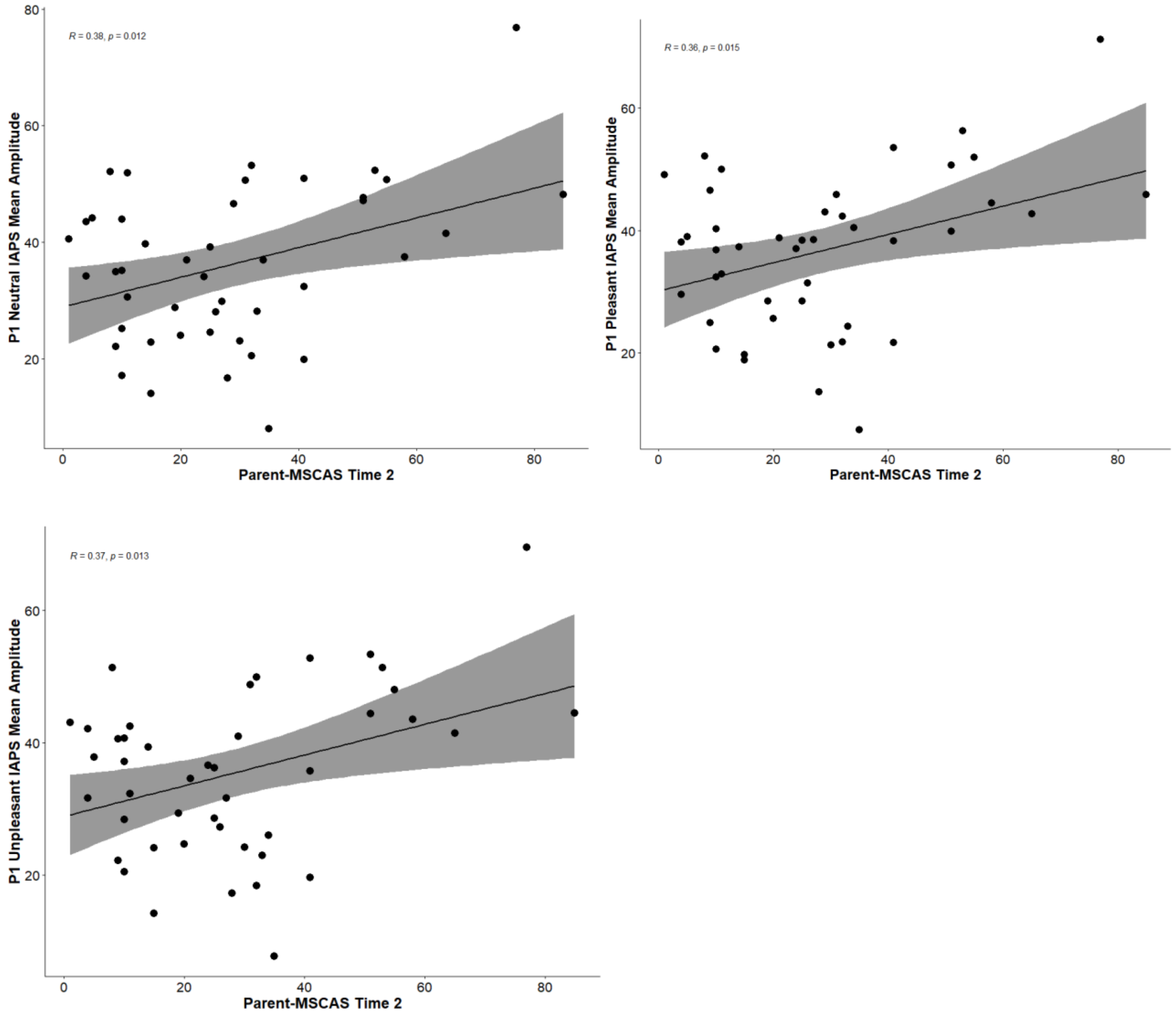


Figure 13. Scatterplots depicting the association between mean amplitude P1 for Neutral, Pleasant, and Unpleasant IAPS images IAPS Task at Time 3 and child anxiety (Parent-MSCAS) at Time 2.

Hypothesis 3. A combined effect of neural correlates of the brain (ERPs) and temporally sensitive behavioral indices (eye tracking) will predict children's anxiety symptoms.

Moderation analysis was used to examine the combined effect of DPT and ERP components (evaluated separately P1, N170, Nc, LPP) in predicting child anxiety. As DPT Time

1 and 3 were not significant predictors of child anxiety at Time 2 and 3, the following models used DPT Time 2 as the predictor and child anxiety at Time 3 as the outcome variable.

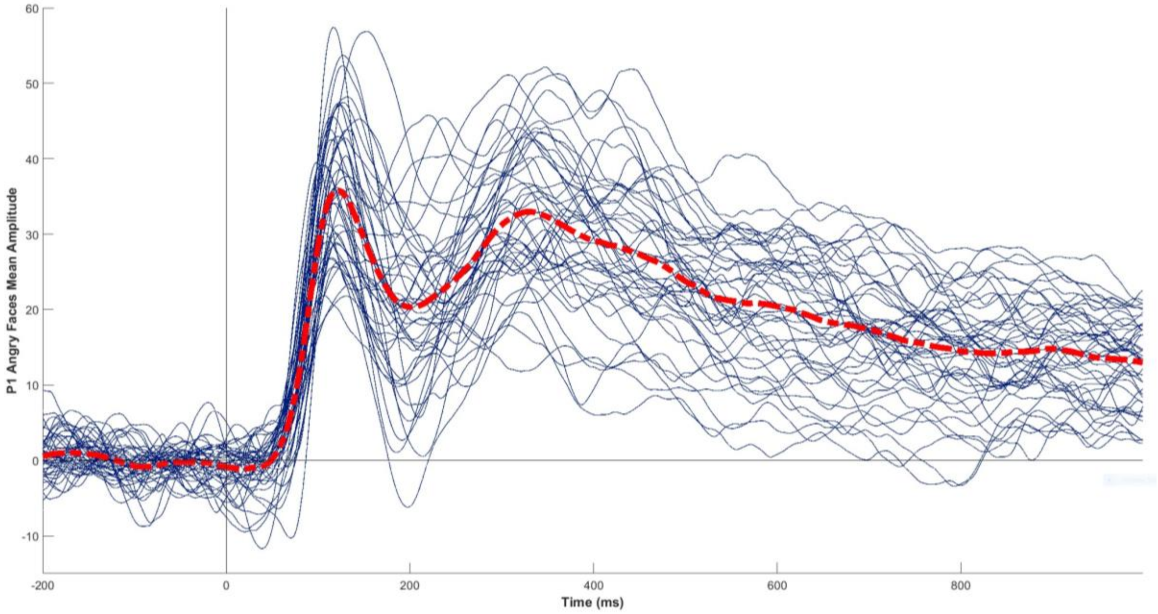
For early visual components, P1 and N170, raw mean amplitude to each condition served as the moderator. For Nc and LPP ERP components, given that we were specifically interested in how sustained attention allocation to emotionally salient faces/scenes may moderate this relation, difference waves were computed to isolate the neural activity for affect: Faces Task: Angry- Neutral, Fearful- Neutral, Happy- Neutral; IAPS Task: Unpleasant- Neutral, Pleasant- Neutral (add reference). Moderation analyses were performed using the PROCESS v4.0 macro for SPSS v26.0.0.1.

DPT and Neural Correlates of Emotional Faces Predicting Anxiety. Specifically, we conducted separate moderation models for each DPT bias score (Angry Bias, Happy Bias) as predictor, for each ERP component (Angry, Fearful, Happy, Neutral condition) as moderator, with parent- reported MSCAS total as outcome. Across all ERP components, DPT Happy Bias was not predictive of child anxiety (*p*s > .11).

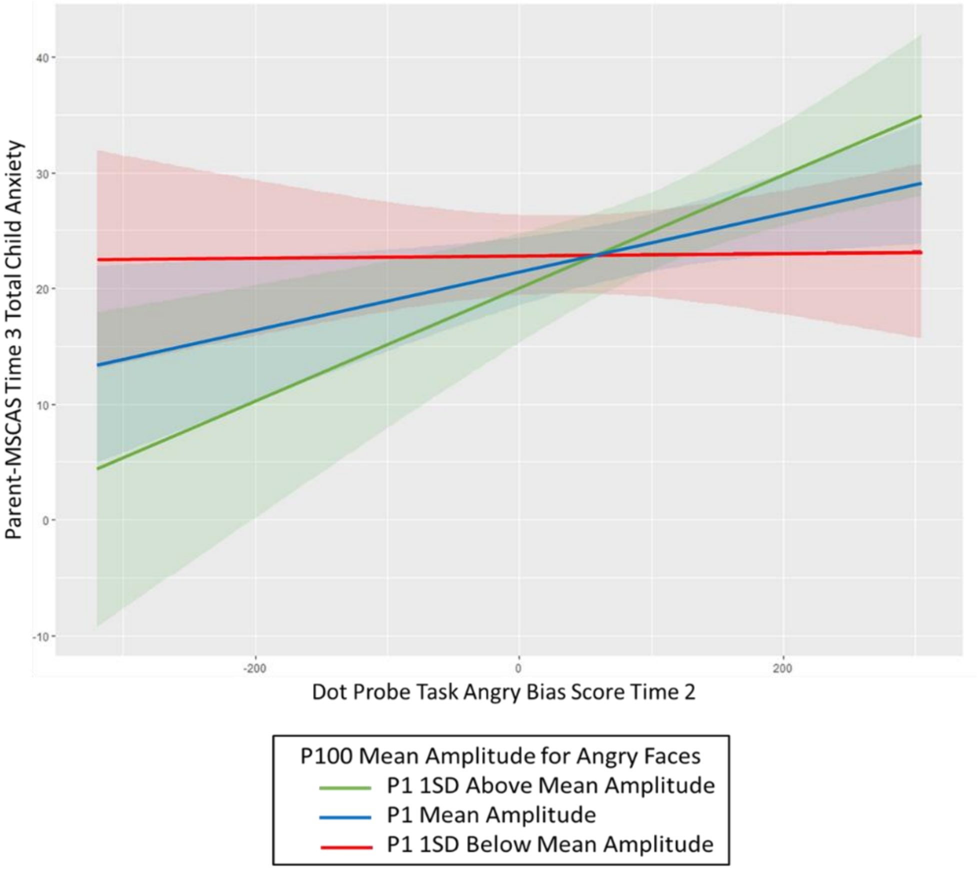
P100

P1 Angry and Happy Face conditions significantly moderated the relation between DPT Angry Bias at Time 2 and Parent-MSCAS at Time 3. The interaction of DPT Time 2 Angry Bias x P1 Angry Faces was a significant predictor of change in Parent-MSCAS Time 3, *b* = .0029, *SE* = .0012, *t* = 2.44, *p* = .019 (FDR adjusted *p* = .038), such that at high levels (1 SD above mean) of P1 mean amplitude for Angry faces (*b* =.049, SE = .016, *t* = 3.14, *p* = .0035, CI95% [.017, .081]) and mean level of P1 (*b* =.025, SE = .010, *t* = 2.41, *p* = .021, CI95% [.004, .046]) significantly predicted Parent-MSCAS anxiety, but not at low levels of P1 (1 SD below mean) (*b* =.0012, SE = .013, *t* = .092, *p* = .93, CI95% [-.025, .027]). See Figure 14. The interaction of DPT

Time 2 Angry Bias x P1 Happy Faces was a significant predictor of change in Parent-MSCAS Time 3, *b* = .0025, *SE* = .0009, *t* = 2.65, *p* = .012 (FDR adjusted *p* = .046), such that at high levels (1 SD above mean) of P1 mean amplitude for Happy faces (*b* =.044, SE = .014, *t* = 3.21, *p* = .003, CI95% [.016, .071]) and mean level of P1 (*b* =.022, SE = .010, *t* = 2.18, *p* = .035, CI95% [.002, .042]) significantly predicted Parent-MSCAS anxiety, but not at low levels of P1 (1 SD below mean) (*b* = -.0002, SE = .012, *t* = -.017, *p* = .99, CI95% [-.025, .025]). See Figure 15. P1 to Fearful Faces (*b* = .0021, *SE* = .0011, *t* = 1.88, *p* = .067 (FDR adjusted *p* = .067) and Neutral Faces (*b* = .002, *SE* = .001, *t* = 2.08, *p* = .044 (FDR adjusted *p* = .059) showed similar patterns but were non-significant predictors of change in Parent-MSCAS Time 3. DPT Happy Bias and P100 was not predictive of child anxiety (*p*s > .21).



(A)



(B)

Figure 14. (A) depicts individual variability in children's P1 mean amplitude response to Angry Emotional Faces. Each line represents a single subject ERPs with a dotted line representing the grand average mean. (B) depicts the moderating role of P1 for Angry Faces at Time 3 in the relation between DPT Angry Bias at Time 2 and child anxiety at Time 3.

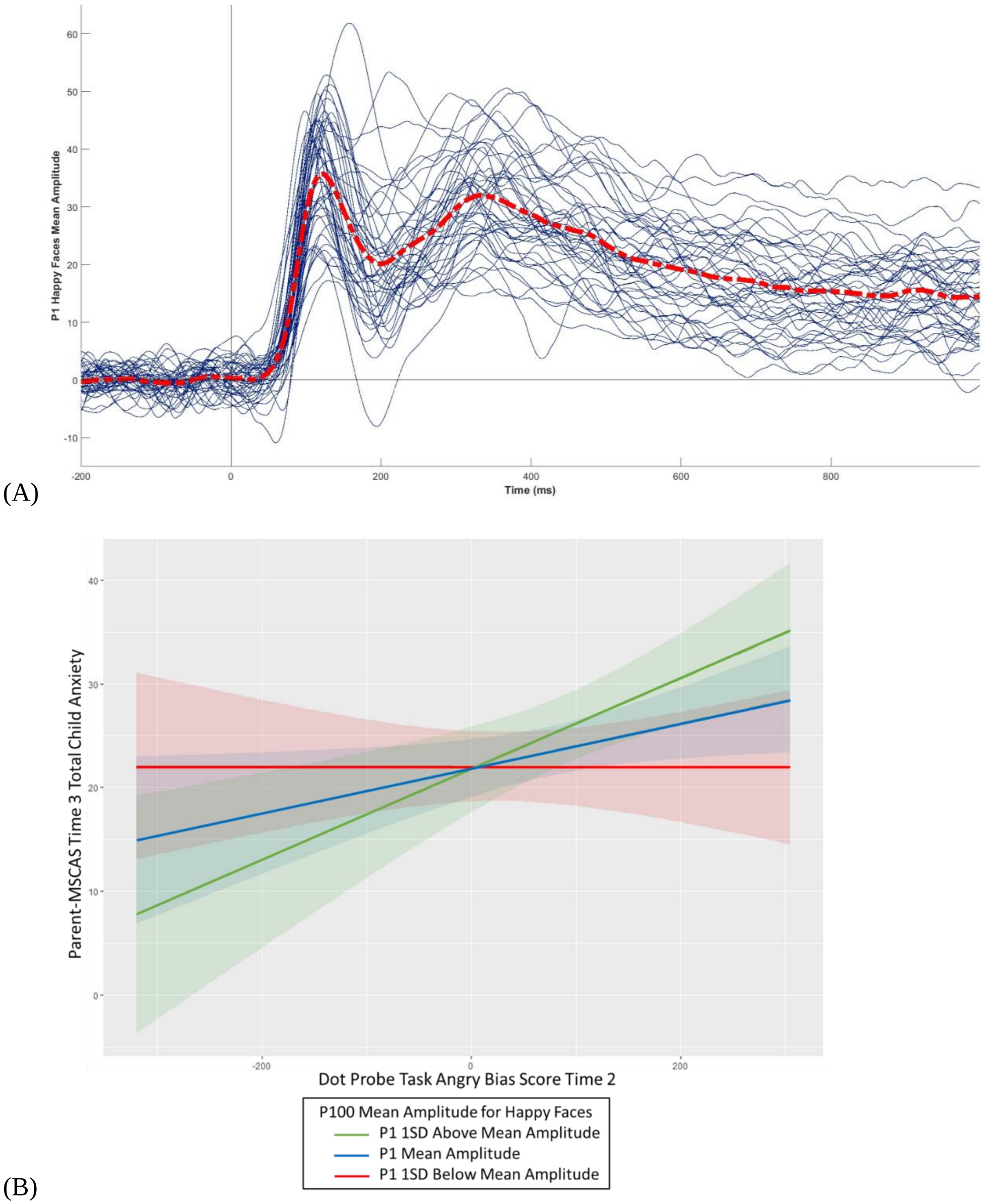


Figure 15. Figure (A) depicts individual variability in children's P1 mean amplitude response to Happy Emotional Faces. Each line represents a single subject ERPs with a dotted line

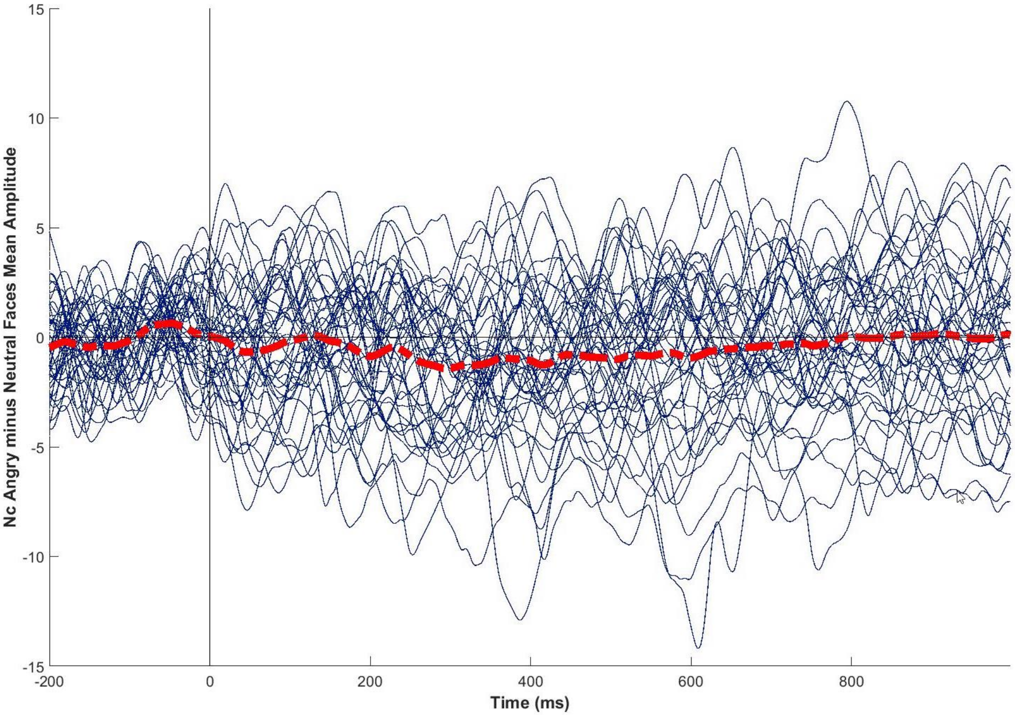
representing the grand average mean. Figure (B) depicts the moderating role of P1 for Happy Faces at Time 3 in the relation between DPT Angry Bias at Time 2 and child anxiety at Time 3.

N170

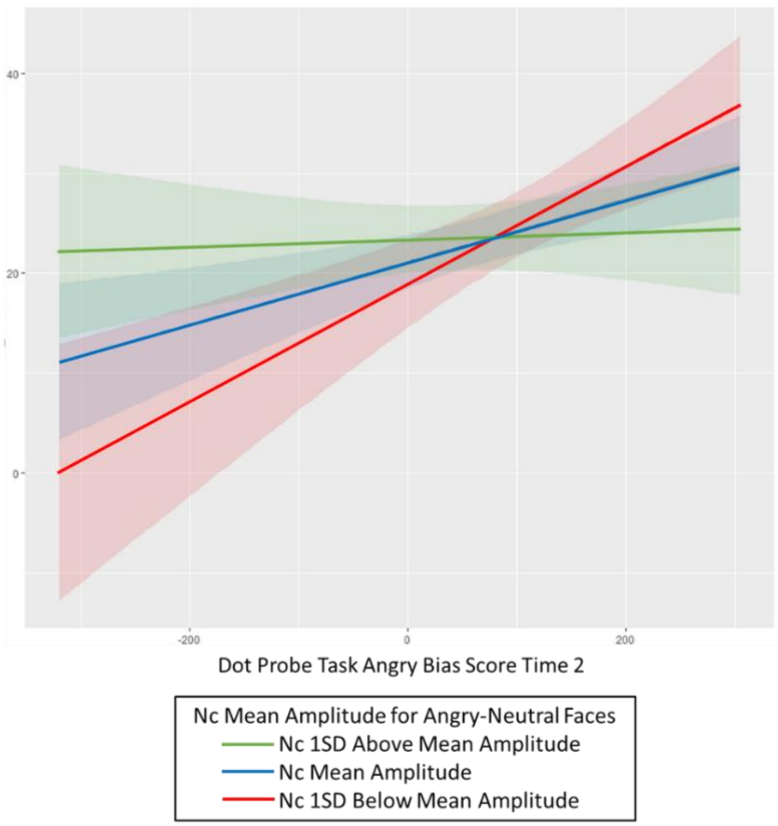
N170 did not significantly moderate the relation between DPT Time 2 Angry Bias/Happy Bias and child anxiety measured by Parent-MSCAS Time 3 in any of the four face conditions (*p*s > .11).

Negative Central (Nc)

Nc Angry- Neutral significantly moderated the relation between DPT Angry Bias at Time 2 and Parent-MSCAS at Time 3.The interaction of DPT Time 2 Angry Bias x Nc Angry- Neutral was a significant predictor of change in Parent-MSCAS Time 3, b = -.0110, *SE* = .0036, t = -3.064, p = .004 (FDR adjusted p = .012), such that at high levels (1 SD above mean) of Nc mean amplitude for Angry- Neutral faces (b =.059, SE = .015, t = 3.94, p = .0003, CI95% [.029, .089]) and mean level of Nc (b =.031, SE = .0097, t = 3.22, p = .003, CI95% [.012, .051]) significantly predicted Parent-MSCAS anxiety, but not at low levels of Nc (1 SD below mean) (b =.0004, SE = .011, t = .325, p = .75, CI95% [-.019, .027]). See Figure 16. Nc Fearful- Neutral Faces (b = .0051, *SE* = .0053, t = .967, p = .34 (FDR adjusted p = .51) and Happy- Neutral Faces (b = -.002, *SE* = .005, t = -.512, p = .612 (FDR adjusted p = .612) were non-significant predictors of change in Parent-MSCAS Time 3. DPT Happy Bias was not predictive of child anxiety (*p*s > .11).


15
10
5
0
-5
-10
-15
Nc Angry minus Neutral Faces Mean Amplitude
-200
0
200
400
600
800
Time (ms)

(A)


40
20
0
Parent-MSCAS Time 3 Total Child Anxiety
-200
0
200
Dot Probe Task Angry Bias Score Time 2
Nc Mean Amplitude for Angry-Neutral Faces
Nc 1SD Above Mean Amplitude
Nc Mean Amplitude
Nc 1SD Below Mean Amplitude

(B)

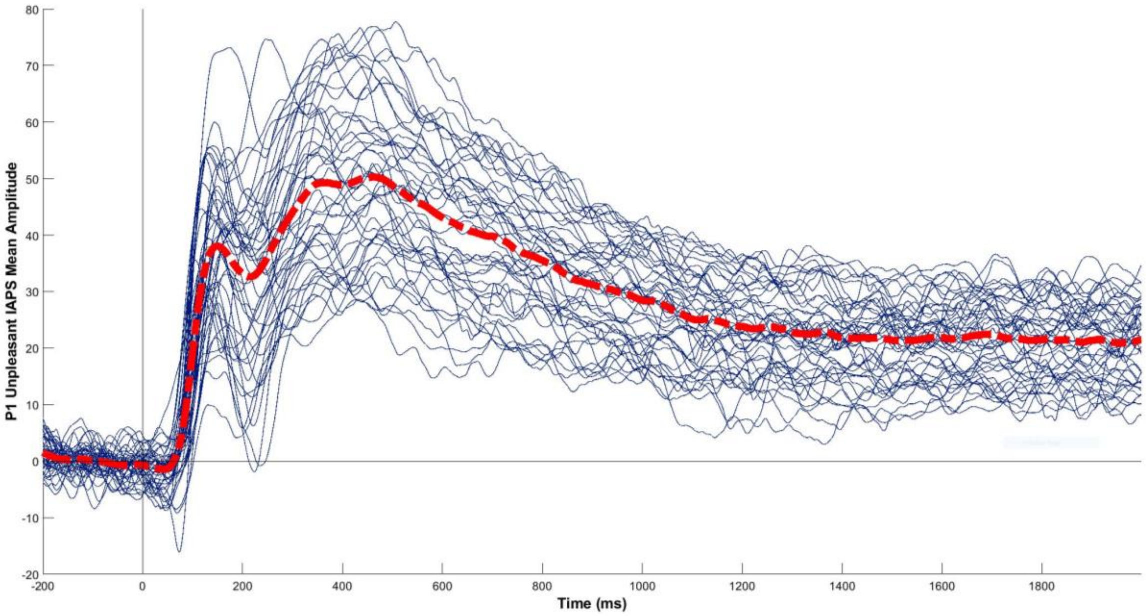
Figure 16. Figure (A) depicts individual variability in children's Nc mean amplitude response to Angry- Neutral Emotional Faces. Each line represents a single subject ERPs with a dotted line representing the grand average mean. Figure (B) depicts the moderating role of Nc for Angry-Neutral Faces at Time 3 in the relation between DPT Angry Bias at Time 2 and child anxiety at Time 3.

DPT and Neural Correlates to Emotion-Evoking Scenes (IAPS) Predicting Anxiety.

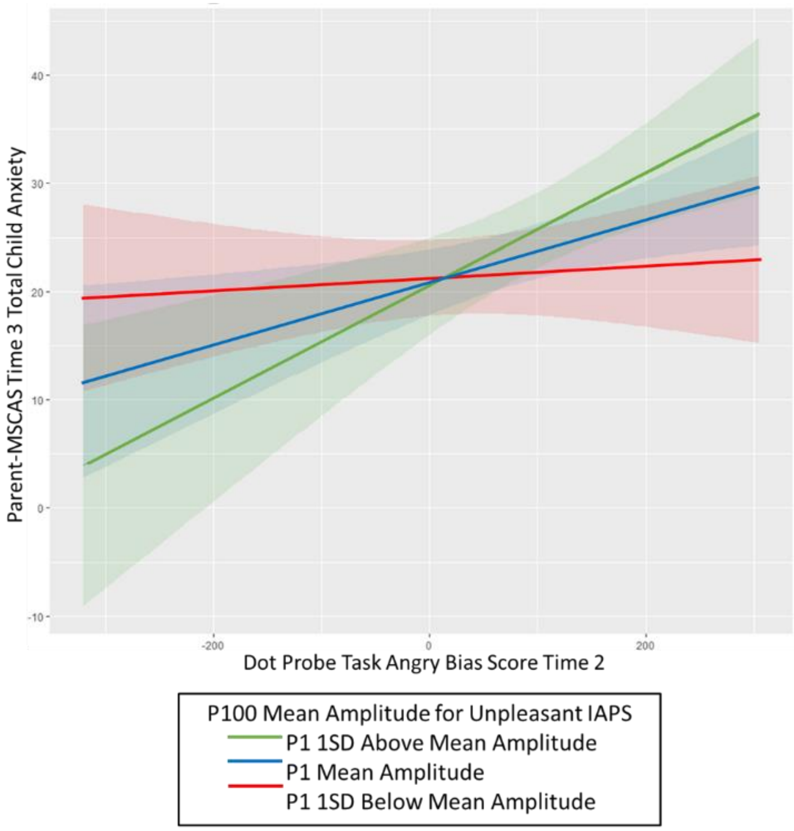
Specifically, we conducted separate moderation models for each DPT bias score (Angry Bias, Happy Bias) as predictor, for each ERP component (Unpleasant, Pleasant, Neutral condition) as moderator, with parent- reported MSCAS total as outcome.

P100

P1 to Unpleasant, Pleasant, and Neutral scenes significantly moderated the relation between DPT Angry Bias at Time 2 and Parent-MSCAS at Time 3.The interaction of DPT Time 2 Angry Bias x P1 Unpleasant scenes was a significant predictor of change in Parent-MSCAS Time 3, *b* = .002, *SE* = .0007, *t* = 2.67, *p* = .011 (FDR adjusted *p* = .017), such that at high levels (1 SD above mean) of P1 mean amplitude for Unpleasant scenes (*b* =.052, SE = .015, *t* = 3.37, *p* = .002, CI95% [.021, .083]) and mean level of P1 (*b* =.029, SE = .011, *t* = 2.66, *p* = .012, CI95% [.007, .051]) significantly predicted Parent-MSCAS anxiety, but not at low levels of P1 (1 SD below mean) (*b* =.006, SE = .012, *t* = .47, *p* = .64, CI95% [-.019, .03]). See Figure 17. The interaction of DPT Time 2 Angry Bias x P1 Pleasant scenes was a significant predictor of change in Parent-MSCAS Time 3, *b* = .002, *SE* = .0007, *t* = 2.84, *p* = .007 (FDR adjusted *p* = .022), such that at high levels (1 SD above mean) of P1 mean amplitude for Pleasant scenes (*b* =.055, SE = .016, *t* = 3.54, *p* = .001, CI95% [.024, .086]) and mean level of P1 (*b* =.031, SE = .011, *t* = 2.83, *p* = .008, CI95% [.009, .052]) significantly predicted Parent-MSCAS anxiety, but not at low levels of P1 (1 SD below mean) (*b* =.006, SE = .012, *t* = .514, *p* = .61, CI95% [-.018, .03]). See Figure 18. The interaction of DPT Time 2 Angry Bias x P1 Neutral scenes was a significant predictor of change in Parent-MSCAS Time 3, *b* = .002, *SE* = .0007, *t* = 2.6, *p* = .024 (FDR adjusted *p* = .024), such that at high levels (1 SD above mean) of P1 mean amplitude for Neutral scenes (*b* =.052, SE = .017, *t* = 3.1, *p* = .004, CI95% [.018, .086]) and mean level of P1(*b* =.03, SE = .011, *t* = 2.61, *p* = .013, CI95% [.007, .053]) significantly predicted Parent-MSCAS anxiety, but not at low levels of P1 (1 SD below mean) (*b* =.007, SE = .013, *t* = .59, *p* = .56, CI95% [-.018, .033]). See Figure 19.

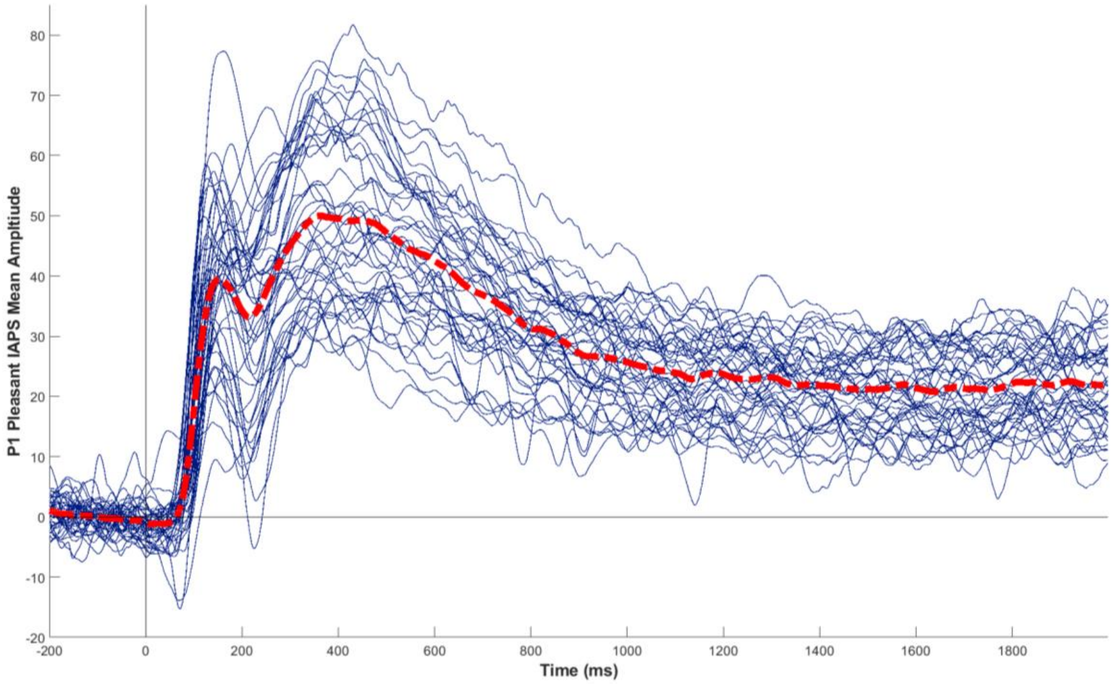


(A)

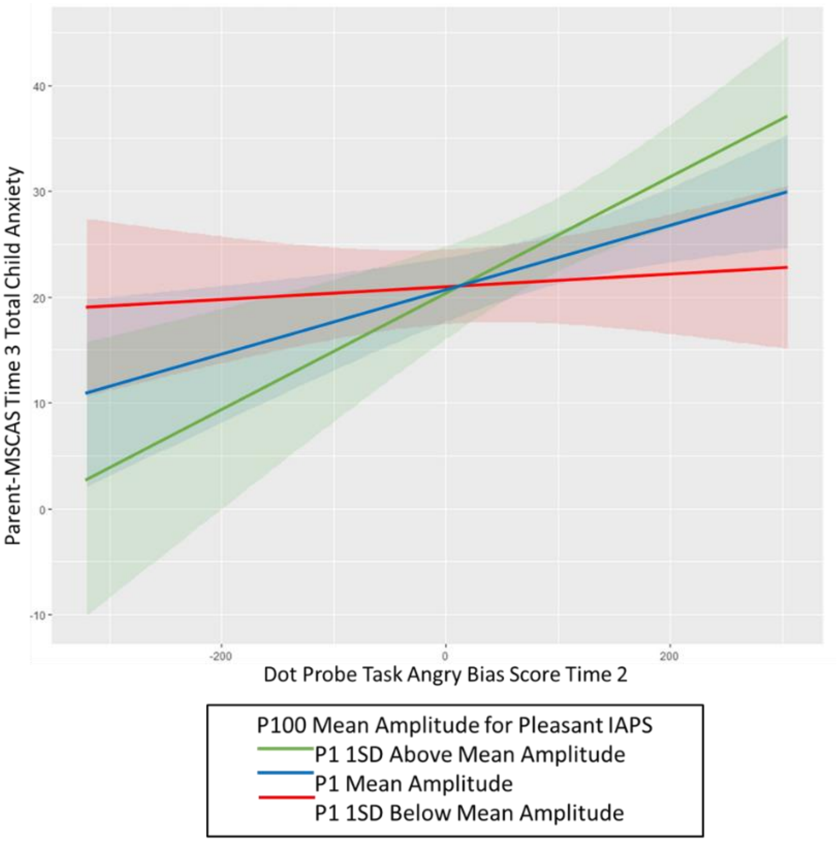


(B)

Figure 17. Figure (A) depicts individual variability in children's P1 mean amplitude response to Unpleasant IAPS images. Each line represents a single subject ERPs with a dotted line representing the grand average mean. Figure (B) depicts the moderating role of P1 for Unpleasant IAPS images at Time 3 in the relation between DPT Angry Bias at Time 2 and child anxiety at Time 3.

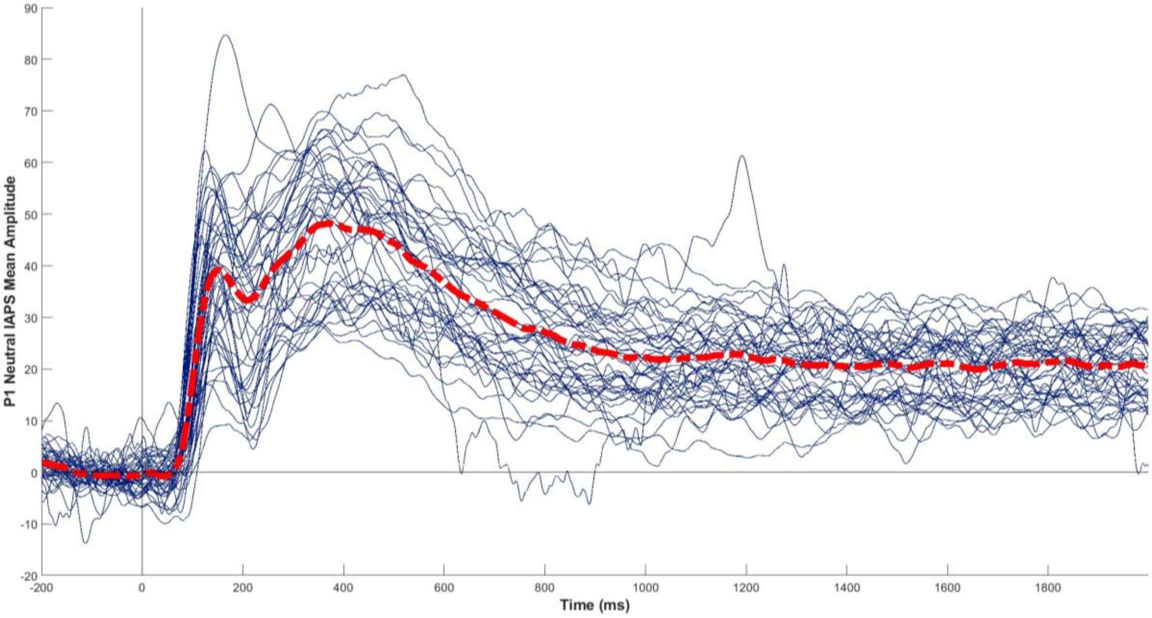

P1 Pleasant IAPS Mean Amplitude
80
70
60
50
40
30
20
10
0
-10
-20
-200
0
200
400
600
800
1000
1200
1400
1600
1800
Time (ms)

(A)

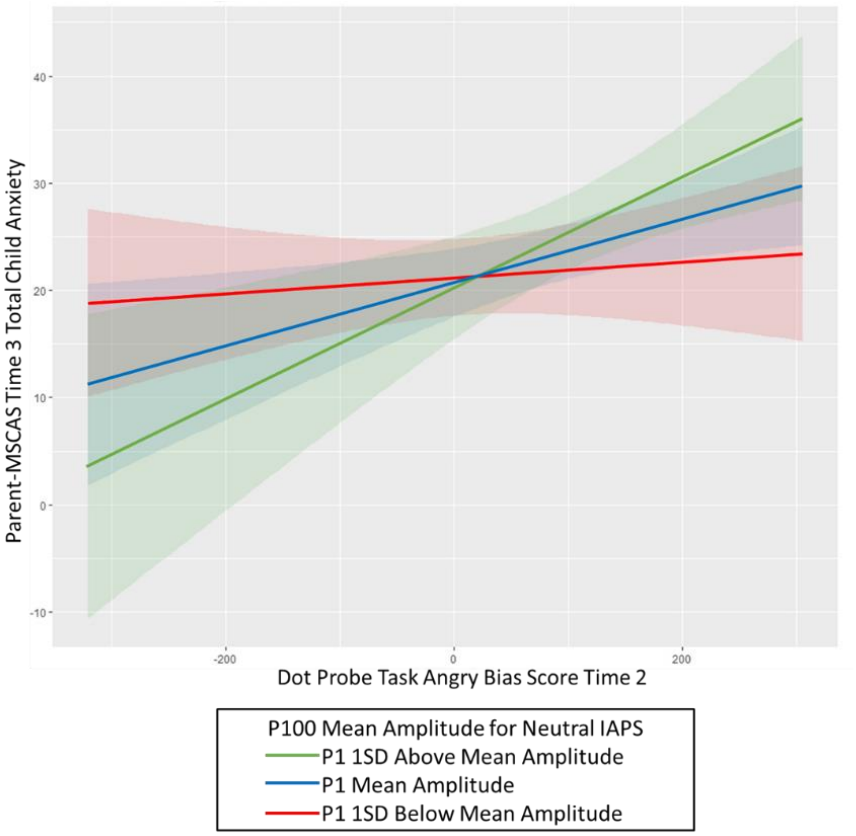

Parent-MSCAS Time 3 Total Child Anxiety
40
30
20
10
0
-10
-200
0
200
Dot Probe Task Angry Bias Score Time 2
P100 Mean Amplitude for Pleasant IAPS
P1 1SD Above Mean Amplitude
P1 Mean Amplitude
P1 1SD Below Mean Amplitude

(B)

Figure 18. Figure (A) depicts individual variability in children's P1 mean amplitude response to Pleasant IAPS images. Each line represents a single subject ERPs with a dotted line representing the grand average mean. Figure (B) depicts the moderating role of P1 for Pleasant IAPS images at Time 3 in the relation between DPT Angry Bias at Time 2 and child anxiety at Time 3.



(A)



(B)

Figure 19. Figure (A) depicts individual variability in children’s P1 mean amplitude response to Neutral IAPS images. Each line represents a single subject ERPs with a dotted line representing the grand average mean. Figure (B) depicts the moderating role of P1 for Neutral IAPS images at Time 3 in the relation between DPT Angry Bias at Time 2 and child anxiety at Time 3.

Late Positive Potential (LPP)

All time windows (early, middle, late) and channel clusters (left, midline, right) of the LPP for Unpleasant, Pleasant, and Neutral conditions and difference waves did not significantly moderate the relation between DPT Time 2 Angry Bias/Happy Bias and child anxiety measured by Parent-MSCAS Time 3 (*p*s > .13).

CHAPTER 5

Discussion

The goal of this study was to examine the role of attention to emotional information and anxiety outcomes by addressing methodological limitations of the extant literature and empirically testing theoretical developmental models of attention bias and anxiety. Importantly, this study used a multi-method approach by combining converging evidence from behavioral, eye-tracking, and measures of brain activity to characterize developmental mechanisms of attention bias and anxiety symptomology. Across three different hypotheses, we tested specific questions regarding the relations between eye tracking and neural correlates of attention to emotional faces and emotion-eliciting scenes, and anxiety symptoms. The findings of this research suggest that attention patterns present early in development play a pivotal role in the risk for anxiety and provide preliminary support for the *Moderation Model* of anxiety (Field & Lester, 2010).

Implications for Selective Attention Mechanisms in Anxiety

The overarching goal of the present investigation was to address methodological limitations of the developmental attention bias literature to better characterize and empirically test theoretical models of attention to threat across early development predicting anxiety outcomes. To date, few studies have combined across measures of attention bias, thus it remains unclear how behavioral indices correspond to neural indices of attention to threat. Further, because few studies have longitudinally evaluated attention bias spanning infancy to middle childhood, it remains relatively unclear how threat bias may predict anxiety outcomes, and how longitudinal presentation of threat bias is reflected in the neural correlates of the brain. To address these open questions, the current study draws on longitudinal data from an eye tracking measure of attention bias (DPT), and measures of the brain reflecting attention processes in middle childhood to examine the complex role of attention in the emergence of anxiety. Overall, we reveal the role of attention to threat as related to symptoms of anxiety, both through eye tracking DPT and neural correlates of the brain (ERP) to emotional faces and scenes. Relations between anxiety symptoms and DPT at specific developmental time points, as well as early relative to later peaking ERP components help shed light on the mechanisms of attention involved in anxiety development, as elaborated below.

Attention bias in early childhood but not infancy, assessed with eye tracking DPT, predicts later childhood anxiety symptoms.

The present analysis shows that attention bias for threat (measured by eye tracking DPT) is predictive of anxiety symptoms, and that only certain developmental time points of attention bias are predictive of anxiety outcomes, while others are not. Specifically, DPT Angry Bias (but not Happy Bias) scores at Time 2 were significantly associated with child anxiety measured at Time 3, such that increased vigilance for threat resulted in higher anxiety symptoms measured approximately two years later. No other combinations of DPT time points and anxiety outcomes were significant. Despite our predictions that multiple DPT time points would predict anxiety outcomes, we found that only DPT Time 2 was predictive.

One possible explanation is that the range of ages at Time 1 included children from 9 months to 4 years of age, which may have introduced additional variance obscuring meaningful associations between attention bias and anxiety outcomes. Alternatively, it could be the case that attention bias is normative during this age and therefore is not yet meaningfully predictive of anxiety outcomes (Field & Lester, 2010). Further, attention bias at Time 2 (ages 2.6-6 years old) may be a better predictor of anxiety because it captures a developmental persistence of attention to threat from Time 1 that is now predictive of anxiety. Alternatively, at Time 2 the age range may be particularly sensitive to attentional processes, as additional cognitive control abilities have not yet fully developed to inhibit attention bias.

We did not see a relation between concurrent measures of eye tracking attention bias and childhood anxiety at Time 3. There is some preliminary research to suggest that attention bias for threat is normative in early childhood, but wanes for non-anxious individuals across development, occurring sometime around middle to late childhood (Field & Lester, 2010). Therefore, a possible explanation for this lack of association may have to do with a tapering of the attention bias around this age (Time 3, 6-8 years old), that is supported by maturation of the prefrontal cortex and increasing ability in attentional control, specifically attention shifting and inhibition (Field & Lester, 2010; Kindt et al., 2000; Shi et al., 2019), which may not yet be occurring at the same rate at our Time 2 (ages 2.6-6 years old) measure of DPT (Moriguchi & Hiraki, 2011). Thus, if attention bias does wane, perhaps our behavioral DPT measure of attention is no longer sensitive enough to capture meaningful individual differences that are predictive of anxiety outcomes, and therefore, a more sensitive neural measure such as ERP is necessary to detect true differences in attention. Another possibility is that the kind of attention bias captured by the DPT (vigilance and avoidance) is only telling a portion of the story, meaning attention related to anxiety likely involves multiple components of selective attention, such as a combination of initial attention allocation (i.e., vigilance) and attentional control (i.e., disengagement) (Shi et al., 2019).

From a developmental perspective, it could be the case that during early development, initial attention allocation (i.e., vigilance) plays a pivotal role in attention bias, but as executive functioning abilities improve in middle to later childhood, attentional control (evidenced by inhibitory processes) may moderate attention bias for threat. This idea is in line with the Attentional Control Theory, which posits that anxiety disrupts attentional control functions, specifically inhibition and shifting, resulting in difficulty in disengagement from threat and facilitated threat detection (Cisler & Koster, 2010; Eysenck et al., 2007; Eysenck & Derakshan, 2011). There is some evidence to suggest that in youth, anxiety is associated with diminished behavioral and neural recruitment of attention and inhibitory control processes (Bechor et al., 2019; Dudeney et al., 2015). However, the current investigation does not directly test this hypothesis. Future research should investigate behavioral attention bias and neural correlates of attention beginning in infancy through late childhood to better characterize the role of initial attention allocation and attentional control as supported by maturation of the prefrontal cortex in predicting anxiety outcomes.

Initial attention allocation (P1) to emotional faces and scenes is related to eye tracking measures of attention bias (DPT) and childhood anxiety symptoms, and significantly moderates the relation between attention bias for threat and anxiety symptoms.

Our results reveal that initial allocation of attention (indexed by P1) to emotional faces and scenes is related to anxiety symptoms in childhood. This finding suggests that attention to emotion eliciting objects/scenes is also predictive of anxiety, meaning that attention bias for threat goes beyond attention for emotional facial expressions, and that it may be more about general initial allocation of attention (or vigilance) for information that is predictive of anxiety outcomes.

Findings regarding the P1 to emotional faces are in line with prior research highlighting the importance of initial attention allocation (indexed by the P1 component) in selective attention for threat and anxiety outcomes (Bigelow et al., 2021; Gupta et al., 2019; Weinberg & Hajcak, 2011). The current study found that for Emotional Faces, P1 to Neutral facial expressions was correlated with DPT Angry Bias Time 2, such that an increased bias towards threat was associated with enhanced neural response to Neutral faces. A similar pattern emerged for P1 to Angry faces but was nonsignificant after correction for multiple comparisons. These findings are in line with prior research that suggest Neutral faces are emotionally ambiguous and may be perceived as threatening similar to that of Angry faces, especially in the context of anxiety in both adults and youth (Denefrio et al., 2019; Hum et al., 2013; Rollins et al., 2021; Wauthia & Rossignol, 2016). Further, P1 for Fearful and Angry Emotional Faces showed only a trend level association with child anxiety measured at Time 2. A larger sample may reveal more robust relations with these other emotional face stimuli. Additionally, while we used a global measure of anxiety that spans subtypes of anxiety, future research should examine social anxiety in relation to attention bias and neural correlates of emotional face processing; these anxiety subtypes may be more related to variance in P1 to angry and fearful faces, compared to our global measure.

Our findings also demonstrate that initial allocation of attention (as indexed with the P1) to emotional objects and scenes is related to childhood anxiety symptoms. To our knowledge, this is the first study to examine the P1 in response to Neutral, Pleasant, and Unpleasant IAPS images in young children. Our data showed enhanced P1 to Neutral, Pleasant, and Unpleasant images was associated with increased DPT Angry Bias Time 2, such that an increased bias towards threat was related with enhanced neural response to all emotional scenes. Further, there was significant relation between P1 for Neutral, Pleasant, and Unpleasant IAPS images and child anxiety at Time 2, such that enhanced P1 was associated with heightened anxiety symptoms. Thus, we find that parent report of child anxiety is predictive of later neural correlates of attention to emotion-eliciting images. Considering that we do not see this same effect in our emotional face data, perhaps the use of emotional scenes provides a more ecologically valid measure of attention bias that encompass subtypes of anxiety symptoms.

Across both tasks, we see that P1 plays a pivotal role in initial attention allocation for emotion. Together, these findings suggest that it is not just emotional facial expressions that are predictive of attention bias to threat and anxiety. In fact, it appears to be more about the general allocation of attention to information that is related to increased anxiety symptoms and attention bias. Specifically, across two different tasks (Emotional Faces, IAPS Task), our data show that P1 moderates the relationship between eye tracking DPT Angry Bias and child anxiety. The relation between DPT and anxiety is only present when P1 is enhanced (more positive), and not present when P1 is small. The importance of the P1 (measured approximately 100ms post-stimulus) in this model supports the theory that initial orienting of attention, specifically vigilance, is pivotal to the presentation of anxiety in young children. Given that we did not have a neural measure of the brain at Time 1 or 2, on open question is whether the brain was already tuned towards threat at these earlier time points, and we are merely capturing that effect in our ERPs at Time 3, or if these results reflect a cascading effect of persistent attention to threat shaping neural brain responses. Future research that includes neural measures of attention in infancy and early childhood can address this open question.

Finally, the relation between P1 in both tasks and DPT provides empirical support for the type of attention processes indexed by the DPT. Specifically, given the findings of this analysis, we conclude that both the P1 and DPT are indexing initial attention allocation processes (i.e., vigilance). This is an important addition to the literature that highlights the temporal sensitivity of the eye tracking version of the DPT to index quick attentional processes.

Attentional Control (Nc) to emotional faces is not independently predictive of eye tracking measures of attention bias (DPT) or childhood anxiety symptoms, but significantly moderates the relation between attention bias for threat and anxiety symptoms.

There was a trend-level association between Nc Fearful-Neutral and DPT Angry Bias scores at Time 1, such that enhanced Angry Bias scores predicted subsequent enhanced Nc for Fearful faces relative to Neutral faces. There were no significant relations between Nc to emotional faces and child anxiety. To our knowledge, prior research has not investigated the relation between Nc and DPT task or anxiety, so future research should explore these relations with a larger sample size and with a population of clinically anxious participants. Overall, given our small sample size, we interpret these null results with caution but perhaps the lack of association between Nc and DPT suggests that these two measures are indexing different aspects of attention, specifically the Nc is indexing attention control processes (Dennis et al., 2009; Hoehl et al., 2008) while our DPT measure indexes initial attention allocation (evidenced by our P1 results and prior research, see Torrence & Troup, 2018). Further, to our knowledge, this is the first study to investigate how Nc is related to anxiety. However, prior research has shown an association between Nc and emotion regulation (Dennis et al., 2009), which involves the ability to flexibly control attention to regulate emotional experiences, and dysregulation is associated with anxiety disorders (Cardinale et al., 2019). Thus, Nc may be tapping into more control processes that are vital to attention-emotion mechanisms associated with anxiety, but future research is necessary to unpack these relations.

Similar to the P1, the Nc for Angry-Neutral faces moderated the relation between DPT Angry Bias and child anxiety. Higher DPT angry bias at Time 2 predicted more anxiety symptoms at Time 3, but only for children who also had an enhanced (more negative) Nc amplitude to Angry versus Neutral faces. Nc amplitude did not moderate the relation between DPT and anxiety when the amplitude difference between angry and neutral faces was small. Given that Nc indexes attentional control to salient stimuli and is sensitive to emotional facial expressions, these findings highlight the importance of attention to threat-specific emotions and suggests that it is not only about the initial vigilance for threat, but also more attentional control and purposeful attention allocation. As such, our measure of Nc alone did not predict anxiety, and was not related to DPT, but only the combination of DPT and Nc was predictive of anxiety. Thus, only the children who exhibited a behavioral vigilance for threat and subsequently two years later an enhanced attention allocation for threat in the brain showed heightened symptoms of anxiety. These findings suggest that both initial attention allocation and enhanced attentional control are contributing to an overall attention bias for threat that is predictive of anxiety symptoms.

It is interesting to think about the Nc findings in comparison to our P1 findings reported above. Taken together, these ERP findings highlight that at the initial attention allocation stages (P1, [100-150ms]), individuals with an attention bias for threat (as measured by DPT) attend more indiscriminately to all emotional information (given that P1 to neutral, unpleasant, and pleasant scenes/objects, as well as to neutral faces played a role in predicting anxiety symptoms), but at later stages of processing (Nc, [275-500ms]), the saliency of the information, particularly threat-relevant information, becomes of high importance in individuals with higher levels of anxiety symptoms (given that Nc only to angry versus neutral faces played a role in predicting anxiety symptoms). These findings highlight that both early and later stages of selective attention processes are underlying attention bias mechanisms in anxiety, but the content that is the focus of the attention is different at different points in the time course of attentional processes.

Face-specific N170 to emotional faces is not related to eye tracking measures of attention bias (DPT) and childhood anxiety symptoms.

N170 for Emotional Faces was not significantly related to DPT Angry/Happy Bias, and child anxiety. These results were surprising, as we expected to see a relation between N170 and both DPT and child anxiety. Prior research has measured the N170 during the DPT task, reporting enhanced N170s in anxious youth (Bechor et al., 2019) and enhanced N170 to angry faces predictive of anxiety in children (O'Toole et al., 2013); however, there are notable discrepancies in the attention bias N170 literature in adult and pediatric populations (Gupta et al., 2019; Torrence & Troup, 2018). In the present analysis, we controlled for the effects of P1 on the N170, whereas prior research showing these relations did not. It is therefore possible that prior findings of relations between N170 and anxiety were driven by variance in P1, and our correction allowed us to better isolate N170 variability and reveal a lack of relation between this component and anxiety. The N170 captures cortical specialization for face processing and is sensitive to emotional faces in beginning in adolescence (~ 14 years of age) and thus, our null results could suggest that our sample was too young (ages 6-8 years) to capture the sensitivity for threatening faces as related to anxiety. However, null findings should be interpreted with caution, and future research, especially that examines N170 as corrected for P1, is needed to disentangle the potential influence of P1 in driving the attention bias and anxiety effects reported in the N170.

Finally, while our data reveled that P1 and Nc moderated the relation between DPT Angry Bias and child anxiety, our findings showed the N170 to emotional faces did not. The N170 is thought to reflect the perceptual encoding of faces, and its sensitivity to emotional facial expressions is debated (Batty & Taylor, 2006), which may explain why the N170 was not a significant moderator of attention to threat and anxiety under the hypothesis that it is emotion-specific attention (and not general facial features) that are related to anxiety. Indeed, the Nc—which is more robustly related to emotional attentional processes per se (Bowman et al., 2021) was a significant moderator.

Sustained attention and appraisal (LPP) of emotion-eliciting objects/scenes is not related to eye tracking measures of attention bias (DPT) and childhood anxiety symptoms.

We found a lack of relation between LPP and DPT. We anticipated this finding due to the time-course of the attentional processes captured in each measure. Specifically, the DPT indexes initial attention allocation (Torrence & Troup, 2018) , whereas the LPP indexes later sustained attention and appraisal (Hajcak et al., 2010). We also did not find a relation between LPP and anxiety, which was contrary to our hypotheses given the extant literature demonstrating enhanced LPPs in youth with heightened anxiety (Fu & Perez-Edgar, 2019; Kujawa et al., 2015). It is possible that these mixed findings are due to variability in the LPP caused by developments in related brain structures occurring over childhood. Specifically, LPP activation has been linked to the visual cortex, amygdala, and prefrontal cortex—all areas that are undergoing age-related changes over the time periods examined in the current and prior studies. Thus, LPP effects are subject to ongoing age-related maturation, which may pose difficulties in revealing relations between LPP and anxiety at different points in development, and over large age-ranges (Decicco et al., 2014; Liu et al., 2012; Sabatinelli et al., 2013). Future research with more precise age-ranges as well as variables that may capture and isolate these underlying maturational processes is needed to characterize the role of brain maturation in LPP neural signatures.

Implications for Developmental Models of Anxiety

The present investigation sought to empirically test developmental models of attention bias and anxiety. Our data did not find empirical support for the *Integral Bias Model,* which posits that development has no influence on attention bias such that individuals born with it will consistently maintain it throughout development. Specifically, to support this model, our longitudinal DPT measure of attention bias should have shown that any developmental time point would predict anxiety and that attention bias remains consistent across development. Perhaps the more sensitive measure of ERPs, if assessed early and consistently across time points (rather than exclusively at Time 3 in our study) would reveal support for the *Integral Bias Model* in that there may be consistency of enhanced ERPs for emotional faces and/or scenes, and these enhanced ERPs at any time point may predict anxiety. However, neither ERPs nor DPT measured at Time 3 were predictive of anxiety at Time 3 , as would have been predicted by *Integral Bias Model*, suggesting this model may not be supported empirically.

In contrast, the current study finds preliminary support for the *Moderation Model*, which proposes that attention bias for threat is present in all individuals early in development, but only individuals that maintain a bias for threat across development are at increased risk for anxiety (Field & Lester, 2010). In other words, in line with the *Moderation Model*, individuals are born with an innate ability for attending to emotion, particularly threat, in the environment but for some individuals, a combination of developmental factors (temperament, environment, parental factors., etc.) contribute to the ongoing maintenance of attention bias that then becomes a risk factor for anxiety (Bayet et al., 2017; Bosquet & Egeland, 2006; Burris et al., 2017; LoBue et al., 2017; Morales et al., 2017; K. Pérez-Edgar et al., 2013; Safar & Moulson, 2020; Waters et al., 2008).

Importantly, our data show that the combination of behavioral attention bias measured at Time 2, plus an enhanced neural brain response to emotional information measured approximately two years later at Time 3 was predictive of anxiety symptoms. Independently, DPT and ERP measures are each accessing attention bias, but critically, together in combination DPT at Time 2 and ERPs at Time 3 show a longitudinal persistence (or maintenance) of attention bias across development that predicts anxiety outcomes. These findings draw preliminary support for the *Moderation Model*, suggesting that attention bias interacts with development to predict anxiety. Thus, the children who show a developmental persistence in attention bias for threat, relative to those who do not, will have different anxiety outcomes. Further, these findings suggest that the brains of children who maintain an attention bias are not only highly tuned to detect threat but may be indiscriminately attending to all emotional information (evidenced by our P1 results) with a high level of vigilance.

Finally, because we see that early DPT (Time 2) predicts later neural correlates of the brain (Time 3), this raises an important question regarding the role of early behavioral threat bias in shaping the developing brain and subsequent risk for anxiety. Data from the present study is not able to directly test this hypothesis, so future research is needed. Support for this hypothesis would come from early (infancy) behavioral measures of attention bias predicting later brain activity, which would reflect a tuning of the brain in response to an ongoing threat bias across development to predict anxiety outcomes. Under this hypothesis, we would not expect to see that early neural correlates of the brain would yet predict anxiety outcomes, as attention bias may shape the brain over the course of development.

Limitations and Future Directions

While the present study represents a pivotal step in the literature for characterizing the developmental progression of anxiety, there were several notable limitations. The present study included a community sample of children instead of a clinical sample diagnosed with anxiety. While it is important to characterize attention bias in a subclinical sample, it is equally important to test these questions in those diagnosed with anxiety. Additionally, our measure of child anxiety encompassed several types of anxiety symptoms including separation anxiety, physical injury fears, social phobia, panic attack, agoraphobia, and generalized anxiety disorder. Future analyses should directly examine the extent to which subtypes of anxiety are associated with behavioral and neural correlates of selective attention. Moreover, though the sample size was relatively large for a *pediatric* ERP study, the sample size is still relatively small and possibly obscuring sex and age-related effects. Finally, the socioeconomic status of participants was generally high and predominately White. Given the established a link between attention bias and adverse early environments (Burris et al., 2022), future research should include a more diverse population.

A critical future direction of this research would be to continue longitudinal investigations that integrate behavioral and neural measures at all time points. Unfortunately, in the present analysis, we only had neural measure at the third time point of data collection. Further, a more comprehensive study is necessary to address outstanding questions regarding executive functioning abilities in attention bias, specifically role of memory in recall of emotion-relevant information and inhibitory control in attention allocation.

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