# The development of sensitivity to threat among children and adolescents

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#### **ABSTRACT**

Several theories of adolescent brain development suggest that adolescence is a sensitive period of development characterized by the onset of internalizing problems, such as anxiety. Sensitivity to threat, a heightened responsiveness to aversive situations, has been suggested to be a precursor to anxiety, highlighting the importance of understanding sensitivity to threat among children and adolescents. Yet relatively little is known about the development of sensitivity to threat. Further, identifying the neural indicators that are associated with heightened sensitivity to threat would help classify which youth are most at risk for anxiety. The primary goals of my dissertation were: 1) to explore whether adolescents, compared to children, have heightened sensitive to threat, 2) assess which neural indicators are associated with heightened sensitivity to threat, and 3) assess whether individual differences (e.g., in consistency of sensitivity to threat across time and situation) help predict which youth are most at risk for anxiety-related problems. Study 1 of my dissertation examined, with concurrent data, whether adolescents have greater neural sensitivity to negative feedback compared to children. Study 2 examined whether children and adolescents differ in their longitudinal trajectories of sensitivity to threat (e.g., consistency across time). I also was interested in whether these trajectories were associated with frontal asymmetry, a neural indicator associated with avoidance motivations. Study 3 extended the findings from Study 2 to examine consistency across threatening situations. While Studies 1 through 3 investigated whether adolescence is a period of heightened sensitivity to threat, Study 4 of my dissertation used a latent class analysis to investigate whether individual differences in sensitivity to threat, impulsivity, and emotion dysregulation are associated with anxiety and/or risk taking. Results indicated that adolescence (especially when defined by pubertal status), may be a normative period for sensitivity to threat. At the same time, not all youth who are sensitive to threat go on to develop anxiety; thus, it may be that for many adolescents, sensitivity to threat

is an adolescent-limited phenomenon, meaning that threat sensitivity may peak in adolescence, but then tapers off into adulthood. Importantly, neural indicators associated with threat sensitivity helped identify which youth may have the highest levels of threat sensitivity. Overall, my dissertation shows that while some level of sensitivity to threat is normative, it is less common for youth to be *consistently* sensitive to threats and importantly, these youth who are consistently sensitive appear to be most at risk. Taken together, the four studies of my dissertation incorporate EEG, longitudinal designs, multiple indicators of development (age and pubertal status), and self-report data to gain a holistic understanding of sensitivity to threat from childhood to adolescence.

*Keywords*: Sensitivity to threat; EEG; Longitudinal; Adolescence; Childhood; Reinforcement Sensitivity Theory; Consistency

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### **CHAPTER 1: GENERAL INTRODUCTION**

Adolescence is thought to be a sensitive period of development, characterized by extensive biological, social, and psychological changes (Spear, 2000). While these changes result in unique opportunities (e.g., increased flexibility to adapt to new demands; Crone & Dahl, 2012; McCormick & Telzer, 2017b), they also can lead to vulnerabilities. Indeed, many mental health disorders, such as anxiety, have their onset in adolescence (Bandelow & Michaelis, 2015; Kessler et al., 2005; Lee et al., 2014). Given that anxiety is one of the most reported mental health problems among North American youth (~20% as of the COVID-19 pandemic; Racine et al., 2021), understanding factors associated with this vulnerability is critical to promote better outcomes for youth with anxiety.

## **Adolescent Brain Development**

Theories of adolescent brain development propose that one contributing factor to adolescents' challenges with mental health is the reorganization of neural circuitry that takes place during this developmental period (e.g., Casey, 2015; Somerville & Casey, 2010; Steinberg, 2008). According to the imbalance model, circuitry within the limbic-striatal system (associated with socioemotional processing) matures early in adolescence (likely due to puberty), while the prefrontal executive system (associated with self-control) undergoes protracted development (Casey, 2015; Luna & Wright, 2016; Shulman et al., 2016; Steinberg, 2008). This asynchrony in maturity is thought to lead to heightened activation of the limbic-striatal region during early to mid-adolescence, when neural connections to the prefrontal cortex that might dampen the activation (if appropriate) are not fully mature. As a result, adolescents are thought to be more likely to

experience heightened reactivity to emotionally provoking events (e.g., aversive events) in comparison to other age groups.

In line with this theory, adolescents tend to show exaggerated reactivity in limbicstriatal regions (e.g., amygdala, striatum, nucleus accumbens) when processing aversive cues, compared to other age groups (Galván & McGlennen, 2013; Guyer et al., 2008; Hare et al., 2008). In other words, adolescents are thought to have heightened sensitivity to threat (i.e., a heightened responsiveness to aversive situations). For example, Hare et al. (2008) used an emotional go/no-go task, in which children and adolescents had to rapidly withhold their responses to different face stimuli (e.g., fear faces, happy faces, neutral faces). Their results showed that adolescents, compared to children, had exaggerated amygdala activity to fearful faces. Relatedly, Guyer et al. (2008) found that adolescents had greater activation in the amygdala while viewing fearful faces compared to adults. In contrast, Dreyfuss et al. (2014) found that adolescents and adults showed greater activation in prefrontal regions than children, but they did not find significant age differences in the striatum, although see Galvan and McGlennen (2013) who showed that adolescents have greater activation in the striatum during aversive processing compared to adults. Mills et al. (2014) found that there was a structural mismatch in developmental timing between the amygdala and prefrontal cortex; however, they did not find clear evidence for the developmental mismatch between the nucleus accumbens and the prefrontal cortex. Overall, while there are inconsistencies depending on which brain regions are investigated, there is some support for the suggestion that adolescence is an age period when neurodevelopmental factors are associated with aversive processing.

Another neurodevelopmental model, the triadic model, posits that during situations of high reward, adolescents would have a *weak* harm-avoidant system (Ernst et al., 2006). This theory is most often considered in the context of risky decision making. In support of the triadic model, Humphreys and colleagues (2016) found that adolescence was marked by reduced sensitivity to negative feedback, compared to childhood and emerging adulthood (see also Feldmann et al., 2021; McCormick & Telzer, 2017a). Fear has also been shown to *decrease* across the lifespan (Gullone, 2000; Marks, 1987). Thus, our understanding of threat sensitivity across development remains unclear. Of concern, heightened sensitivity to threat has been associated with anxiety (Balle et al., 2013; Bar-Haim et al., 2007; Johnson et al., 2003; Katz et al., 2020; Pérez-Edgar et al., 2010; Vervoort et al., 2010); thus, it is critical to advance our understanding of the development of sensitivity to threat.

## **Pubertal Development**

Puberty is thought to be a key reason for the brain changes that occur during adolescence (Casey, 2015; Crone & Dahl, 2012; Nelson et al., 2005; Somerville & Casey, 2010). Yet, chronological age most often is used as a developmental marker (Vijayakumar et al., 2021). To gain a more holistic understanding of the development of threat sensitivity, it is important to move beyond using only age as a developmental marker. Puberty begins with adrenarche, which is triggered by the hypothalamic-pituitary-adrenal (HPA) axis. This stage typically begins between the ages of 6 to 9 in females and 7 to 10 in males (Dorn et al., 2006; Vijayakumar et al., 2018). The hormones released during this stage are responsible for the initial development of some secondary sex characteristics (e.g., pubic hair, acne; Patton & Viner, 2007).

The second phase of puberty, gonadarche, is triggered by the hypothalamic-pituitary-gonadal (HPG) axis. Sex steroid hormones (e.g., estrogen and testosterone) are released and ultimately contribute to the development of primary sex characteristics (ovaries and testes) as well as other secondary sex characteristics, such as breast development and menstruation in females and testicular development in males (Dorn et al., 2006; Vijayakumar et al., 2018). Like the first stage of puberty, gonadarche occurs earlier in females than males, approximately between the ages of 9-15 for females and between 10-16 for males. In this phase of puberty, gonadal hormones may induce neural organization effects in areas of the brain associated with social and emotional processing (e.g., the amygdala; Neufang et al., 2009; Sisk & Zehr, 2005; Somerville et al., 2010). Increases in gonadal hormones have been shown to impact social interactions, stress response, and the salience of social stimuli (Nelson et al., 2005; Sisk & Foster, 2004). Thus, changes in hormones during puberty likely are an important factor that contributes to heightened reactivity to emotionally salient events during adolescence.

At the same time, the physical changes associated with puberty can have a psychological and social impact. These physical changes (e.g., breast development for girls) may alter how others interact and perceive the adolescent and can ultimately impact adolescents' own self-image and mental health (Brooks-Gunn & Warren, 1989; Mendle & Koch, 2019; Ullsperger & Nikolas, 2017), especially given that negative social evaluation is particularly salient to adolescence (Forbes & Dahl, 2010; Somerville, 2013). Overall, interactions between biological, social, and psychological processes associated with pubertal maturation may contribute to adolescence being a sensitive period of

development, characterized by heightened reactivity to threats (Guyer et al., 2008; Moore et al., 2012; Quevedo et al., 2009).

## The Reinforcement Sensitivity Theory

The term sensitivity to threat comes from Gray's (1970) influential theory for motivation, the Reinforcement Sensitivity Theory. Gray (1970) originally proposed three neural systems that underlie individual differences in motivation: The Behavioral Approach System (BAS), the Fight/Flight System (FFS) and the Behavioral Inhibition System (BIS). The BAS was hypothesized to be activated by conditioned appetitive stimuli (e.g., rewarding) when signals of punishment are absent. Greater activation of the BAS was thought to be associated with increased tendency for impulsive behaviors. The FFS instead was hypothesized to be activated by unconditioned aversive stimuli (e.g., pain-inducing). Greater activation of the FFS was thought to be associated with emotional responses such as rage and panic. The BIS was considered a measure of sensitivity to threat, also called sensitivity to punishment, activated by conditioned aversive stimuli (absence of reward or in situations of threat or punishment), resulting in withdrawal behaviors. Greater activation of BIS was thought to be associated with trait levels of anxiety.

The Reinforcement Sensitivity Theory has been used as a framework to investigate why individuals may be driven to engage in or avoid certain behaviors (see Corr, 2004; Corr et al., 2013). Sensitivity to threat among children and adolescents may be a particularly important construct to examine, as the predisposition to avoid threat may be a risk factor in the development of anxiety (Degnan and Fox, 2007). Indeed, children and adolescents who are more sensitive to threat have a greater likelihood of developing

anxiety compared to those who are less sensitive to threat (Balle et al., 2013; Bar-Haim et al., 2007; Johnson et al., 2003; Katz et al., 2020; Perez-Edgar et al., 2010, 2011; Vervoort et al., 2010).

Sensitivity to threat has most often been measured using Carver and White's (1994) Behavioral Inhibition Scale. Originally, this measure was designed as a self-report measure for adults – it was first tested only among university students. Since then, the scale has been widely used among a variety of different samples, including children and adolescents (e.g., Bjørnebekk, 2009; Cooper et al., 2007; Coplan et al., 2006; Muris et al., 2005). Thus, researchers have since been able to investigate the development of sensitivity to threat across the lifespan.

#### The Development of Sensitivity to Threat

Sensitivity to threat was originally conceptualized as a personality *trait*, and thus, often is assumed to be relatively stable across development. In a sample of adults, Naragon-Gainey et al. (2013) found that sensitivity to threat (and neuroticism, a tendency to experience negative emotions) were largely stable across three time points over the course of one year. Similarly, De-Decker and colleagues (2017) found 2-year-longitudinal stability of BIS scores among children (aged 5.5 to 11 years at baseline). Takahashi et al. (2007) investigated the stability of sensitivity to threat among monozygotic and dizygotic twins over time among young adults. They found that genetic factors significantly predicted the stability of BIS and thus they concluded that BIS may have genetic trait-like stability over time.

There also has been work, however, suggesting that sensitivity to threat may actually be higher during different stages of development. Several cross-sectional studies

have shown that sensitivity to threat may increase from childhood to early adulthood. For example, Pagliaccio et al. (2016) found a cubic slope for BIS, which was characterized by a steep increase from childhood to young adulthood, and then a shallow decline from young adulthood to later adulthood. Gray and colleagues (2016) found that BIS peaked in mid-late adolescents across a sample ranging from 11 to 30 years old. Vervoort and colleagues (2010) also found that BIS scores were positively correlated with age in a sample of children and adolescents (although see Braams et al. (2015) who did not find that BIS was associated with age in a sample of participants ranging from 8 to 27 years old).

Although some research has investigated the stability of sensitivity to threat at a given age group (e.g., among adults), much less research has investigated longitudinal change in sensitivity to threat across different stages of development. Of note, in a two-year longitudinal study Urošević et al. (2012) found that females showed increases in BIS in a sample of early adolescents to young adults. There has been, however, a larger body of research that has investigated the development of behavioral inhibition, a related construct characterized by withdrawal and avoidance of unfamiliar or novel situations (Garcia Coll et al., 1984; Kagan et al., 1984). Research on behavioral inhibition has shown that this temperament style is relatively stable across development. For example, Caspi and Silva (1995) found that 3-year-olds classified as behaviorally inhibited were more harm avoidant (i.e., avoids danger/threats and prefers safe activities) and less flexible (i.e., overcontrolled) at age 18 than uninhibited 3-year-olds. Gest (1997) also found that behavioral inhibition was quite stable in a longitudinal study among children (aged 8 to 12 years at baseline) who were followed into early adulthood. Further, *stable* 

behavioral inhibition (i.e., consistent across time) during childhood is associated with increased odds of anxiety disorders in adolescence (Chronis-Tuscano et al., 2009; Frenkel et al., 2015).

Despite the obvious similarity in naming conventions, behavioural inhibition and the behavioral inhibition system have been studied as two distinct processes. Gray (1970) originally conceptualized BIS as withdrawal or avoidance of aversive stimuli while behavioral inhibition was conceptualized to understand temperament profiles in toddlers and young children (Garcia Coll et al., 1984; Kagan et al., 1984). Behavioral inhibition was first conceptualized by Kagan and his colleagues, who differentiated infants based on their motor and emotional reactivity. Infants who displayed vigorous motor activity and frequent crying were classified as 'high reactive' (~20% of the sample), while infants with low motor activity and low crying were classified as 'low reactive' (~40%). Two other subgroups of infants were classified as 'distressed' infants who had low motor activity but frequent crying and 'aroused' infants who had high motor activity but low crying. Importantly, high reactive infants (as young as 4 months of age) are more likely to be classified as behaviorally inhibited toddlers than the other subgroups (Garcia Coll et al., 1984; Kagan et al., 1984, 2007; Kagan & Snidman, 1991).

In young children (as opposed to infants) behavioral inhibition is typically measured in a lab setting, where children are exposed to novel stimuli (e.g., unfamiliar toys) and researchers are interested in different behavioral measures, including latency to approach the novel stimuli, proximity to parent, etc.). BIS, on the other hand, assesses reactivity to a range of different threats (e.g., making mistakes, receiving negative feedback). Despite differences in measurement, behavioral inhibition and BIS have many

overlapping features, including avoidance motivation, heightened activation in limbic regions, attentional bias to threat, and clear associations with anxiety (see Barker et al., 2019 for an overview of the similarities and differences between these constructs). There has been, however, little empirical work attempting to integrate these two distinct lines of research, thus the extent of overlap in these constructs is not fully known. Taken together, our understanding of the development of sensitivity to threat comes largely from the literature on behavioral inhibition, a related but distinct construct. Thus, it is critical to advance our understanding of the development of sensitivity to threat.

#### Electroencephalography (EEG)

Another way to further our understanding of threat sensitivity among children and adolescence is to investigate *neural indicators* associated with different types of threats. Neural indicators are critical to investigate as they can potentially help distinguish who is most at risk at earlier ages (e.g., before they can self-report anxiety-related problems). My dissertation uses electroencephalography (EEG) to identify neural indicators associated with threat sensitivity among children and adolescents.

EEG is a non-invasive procedure used to track and record electrical activity in the brain that is related to different cognitive, sensory, or motor processes (Luck, 2014). EEG records electrical activity at the scalp from neurons in the brain. As a brief overview, neurons are interconnected via synapses that generate subtle electrical impulses. Any one neuron's signal would be difficult to record; however, when hundreds of thousands of neurons fire in unison, they generate a large electrical field that is detectable at the scalp (Luck, 2005, 2014). This synchronized activity is thought to result primarily from pyramidal cells given that these cells have a perpendicular orientation to the scalp— other

types of cells that do not have perpendicular orientation disperse electrical activity in all different directions, and thus this activity cancels out.

Many EEG researchers are interested in event-related potentials— an average EEG response that is *time-locked* to an event (e.g., stimulus, response, feedback). For example, a participant may be completing a task in which they continually receive positive or negative feedback. Every instance of feedback is considered an event, and thus ERPs allow for an assessment of electrical activity in the brain directly after receiving different types of feedback. Across the task, participants complete many trials for each type of feedback. The EEG data is then averaged across the trials (separately for both positive and negative feedback) creating an ERP waveform. Overall ERPs are useful for investigating underlying neurocognitive processes that may be associated with specific task events (e.g., receiving negative feedback).

EEG allows for millisecond precision; therefore, an ERP waveform can be captured within one second after an event has occurred. Earlier components of an ERP waveform (<~100ms) are often thought to be associated with external aspects of the stimulus (e.g., visual properties such as brightness or shape) whereas later components are considered to be associated with higher order cognitive processes (e.g., attention to the stimulus) (Luck, 2005).

Importantly, different events elicit different ERPs. For example, the error-related negativity (ERN), a negative waveform that peaks around 50ms following the commission of an error (e.g., Gehring et al., 1993), is typically larger when individuals have greater motivation to avoid errors (Hajcak & Foti, 2008; Meyer, 2017), whereas the P3, a positive waveform that peaks around 300ms after a stimulus is presented, is an ERP

component that is typically larger when an individual is paying more attention to feedback (Huang et al., 2015; Luck, 2005). My dissertation will focus on ERPs that are elicited in response to aversive events (e.g., the ERN when making mistakes, the P3 when receiving negative feedback), given that sensitivity to threat is characterized by a heightened responsiveness to *aversive* situations.

Although ERPs can help assess neural activation after a stimulus, our brain is a continuous oscillator and thus is generating activity even in the absence of a stimulus. Therefore, instead of only looking at EEG activity in response to an event, we also can investigate different patterns of activity that are naturally occurring while at rest. Indeed, different patterns of brain activity during rest can be used to assess different cognitive, affective, or motivational drives (Luck, 2014). One pattern of activity that is particularly relevant when assessing sensitivity to threat is right frontal asymmetry. Right frontal asymmetry is measured using the alpha frequency band (8-13 hz) at rest and this type of activation is thought to be associated with greater avoidance motivations (Borod, 1993; Fox, 1991). Thus, right frontal asymmetry also will be examined in this dissertation as a potentially important neural indicator associated with threat sensitivity.

#### **The Current Studies**

Although sensitivity to threat is thought to be an important factor associated with anxiety among youth, relatively little is known about the development of sensitivity to threat. Further, identifying which neural indicators are associated with heightened sensitivity to threat would be an important step to help classify which youth are most at risk for anxiety. The primary goals of my dissertation were 1) to explore whether adolescents, compared to children, are more sensitive to threat, 2) assess what neural

indicators are associated with heightened sensitivity to threat 3) assess whether individual differences (e.g., in consistency across time and situation) help predict which youth are most at risk for anxiety-related problems. The four studies of my dissertation utilize a multi-methodological approach incorporating EEG, longitudinal designs, multiple indicators of development (age and pubertal status), and self-report data to gain a holistic understanding of sensitivity to threat from childhood to adolescence.

The first study of my dissertation investigated whether adolescents, compared to children (as measured by both age and pubertal status), have greater neural sensitivity to negative feedback. In this study, I also considered whether individual differences in worry, an anxiety-related construct characterized by apprehensive expectations about the future (Aldao et al., 2013; Borkovec et al., 1998), was associated with sensitivity to negative feedback. Indeed, according to the RST, heightened sensitivity to aversive processes is thought to be associated with anxiety-related processes (e.g., worry). Thus, according to this theory, I would expect that children and adolescents with high levels of worry would have greater levels of sensitivity to negative feedback than those with low levels of worry. The imbalance model, however, suggests that adolescents in general are thought to have heightened sensitive to emotionally provoking events (e.g., receiving negative feedback) in comparison to other age groups. That is, in the heat of the moment—directly after receiving negative feedback—both adolescent worriers and lowworriers might show sensitivity to the feedback. Thus, adolescents who report low levels of worry were an important group of interest in this study. If only adolescent worriers were sensitive to negative feedback (i.e., low-worriers were not), then sensitivity to negative feedback may be linked to higher rates of worry (in line with the RST). If,

however, adolescent non-worriers also have high neural sensitivity, then adolescents in general may be sensitive to negative feedback (in line with the imbalance model).

In Study 2, I investigated whether longitudinal trajectories of self-reported sensitivity to threat across childhood and adolescence are associated with frontal asymmetry (a neural indicator associated with avoidance motivations). According to RST, avoidance motivation is considered an important aspect of threat sensitivity. Further, Degnan and Fox (2007) suggest that individuals who have greater right frontal asymmetry may have a lower threshold for dealing with aversive situations, and thus, may be more likely to *consistently* report high sensitivity to threat. Despite this theorized relationship, no study has examined whether consistently high threat sensitivity across time is associated with this neural indicator of avoidance motivation. I expected that 1) adolescents would be more likely to self-report consistently high sensitivity to threat across time compared to children, and 2) consistently high threat sensitivity over time would be associated with right frontal asymmetry.

Given the importance of consistency across time, in Study 3 I extended this work to examine consistency across threatening *situations*. Indeed, there are a variety of different situations that youth may find aversive, such as receiving negative feed-back, making mistakes, and seeing angry faces. No study, however, has investigated whether individuals who self-report high sensitivity to threat have consistently high neural activation across different types of threats. While this analysis was exploratory, I expected that individuals who self-report higher sensitivity to threat would have consistently higher neural activation to different threats. I also predicted that adolescents

(those with more advanced pubertal development and older age) would be more likely to have consistently higher neural activation to threats.

Finally, in Study 4, I used latent class analysis to identify distinct groups of youth at risk for anxiety. Although adolescence is considered a sensitive period of development characterized by the onset of anxiety and risk taking, not all youth are anxious and/or engage in risks. In this study, I investigated several factors that might help differentiate youth with anxiety (e.g., threat sensitivity and emotion dysregulation) and youth who take risks (e.g., impulsivity and emotion dysregulation). I also assessed group differences on the ERN, an ERP that has been differentially associated with threat sensitivity and impulsivity. This is particularly important as neural indicators could potentially help predict later development of internalizing or externalizing problems (e.g., anxiety and/or risk taking) at younger ages (e.g., before children are able to self-report issues with anxiety). Although the latent class was exploratory, it was expected that groups characterized by higher levels of sensitivity to threat in combination with emotion dysregulation would be more at risk for anxiety, while groups characterized by high impulsivity and high emotion dysregulation would engage in higher levels of risk taking. Further, I expected that groups characterized by higher levels of sensitivity to threat would have a larger ERN, while groups characterized by higher impulsivity would have a smaller ERN. Finally, given that adolescence is thought to be a time of heightened anxiety and risk taking, I expected that adolescents, compared to children, would be more likely to be in groups with the highest risk for anxiety (i.e., groups with higher levels of sensitivity to threat in conjunction with emotion dysregulation) and risk taking (i.e., groups with higher levels of impulsivity in conjunction with emotion dysregulation).

Taken together, my dissertation offers a collection of studies that use multiple methods (and tasks) to investigate the development of sensitivity to threat among children and adolescents. This research provides support for the notion that adolescence is a particularly vulnerable time for heightened sensitivity to threat. However, Study 4 also demonstrates that there are individual differences in sensitivity to threat across development. Overall, advancing our understanding of sensitivity to threat may be an important way to identify youth most at risk for anxiety.

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### **CHAPTER 2: STUDY 1**

Sensitivity to negative feedback among children and adolescents: An ERP study comparing developmental differences between high-worriers and low-worriers<sup>1</sup>

Adolescence often is considered a transitional period marked by physical, psychological, and social changes (Spear, 2000). One notable change is the increase in adolescents' sensitivity to emotionally salient events (e.g., sensitivity to negative feedback). Indeed, compared to children, adolescents tend to report more sensitivity to negative feedback (O'Brien & Bierman, 1988; Vervoort et al., 2010; Westenberg, Drewes, Goedhart, Siebelink, & Treffers, 2004). For example, O'Brien and Bierman (1988) found that adolescents (grade 8) were more likely than children (grade 5) to report that rejection impacted their sense of self-worth. Further, Westenberg and colleagues (2004) found that fear of negative social evaluation was higher among adolescence compared to children (age range in the study was 8 to 19). Although these studies highlight social negative feedback (e.g., rejection), sensitivity to negative feedback also includes an emotionally salient event, such as receiving negative feedback about performance.

Recently, a number of neurodevelopmental imbalance models have been used to help explain why adolescents in general (i.e., not just in social settings)—compared to children— may be more sensitive to emotionally salient experiences, such as receiving negative feedback (Casey, 2015; Somerville, Jones, & Casey, 2010; Steinberg, 2008).

According to these models, adolescence behaviour may be affected by an imbalance

<sup>&</sup>lt;sup>1</sup>This chapter is based on the published article: Heffer, T., & Willoughby, T. (2020). Sensitivity to negative feedback among children and adolescents: An ERP study comparing developmental differences between high-worriers and low-worriers. *Cognitive, Affective & Behavioral Neuroscience*, 20(3), 624–635. doi:10.3758/s13415-020-00791-8

between an early maturing limbic-striatal system (possibly related to puberty), associated with affective processing, and a slower developing prefrontal cortex system, associated with cognitive control. This asynchrony is thought to lead to heightened activation of the limbic-striatal region during early to mid-adolescence when neural connections to the prefrontal cortex that might dampen the activation (if appropriate) are not fully mature, thus making this age group more sensitive to emotionally salient stimuli compared to children.

In line with these theories, studies have found that subcortical regions (e.g., the amygdala) increase in volume across puberty (Goddings et al., 2014) and mature earlier than higher-order cortices (e.g., prefrontal cortex; Galvan et al., 2006; Gogtay et al., 2004; Mills, Goddings, Clasen, Giedd, & Blakemore, 2014). Adolescents, compared to children, also have heighted activation in limbic regions when viewing negative faces (Hare et al., 2008) and when receiving negative feedback (Bolling et al., 2011; Moor, van Leijenhorst, Rombouts, Crone, & van der Molen, 2010). Thus, there has been some work suggesting that adolescents may have greater neural sensitivity to negative feedback than children. At the same time, there may be important individual differences to consider when investigating sensitivity to negative feedback. For instance, adolescent worriers report greater sensitivity to negative feedback compared to adolescents with low levels of worry (e.g., Balle, Tortella-Feliu, & Bornas, 2013). Studies using event-related potentials (ERPs) also have found that worriers have greater P3 activation (an ERP component that is typically larger when an individual is paying more attention to the feedback; Huang et al., 2015; Luck, 2005) to negative feedback compared to low worriers (De Pascalis et al., 2004; Miltner et al., 2005; Sewell, Palermo, Atkinson, & McArthur, 2008; although see

Bar-Haim, Lamy, & Glickman, 2005 for a study that found no differences in the P3 between individuals with high and low anxiety). Thus, worriers tend be more sensitive to negative feedback than low-worriers. Of note, however, these ERP studies have primarily focused on university students.

There is a paucity of research investigating whether individual differences in worry among *adolescents and children* might affect their sensitivity to negative feedback using the P3. In a sample of adolescents, Reeb-Sutherland et al., (2009) found a trend whereby high sensitivity to negative feedback and larger P3 amplitudes was associated with greater anxiety. Beyond that, little work that investigated not only individual differences (e.g., worry) in adolescents' neural sensitivity to negative feedback, but also how adolescents compare to children.

It may be that adolescents' sensitivity to negative feedback is tied to worry. In this case, we would expect only adolescents who report higher levels of worry to have a larger P3 amplitude to negative feedback— not adolescents who report low levels of worry. The imbalance neurodevelopmental models, in contrast, might suggest that adolescents *in general* likely are sensitive to emotionally salient stimuli; that is, in the heat of the moment—directly after receiving negative feedback—both adolescent worriers and low-worriers might show sensitivity to the feedback. Thus, adolescents who report low levels of worry are a key group of interest in this study.

## **The Current Study**

The goal of this ERP study is to investigate whether adolescents and children with high versus low levels of worry differ in their sensitivity to negative feedback (when receiving loss-feedback about their performance on a task). We had three main research questions: (1) Do adolescents have a greater neural sensitivity to negative feedback than

children (main effect of age group)? (2) Do worriers have greater neural sensitivity to feedback than low-worriers (main effect of worry)? (3) Do worriers and low-worriers show similar sensitivity to negative feedback *only* in adolescence, but not in childhood (interaction between worry and age group)?

Overall, we expect that adolescents will have a greater P3 amplitude to negative feedback than children, and worriers will have a greater P3 amplitude to negative feedback than low-worriers. In terms of the interaction, given the lack of research in this area, this analysis is more exploratory. It may be that adolescents' sensitivity to negative feedback is tied to worry, or as the neural developmental models might suggest, it may be that adolescents *in general* are sensitive to negative feedback. It also is not clear whether adolescent worriers will have even larger P3 amplitudes than adolescent low-worriers. In terms of the children, if worry is associated with greater attention to negative feedback (in line with ERP studies using university students), then we would expect that only children who are worriers will have a large P3 amplitude to negative feedback compared to children who are low worriers.

We also were interested in comparing how the results might differ depending on whether pubertal status or grade-level is used to classify adolescents versus children. Importantly, neurodevelopmental imbalance models highlight that puberty might be a key reason for the brain changes that occur in adolescence (Casey, 2015; Somerville et al., 2010; Steinberg, 2008). Further, previous research has found that pubertal development is a better marker than age (e.g., van den Bos, de Rooij, Miers, Bokhorst, & Westenberg, 2014). Thus, another goal of our study was to test whether there were any differences in the results when using grade versus pubertal status to distinguish between children and

adolescents. We conducted the analyses first using grade and then again using pubertal status as a way to identify any differences between these approaches. Critically, since theory and previous research highlight the importance of puberty, we expect that pubertal development will be a more sensitive measure than grade status.

Although we were primarily interested in group differences in sensitivity to negative feedback, we also provided participants with positive feedback during our task. Thus, while worriers may be particularly concerned with negative feedback, neurodevelopmental models suggest that adolescents may be sensitive to emotionally salient events in general (e.g., both negative *and* positive feedback). As a secondary analysis, we investigated whether groups differed in their sensitivity to positive feedback (see supplemental materials).

#### Method

## **Participants**

The current sample included 127 students (50.4% female; age range: 8-14; *M*age = 11.26, standard deviation = 1.71) from several elementary and high schools in southern Ontario, Canada. Students were part of a larger study examining the relationship between wellbeing and youth health-risk behaviours. Parents were asked to identify if their child had any illnesses or disabilities (either physical or mental). One participant was excluded from the study based on a diagnosis of autism. Parent report indicated that 87.2% of the children and adolescents were White, 2.6% were Hispanic, 0.9% were Black, and 8.5% were Mixed (a further 0.9% of parents indicated that they preferred not to answer the question). Mean levels of parental education fell between "some college, university, or

apprenticeship program" and "completed a college/apprenticeship and/or technical diploma".

## Procedure

Students were invited to participate in the study through visits to schools. Surveys were completed in classrooms during school hours and all participants received gifts (e.g., backpacks) as compensation. Participants also completed a Mobile Lab component where they each played computer tasks on their own while EEG was recorded. There were 12 participants who did not fill out the worry scale; therefore, they were not included in this study. Six participants did not complete the task due to equipment issues, and eight participants were not included because their ERP data was not usable (e.g., contained a large number of muscle/movement artifacts). Thus, the final sample included 100 participants. The University Ethics Board approved this study and participants provided informed assent and their parents provided informed consent

## **Primary Measure**

**Worry.** Participants reported the extent to which they agreed with 3 items examining worry ("I know I should not worry about things but I just cannot help it", "I worry about getting in trouble", "I worry about making mistakes") on a scale ranging from 1 (*Almost Never*) to 4 (*Almost Always*). Higher scores indicated higher levels of worry. Cronbach's alpha was 0.844.

**Age Group.** To distinguish between children and adolescents based on age group, anyone in grades 3 to 5 was considered a child (*M*age= 9.627, *SD*= .618) and anyone in grades 6 to 8 was considered an adolescent (*M*age= 12.404, *SD*= 1.100).

Pubertal Status. Pubertal status was assessed using the Puberty Development Scale (PDS; Petersen, Crockett, Richards, & Boxer, 1988). The PDS assesses body hair, facial hair, and voice development in boys, and body hair, menarche, and breast development in girls. All items were rated on a 4-point scale from 1 (not yet started changing) to 4 (change seems complete). For boys, their scores were summed such that any score of 5 or lower (with no 3-point responses) were considered pre/early puberty, while a score of 6 or more was considered mid-later puberty (Carskadon & Acebo, 1993). For girls, a score of three or less, without menarche, was categorized as pre-early puberty, while a score of three or more, plus a yes to menarche, indicated mid-late puberty (see Carskadon & Acebo, 1993 for scoring scheme). The PDS scale exhibits good reliability and validity (Carskadon & Acebo, 1993; Petersen et al., 1988).

Balloon Analogue Risk Task. The Balloon Analogue Risk Task (BART) is a behavioural task that has been used to measure risky decision-making (Lejuez et al., 2002). Traditionally, participants are instructed to inflate a series of balloons in order to earn points. The goal is to pump each balloon up as much as possible as each pump incrementally adds points for that trial. As the balloon gets larger, however, it is more likely to pop, in which case the participants lose the points that they accumulated on that trial (Lejuez et al., 2002). They still keep the points they received on previous trials. Given that this task provides feedback associated with losing (i.e., when the balloon pops and points are lost) and winning (i.e., when the balloon does not pop and points are won), it facilitates the examination of sensitivity to negative feedback as well as sensitivity to positive feedback using ERPs (Chandrakumar, Feuerriegel, Bode, Grech, & Keage, 2018; Fein & Chang, 2008; Gu, Zhang, Luo, Wang, & Broster, 2018; Takács et al., 2015).

In order to use the BART for an ERP study, there were important modifications to make to the task. First, studies using the BART often allow participants to inflate the balloon at their own pace (e.g., Fein & Chang, 2008; Gu et al., 2018; Kessler, Hewig, Weichold, Silbereisen, & Miltner, 2017; Kiat, Straley, & Cheadle, 2016; Takács et al., 2015; Webber, Soder, Potts, Park, & Bornovalova, 2017; Xu et al., 2016). One limitation associated with allowing participants to sequentially pump the balloon at their own pace is that researchers are unable to time-lock the ERP to the exact moment participants decide that they are going to cash out. In other words, the researchers are unable to timelock the ERP to the 'win' feedback because the point at which the participant decides they are going to cash out is not identifiable. To address this concern, we had participants choose the number of pumps they wanted to inflate the balloon at the beginning of the trial (Euser et al., 2013; Pleskac, Wallsten, Wang, & Lejuez, 2008; Yau et al., 2015). Participants then observed the balloon as it either safely reached the inflation number they picked (i.e., they won the points for that trial), or the balloon burst before reaching that point (i.e., they lost the points for that trial). Participants in this case do not know that they have won points during the trial until they receive feedback—making feedback salient for both wins and losses. This approach allowed us to time-lock the ERPs to the exact moment the participant receives feedback during that trial.

Another limitation that is important to address before using the BART for an ERP study is the feedback stimulus used in the task. In contrast to the win feedback, the loss feedback often is an exploding balloon, while the win feedback consists of a balloon with text in the middle or just a screen informing the participants of the win (Euser et al., 2013; Fein & Chang, 2008; Gu et al., 2018; Kessler et al., 2017; Kiat et al., 2016; Kóbor

et al., 2015; Xu et al., 2016). Therefore, it is difficult to disentangle whether participants are sensitive to the feedback itself, or if they are just more sensitive to a startling explosion. To address this concern, we modified the task to ensure that the stimulus for wins and losses were comparable (i.e., similar feedback was given for both wins and losses). Specifically, for both win and loss feedback, we made the text, font, and balloon size consistent, and both feedback messages were written inside of the balloon. We also made sure that the loss feedback was no longer a startling explosion but instead depicted a balloon with a few marks in it to represent that it had popped. This modification ensured that sensitivity to loss would not be driven by the stimulus used to provide the feedback (e.g., a startling explosion). Overall, these modifications allowed us to directly compare sensitivity to wins and sensitivity to losses without concern that results would be confounded by the stimulus or by not being able to examine feedback to wins in the same way as losses.

The task consisted of 90 trials with a maximum breaking point of 20 pumps. The probability of the balloon popping increased as the number of pumps chosen increased (e.g., choosing to pump the balloon up to '15' had a greater likelihood of it popping compared to pumping the balloon up to '5'). After feedback was presented, a new balloon appeared after 1000 ms. Participants earned one point for every pump of the balloon and points for all the "win" trials were summed to calculate their total points. Participants were instructed that the goal of the task was to earn as many points as possible.

## **Electrophysiological Recording**

Electroencephalography (EEG) was recorded continuously from a BioSemi ActiveTwo system using a 96-channel montage and 7 face sensors. The data were digitized at a sampling rate of 512 Hz. Our pre-processing pipeline identify scalp

channels, time course activations, and independent components that represented unreliable and non-stationary signals.

# **Pre-processing (Channels)**

Pre-processing was automated (using MATLAB 2012b scripts) to be carried out using EEGLAB (Delorme & Makeig, 2004) version 13.6.5b and was then executed using Octave on Compute Canada's high performance computer cluster (Cedar; see Desjardins & Segalowitz, 2013; van Noordt, Desjardins, & Segalowitz, 2015; van Noordt, Desjardins, Gogo, Tekok-Kilic, & Segalowitz, 2017 for more details). The data were first separated into 1 second non-overlapping time windows. For each time window, the voltage variance across each channel was calculated (a 20% trimmed mean was used). Channels were flagged as unreliable if they had a z-score six times greater than the voltage variance across all channels. Time-periods (i.e., the 1 second time windows) were considered unreliable if more than 10% of the channels were identified as having extreme voltage variances. Finally, any channels that were flagged in more than 20% of the time-periods were considered unreliable throughout the recording.

To minimize spatial bias introduced by variance in channel artifacts across subjects, we used an interpolated average reference procedure. Channels containing clean signal are used to interpolate to 19 spatially balanced sites arranged in the 10-20 layout. The average of these 19 interpolated sites are used as the reference, and subsequently subtracted from each of the original channels containing clean signal. The data were filtered with a 1Hz high pass and 30 Hz low pass filter given that cortical activity would not be expected to exceed 30 Hz. After this step, the data were again checked for the same issues reported above: (1) channels that are unreliable within a given time-period,

(2) time-periods that are unreliable, (3) and channels that are unreliable throughout the recording. Specifically, any channels that were unlike its neighbouring channels (e.g., had a low correlation with channels around it), were flagged. A channel was flagged as unreliable if it had a z-score that was 2.326 times greater than the mean of the 20% trimmed distribution of correlation coefficients. Time-periods were considered unreliable if more than 10% of the channels within the window were flagged as unreliable. Any individual channels that were flagged in more than 10% of time-periods were considered unreliable across the entire recording. Bridged channels (i.e., channels that are highly correlated with invariable signal) were identified after dividing the average maximum correlation by the standard deviation of the distribution of correlation coefficients.

Channels that had a positive z-score that was eight times greater than the 40% trimmed distribution of coefficients were flagged as bridged channels.

# **Pre-Processing (Components)**

After pre-processing the channel data, all data (channels and time periods) that had not been flagged as unreliable was concatenated back into continuous data. These data were then submitted to an initial Adaptive Mixture of Independent Component Analysis (AMICA) to identify different components of the EEG data (e.g., heart rate components, cortical components etc.). This process helps to separate brain activity (neural components) from non-neural activity (e.g., eye blinks).

During this procedure, the data were windowed into 1 second time epochs.

Unreliable components were detected by comparing each individual component to the variance among all components. Components were flagged if they had a z-score that was 2.326 times greater than the trimmed mean. Time-periods that had more than 10% of its

components flagged were considered unreliable. The data were then concatenated into the continuous time course and submitted to three simultaneous AMICA decompositions to assess whether components were replicable (i.e., is muscle movement consistently being classified as muscle movement when the process is repeated multiple times). The procedure above for identifying unreliable components (within 1 second epochs) was completed again using the continuous time series data. Next, a dipole (which identifies the position and orientation for the distribution of positive and negative voltages) was fit using the dipfit plugin in Matlab (Oostenveld, Fries, Maris, & Schoffelen, 2011). Components with a dipole fit residual variance greater than 15% were flagged. Finally, components were classified using the ICMARC plugin. This process assesses each component against a crowd-sourced database to identify activation consistent with five different categories: eye blinks, neural, heart, lateral eye movements, muscle contamination, and mixed signal.

After pre-processing, a quality control review was completed to ensure that the decisions made during pre-processing were appropriate. This procedure was completed by one trained research assistant who assessed the accuracy of the independent component classifications. For example, the research assistant would identify whether cortical components were correctly distinguished from non-cortical components (e.g., muscle, eye blinks, etc.) based on topographical projection, continuous activation, dipole fit and power spectrum profile. Thus, the quality control review involved using the independent components to help with artifact correction (see Table 1.1 for summary results of the artifact procedure).

## **EEG** post-processing

EEG data were then segmented into single trials and time-locked to the onset of the win/lose BART feedback stimuli. Epochs (-200 to 600 ms) were extracted to feedback onset and baseline corrected using the -200 to 0 ms pre-stimulus window. At this step, a final quality check was completed to identify (and remove) channels that had extreme voltage fluctuations (+/-50 mV). Channels that were flagged during pre-processing were interpolated in order to reconstitute the full montage of 103 channels (96 scalp, 7 exogenous) using spherical spline. Similar to previous studies (Hassall, Holland, & Krigolson, 2013; Kessler et al., 2017), the current study used central midline sites (Cz: electrodes A19 and B19 on our montage) to identify the P3 activation.

Table 1.1. Means and standard deviations from artifact detection procedure

| Artifact Category                  | Mean (%) | SD (%) |
|------------------------------------|----------|--------|
| Time                               |          |        |
| Extreme voltage variance           | 1.93     | 1.84   |
| Low channel correlation            | 0.13     | 0.29   |
| ICA variance 1                     | 8.46     | 5.56   |
| ICA variance 2                     | 1.75     | 1.60   |
| All methods                        | 12.26    | 7.92   |
| Channels                           |          |        |
| Extreme voltage variance           | 2.28     | 1.93   |
| Low channel correlation            | 10.79    | 4.65   |
| Bridge channels                    | 3.78     | 3.05   |
| All methods                        | 16.85    | 5.50   |
| Components                         |          |        |
| Residual variance                  | 49.45    | 10.70  |
| Neural components                  | 44.67    |        |
| Biological (non-neural) components | 28.94    | 7.95   |

# Statistical analyses

Statistical analyses were carried out using STATSLAB, an open-source toolbox that implements robust statistics for analysis of single trial EEG data (Campopiano, van Noordt, & Segalowitz, 2018). This software uses percentile bootstrap and trimmed means, techniques that are robust to distribution characteristics such as skew, outliers, uneven tails, and various model assumption violations (see Wilcox, 2017).

In STATSLAB, single trial data for channels A19 and B19 were extracted and averaged together. For each subject, the single trial data were re-sampled, with replacement, to generate a surrogate sampling distribution. The 20% trimmed mean was taken across trials, at each time point (i.e., removing the most extreme voltages at each time point), to generate a robust bootstrapped ERP. This process was repeated for each condition and the difference taken. Iterating this process of re-sampling, trimming and scoring the difference wave was done 1000 times to generate a distribution of differences between conditions (see Campopiano, van Noordt, & Segalowitz, 2018 for details). The 95% confidence interval was obtained to test significant differences between ERP wave forms for each condition. To investigate sensitivity to negative feedback, we ran two 2x2 ANOVAs: (1) worry status (worry vs low-worry) and grade group (younger vs older) as the between-subject independent variables and (2) worry status (worry vs low-worry) and puberty status (early-pre puberty vs mid-late puberty) as the between-subject independent variables.

#### Results

## **Descriptive Results**

We used grade (grade 3 to 5 = children, grade 6 to 8 = adolescent) and puberty (pre to early puberty = children, mid to late puberty = adolescent) to differentiate between

children and adolescents. In order to be consistent with previous research investigating worry and the P3, a median split was used to differentiate between those who had higher vs lower levels of worry (e.g., De Pascalis et al. 2004; Bar-ham et al. 2005; Miltner et al., 2005; Reeb-Surtherland et al., 2009). This created four groups based on grade: (1) younger low-worriers (N = 29, M = 1.573, SD = .417), (2) younger worriers (N = 18, M = 2.954, SD = .636), (3) older low-worriers (N = 37, M = 1.703, SD = .483), and (4) older worriers (N = 31, M = 3.194, SD = .485); and four groups based on puberty status: (1) pre-early puberty low-worriers (N = 28, M = 1.655, SD = .411), (2) pre-early puberty worriers (N = 12, M = 2.958, SD = .746), (3) mid-late puberty low-worriers (N = 39, M = 1.658, SD = .498), and (4) mid-late puberty worriers (N = 36, M = 3.176, SD = .461).

## **BART Behavioural Results**

On average, participants received win-feedback on 47.70 trials and loss-feedback on 48.30 trials. There were no group differences in the amount of win-feedback received or in the amount of loss-feedback received, regardless of whether groups were created using grade-level, F(3,105) = .023, p = .995,  $\eta_p^2 = .001$ , or pubertal status, F(3,105) = .152, p = .928,  $\eta_p^2 = .004$ . There were also no differences between the groups on the percent of trials retained after quality control for either wins or losses (Ms = 62% - 66%), regardless of whether groups were created using grade-level, F(3,97) = 1.44, p = .237,  $\eta p^2 = .048$ , or pubertal status F(3,97) = 0.953, p = .419,  $\eta p^2 = .033$ .

The key variables of interest for the BART behavioural data were: (1) total number of points earned, (2) total number of pumps, (3) reaction time after loss feedback minus reaction time after win feedback (a positive reaction time suggests a longer reaction time to losses compared to wins, while a negative reaction time suggests a longer

reaction time to wins compared to losses), (4) change in number of pumps (from the previous trial) after a loss, (5) change in number of pumps (from the previous trial) after a win. For each of the outcome variables, two 2x2 ANOVA's were conducted: (1) with grade (younger vs older) and worry status (high-worry vs low-worry) as the independent variables and (2) with puberty (pre-early puberty vs mid-later puberty) and worry status (high-worry vs low-worry) as the independent variables.

We also assessed whether participants changed the number of pumps they chose based on the feedback from the previous trial. We found that the older age group decreased the number of pumps after receiving win feedback a greater number of times (mean number = 21.266, SD = 5.304) compared to the younger age group (mean number = 18.867, SD = 5.480), F(1, 105) = 4.229, p = .042,  $\eta_p^2 = .039$ . The older age group was more likely to increase their number of pumps following loss feedback (M = 22.688, SD = 4.866) compared to the younger group (M = 20.222, SD = 5.830), F(1, 105) = 5.451, p = .021,  $\eta_p^2 = .049$ .

The mid-late puberty group increased their number of pumps following loss feedback (M = 22.542, SD = 4.930) more often than the pre-early puberty group (M = 19.973, SD = 5.918), F(1, 105) = 5.451, p = .021,  $\eta_p^2 = .049$ . In addition, we found a significant interaction between pubertal status and worry status on reaction time after loss feedback – win feedback, F(1, 105) = 5.231, p = .024,  $\eta_p^2 = .047$ . Simple effects analyses revealed that among the mid-later puberty group, there were no differences found between worriers (M = 13.734, SD = 202.861) and low-worriers (M = 35.400, SD = 190.806); both groups had a longer reaction time to loss feedback than to win feedback, t(70) = .467, p = .642, d = .110. Among the early puberty group, there was a significant

difference between worriers (M = 92.178, SD = 236.983) and low-worriers (M = -81.749, SD = 740.428) such that the worriers had a longer reaction time after loss feedback (vs win feedback) than the low-worry group, t(33.642) = 2.311, p = .027, d = .680. There were no other significant main effects or interactions for any of the other BART outcome variables.

#### **ERP Results**

We had three main research questions in terms of the ERP data: (1) Do adolescents have a greater neural sensitivity to negative feedback than children (main effect of age group)? (2) Do worriers have greater neural sensitivity to feedback than low-worriers (main effect of worry)? (3) Do adolescents worriers and low-worriers show similar sensitivity to negative feedback, and does that differ among children (interaction between worry and age group)? For all three research questions, we conducted analyses first using grade level and then again using pubertal status. Results for sensitivity to positive feedback can be found in Supplemental Figure 1.

# **Analysis Using Grade Level.**

Do adolescents have greater sensitivity to negative feedback than children? We found a significant main effect of grade level, t(98) = -1.639, p < .001, CI [-.571, -2.763]. Adolescents (older grade) had greater sensitivity to negative feedback than children (younger grade).

Do worriers have greater sensitivity to negative feedback than low-worriers? We found a significant main effect of worry status, t(98) = -2.890, p < .001, CI [-1.757, -3.975]. Worriers had greater sensitivity to negative feedback than low-worriers.

Do adolescents worriers and low-worriers show similar sensitivity to negative feedback, and does that differ among children (interaction between worry and age group)? We found a significant 2-way interaction between worry status (high-worry vs low-worry) and grade level (younger grade vs older grade) for negative feedback as indicated by the P3 (see Figure 1.1: the non overlapping confidence intervals around 300ms highlight that the difference between worriers and low-worriers is significantly different among children and adolescents). Specifically, as seen in Figure 1.2, worriers had a larger P3 amplitude to negative feedback compared to low-worriers regardless of whether they were children or adolescents. Of note, children and adolescent worriers did not differ on their P3 amplitude to negative feedback (see Figure 1.3). The difference between high-worriers and low-worriers, however, was much smaller among adolescents than with children (see interaction Figure 1.1).

# **Analysis Using Puberty Status.**

Do adolescents have greater sensitivity to negative feedback than children? We found a significant main effect of pubertal status, t(98) = -1.292, p = .018, CI [-0.179, -2.473]. Adolescents (mid-late puberty) had greater sensitivity to negative feedback than children (pre-early puberty status).

Do worriers have greater sensitivity to negative feedback than low-worriers? We found a significant main effect of worry status, t(98) = -2.989, p < .001, CI [-1.957, -4.143]. Worriers had greater sensitivity to negative feedback than low-worriers.

Do adolescents worriers and low-worriers show similar sensitivity to negative feedback, and does that differ among children (interaction between worry and age group)? We found a significant 2-way interaction between worry status (high-worry vs

low-worry) and pubertal status (pre-early vs mid-late) for negative feedback as indicated by the P3 (see Figure 1.1: the non overlapping confidence intervals around 300ms highlight that the difference between worriers and low-worriers is significantly different among children and adolescents). Specifically, as seen in Figure 1.2, worriers had a larger P3 amplitude to negative feedback compared to low-worriers regardless of whether they were children or adolescents. Of note, children and adolescent worriers did not differ on their P3 amplitude to negative feedback (see Figure 1.3). The difference between highworriers and low-worriers, however, was much smaller among adolescents than with children (see interaction Figure 1.1).

# Loss Feedback Interaction Worry - No Worry

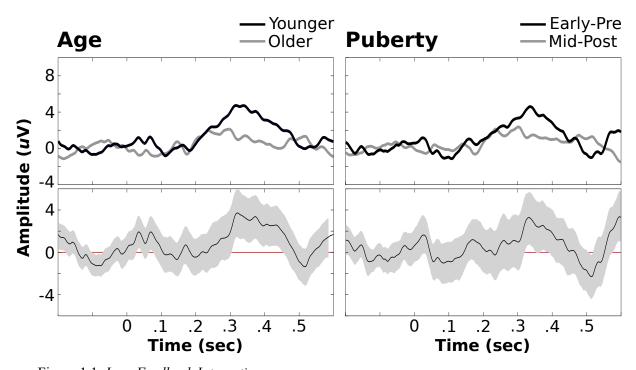


Figure 1.1. *Loss Feedback Interaction*. *Note*. Top panels show the difference between worriers and low-worriers for adolescence (grey line) and children (black line). Figures are displayed for both age group (left) puberty group

(right). Bottom panels for each figure shows the 95% bootstrapped confidence intervals for the difference scores between children and adolescents. Confidence intervals not overlapping with the red horizontal line indicate a significant difference at that time point.

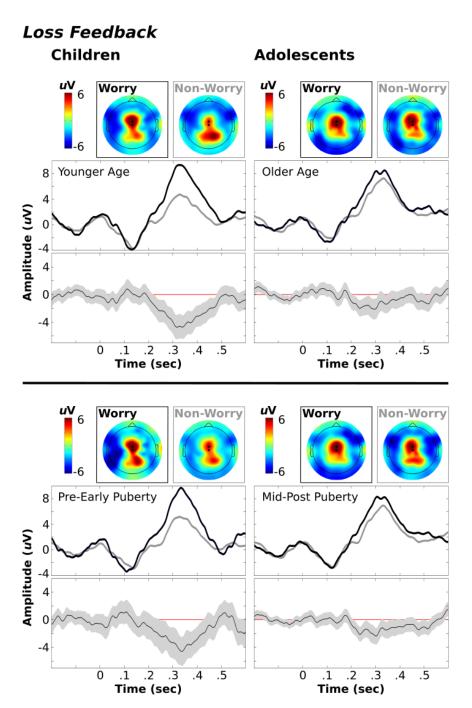


Figure 1.2. Waveforms and topographical maps for ERPs *Note.* Waveforms and topographical maps show the ERPs to loss feedback for worriers and low-worriers separately for both adolescents (right figures) and children (left figures). Figures are displayed for both puberty group (bottom figures) and grade group (top figures). Black dots on topographical maps indicate the channel cluster used for analysis. Bottom panels for each figure shows the 95% bootstrapped confidence intervals for the difference between worriers and low worries [loss for worriers-loss for low worriers]. Confidence intervals that do not overlap with the zero line (red) depict a significant difference at that time point.

# Main Effect (Worry)

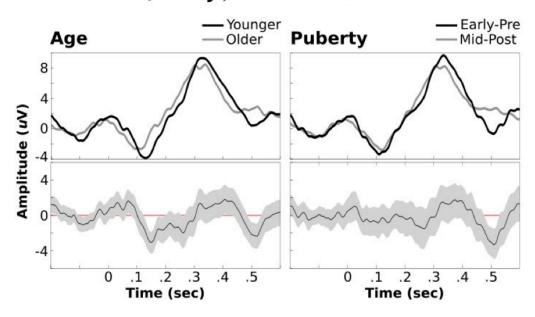


Figure 1.3. *Main effect of Worry*. *Note*. Results highlighting that children and adolescent worriers were not significantly different—as indicated by the confidence interval overlapping with the zero line at 300 ms.

## Discussion

The purpose of the current ERP study was to investigate sensitivity to negative feedback among children and adolescents who are high and low on worry. Current neurodevelopmental models suggest that adolescence is a time of sensitivity to emotionally salient experiences (e.g., sensitivity to negative feedback; Casey, 2015; Somerville et al., 2010; Steinberg, 2008). Our findings provide support for these models by highlighting that adolescents in general had a neural sensitivity to negative feedback. Indeed, even adolescents who were low on worry demonstrated a large P3 response to negative feedback, providing support for adolescents as a sensitivity period for emotionally arousing stimuli (e.g., receiving negative feedback). This finding is in-line with other research suggesting that adolescents may be particularly sensitive to "hot" tasks that are emotionally arousing compared to "cold" tasks (Grose-Fifer, Rodrigues, Hoover, & Zottoli, 2013; Prencipe et al., 2011). Receiving negative feedback appears to be an emotionally salient event. This result also highlights that sensitivity to feedback is not necessarily tied to worry.

We also found that both children and adolescents with high levels of worry are sensitive to negative feedback (i.e., have a large P3 amplitude to negative feedback). Of concern, heightened attention towards threatening/negative events has been speculated to play an important role in the development of anxiety (see, Pérez-Edgar, 2018). Thus, the current study highlights that the P3 may be an important way to identify individuals who have a large physiological reaction to negative feedback. Given that even younger children who were worriers had a large P3 amplitude, the P3 may be a useful tool to

identify individuals who have a sensitivity to negative feedback at young ages—perhaps allowing for earlier intervention.

We also were interested in comparing whether our results differed depending on whether grade level or puberty status was used to define adolescence. For the ERP results, our findings remained consistent regardless of the method used to categorize children vs adolescents (see Figure 1.1). For the behavioural results, there were some consistent findings across methods, but there were also some differences found between using grade level versus puberty status. In terms of the consistent findings, we found that adolescents (either defined by mid-late puberty or older age) were more likely to increase their number of pumps following loss feedback compared to children. This finding might suggest that when adolescents (compared to children) receive losing feedback, they may be more willing to take a risk (e.g., increase their number of pumps), perhaps in an attempt to receive more points to make up for the loss.

In terms of the inconsistent results, we found that adolescents (defined based on older age) were more likely to decrease their number of pumps after receiving win feedback compared to the younger age group. This result was not found when adolescence was defined by pubertal status. It is not entirely clear why the older age group would decrease their number of pumps after a win. It could be that they were trying to protect the points they had just won by using a safer strategy on the following trial.

When adolescence was defined by puberty status, we found a significant interaction between puberty status and worry status on their reaction time after loss feedback – win feedback. Specifically, adolescents, and children who were high worriers had a longer reaction time after receiving loss feedback (vs win feedback) compared to

the children non-worriers. In other words, when adolescents and high worriers receive negative feedback, they took longer to decide how much to pump the next balloon; thus, they may be taking longer to "recover" from or are more impacted by negative feedback than the children who were low on worry. Of interest, this finding is consistent with the ERP results suggesting that adolescents and high worriers demonstrate a sensitivity to negative feedback. This finding was not significant when adolescence was defined by grade level. Given that the puberty results were more in line with the ERP results, it may suggest that puberty is a better marker of adolescent's attentional bias to negative feedback than age (in line with previous findings; van den Bos, de Rooij, Miers, Bokhorst, & Westenberg, 2014).

There were no other significant main effects or interactions for any of the other BART outcome variables (e.g., number of pumps). Of note, other ERP studies have failed to find consistent group differences in the BART behavioural outcomes (Kóbor et al., 2015; Takács et al., 2015; Yau et al., 2015). Given that ERP studies often modify the BART task to make it more appropriate to identify ERP components (e.g., include more trials, make stimuli comparable, etc.), these modifications may help explain why ERP studies are not consistently finding the behavioural results that other non-ERP studies are demonstrating (e.g., Lejuez et al., 2007, 2002; White et al., 2008).

In a secondary analysis investigating sensitivity to win-feedback, we found that there were no differences between adolescent worriers and low-worriers. Children with higher levels of worry, however, had a larger neural reaction to positive feedback than children with lower levels of worry. This finding was not expected and requires further investigation. Of interest, all groups had larger neural sensitivity to negative feedback

than to positive feedback— in line with Kahneman and Tversky's (1979) who suggested that "losses loom larger than gains."

Despite key strengths of this study, including a large EEG sample and the inclusion of pubertal developmental as indicators of adolescence, the current study is not without limitations. First, we had participants choose the number of pumps they wanted to inflate the balloon at the *beginning* of the trial. This approach may remove some of the impulsivity involved in pumping up the balloon in real time. Second, our worry measure was a composite of three items as opposed to a complete full-scale worry measure. As the data were part of a larger study assessing a wide range of constructs, it was not feasible to include every item from a worry scale. Of note, however, the alpha for the measure used in this study was 0.838, demonstrating good reliability (Cronbach, 1951, Klein, 1999).

Overall, our findings lend support to theoretical models highlighting that adolescents may be more sensitive to emotionally salient events (e.g., receiving negative feedback) than children. Importantly, we found individual differences in sensitivity to negative feedback; worriers had even greater sensitivity than non-worriers, but this difference was much smaller among adolescents. These findings support current neurodevelopmental models highlighting adolescence as a time of sensitivity to emotionally salient stimuli. Further, our study highlights the importance of investigating individual differences among adolescents and children. Indeed, by separating worriers from non-worriers in both samples, we were able to test whether adolescents in general demonstrate a sensitivity, or whether this sensitivity is linked to worry status. Future studies should continue to investigate individual differences among children and

adolescents' sensitivity to emotionally salient events as a way of furthering our understanding of adolescent neurodevelopment.

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#### **CHAPTER 3: STUDY 2**

A longitudinal study investigating trajectories of sensitivity to threat over time and their association with alpha asymmetry among children and adolescents<sup>2</sup>

According to Gray's original Reinforcement Sensitivity Theory (1970), motivation is driven by individual differences in sensitivity to reward and sensitivity to threat. Sensitivity to reward (SR; heightened responsiveness to reward/pleasure) and sensitivity to threat (ST; heightened responsiveness to threat), also called sensitivity to punishment, can help explain why individuals may be driven to engage in or avoid certain behaviors (see Corr, 2004; Corr et al., 2013). ST in children and adolescents may be a particularly important construct to examine, as the predisposition to avoid threat may be a risk factor in the development of anxiety (Degnan & Fox, 2007). Indeed, children and adolescents who are more sensitive to threat have a greater likelihood of developing anxiety compared to those who are less sensitive to threat (Balle et al., 2013; Bar-Haim et al., 2007; Johnson et al., 2003; Katz et al., 2020; Pérez-Edgar et al., 2010, 2011; Vervoort et al., 2010). Thus, investigating sensitivity to threat is critical in order to advance our understanding of the development of anxiety in youth.

## **Right Frontal Asymmetry and Avoidance Motivation**

Avoidance motivation (i.e., the strong desire to avoid threats) is thought to be one of the core components of threat sensitivity (Gray, 1970; Gray & McNaughton, 2000). One way to measure avoidance motivation is right frontal asymmetry (neural activation associated with avoidance tendencies; Borod, 1992; Fox, 1991).

<sup>&</sup>lt;sup>2</sup>This chapter is based on the published article: Heffer, T., & Willoughby, T. (2020). A longitudinal study investigating trajectories of sensitivity to threat over time and their association with alpha asymmetry among children and adolescents. *Developmental Cognitive Neuroscience*, 100863. https://doi.org/10.1016/j.dcn.2020.100863

There is a long line of research using electroencephalography (EEG) to measure cortical activation in the frontal hemispheres (see Briesemeister et al., 2013 for a review). This research has highlighted that right anterior cortical activity is a biological substrate of avoidance motivation, whereas left anterior cortical activity is a biological substrate of approach motivation (Thibodeau et al., 2006).

Evidence for this classification emerged from studies on individuals with brain damage (and animal research) whereby damage (or disruption) to the right versus left frontal hemispheres impacted emotion differentially (Silberman & Weingartner, 1986). Patients with damage to the right frontal hemisphere (i.e., greater activation in the left hemisphere) tended to express more euphoria and positive moods, whereas those with damage to the left frontal hemisphere (i.e., greater activation in the right hemisphere) expressed more negative/avoidant moods (Lipsey et al., 1983; Robinson et al., 1983, 1984; Sackeim, 1982). Given these findings, researchers became interested in individual differences in the asymmetry between the frontal hemispheres among non-brain damaged populations. Subsequent studies have confirmed that individuals in normative populations differ in their tendency to have greater right [versus left] or greater left [versus right] cortical activation (Henderson et al., 2004; Lopez-Duran et al., 2012; McManis et al., 2002).

Frontal asymmetry is measured using the alpha frequency band (8-13 hz). Alpha power is inversely related to cortical activity (Gevins et al., 1997); thus, *lower* levels of alpha power reflect greater cortical activation. To obtain a measure of frontal alpha asymmetry, researchers subtract alpha activation in the left anterior cortex from alpha activation in the right anterior cortex (Tomarken et al., 1992). This creates a continuous

variable, with positive scores (greater right than left *alpha* activation) representing greater relative left cortical activation and negative scores (greater left than right *alpha* activation) representing greater relative right cortical activation. For clarity, in the present study we use the term 'right frontal asymmetry' to indicate frontal alpha asymmetry scores associated with avoidance tendencies [i.e., greater right (versus left) cortical activation].

# **Threat Sensitivity and Frontal Asymmetry**

Importantly, individuals with greater right frontal asymmetry should also self-report greater sensitivity to threat, given that avoidance is thought to be a key component of threat sensitivity. Despite this theorized relationship, there are inconsistencies within the literature on threat sensitivity and frontal asymmetry. Some work has found that those with greater threat sensitivity— or related constructs such as shyness and behavioral inhibition (characterized by avoidant coping styles and attentional bias to threat; Barker et al., 2019; Perez-Edgar & Fox, 2005)— have greater right frontal asymmetry (Poole et al., 2018; Sutton & Davidson, 1997; Wacker et al., 2009). Other studies, however, have found no relationship (Amodio et al., 2008; Coan & Allen, 2003; Harmon-Jones & Allen, 1997; Hewig et al., 2006).

It could be, however, that *stable* threat sensitivity (i.e., consistently high ST over time) is associated with right frontal asymmetry. Indeed, Degnan and Fox (2007) suggest that individuals who have greater right frontal asymmetry may have a lower threshold for dealing with threatening situations, and thus may be more likely to consistently report a high ST. Although no research has directly tested whether consistently high threat sensitivity is associated with right frontal asymmetry, infants and young children who are

consistently classified as behaviorally inhibited or shy have greater right frontal asymmetry than those who are less consistently classified (Fox et al., 2001; Henderson et al., 2001; McManis et al., 2002; Poole et al., 2019). Less is known about stability of threat sensitivity and alpha asymmetry, especially among children and adolescents.

# Threat Sensitivity among Children and Adolescents

Childhood and adolescence are important age groups to investigate because adolescence is proposed to be a time of heightened sensitivity to emotionally salient events (e.g., threatening events) compared to children (Casey, 2015; Somerville et al., 2010; Steinberg, 2008). For example, Casey argues in an Imbalance Model that there is asynchrony in the maturation of neural circuits within and between different brain systems, with circuitry within the subcortical limbic-striatal brain system (associated with socioemotional processing) maturing early in adolescence (likely due to puberty), but interconnections to the prefrontal executive system (associated with self-control and potential suppression of socioemotional impulses) maturing later in adolescence. This asynchrony in maturity is thought to lead to heightened activation of the limbic-striatal region during early to mid-adolescence, when neural connections to the prefrontal cortex that might dampen the activation (if appropriate) are not fully mature. As a result, adolescents are thought to be more likely to experience heightened aversive reactions to emotionally provoking negative/threatening events in comparison to children.

In line with these theories, studies have found that subcortical regions (e.g., the amygdala) increase in volume across puberty (Goddings et al., 2014) and mature earlier than higher-order cortices (e.g., prefrontal cortex; Galvan et al., 2006; Gogtay et al., 2004; Mills, Goddings, Clasen, Giedd, & Blakemore, 2014). Greater pubertal

development also has been found to be associated with heightened emotional processing (Dahl & Gunnar, 2009; Goddings et al., 2012, 2019; Schmitz et al., 2014). Indeed, adolescents, compared to children, have been found to have greater sensitivity to threat (Heffer & Willoughby, 2020; O'Brien & Bierman, 1988; Vervoort et al., 2010; Westenberg et al., 2004). Van den Bos and colleagues (2014) also found that threat sensitivity was more strongly associated with pubertal development than age. Thus, studies find that adolescents may be more sensitive to threats than children. To the best of our knowledge, the question of whether adolescents are more likely than children to report high-stable ST has not been addressed in the literature. Further, whether or not high-stable ST would be associated with right frontal asymmetry remains unknown.

#### **The Current Study**

The present longitudinal study sought to investigate whether consistently high ST is associated with greater neural avoidance motivations (i.e., great right frontal asymmetry) among children and adolescents. First, we used latent class growth curve analysis to investigate whether there are distinct subgroups of children and adolescents based on their self-reported ST across three years. Although this analysis is exploratory, we expected to find a high-stable ST group. We also examined predictors of group membership (e.g., characteristics that predict being in the high-stable ST group). Given that adolescence is thought to be a time of sensitivity to emotionally threatening events, we examined whether older age and more advanced pubertal development would be linked to a greater likelihood of being in the high-stable ST group. We expect, based on Casey's Imbalance Model that adolescents would be more likely to report stable high levels of ST than children. Critically, we also examined whether the groups found in the

latent class growth curve analysis would differ on right frontal asymmetry scores. We hypothesized that a group characterized by high-stable ST would have greater right frontal asymmetry compared to groups with lower or less stable ST.

#### Method

## **Participants**

Participants (*N* = 361, age range = 8-14 at year 1, 47.5% female) were drawn from several elementary and high schools in southern Ontario, Canada, and were surveyed annually across three years. Students were part of a larger study examining the relationship between wellbeing and youth health-risk behaviors. Parents were asked to identify if their child had any illnesses or disabilities (either physical or mental). Two participants were excluded because of a diagnosis of autism, one participant was excluded because they are prone to seizures, and one participant was excluded because of a diagnosis of cerebral palsy. Parent report indicated that 83.7% of the children and adolescents were White, 1.9% were Black, 0.8% were Asian, 1.4% were Hispanic, 0.6 Indigenous, and 5.5% were Mixed (a further 0.6% of parents indicated that they preferred not to answer the question). On average, parental education was "completed a college/apprenticeship and/or technical diploma".

#### **Procedure**

Students were invited to participate in the study through visits to schools. Surveys were completed in classrooms during school hours and all participants received gifts (e.g., backpacks) as compensation. All students who completed the survey in the first year were invited to participate again in the second year. Participants also completed a Mobile Lab component in which their resting EEG was recorded. Given the size of the

sample, data collection for the Mobile Lab began in year 2 of the study and finished in year 3. Resting EEG was collected for a total of 4 minutes (2 minutes with eyes open and 2 minutes with eyes closed) while they were seated comfortably. There were 18 participants who had equipment issues during the task (e.g., the event markers did not show up) and two participants did not complete the task. There also were 16 participants who were not included because their EEG data was not usable (e.g., contained a larger number of muscle/movement artifacts). Thus, the final sample included 322 participants. The University Ethics Board approved this study and participants provided informed assent and their parents provided informed consent.

## **Missing Data Analysis**

Missing data occurred within each assessment because some participants did not complete the questionnaire (average missing data = 2.433%), and because some participants were absent during the time of the survey. The percentage of participants absent for the survey at each time point was 6.4% at Year 1, 4.4% at Year 2, and 22.7% at Year 3, respectively. Missing data was primarily due to absenteeism but also occasionally due to time conflicts, students declining to participate in one part of the survey, RA mistakes (e.g., not inviting a child to complete the survey), or students moving to another school district with no contact information. Participants who were absent at one or two of the time points were not significantly different from participants who were there at all three time points on any of the study measures (p > .05). Missing data were imputed using the expectation-maximization algorithm (EM). EM retains cases that are missing survey waves and thus avoids the biased parameter estimates that can occur with pairwise or listwise deletion (Schafer & Graham, 2002).

#### Measures

**Demographics.** Pubertal status, age, sex, and parental education (one item per parent [averaged together] using a scale of 1= did not finish high school to 6 = professional degree) were collected at all three years. Pubertal status was assessed using the Puberty Development Scale (PDS; Petersen, Crockett, Richards, & Boxer, 1988). The PDS is a self-report measure that assesses body hair, facial hair, and voice development in boys, and body hair, menarche, and breast development in girls. All items were rated on a 4-point scale from 1 (not yet started changing) to 4 (change seems complete). The PDS scale exhibits good reliability and validity (Carskadon & Acebo, 1993; Petersen et al., 1988).

Sensitivity to Threat. At Years 1 to 3, participants reported the extent to which they agreed with three items specifically examining ST from the Behavioural Inhibition Scale (Carver & White, 1994; "Criticism hurts me quite a bit", "I feel worried when I think I have done poorly at something", "I feel pretty worried or upset when I think or know somebody is angry at me") on a scale ranging from 1 (*Strongly Disagree*) to 4 (*Strongly Agree*). Higher scores indicate higher levels of threat sensitivity. Cronbach's alpha was 0.77, 0.80, 0.78 at years 1-3, respectively. Of note, we ran an exploratory factor analysis with our items and found that they formed one factor (all factor loadings >.82). We also ran a repeated measures ANOVA to investigate whether the sensitivity to threat increased over time. A repeated measures ANOVA with a Greenhouse-Geisser correction determined that mean sensitivity to threat was significantly different across time points, F(1.9, 684) = 4.942, p = 0.08. Post hoc tests using the Bonferroni correction revealed that sensitivity to threat increased between Time 1 and Time 3 ( $M_{\rm diff} = .124$ , SE

= .041, p = .008; see Table 2.2 for means at each time point). This finding is consistent with the idea that sensitivity to threat may increase across adolescence.

## **Electrophysiological Recording**

Electroencephalography (EEG) was recorded continuously from a BioSemi ActiveTwo system using a 96-channel montage and 7 face sensors. The data were digitized at a sampling rate of 512 Hz. Pre-processing was conducted to identify (1) channels/components that were unreliable within a given time-period, (2) time-periods that were unreliable, (3) and channels/components that were unreliable throughout the recording.

## **Pre-processing (Channels)**

Pre-processing was automated (using MATLAB 2012b scripts) to be carried out using EEGLAB (Delorme & Makeig, 2004) version 13.6.5b and was then executed using Octave on Compute Canada's high performance computer cluster (Cedar; see Desjardins & Segalowitz, 2013; van Noordt, Desjardins, & Segalowitz, 2015; van Noordt, Desjardins, Gogo, Tekok-Kilic, & Segalowitz, 2017 for more details). The data were first separated into 1 second non-overlapping time windows. For each time window, the voltage variance across each channel was calculated (a 20% trimmed mean was used). Channels were flagged as unreliable if they had a z-score six times greater than the voltage variance across all channels. Time-periods (i.e., the 1 second time windows) were considered unreliable if more than 10% of the channels were identified as having extreme voltage variances. Finally, any channels that were flagged in more than 20% of the time-periods were considered unreliable throughout the recording.

The data were re-referenced to an interpolated average of 19 sites, excluding flagged channels. The data were filtered with a 1 Hz high pass and 30 Hz low pass filter given that cortical activity would not be expected to exceed 30 Hz. After this step, the data were again checked for the same issues reported above: (1) channels that are unreliable within a given time-period, (2) time-periods that are unreliable, (3) and channels that are unreliable throughout the recording. Specifically, any channels that were unlike its neighbouring channels (e.g., had a low correlation with channels around it), were flagged. A channel was flagged as unreliable if it had a z-score that was 2.326 times greater than the mean of the 20% trimmed distribution of correlation coefficients. Time-periods were considered unreliable if more than 10% of the channels within the window were flagged as unreliable. Any individual channels that were flagged in more than 10% of time-periods were considered unreliable across the entire recording. Bridged channels (i.e., channels that are highly correlated with invariable signal) were identified after dividing the average maximum correlation by the standard deviation of the distribution of correlation coefficients. Channels that had a positive z-score that was eight times greater than the 40% trimmed distribution of coefficients were flagged as bridged channels.

## **Pre-Processing (Components)**

After pre-processing the channel data, all data that had not been flagged as unreliable was concatenated back into continuous data. These data were then submitted to an initial Adaptive Mixture of Independent Component Analysis (AMICA) to identify different components of the EEG data (e.g., heart rate components, eye blink

components, cortical components etc.). This process helps to separate brain activity (neural components) from non-neural activity (e.g., muscle movement).

During this procedure, the data were windowed into 1 second time epochs. Unreliable components were detected by comparing each individual component to the variance among all components. Components were flagged if they had a z-score that was 2.326 times greater than the trimmed mean. Time-periods that had more than 10% of its components flagged were considered unreliable. The data were then concatenated into the continuous time course and submitted to three simultaneous AMICA decompositions to assess whether components were replicable (i.e., is muscle movement consistently being classified as muscle movement when the process is repeated multiple times). The procedure above for identifying unreliable components (within 1 second epochs) was completed again using the continuous time series data. Next, a dipole (which identifies the position and orientation for the distribution of positive and negative voltages) was fit using the dipfit plugin in Matlab (Oostenveld, Fries, Maris, & Schoffelen, 2011). Components with a dipole fit residual variance greater than 15% were flagged. Finally, components were classified using the ICMARC plugin. This process assesses each component against a crowd-sourced database to identify activation consistent with five different categories: eye blinks, neural, heart, lateral eye movements, muscle contamination, and mixed signal.

After pre-processing, a manual quality control review was completed to ensure that the decisions made during pre-processing were appropriate. This procedure was completed by one trained research assistant who assessed the accuracy of the independent component classifications. For example, the research assistant would identify whether

cortical components were correctly distinguished from non-cortical components (e.g., muscle, eye blinks, etc.) based on topographical projection, continuous activation, dipole fit and power spectrum profile. Thus, the quality control review involved using the independent components to help with artifact correction.

## **EEG** post-processing

Resting EEG was recorded for a total of 4 minutes (2 minutes with eyes open [EO], 2 minutes with eyes closed [EC]). Consistent with previous studies, frontal alpha (8-13 Hz) was measured at F3 (left scalp location) and F4 (right scalp location; Allen et al., 2004; Davidson, 2000; Poole et al., 2019; Schmidt, 1999). The average of EO and EC conditions were taken. The data were then log(ln) transformed to correct for skewed distributions. To get a measure of alpha asymmetry, power from the left site was subtracted from power from the right site (Ln F4-Ln F3). Positive scores (greater right than left *alpha* activation) represent greater relative left cortical activation while negative scores (greater left than right *alpha* activation) represent greater relative right cortical activation. The range of alpha asymmetry scores for this sample was -2.87 to 2.59 (M = -622, SD = .717).

## Plan of Analysis

A latent class growth curve analysis was conducted using Mplus 7 (Muthén & Muthén, 2012). We used *MplusAutomation* (Hallquist & Wiley, 2018), a package in R (R Core Team, 2019), to automate the latent class growth curve analysis and extract the model parameters from Mplus. ST was measured at all three time points and used as latent class indicators. In order to determine the number of groups that were best represented by the data, four criteria were considered: 1) interpretability of the classes, 2)

Bayesian information criterion (BIC), such that smaller values of BIC indicate a better fit model, 3) significance of the Lo-Mendell-Rubin Likelihood Ratio Test (LMR-LRT) significance value— once non-significance is reached, the number of classes prior to non-significance is defined as the appropriate number, and 4) average latent class conditional probabilities are close to 1.00 (Nylund et al., 2007). After establishing the existence of latent classes, a multinomial logistic regression was run to establish whether demographic variables at year 1 (sex, age, parental education, and pubertal status) predicted group membership (see Figure 2.1 for correlations between demographic variables).

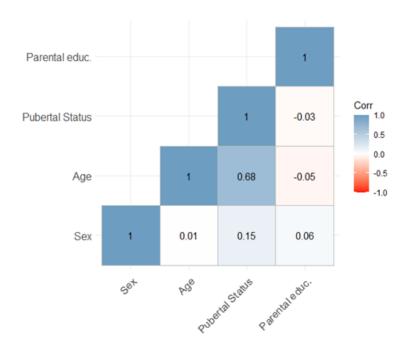


Figure 2.1. Bivariate correlations for the demographic variables. *Note.* The plot was made using ggcorrplot in R (Lishinski, 2018). Of note, sex was coded as 0 = male, 1 = female.

Class differences in alpha asymmetry were examined using an ANCOVA, with alpha asymmetry as the dependent variable and class as the independent variable. Sex, parental education, age, and pubertal status were included in the analysis as covariates. Of note, the EEG data collection occurred in year 2 and year 3 of the study; therefore, age and pubertal status may be different depending on what year the EEG data was collected. To account for this, we created variables that used year 2 demographics for participants who completed the lab in year 2, and year 3 demographics for participants who completed the lab in year 3. Thus, we were able to control for age and pubertal status in the year that participants completed the mobile lab.

#### Results

## Latent class growth curve analysis

The latent class growth analysis was conducted for 1-4 classes. The three-class solution was chosen as the best classification of the data (see Table 2.1). This classification had the lowest BIC, and a LMR-LRT significance value that was significant at 3 classes but not at 4 classes, indicating that three classes was a better fit to the data. This solution also was interpretable and had conditional probabilities close to 1.00. The three groups were characterized as follows: low-stable ST (LowStb ST; 14.0% of the sample), moderate-increasing ST (ModInc ST; 54.3% of the sample) and high-stable ST (HighStb ST; 31.7% of the sample). See Figure 2.2 for an illustration of the groups. The means for threat sensitivity across all three time points for each group, and the slopes, are presented in Table 2.2. ANOVAs revealed that the three groups were significantly different from each other on ST at all three years (ps < .001).

Table 2.1. Latent Class Analysis fit indices.

| Number of | BIC     | Entropy | Conditional   | LMR          | BLRT         |
|-----------|---------|---------|---------------|--------------|--------------|
| Classes   |         |         | Probabilities | Significance | Significance |
| 2 Classes | 2221.13 | 0.78    | 0.91-0.95     | 0.0006       | < 0.00       |
| 3 Classes | 2180.03 | 0.70    | 0.85-0.93     | 0.0008       | < 0.00       |
| 4 Classes | 2181.65 | 0.71    | 0.76-0.90     | 0.1097       | < 0.00       |

*Note.* BIC= Bayesian information criterion. LMR = Lo-Mendell-Rubin, BLRT= Bootstrapped Likelihood Ratio Test.

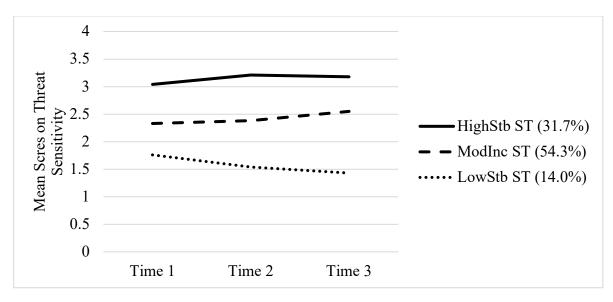


Figure 2.2. Results of the latent class growth curve analysis. Note. ST = Sensitivity to threat.

Table 2.2. Group Means on Sensitivity to Threat and Their Slopes.

|            | Low-stable ST | Mod-increasing ST | High-stable ST | Overall ST |
|------------|---------------|-------------------|----------------|------------|
| Mean1(SD)  | 1.76(0.73)    | 2.33(0.64)        | 3.04(0.55)     | 2.47(0.76) |
| Mean2(SD)  | 1.54(0.51)    | 2.38(0.57)        | 3.21(0.44)     | 2.52(0.75) |
| Mean3(SD)  | 1.43(0.40)    | 2.55(0.32)        | 3.18(0.36)     | 2.59(0.65) |
| Slope (SD) | -0.15(0.09)   | 0.13(0.03)***     | 0.05(0.04)     |            |

*Note.* Mod = moderate, ST= sensitivity to threat. Means 1, 2, and 3 represent the means at Years 1, 2 and 3 of the study, respectively. SD= Standard deviation. \*\*\*p < .001

# **Predictors of Group Membership**

Multinomial logistic regression was used to predict whether sex, parental education, age, and pubertal status were associated with group membership. Means and standard deviations for the demographic variables across the different groups are presented in Table 2.3. Group status (LowStb ST, ModInc ST, HighStb ST) was entered as the dependent variable and sex, parental education, age, and pubertal status were entered as the independent variables. The overall model was significant  $\chi 2(8) = 48.38$ , p < .001. Sex (p < .001), parental education (p = .009), and pubertal status (p = .002) significantly differentiated among the classes. Females had greater odds of being in the HighStb ST (OR = 5.094, p < .001) and ModInc ST (OR = 3.631, p = .001) groups than in the LowStb ST group. Further, individuals with higher parental education had greater odds of being in the HighStb ST group compared to the ModInc ST group (OR = 1.554, p = .003) and compared to LowStb ST group (OR = 1.531, p = .046). Participants with greater pubertal development had higher odds of being in the HighStb ST group

compared to the ModInc ST group (OR = 2.217, p = .011) and compared to the LowStb ST group (OR = 4.869, p = .004). There were no other significant differences (of note, we also re-ran the model with only age, sex, and parental education as predictors. In this model, age was not a significant predictor of class, p = .066).

Table 2.3. Means and standard deviations of demographic variables as a function of group

| Demographic Variables | Low-stable ST | Mod-increasing ST | High-stable ST |
|-----------------------|---------------|-------------------|----------------|
| Sex                   | 20.0% Female  | 47.7% Female      | 59.6% Female   |
| Parental Education    | 4.04(0.94)    | 4.05(0.87)        | 4.31(0.84)     |
| Age                   | 9.76(1.41)    | 9.67(1.47)        | 10.00(1.40)    |
| Pubertal Status       | 1.25(0.40)    | 1.36(0.50)        | 1.57(0.65)     |
|                       |               |                   |                |

*Note.* Mod = moderate, ST= sensitivity to threat.

# **Differences among Classes on Alpha Asymmetry**

An ANCOVA was run with alpha asymmetry scores as the dependent variable and class (LowStb ST, ModInc ST, HighStb ST) as the between-subjects factor. Sex, parental education, age, and pubertal status were included as covariates. There was a significant main effect of class, F(2, 299)=3.383, p=.035. Post hoc analyses revealed that the HighStb ST group had more negative alpha asymmetry scores (i.e., right frontal asymmetry; M=-.777, SD=.686) than the ModInc ST group (M=-.551, SD=.746) and

the LowStb ST group (M= -.547, SD= .623), ps < .05. There were no differences found between the ModInc ST group and the LowStb ST group (p= .976). The covariates were not associated with alpha asymmetry (p > .05; see Table 2.4).

Table 2.4. Results of the ANCOVA for Group Differences on Alpha Asymmetry

|                    | df | F     | p     | $n^2p$ |
|--------------------|----|-------|-------|--------|
| Sex                | 1  | 1.486 | .224  | .005   |
| Parental Education | 1  | .038  | .845  | .000   |
| Age                | 1  | 2.219 | .137  | .007   |
| Pubertal Status    | 1  | 1.672 | .197  | .006   |
| Group membership   | 2  | 3.383 | .035* | .022   |

Note: \*p < .05.

#### Discussion

Avoidance motivation is thought to be an important component of threat sensitivity. However, research on right frontal asymmetry, a neural index of avoidance tendencies, and threat sensitivity is mixed. It may be that *stable* threat sensitivity (i.e., consistently high ST over time) is associated with right frontal asymmetry. Indeed, Degnan and Fox (2007) suggest that individuals who have greater right frontal asymmetry may have a lower threshold for dealing with threatening situations, and thus may be more likely to consistently report a high ST. The current study examined whether developmental trajectories of threat sensitivity (e.g., consistently reporting high ST) are associated with right frontal asymmetry in a sample of children and adolescents. This age group is particularly important to examine given that adolescence is thought to be a time of increased sensitivity to emotionally salient events (Casey, 2015; Somerville et al., 2010; Steinberg, 2008)—perhaps heightening their ST compared to children. To address these questions, we first conducted a latent class growth curve analysis to investigate different trajectories of ST. Next, we examined predictors of group membership, specifically to identify whether adolescents (as measured by age and pubertal status) were more likely to be part of the high-stable ST group. Critically, once we established the developmental trajectories, we investigated whether these trajectories were associated with right frontal asymmetry.

Results from the latent class growth curve analysis identified three distinct trajectories: as predicted, a HighStb ST group was found, representing a third of the sample. We also found a smaller LowStb ST group (14.0% of the sample), and a ModInc ST group, representing 54.3% of the sample. The most common trajectory among this

age group, therefore, was moderate yet increasing ST across the three years. This finding suggests that it may be normative for children and adolescents to report slightly higher levels of ST as they get older. Further, 32% of our sample were classified as HighStb ST, highlighting that a relatively large proportion of children and adolescents are reporting consistently high sensitivity to threat.

Pubertal status, but not age, predicted greater odds of being in the HighStb ST group than in the other two groups. Indeed, neurodevelopmental imbalance models highlight that changes in neural circuitries in early adolescence, hypothesized to lead to increased sensitivity to emotionally salient events, may be a result of pubertal development. Our results are consistent with this model: more advanced pubertal development, rather than age, was a better indicator of being in the HighStb ST. A strength of this study is that we used both age and pubertal status as predictors of group membership. Indeed, if we had only used age in our model, we would have missed an important finding relating to puberty (one that is in line with the Casey's Imbalance Model, 2015).

We also found that females had greater odds of being in the HighStb ST and ModInc ST groups compared to LowStb ST group. This is perhaps not surprising given that females tend to reach puberty earlier, and thus, may have increased ST, resulting in greater odds of being in the higher ST groups at Time 1 in comparison to males. This finding is consistent with some studies showing that females report greater ST than males (Santesso et al., 2011; Tull et al., 2010). We also found that participants with *greater* parental education had higher odds of being in the HighStb ST group compared to the ModInc ST group and the LowStb ST group. Although this finding was not among our

main hypotheses, we speculate that perhaps children and adolescents who have parents with higher levels of education may feel more pressure to succeed and thus may report feeling worse about threatening events (e.g., receiving criticism).

A key interest in this study was whether frontal asymmetry was associated with the trajectories of ST. We found that the HighStb ST group had greater right frontal asymmetry scores compared to the other groups. These results are consistent with previous research suggesting that *stable* and higher behavioral inhibition (a related construct) is associated with right frontal asymmetry in a small group of infants and young children (e.g., Chronis-Tuscano et al., 2009; Fox et al., 2001). Therefore, when individuals report or exhibit stable high ST, they show neural activation consistent with greater avoidance motivation. A strength of our study was the combining of EEG methods with self-report. This combination provides a more comprehensive understanding of ST across development. Our findings indicate that not only do those with more advanced pubertal development have greater odds of being in the HighStb ST group, there also are neural differences associated with this pattern of reporting.

Despite the strengths of our study, there are several limitations. First, EEG was collected across two years of the study; thus, not all student's EEG data was collected in the same year. This is not surprising given the size of our sample of children and adolescents. Although a large sample was critical to identify distinct groups of children and adolescents on threat sensitivity, the design of our study does not allow for us to investigate whether alpha asymmetry is a predictor of stable threat sensitivity. To test this question, an optimal design would be to collect EEG and sensitivity to threat data at each time point. In doing so, future research would be able to examine the direction of effects

between threat sensitivity and alpha asymmetry over time (i.e., does greater right frontal asymmetry predict more stable threat sensitivity and/or does more stable threat sensitivity predict greater right frontal asymmetry over time).

Second, our sensitivity to threat measure was a composite of three items from the BIS measure as opposed to the full BIS measure. As the data were part of a larger study assessing a wide range of constructs, it was not feasible to include every item from the BIS scale. Of note, however, the alpha for the measure used in this study ranged from .77 to .80 across the three years, demonstrating good reliability (Cronbach, 1951). Third, our measure of threat sensitivity was designed in accordance with the original Reinforcement Sensitivity Theory; however, revisions to the theory suggest that anxiety may result from conflict between both avoidance and approach motivation (Gray & McNaughton, 2000). Future research should investigate whether frontal asymmetry is associated with a revised measure of the Reinforcement Sensitivity Theory, one that addresses this approach/avoidance conflict. Fourth, our study had a large percent (22.7%) of missing data at year 3 due primarily to absenteeism. Given that the questionnaires used for this study were administered during class time, we had no control over whether students would be absent or unavailable during that time period. Finally, our overall sample had a mean alpha asymmetry score of -.622; thus, our overall sample tended to have greater right than left frontal asymmetry. Although this was not expected, some studies also have found greater right than left frontal asymmetry among children and adolescents (e.g., Winegust et al., 2014).

Overall, this large longitudinal study has important developmental implications.

In support of current neurodevelopmental models, more advanced pubertal development

may be an important measure for identifying those who will report stable high ST. We did not find this same pattern of results with age; thus, our results suggest that puberty is a better marker of distinct trajectories of ST than age. Additionally, the HighStb ST group had greater right frontal asymmetry than the other groups. Thus, the current study highlights that sensitivity to threat seems to have important neurological underpinnings associated with both puberty and alpha activation in the brain.

Although advanced pubertal development predicted membership in the HighStb ST group, it is important to note that puberty would not be expected to increase ST among all youth. Instead, our results suggest that advanced pubertal development increases the odds of being specifically in the HighStb ST group. However, this group represented only 31% of the sample; thus, there are clear individual differences in ST across development. Future research should extend these findings to investigate how these trajectories of ST may change beyond adolescence (i.e., is there a percentage of the HighStb ST group that *remains* consistently sensitive to threat into adulthood?). Given that stable ST has been found to be associated with anxiety, identifying groups of individuals with (and neural predictors of) high/stable ST is of critical importance.

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#### **CHAPTER 4: STUDY 3**

# Investigating the consistency of ERPs across threatening situations among children and adolescents<sup>3</sup>

Several theories of adolescent development posit that adolescence may be a time of heightened sensitivity to emotionally salient events (Casey, 2015; Somerville et al., 2010; Steinberg et al., 2008). Indeed, adolescents tend to report greater sensitivity to threat— one type of emotionally salient event— compared to children (O'Brien and Bierman 1988; Vervoort et al. 2010). In contrast, there also is some work suggesting that adolescents may have lower threat sensitivity compared to children (e.g., Humphreys et al. 2016; McCormick and Telzer 2017); see Ernst and colleague's (2006) Triadic Model which posits that adolescents have a strong reward system but a *weak* harm-avoidant system. Thus, the relationship between threat sensitivity and development remains unclear. Of concern, heightened sensitivity to threats has been found to be associated with anxiety (e.g., Balle et al., 2013; Bar-Haim et al., 2007; Johnson et al., 2003; Katz et al., 2020; Pérez-Edgar et al., 2010, 2011; Vervoort et al., 2010); therefore, it is critical to advance our understanding of threat sensitivity among youth.

There are a variety of different situations, however, that youth may find threatening, such as receiving negative feedback, making mistakes, and seeing angry faces. In survey research, these threatening situations are generally combined into one overall measure of threat sensitivity [e.g., Behavioral Inhibition Scale (BIS; Carver & White, 1994); Sensitivity to Punishment Scale (Torrubia et al., 2001)].

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For example, the BIS includes questions assessing responsiveness to negative feedback (e.g., "Criticism or scolding hurts me quite a bit"), making mistakes (e.g., "I worry about making mistakes"), and worrying about whether someone is angry at you ("I feel pretty worried or upset when I think or know somebody is angry at me"). Thus, in survey research, the assumption is that people who are high on sensitivity to threat in one situation also tend to be high in other situations. Within the neuroscience literature, however, different threatening situations are treated as distinct events, each being investigated in isolation from each other. For example, a task where someone receives negative feedback about their performance (e.g., a gambling task) is not compared to a task where someone makes mistakes (e.g., during a go/no-go task); yet both of these situations are captured within the same self-report survey. Research has yet to investigate (1) individual differences in the consistency of ERP activation across different threatrelated events (e.g., Do some participants have consistently high neural activation across different threat-related events, while others show heightened neural activation to only one or two events?) and (2) what demographic and self-report factors are associated with individual differences in neural activation across different tasks (e.g., do adolescents have more consistently high neural activation to threats than children? Do individuals who self-report greater threat sensitivity have consistently higher activation across these tasks?).

#### ERPs to threatening situations

One way to investigate how an individual reacts to different types of threats is to consider their neural activation directly after a threatening event occurs. Event-related potentials (ERPs: an averaged EEG response that is time-locked to an event; Luck, 2005)

can provide a sensitive measure of neural activation directly after a threatening event happens (e.g., after an individual receives negative feedback). We have elected to investigate three different types of threatening events that are consistent with self-report measures of threat sensitivity: receiving negative feedback, making mistakes, and viewing angry faces. Below, we discuss three ERPs that are elicited in response to these types of events and have previously been associated with self-reported threat sensitivity.

Negative feedback (P3). The P3 is an ERP component that is associated with paying attention to feedback (Huang et al., 2015; Luck, 2005). Previous research has found that individuals who have greater sensitivity to threat tend to have larger P3 amplitudes to negative feedback than those with lower sensitivity to threat (e.g., De Pascalis et al., 2004; Heffer & Willoughby, 2020; Miltner et al., 2005). Further, Reeb-Sutherland et al. (2009) found a trend whereby high sensitivity to negative feedback and larger P3 amplitudes were associated with greater anxiety.

Making mistakes (ERN). The error-related negativity (ERN) is an ERP that is associated with performance monitoring, specifically when making mistakes during an inhibitory control task. Indeed, this ERP corresponds to the motivational significance of errors, whereby a larger ERN is associated with greater motivation to avoid errors (Hajcak & Foti, 2008; Meyer, 2017). Individuals with greater threat sensitivity or anxiety tend to have larger ERNs when making errors than those with lower threat sensitivity or anxiety (Boksem et al., 2008; Chong & Meyer, 2019; Hajcak et al., 2003; Ladouceur et al., 2006; Meyer, 2017; Meyer & Hajcak, 2019; Weinberg et al., 2010).

**Viewing angry faces (N170).** N170 is an ERP that is elicited to faces (e.g., angry faces). Previous research has found that the N170 is larger in response to angry faces

compared to other emotional expressions (e.g., neutral or happy Denefrio et al., 2019; Hinojosa et al., 2015; Jetha et al., 2013; Kolassa et al., 2009, 2007; Rossignol et al., 2005). Further, individuals with greater threat sensitivity (or anxiety) tend to have a larger N170 to angry faces than those with less sensitivity to threat or anxiety (Bechor et al., 2019; Kolassa & Miltner, 2006; O'Toole et al., 2013; Wieser et al., 2010).

Age-related differences in ERPs. Of note, there has been some work identifying age-related differences in these ERPs across development (Downes et al., 2017). Specifically, there is evidence that the ERN (e.g., Davies et al., 2004; DuPuis et al., 2015; Kim et al., 2005; Santesso et al., 2006; Wiersema et al., 2007) and the P3 (e.g., Heffer & Willoughby, 2020; van Dinteren et al., 2014) tend to be larger among older participants. Other studies, however, have not found this pattern of age-related changes among the ERN or the P3 (e.g., Eppinger et al., 2009; Grose-Fifer et al., 2014). Age-related changes in the N170 are less consistent. Some studies have found that this ERP also gets larger with age (e.g., Hileman et al., 2011), while others have shown that the N170 fluctuates across development, showing more positive values around late childhood and early adolescence followed by greater negativity into adulthood (Batty & Taylor, 2006; Kuefner et al., 2010; Taylor et al., 2004). Overall, this research highlights that age may be an important factor to consider when investigating the ERN, P3, and N170. This research, however, has rarely taken into consideration individual differences that may also affect ERP amplitudes. Indeed, youth who are in the *same age group* have a larger N170s, ERNs or P3 when they have greater anxiety-related symptoms than when they do not have anxiety-related symptoms (e.g., Chong & Meyer, 2019; Heffer & Willoughby,

2020; O'Toole et al., 2013). Thus, it is unlikely that these changes in amplitude across development are simply the result of age.

To date, these ERPs have been investigated in isolation and no study has investigated whether individuals have neural consistency across these ERPs. In other words, it is not clear whether the same individuals have a high neural sensitivity across these different threat-related events (i.e., are individuals consistently sensitive to different threats?). Based on self-report measures of sensitivity to threat—that incorporate these different threatening situations all into one measure— we might expect that individuals will be consistently sensitive (or not) across these different situations. From a neuroscience perspective, however, these threat-related events are examined in separate lines of research and each of these ERPs are thought to have different neural generators. For example, studies that have combined fMRI and EEG have suggested that the ERN is generated in the anterior cingulate cortex (Debener et al., 2005; Mathalon et al., 2003) – an important region involved in goal-directed behavior (Holroyd & Yeung, 2012). The N170, however, is thought to be activated in face processing regions (e.g., superior temporal sulcus or the fusiform gyrus; Sadeh et al., 2010), while the P3 is a neural indicator associated with attention (Huang et al., 2015; Luck, 2005). Thus, within the neuroscience field, these different threatening events are thought to be distinct and related to different neural processes. No study has investigated individual differences in consistency of neural activation across these different tasks. Importantly, cumulative neural-level sensitivity across these different threats (e.g., across a number of situations) may be important to consider when targeting individuals at risk factors for anxiety, given

that these individuals would have a high reactivity to threat across multiple situations (and multiple neural generators).

At the same time, there may be some children and adolescents who are not concerned with these threatening situations (e.g., they may be consistently low on these ERPs). Indeed, some individuals may be less bothered by these types of threats, and therefore may pay less attention to negative feedback, errors, or angry faces. For instance, impulsive individuals tend to be less concerned with threatening situations and instead engage in non-reflective, stimulus-driven responses (Nigg, 2017). Previous research has found that impulsive individuals tend to have smaller P3 amplitudes (Justus et al., 2001; Ruchsow et al., 2008) and smaller ERN amplitudes (Checa et al., 2014; Pailing et al., 2002; Ruchsow et al., 2005; Stahl & Gibbons, 2007; J. B. Taylor et al., 2018) compared to individuals who are less impulsive. Less is known about whether impulsive individuals have smaller N170 activation to angry faces; thus, this latter analysis is more exploratory.

### The Current study

The current study seeks to assess whether consistently high neural activation to threats across different tasks is associated with both demographic and self-report factors (sensitivity to threat, impulsivity, age, pubertal status, sex, and parental education). While this analysis is exploratory, we expect that individuals who self-report higher sensitivity to threat and lower impulsivity will have consistently higher neural activation to threats. We also predict that adolescents (those with more advanced pubertal development and older age), will be more likely to have consistently higher neural activation to threats.

In a follow up analysis, we further investigate whether the results will replicate when using a difference score for each of these threatening events (i.e., P3 loss - P3 wins;

N170 angry - N170 neutral; ERN - CRN). A difference score specifically examines whether individuals have higher neural activation to threats than to non-threatening events. One difference between this analysis and the previous analysis is that difference scores offer a way to investigate whether individuals have neural activation that is specific to threats. In other words, difference scores provide a method for checking if individuals have greater activation to threats than non-threats. At the same time, however, only investigating difference scores can sometimes make interpretation of the results unclear. For example, an individual who has high neural activation to receiving negative feedback and high activation to receiving positive feedback would have a low difference score, but their score could be identical to a person who has low neural activation to negative feedback and low neural activation to positive feedback. Given the different strengths and weaknesses of these analyses, we include both an analysis using only the threat-related ERPs and an analysis using the difference score.

### Method

## **Participants**

Participants (N = 228,  $M_{\rm age} = 10.57$ , SD = 1.77; age range = 8-14, 49.36% female) were drawn from several elementary and high schools in southern Ontario, Canada and were part of a larger study examining the associations between wellbeing and youth health-risk behaviors. Parent report indicated that 82.96% of the children and adolescents were White, 1.89% were Black, 1.42% were Asian, 2.36% were Hispanic, 0.47% Indigenous, and 9.43% were Mixed (a further 0.47% of parents indicated that they preferred not to answer the question).

### Procedure

Students were invited to participate in the study through visits to schools. Surveys were completed in classrooms during school hours and all participants received gifts (e.g., backpacks) as compensation. Participants also completed a Mobile Lab component in which EEG data was recorded. Parents were asked to identify if their child had any illnesses or disabilities (either physical or mental). One participant was excluded because of a diagnosis of autism. Eleven people were excluded because of equipment issues (e.g., the event markers did not show up) on at least one of the tasks. Fifteen people were excluded because EEG data was not usable (e.g., contained a larger number of muscle/movement artifacts) on at least one of the tasks. Two participants did not complete one of the tasks and five participants did not follow the instructions (e.g., they were off task). We also had 33 participants who had less than 6 trials on the ERN, which can be cause for concern (Olvet & Hajcak, 2009). Thus, we removed these participants from our analyses. The final sample included 161 participants. Of note, the final sample was fairly equally distributed among children 8-11 (N = 91) and adolescents 12-14 (N = 91) 70). The University Ethics Board approved this study and participants provided informed assent and their parents provided informed consent.

## **Missing Data Analysis**

Missing data occurred because some participants did not finish the questionnaire (average missing data = 5.09%) and because some participants were absent during the time of the survey. The percentage of students who completed the survey was 93.43%. Missing data was primarily due to absenteeism, but also occasionally due to time conflicts, RA mistakes (e.g., not inviting a child to complete the survey), or students moving to another school district with no contact information. Missing data were imputed

using the expectation-maximization algorithm (EM). EM retains cases that are missing survey waves and thus avoids the biased parameter estimates that can occur with pairwise or listwise deletion (Schafer & Graham, 2002).

### Measures

Demographics. Pubertal status, age, sex, and parental education were collected. Parental education was measured with one item per parent on the following scale: 1 (did not finish high school); 2 (high school diploma); 3 (some university/college); 4 (associate degree/diploma); 5 (undergraduate degree); 6 (graduate degree). The average level of parental education for this sample was a 4, "completed an associate degree and/or technical diploma". Pubertal status was assessed using the Puberty Development Scale (PDS; Petersen et al., 1988). The PDS is a self-report measure that assesses body hair, facial hair, and voice development in boys, and body hair, menarche, and breast development in girls. All items were rated on a 4-point scale from 1 (not yet started changing) to 4 (change seems complete). The PDS scale exhibits good reliability and validity (Carskadon & Acebo, 1993; Petersen et al., 1988).

Sensitivity to Threat. Participants reported the extent to which they agreed with three items specifically examining sensitivity to threat from the Behavioral Inhibition Scale (Carver & White, 1994; "Criticism hurts me quite a bit", "I feel worried when I think I have done poorly at something", "I feel pretty worried or upset when I think or know somebody is angry at me") on a scale ranging from 1 (*strongly disagree*) to 4 (*strongly agree*). Higher scores indicate higher levels of threat sensitivity. Cronbach's alpha was 0.73.

Impulsivity. Impulsivity was measured using 4 items ("I do not consider the consequences before I act", "I say things without thinking", "I often act on the spur of the moment", "I do things without thinking" Baars et al., 2015; Barratt, 1959; Patton et al., 1995; Van der Elst et al., 2012). Items were assessed on a 4-point scale from 1 (almost never) to 4 (almost always). Higher scores indicate higher impulsivity. Cronbach's alpha for this scale was 0.79.

**Go/No-go task.** Participants completed the go/no-go task (DuPuis et al., 2015) while EEG was recorded. Participants were instructed to continuously push a button every time a stimulus appeared (a Go trial) unless the newly presented stimulus matched the previously presented stimulus (i.e., the same stimulus appeared twice in a row), in which case the participant needed to refrain from pushing the button on that trial (a No-go Trial). We were particularly interested in the ERN, an ERP elicited when participants make mistakes during this task. Stimuli were presented 1000 ms apart and there were a total of 225 trials. On average, participants committed 17 errors (sd = 8.25) on no-go trials. The average reaction time to a no-go trial was 362 ms (sd = 47.89 ms). To create the difference score, we also extracted the correct-response negativity (CRN), an ERP elicited when participants correctly push a button during a go trial.

Balloon Analogue Risk Task. The Balloon Analogue Risk Task (BART) is a behavioral task that has been used to measure risky decision-making (Lejuez et al., 2002). We used a modified version of the BART in order to use this task for an ERP study (see Heffer & Willoughby, 2020). Participants were instructed to inflate a series of balloons in order to earn points. Participants indicated the number of pumps they wanted to inflate the balloon at the beginning of the trial (Euser et al., 2013; Pleskac et al., 2008; Yau et

al., 2015). Participants then observed the balloon as it either safely reached the inflation number they picked (i.e., they won the points for that trial), or the balloon burst before reaching that point (i.e., they lost the points for that trial). Given that this task provides feedback associated with losing (i.e., when the balloon pops and points are lost), it facilitates the examination of sensitivity to negative and positive feedback using ERPs (Chandrakumar et al., 2018; Fein & Chang, 2008; Gu et al., 2018; Takács et al., 2015).

The task consisted of 90 trials with a maximum breaking point of 20 pumps. The probability of the balloon popping increased as the number of pumps chosen increased (e.g., choosing to pump the balloon up to '15' had a greater likelihood of it popping compared to pumping the balloon up to '5'). After feedback was presented, a new balloon appeared after 1000 ms. Participants earned one point for every pump of the balloon and points for all the "win" trials were summed to calculate their total points. Participants were instructed that the goal of the task was to earn as many points as possible.

Face-processing Task. Participants also completed a face-processing task. During this task, participants were shown pictures of different emotional faces (happy, neutral, fear, and anger), as well as other stimuli (e.g., butterflies, houses, and checkerboards). Participants were instructed that the point of the task was to 'catch the butterflies' by clicking a button whenever a butterfly appeared on the screen. This instruction was given to keep children and adolescents' attention during the task; however, our main goal was to investigate face-processing to angry faces and angry compared to neutral faces. There were four blocks included in this task and the angry face was presented 60 times throughout the task. Overall, there were 496 trials: 240 face trials and 256 non-face trials (checkerboards, houses, and butterflies).

## **Electrophysiological Recording**

Electroencephalography (EEG) was recorded continuously from a BioSemi ActiveTwo system using a 96-channel montage and 7 face sensors. The data were digitized at a sampling rate of 512 Hz. Pre-processing was conducted to identify (1) channels/components that were unreliable within a given time-period, (2) time-periods that were unreliable, (3) and channels/components that were unreliable throughout the recording.

# **Pre-processing (Channels)**

Pre-processing was automated (using MATLAB 2012b scripts) to be carried out using EEGLAB (Delorme & Makeig, 2004) version 13.6.5b and was then executed using Octave on Compute Canada's high performance computer cluster (Cedar: see Desjardins & Segalowitz, 2013; Desjardins et al., 2020; van Noordt et al., 2017, 2015 for more details). The data were first separated into 1 second non-overlapping time windows. For each time window, the voltage variance across each channel was calculated (a 20% trimmed mean was used). Channels were flagged as unreliable if they had a z-score six times greater than the voltage variance across all channels. Time-periods (i.e., the 1 second time windows) were considered unreliable if more than 10% of the channels were identified as having extreme voltage variances. Finally, any channels that were flagged in more than 20% of the time-periods were considered unreliable throughout the recording.

The data were re-referenced to an interpolated average of 19 sites, excluding flagged channels. The data were filtered with a 1 Hz high pass and 30 Hz low pass filter given that cortical activity would not be expected to exceed 30 Hz. After this step, the data were again checked for the same issues reported above: (1) channels that are

unreliable within a given time-period, (2) time-periods that are unreliable, (3) and channels that are unreliable throughout the recording. Specifically, any channels that were unlike its neighbouring channels (e.g., had a low correlation with channels around it), were flagged. A channel was flagged as unreliable if it had a z-score that was 2.326 times greater than the mean of the 20% trimmed distribution of correlation coefficients. Time-periods were considered unreliable if more than 10% of the channels within the window were flagged as unreliable. Any individual channels that were flagged in more than 10% of time-periods were considered unreliable across the entire recording. Bridged channels (i.e., channels that are highly correlated with invariable signal) were identified after dividing the average maximum correlation by the standard deviation of the distribution of correlation coefficients. Channels that had a positive z-score that was eight times greater than the 40% trimmed distribution of coefficients were flagged as bridged channels.

## **Pre-Processing (Components)**

After pre-processing the channel data, all data that had not been flagged as unreliable was concatenated back into continuous data. These data were then submitted to an initial Adaptive Mixture of Independent Component Analysis (AMICA) to identify different components of the EEG data (e.g., heart rate components, eye blink components, cortical components etc.). This process helps to separate brain activity (neural components) from non-neural activity (e.g., muscle movement).

During this procedure, the data were windowed into 1 second time epochs.

Unreliable components were detected by comparing each individual component to the variance among all components. Components were flagged if they had a z-score that was

2.326 times greater than the trimmed mean. Time-periods that had more than 10% of its components flagged were considered unreliable. The data were then concatenated into the continuous time course and submitted to three simultaneous AMICA decompositions to assess whether components were replicable (i.e., is muscle movement consistently being classified as muscle movement when the process is repeated multiple times). The procedure above for identifying unreliable components (within 1 second epochs) was completed again using the continuous time series data. Next, a dipole (which identifies the position and orientation for the distribution of positive and negative voltages) was fit using the dipfit plugin in Matlab (Oostenveld et al., 2011). Components with a dipole fit residual variance greater than 15% were flagged. Finally, components were classified using the ICMARC plugin. This process assesses each component against a crowd-sourced database to identify activation consistent with five different categories: eye blinks, neural, heart, lateral eye movements, muscle contamination, and mixed signal.

After pre-processing, a manual quality control review was completed to ensure that the decisions made during pre-processing were appropriate. This procedure was completed by one trained research assistant who assessed the accuracy of the independent component classifications. For example, the research assistant would identify whether cortical components were correctly distinguished from non-cortical components (e.g., muscle, eye blinks, etc.) based on topographical projection, continuous activation, dipole fit and power spectrum profile. Thus, the quality control review involved using the independent components to help with artifact correction.

## **EEG** post-processing

EEG data were then segmented into single trials and time-locked to the onset of the (1) no-go response (and correct response) from the Go/No-Go task, (2) negative feedback (and positive feedback) from the BART task, and (3) angry faces (and neutral faces) from the face-processing task. A final quality check was completed to identify (and remove) channels that had extreme voltage fluctuations (+/-50 mV). Channels that were removed during pre-processing were interpolated (i.e., rebuilt using the remaining channel data) to the full montage of 103 channels (96 scalp, 7 exogenous) using spherical spline. The current study used fronto-central midline sites (FCz: electrodes A8 and B8 on our montage) to identify the ERN and CRN during the no-go/task and epochs were baseline corrected at -600 to -400. Similar to previous studies (e.g., Fein & Chang, 2008; Hassall et al., 2013; Heffer & Willoughby, 2020), the current study used central midline sites (Cz: electrodes A19 and B19 on our montage) to identify the P3 activation during the BART task; epochs were baseline corrected at -200 to 0. Finally, posterior-temporal sites (P7 and P8; electrodes C2, C3, C12, and C13 on our montage) were used to identify the N170 during the face processing task; epochs were baseline corrected at -200 to 0.

### Plan of Analysis

We used STATSLAB, an open-source toolbox that implements robust statistics for analysis of EEG data to extract the ERPs for each task (Campopiano et al., 2018). This software allows for testing using percentile bootstrap and trimmed means, a technique that is robust to distribution characteristics such as skew, outliers, uneven tails, and various model assumption violations (see Wilcox, 2017).

In STATSLAB, single trial data for our channels were extracted and averaged together. For each subject, the single trial data were resampled, with replacement, to

generate a surrogate sampling distribution. The 20% trimmed mean was taken across trials, at each time point (i.e., removing the most extreme voltages at each time point), to generate a robust bootstrapped ERP. Iterating this process of resampling, trimming, and scoring the difference wave was performed 1,000 times (see Campopiano et al., 2018 for details). The P3 was extracted at the most positive points (315ms for losses; 307ms for wins), all other ERPs were extracted at the most negative points (176ms for anger N170; 174ms for neutral N170; 35ms for ERN; 10ms for CRN). See Figure 3.1 for the ERPs and corresponding topographies.

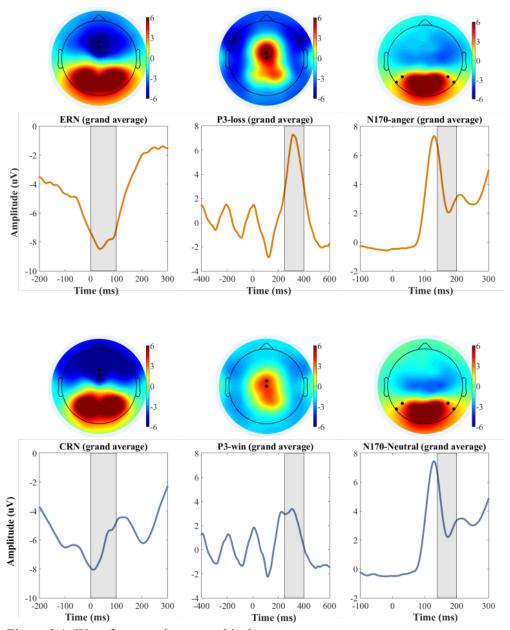


Figure 3.1. Waveforms and topographical maps.

Note. Waveforms and topographical maps show the ERN and CRN during the go/no-go task(0-100ms), the P3 to losses and to wins during the BART task (250-400ms), and the N170 to angry faces and to neutral faces during the face-processing task (140-200ms). Black dots on topographical maps indicate the channel cluster used for analysis. Of note, the N170 does not cross zero in our sample, due to a large/dominating P1 amplitude; this finding is typical among children and adolescent populations (see Kuefner et al., 2010; Taylor et al., 2004). The orange waveforms represent neural activation to threatening situations; the blue waveforms represent neural activation to non-threatening situations.

We next created a variable to identify consistently high neural activation across the tasks. For the BART task, given that the P3 is a positive waveform, scores above the mean reflect having high neural activation to threats. For both the go/no-go task and the face processing task, given that the ERN and the N170 are negative waveforms, scores below the mean reflect having high neural activation to threats. We created a consistency variable, whereby a score of 4 represented having consistently high neural activation on all three ERPs, a score of 3 represented having high neural activation on two out of three tasks, a score of 2 represented having high neural activation on one out of three tasks, and a score of 1 represented having high neural activation on none of the tasks (i.e., low neural activation across all three tasks). Thus, higher scores represent more situations where individuals had high neural activation to threats, while lower scores represent less situations where individuals had high neural activation to threats.

In a follow up analysis, we replicated this analysis using the difference score for each ERP (P3 loss- P3 win; angry N170- neutral N170; ERN- CRN). For the BART task, participants with scores above zero would have a larger P3 amplitude to loss feedback compared to win feedback. For both the go/no-go task and the face processing task, scores below zero reflect having larger ERP activation to the threat (mistakes and angry faces) compared to the non-threatening situations (successful button presses and neutral faces). In this case, we created a consistency variable whereby a score of 4 represented having consistently higher neural activation to threats than non-threats on all three ERPs, a score of 3 represented having higher neural activation to threats than non-threats on two out of three tasks, a score of 2 represented having higher neural activation to threats than non-threats on one out of three tasks, and a score of 1 represented having higher neural

activation to threats than non-threats on none of the tasks (i.e., lower neural activation to threats than to non-threats across all three tasks). Thus, a higher difference score reflects more situations in which an individual has higher neural activation to threats than to non-threats.

#### Results

Means and standard deviations for all study variables are reported in Table 3.1. Of interest, the mean score on neural consistency to threats was 2.47(SD=0.85), suggesting that on average, participants had high neural activation to threats on one or two tasks. Approximately, 11.8% of participants had consistently high neural activation to all three tasks, 34.8% of participants had high neural activation to two out of three tasks, 41.6% of participants had high neural activation to one out of three tasks, and 11.8% of participants had low neural activation on all three tasks. For the difference score, the average was 2.86 (SD=0.84), with higher scores representing consistently higher neural activation to threats than non-threats. Approximately, 24.8% of participants had consistently higher neural activation to threats than non-threats on all three tasks, 41% of participants had higher neural activation to threats than non-threats on two out of three tasks, 29.8% of participants had higher neural activation to threats than non-threats on one out of three tasks, and 4.4% of participants had no tasks whether they had higher neural activation to threats than non-threats.

Table 3.1. Means and Standard Deviations of Study Variables

| Variables                       | Mean(SD)    |
|---------------------------------|-------------|
| Threat Sensitivity              | 2.52(0.73)  |
| Impulsivity                     | 1.92(0.62)  |
| Age                             | 11.27(1.80) |
| Pubertal Status                 | 1.94(0.83)  |
| Sex (% female)                  | 47.8%       |
| Parental Educ.                  | 4.15(0.87)  |
| Consistency of ERPs to Threats  | 2.47(0.85)  |
| Consistency of Difference Score | 2.86(0.84)  |

*Note*. Parental Educ. = Parental education, SD = Standard deviation.

What factors predict consistently high neural activation to threats? A linear regression was used investigate what factors (sensitivity to threat, impulsivity, age, pubertal status, sex, and parental education) predict consistently high neural activation to threats. Table 3.2 contains the results of the linear regression. Sensitivity to threat [ $\beta$ = .236, p = .017], impulsivity [ $\beta$ = -.374, p = .002], and sex [ $\beta$ = -.284, p = .043], were the only significantly predictors of consistent neural activation to threats. Specifically, higher self-reported threat sensitivity and lower self-reported impulsivity predicted having consistently higher neural activation to threats. Additionally, males had consistently higher neural activation to threats than females.

Table 3.2. Regression Results using Stability of ERPs to Threats as the Criterion

| Predictor          | Beta   | Std. Error | t      | Sig.  |
|--------------------|--------|------------|--------|-------|
| Threat Sensitivity | 0.236  | 0.098      | 2.415  | 0.017 |
| Impulsivity        | -0.374 | 0.116      | -3.219 | 0.002 |
| Age                | 0.021  | 0.055      | 0.381  | 0.704 |
| Pubertal Status    | 0.072  | 0.125      | 0.574  | 0.567 |
| Sex                | -0.284 | 0.139      | -2.045 | 0.043 |
| Parental Educ.     | -0.027 | 0.077      | -0.344 | 0.731 |

Note. Parental Educ. = Parental education, Std. Error = Standard error, Sig. = p-value

What factors predict consistently higher neural activation to threats than to non-threats (i.e., using the difference score)? A linear regression was used investigate what factors (sensitivity to threat, impulsivity, age, pubertal status, sex, and parental education) predict consistently higher neural activation to threats than non-threats (i.e., difference score). Table 3 contains the results of the linear regression. Sensitivity to threats [ $\beta$ = .208, p = .036] was the only significantly predictor of the difference score. Specifically, higher self-reported threat sensitivity predicted having consistently higher neural activation to threats than to non-threats.

Table 3.3. Regression Results using Stability of ERPs Difference score as the Criterion

| Predictor          | Beta   | Std. Error | t      | Sig.  |
|--------------------|--------|------------|--------|-------|
| Threat Sensitivity | 0.208  | 0.098      | 2.116  | 0.036 |
| Impulsivity        | -0.160 | 0.117      | -1.370 | 0.173 |
| Age                | 0.040  | 0.056      | 0.714  | 0.476 |
| Pubertal Status    | 0.014  | 0.126      | 0.110  | 0.912 |
| Sex                | -0.267 | 0.140      | -1.911 | 0.058 |
| Parental Educ.     | -0.091 | 0.078      | -1.168 | 0.245 |

Note. Parental Educ. = Parental education, Std. Error = Standard error, Sig. = p-value

## **Discussion**

Threat sensitivity frequently has been characterized as a risk factor for the development of anxiety (e.g., Bar-Haim et al., 2007). Self-report measures of threat sensitivity often combine different threat-related situations (e.g., making a mistake, receiving negative feedback, worrying about someone being angry with you) into one measure. Neuroscience research, on the other hand, often investigates these threat-related situations separately using different tasks. The current study used three EEG tasks to investigate consistency of neural activation to threats. We were interested in what demographic and self-report factors are associated with consistently high neural activation to threats (e.g., do adolescents have more consistently high neural activation to threats than children? Do individuals who self-report greater threat sensitivity have consistently high neural activation across these tasks?).

First, we created a measure of neural consistency to threats. Using three different ERPs (P3, N170, and ERN) and three different tasks (the BART, a go/no-go task, a face-processing task) we found that it was quite common for youth to have high neural sensitivity to threats on at least one or two tasks (M = 2.4, SD = 0.85). It was less common, however, to have consistently high neural activation to threats on all three tasks ( $\sim$ 12% of the sample). Our results show that although self-report measures of threat sensitivity group these different threat-related events together, not all youth have consistently high neural activation to receiving negative feedback, angry faces, and making mistakes.

Our results show that self-reported impulsivity was a predictor of consistently low neural activation, while self-reported threat sensitivity was a predictor of consistently high neural activation to threats. We also found that males had consistently higher neural activation to threats than females. The latter finding was not part of our original predictions. It is not entirely clear why males would have higher neural consistency to threats than females. Given that this is the first study investigating neural consistency across multiple tasks, future research is needed to tease apart this association.

On the other hand, our findings regarding impulsivity and threat sensitivity were in line with our predictions. Indeed, individuals with high self-reported impulsivity may be less troubled by different types of threats, given that they are more likely to engage in non-reflective, stimulus-driven responding (Nigg, 2017). At the same time, individuals with high self-reported threat sensitivity seem to have higher neural sensitivity to a variety of different threats. Therefore, investigating *consistent* neural activation across different tasks may be an important way to identify youth who are at the greatest risk for impulsivity and threat sensitivity. Indeed, if individuals have a consistent response across three different threats, it would be more likely that the individuals' threat sensitivity is being accurately classified. This result is in line with the cumulative risk hypothesis (i.e., a greater number of risk factors is associated with more problem behaviors; e.g., Appleyard et al., 2005). Thus, individuals who have consistently high (or low) neural activation across multiple situations would be the most likely to also self-report high levels of sensitivity to threat (or impulsivity). Identifying youth with consistent neural activation to different threats may be an important avenue for researchers interested in the development of anxiety. Indeed, given that many youth show high neural activation to at least one threatening event, cumulative neural activation to a variety of different threats

may be a promising approach to identify youth who are truly at risk for the development of anxiety.

Surprisingly, we did not find that adolescents (i.e., individuals with more advanced pubertal status or older age) had consistently higher neural activation to threats than children. We expected that adolescence may be a time of heightened sensitivity to emotionally salient events, such as threatening events (e.g., Casey, 2015; Somerville et al., 2010; Steinberg et al., 2008), and therefore, we thought that adolescents would have heightened neural activation across a variety of different threatening events. This non-significant finding, however, suggests that children also show consistently high neural sensitivity to different threats (see Chong & Meyer, 2019; Heffer & Willoughby, 2020; O'Toole et al., 2013, for other studies showing that children with anxiety-related symptoms can show high ERP activation to these different threatening situations). Thus, youth who demonstrate consistently high neural sensitivity to different threats should be further investigated, especially when considering *early* interventions aimed at identifying youth who may self-report sensitivity to threats.

In a follow up analysis, we also wanted to investigate whether our results were consistent when using the difference scores for each ERP (i.e., P3 loss - P3 wins; N170 angry - N170 neutral; ERN - CRN). The main conclusion from our study was replicated when using the difference score: youth with higher self-reported threat sensitivity had consistently higher neural activation to threats than to non-threats. However, we did not replicate our findings regarding impulsivity and sex. There may be several reasons for the latter findings. In terms of impulsivity, for example, if impulsive individuals are less reflective during the task, they may have been less sensitive to *both* threatening events

and non-threatening events, providing them with a difference score that thus is similar to others who have high neural activation to both threats and non-threats. Again, this may be one disadvantage of the difference score—individuals with different patterns of neural activation can end up with the same value on a difference score measure. Additionally, in two out of three of our tasks the non-threatening event was a positive event (receiving win feedback and making a correct response). Previous research has found that some individuals have high sensitivity to both negative and positive stimuli (e.g., Coplan et al. 2006). Thus, individuals who find threatening events aversive (but also find positive events exciting) may not be well represented by a difference score. Future research is needed to replicate these results using multiple threat-related situations in comparison to neutral events.

Our study has important strengths, including a large sample, inclusion of three different ERP tasks, and the use of multiple methods (e.g., self-report and EEG). At the same time, our study is not without limitations. First, we did not include the full scale for either self-report sensitivity to threat or self-reported impulsivity as the data were part of a larger study assessing a wide range of constructs and it was not feasible to include every item from each scale due to time constraints. Future research would benefit from investigating group differences in threat-sensitivity and impulsivity using the full scales. Second, our study is concurrent; thus, casual inferences cannot be concluded (e.g., we are unable to ascertain whether more consistent neural activation across tasks *leads* to greater self-reported sensitivity to threat and/or whether greater self-reported sensitivity to threat leads to more consistent neural sensitivity). Longitudinal studies investigating both self-report measures and neural activation at each time point are necessary before drawing

these conclusions. Finally, we did not assess whether there were individual differences in specific combinations of tasks (e.g., individuals who have high neural activation to negative feedback, low neural activation to making mistakes, but high neural activation to angry faces). Given that our main interest was in *consistent* threat sensitivity, this breakdown was not necessary to answer our research question.

Despite these limitations, our study has important implications. A small (~12% of the sample), but important percentage of the sample was identified as having consistently high neural response to threats. Further, consistently higher neural activation to threats (and higher neural activation to threats than to non-threats) was associated with higher self-reported threat sensitivity. Our results suggest that although it is common for youth to have high neural activation in response to one threat-related tasks, it is far less common for youth to have *consistently* high neural activation to threats. Threat sensitivity is thought to be associated with the development of anxiety; however, not all youth who are sensitive to threats develop anxiety (e.g., Pérez-Edgar et al., 2010). Given that anxiety affects roughly 7–15% of youth (Beesdo et al., 2009; Ghandour et al., 2019), consistency of neural activation to threats may be an important group to investigate in order to identify non-normative levels of threat sensitivity.

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## **CHAPTER 5: STUDY 4**

A person-centered examination of emotion dysregulation, sensitivity to threat, and impulsivity among children and adolescents: An ERP study<sup>4</sup>

Adolescence often has been suggested to be a sensitive period of development, characterized by the onset of both internalizing problems (e.g., social anxiety; Beesdo, Knappe, & Pine, 2009) and externalizing problems (e.g., risk taking; Casey & Caudle, 2013; Casey, Jones, & Hare, 2008; Dahl, 2004; Ernst, 2014). Yet, not all youth are socially anxious and/or engaging in extreme risks. Identifying factors that are differentially associated with these outcomes is critical in order to gain a better understanding of adolescent development. There are several important constructs that may help differentiate youth who may be more likely to develop anxiety versus risktaking problems. Previous research has found that heightened sensitivity to threat (heightened responsiveness to threat) is associated with anxiety (Balle, Tortella-Feliu, & Bornas, 2013; Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007; Johnson, Turner, & Iwata, 2003; Katz, Matanky, Aviram, & Yovel, 2020; Pérez-Edgar et al., 2010, 2011), while *impulsivity* (non-reflective stimulus-driven response; Nigg, 2017) has been found to be associated with risk taking (Khurana, Romer, Betancourt, & Hurt, 2018; Romer et al., 2009). At the same time, both risk taking (Leith & Baumeister, 1996; Tull, Weiss, Adams, & Gratz, 2012; Weiss, Sullivan, & Tull, 2015)

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and anxiety (Cisler & Olatunji, 2012; Hannesdottir & Ollendick, 2007; Jazaieri, Morrison, Goldin, & Gross, 2015; Mennin, McLaughlin, & Flanagan, 2009; Neumann, van Lier, Gratz, & Koot, 2010; Suveg & Zeman, 2004; Tortella-Feliu, Balle, & Sesé, 2010) have been linked to *emotion dysregulation* (poor control over emotions). The current study used latent class analysis to investigate whether there are youth with different profiles of sensitivity to threat, impulsivity, and emotion dysregulation and whether these profiles are associated with a variety of factors (risk taking, social anxiety, age, pubertal status, sex, and parental education). A critical component of our study also was to investigate whether groups differ on the error-related negativity (ERN: An ERP elicited when making mistakes on an inhibitory control task), given that this neural indicator has been associated with both threat sensitivity and impulsivity (e.g., Boksem, Tops, Kostermans, & De Cremer, 2008; Checa, Castellanos, Abundis-Gutiérrez, & Rosario Rueda, 2014; Hajcak, McDonald, & Simons, 2003; Meyer, 2017; Ruchsow, Spitzer, Grön, Grothe, & Kiefer, 2005). Thus, the ERN may be an important way to distinguish between different profiles of individuals who may be at risk for the development of anxiety and/or risk-taking problems.

Neurodevelopmental imbalance models can help explain why adolescence may be a sensitive period for development. Specifically, asynchrony in the maturation of neural connections within and between the prefrontal executive system (associated with self-control and potential suppression of socioemotional impulses) and the subcortical limbic-striatal system (associated with socioemotional processing) is thought to contribute to adolescents being more sensitive to emotionally salient events than children (Casey,

2015; Somerville, Jones, & Casey, 2010; Steinberg, 2008). According to these models, circuitry within the subcortical limbic-striatal system matures early in adolescence (likely due to puberty), but interconnections to the prefrontal executive system mature later in adolescence. This asynchrony in maturity is thought to lead to heightened activation of the limbic-striatal region during a time when neural connections to the prefrontal cortex that might dampen the activation (if appropriate) are not fully mature. As a result, adolescents may be more susceptible than children to impulsive or emotionally driven responses (e.g., heightened sensitivity to threat), during a time when their ability to regulate their emotions is not yet mature.

Some researchers have investigated the imbalance model by assessing associations between neural activity in the prefrontal executive system and subcortical regions (e.g., amygdala, striatum). For example, Galvan and colleagues (2006) found that adolescents, compared to children and adults, had exaggerated activity in the accumbens relative to prefrontal activation during and fMRI task. Long-range neural connections between frontal regions and subcortical regions also have been found to increase from childhood to adolescence (Hwang, Velanova, & Luna, 2010). Hare et al. (2008) used an emotional go/no-go task and found that adolescents, compared to children, have exaggerated amygdala activity to fearful faces. They also found that stronger connectivity between the ventral medial prefrontal cortex and the amygdala was associated with habituation of the amygdala activity across trials. Dreyfuss and colleagues (2014) found that adolescents and adults showed greater activation in prefrontal regions than children, but they did not find significant age differences in the striatum. Mills and colleagues (2014) found that there was a structural mismatch in developmental timing between the

amygdala and prefrontal cortex; however, they did not find clear evidence for the developmental mismatch between the nucleus accumbens and the prefrontal cortex.

Overall, while there are some inconsistencies depending on what regions are investigated, there is some support for the imbalance model, suggesting that adolescence may be a sensitive period of development.

Puberty is thought to play an important role in why adolescence may be a sensitive period of development (Casey, 2015; Somerville, Jones, & Casey, 2010; Steinberg, 2008). Previous research, however, often uses age rather than puberty as a key measure to investigate developmental differences between children and adolescents. While puberty and age are of course associated, puberty is marked by important changes in hormone levels that can impact adolescent brain development (Blakemore, Burnett, & Dahl, 2010; Goddings et al., 2014; Sisk & Zehr, 2005; Vijayakumar, Op de Macks, Shirtcliff, & Pfeifer, 2018). Indeed, there is considerable variability in the age at which different features of puberty develop (see Berenbaum, Beltz, & Corley, 2015 for an overview of the timing and measurement of pubertal development). Puberty is not a single event; thus, it is important to differentially measure a variety of physical signs associated with gonadal and adrenal hormonal development [e.g., body hair, breast development and menarche (in females), voice change and facial hair (in males)], especially when using self-reported measures of pubertal development which rely on youth self-identifying these features (Shirtcliff, Dahl, & Pollak, 2009). Previous research has found that self-reported pubertal development (as measured by the Pubertal Development Scale) is associated with biological pubertal development (Schmitz et al., 2004; Shirtcliff et al., 2009). Taken together, it is important to investigate pubertal status

(in addition to assessing age) in order to gain a better understanding of adolescent brain development.

In line with research on adolescent brain development, adolescents also may selfreport greater sensitivity to threats, impulsivity, and emotion dysregulation, compared to children. For example, researchers have found that adolescents experience heightened sensitivity to threat compared to children (e.g., Heffer & Willoughby, 2020; O'Brien & Bierman, 1988; Vervoort et al., 2010; Westenberg, Drewes, Goedhart, Siebelink, & Treffers, 2004). Research on age-related differences in impulsivity has been mixed. While some researchers have found that adolescents are more impulsive than children (Collado, Felton, MacPherson, & Lejuez, 2014; Dreyfuss et al., 2014; Figner, Mackinlay, Wilkening, & Weber, 2009; Kasen, Cohen, & Chen, 2011; Khurana et al., 2018), others have found that impulsivity decreases from childhood to adolescence (Harden & Tucker-Drob, 2011; Quinn & Harden, 2013; Steinberg et al., 2008). Further, some researchers have found that dysregulation decreases throughout adolescence (Ahmed, Bittencourt-Hewitt, & Sebastian, 2015; Gee et al., 2013), but adolescents in particular may have difficulties with emotion regulation during 'hot' situations (i.e., when they are stressed or emotionally-aroused; e.g., Prencipe et al., 2011; Zelazo, Qu, & Kesek, 2010).

There also has been some research investigating the associations between impulsivity, sensitivity to threat and emotion dysregulation. For example, among adult samples, higher levels of emotion dysregulation has been associated with greater threat sensitivity (Schreiber, Grant, & Odlaug, 2012; Slessareva & Muraven, 2004) and impulsivity (Jakubczyk et al., 2018; Schreiber et al., 2012). Khurana et al. (2018) used a latent growth curve analysis and identified two different groups of impulsive adolescents:

high-increasing and low-stable. They found that adolescents in the high-increasing impulsive group had lower top-down control than those in the low-stable group. Overall, this work highlights that impulsivity and sensitivity to threat have both been separately associated with poor emotion regulation.

Of course, there likely are important individual differences among adolescents in the amount of sensitivity to threat, impulsivity, and dysregulation that they experience (Crone, van Duijvenvoorde, & Peper, 2016; Somerville et al., 2010). For example, although Hare and colleagues (2008) found that adolescents had exaggerated amygdala activity in an emotional-processing task compared to children and adults, there also was a great deal of variability in activity among the adolescents. Van Duijenvoorde et al. (2015) found that some adolescents were more sensitive to threat (e.g., avoiding risks), while others showed more impulsive tendencies. To address these individual differences and provide a more holistic understanding of adolescent's sensitivity to threat, impulsivity, and emotion dysregulation, a person-centered approach is needed.

A *person-centered* approach can be used to explore whether there are distinct subgroups of individuals who have different combinations of dysregulation, threat sensitivity, and impulsivity within the larger sample. For example, there may be a group within the population that has high dysregulation, high sensitivity to threat, but is less impulsive (this group may be at risk for the development of anxiety), whereas a separate group of youth may have high dysregulation, high impulsivity, but is less sensitive to threats (this group may be more likely to engage in risk taking). Both groups may be characterized by high dysregulation (a measure associated with both risk taking and anxiety) but would have differential levels of impulsivity and sensitivity to threat.

Identifying subgroups of individuals who vary on these measures— as opposed to investigating associations among variables— is of key importance to gain a better understanding of adolescent development and to identify those who are risk for the development of anxiety and/or risk taking. Indeed, a person-centered analysis can capture important individual differences that may otherwise be missed in a variable-centered approach (Howard & Hoffman, 2018).

# The Error Related Negativity

It is critical also to investigate whether groups of youth are distinguishable based on neural indicators. Neural indicators could potentially help predict later development of internalizing or externalizing problems (e.g., social anxiety and/or risk taking) at younger ages (e.g., before children are able to self-report issues with anxiety). The ERN (errorrelated negativity) may be a potential biomarker used to help distinguish between the different profiles of adolescents. The ERN is thought to be associated with performance monitoring, specifically the motivational significance of errors; whereby a larger ERN is associated with greater motivation to avoid errors (e.g., Hajcak & Foti, 2008; Meyer, Hajcak, Glenn, Kujawa, & Klein, 2017). Previous research has found that impulsive individuals tend to have smaller ERN amplitudes than those who are less impulsive (Checa et al., 2014; Pailing, Segalowitz, Dywan, & Davies, 2002; Ruchsow et al., 2005; Stahl & Gibbons, 2007; Taylor, Visser, Fueggle, Bellgrove, & Fox, 2018); perhaps as a result of reduced behavioral monitoring. In contrast, individuals with greater threat sensitivity or anxiety tend to have larger ERNs when making errors than those with lower threat sensitivity or anxiety (Boksem et al., 2008; Chong & Meyer, 2019; Hajcak et al., 2003; Ladouceur, Dahl, Birmaher, Axelson, & Ryan, 2006; Meyer, 2017; Meyer &

Hajcak, 2019; Weinberg, Olvet, & Hajcak, 2010). No research, however, has taken into consideration whether different patterns of dysregulation, sensitivity to threat, and impulsivity are differentially associated with the ERN. Thus, it remains unclear as to whether the ERN may be a biomarker that can help to distinguish between different profiles of adolescents (e.g., those who may be more likely to engage in risk taking compared to those who may be more likely to develop anxiety).

# **Current study**

The current study seeks to address three questions: (1) Using a person-centered latent-class approach, are there distinct groups of individuals who vary in levels of emotion dysregulation, sensitivity to threat, and impulsivity? (2) If there are distinct groups, what factors (risk taking, social anxiety, age, pubertal status, sex, and parental education) predict group membership? (3) Do groups show different neural activation on the ERN during an inhibitory control task?

### Method

## **Participants**

Participants (N = 1314, age range = 8-15, 49.96% female) were drawn from several elementary and high schools in southern Ontario, Canada and were part of a larger study examining the associations between wellbeing and youth health-risk behaviors. Most participants were between the ages of 9 and 14 and the sample had fairly even distribution among these ages. Parent report indicated that 84.20% of the children and adolescents were White, 1.70% were Black, 2.12% were Asian, 2.76% were Hispanic, 0.85% Indigenous, and 7.53% were Mixed (a further 0.85% of parents indicated that they preferred not to answer the question). Data on socioeconomic status

indicated that mean levels of education for mothers and fathers was, on average, "completed an associate degree and/or technical diploma".

### **Procedure**

Students were invited to participate in the study through visits to schools. Surveys were completed in classrooms during school hours and all participants received gifts (e.g., backpacks) as compensation. The survey was split into two sections to reduce fatigue, with both sections completed within a 1-month period sometime between January and April. Starting in year 2 of the study, a subsample (N = 468) of participants also completed a Mobile Lab component in which EEG data was recorded. Parents were asked to identify if their child had any illnesses or disabilities (either physical or mental). Two participants were excluded because of a diagnosis of autism, one participant was excluded because they are prone to seizures, and one participant was excluded because of a diagnosis of cerebral palsy. There were 14 participants who had equipment issues during the task (e.g., the event markers did not show up) and three participants did not complete the task. There also were 16 participants who were not included because their EEG data was not usable (e.g., contained a larger number of muscle/movement artifacts). Seven participants did not follow the instructions (e.g., they were off task). Thus, the final sample included 424 participants. The sample of participants who had useable EEG data did not differ on any of the study variables compared to the sample of participants who were excluded (p's > .05). The University Ethics Board approved this study and participants provided informed assent and their parents provided informed consent. Of note, there also were no significant differences between the full sample and the mobile lab sample, with one exception. The age of participants in the mobile lab (M = 11.45, SD

= 1.78) on average, was younger than the age of participants in the full sample (M = 11.77, SD = 1.72), p = .003.

## **Missing Data Analysis**

Missing data occurred because some participants did not finish the questionnaire (average missing data for the first section of the survey = 1.764%; average missing data for the second section of the survey = 4.788%) and because some participants were absent during the time of the survey. The percentage of students who completed the survey was 82% for the first section and 81% for the second section. Missing data was primarily due to absenteeism but also occasionally due to time conflicts, students declining to participate in one part of the survey, RA mistakes (e.g., not inviting a child to complete the survey), or students moving to another school district with no contact information. Missing data were imputed using the expectation-maximization algorithm (EM). EM retains cases that are missing survey waves and thus avoids the biased parameter estimates that can occur with pairwise or listwise deletion (Schafer & Graham, 2002).

#### Measures

**Demographics.** Pubertal status, age, sex, and parental education (one item per parent, averaged together) using a scale of 1 = did not finish high school to 6 = professional degree) were collected. Pubertal status was assessed using the Puberty Development Scale (PDS; Petersen, Crockett, Richards, & Boxer, 1988). The PDS is a self-report measure that assesses body hair, facial hair, and voice development in boys, and body hair, menarche, and breast development in girls. All items were rated on a 4-point scale from 1 (not yet started changing) to 4 (change seems complete). The PDS

scale exhibits good reliability and validity (Carskadon & Acebo, 1993; Petersen et al., 1988). In our sample, Cronbach alpha was .81 for boys and .80 for girls.

**Emotion Dysregulation.** Emotion dysregulation was measured using three items from the Difficulties with Emotion Regulation Scale (DERS; Gratz & Roemer, 2004). Participants reported the extent to which they agreed with items ("When I'm upset or stressed, I have difficulty concentrating", "When I'm upset or stressed, I have difficulty thinking about anything else", "When I'm upset or stressed, I start to feel bad about myself') on a scale from 1 (almost never) to 4 (almost always). Higher scores indicate higher levels of emotion dysregulation. The Cronbach alpha in the present study was 0.81. Of note, the original DERS contains 36 items with six different subscales. Given that this study is part of a larger study investigating a wide range of health-risk behaviors among youth, it was not feasible to include all items. Previous research has investigated the DERS as a unitary construct and found that using a shortened scale with a subset of items is related to expected adjustment indicators (e.g., sleep, non-suicidal self-injury; Heffer & Willoughby, 2018; Semplonius, Good, & Willoughby, 2015; Tavernier & Willoughby, 2015). Regarding the current study, we ran an exploratory factor analysis with our DERS items and found that the items formed one factor (all factor loadings > 0.77).

Sensitivity to Threat. Participants reported the extent to which they agreed with three items specifically examining sensitivity to threat from the Behavioral Inhibition Scale (Carver & White, 1994; "Criticism hurts me quite a bit", "I feel worried when I think I have done poorly at something", "I feel pretty worried or upset when I think or know somebody is angry at me") on a scale ranging from 1 (*strongly disagree*) to 4

(*strongly agree*). Higher scores indicate higher levels of threat sensitivity. Cronbach's alpha was 0.82.

**Impulsivity.** Impulsivity was measured using 4 items ("I do not consider the consequences before I act", "I say things without thinking", "I often act on the spur of the moment", "I do things without thinking"; Baars, Nije Bijvank, Tonnaer, & Jolles, 2015; Barratt, 1959; Patton, Stanford, & Barratt, 1995; Van der Elst et al., 2012). Items were assessed on a 4-point scale from 1 (*almost never*) to 4 (*almost always*). Higher scores indicate higher impulsivity. Cronbach's alpha for this scale was .83.

Risk Taking. Risk taking was assessed by asking students the extent to which they engaged in 21 risky behaviors in the past year (e.g., rode a bike without a helmet, cheated on a test, skipped school without permission, etc.). The list of risky behaviors was adapted from the Risk Involvement and Perception Scale (Shapiro, Siegel, Scovill, & Hays, 1998) and overlaps with behaviors generated from other studies (e.g., Gonzalez et al., 1994; Gullone, Moore, Moss, & Boyd, 2000). Response options ranged from 0 (0 times) to 4 (10 or more times). We calculated the average for each student's risk-taking engagement; higher scores reflect higher risk taking.

Social anxiety. Four items from the Social Anxiety Scale for Children – Revised (SASC-R; La Greca & Stone, 1993) were used to assess symptoms of social anxiety. These items (e.g., "I am afraid other students my age will not like me", "I am quiet when I am with a group of other students my age") were measured on a 4-point Likert scale ranging from 1 (almost never) to 4 (almost always). Higher scores indicated higher levels of social anxiety. Cronbach's alpha for this scale was 0.71. Typically, the SASC-R contains 18 items, with three subscales. Given the nature of our study, we were unable to

include all items and subscales. Previous research, however, has used this shortened 1-factor version of the SASC-R (Daly & Willoughby, 2020).

**Go/No-go task.** Participants completed the go/no-go task (DuPuis et al., 2015) while EEG was recorded. Participants were instructed to continuously push a button every time a stimulus appeared (a Go trial) unless the newly presented stimulus matched the previously presented stimulus (i.e., the same stimulus appeared twice in a row), in which case the participant needed to refrain from pushing the button on that trial (a No-go Trial). Stimuli were presented 1000 ms apart and there were a total of 225 trials. On average, participants committed 20 errors (sd = 9.78). The average reaction time to a no-go trial was 363 ms (sd = 53.72 ms).

## **Electrophysiological Recording**

Electroencephalography (EEG) was recorded continuously from a BioSemi ActiveTwo system using a 96-channel montage and 7 face sensors. The data were digitized at a sampling rate of 512 Hz. Pre-processing was conducted to identify (1) channels/components that were unreliable within a given time-period, (2) time-periods that were unreliable, (3) and channels/components that were unreliable throughout the recording.

# **Pre-processing (Channels)**

Pre-processing was automated (using MATLAB 2012b) using EEGLAB (Delorme & Makeig, 2004) version 13.6.5b, executed using Octave on Compute Canada's high performance computer cluster (Cedar: see Desjardins & Segalowitz, 2013; Desjardins, van Noordt, Huberty, Segalowitz, & Elsabbagh, 2020; van Noordt, Desjardins, Gogo, Tekok-Kilic, & Segalowitz, 2017; van Noordt, Desjardins, &

Segalowitz, 2015 for more details). EEG Integrated Platform Lossless (EEG-IP-L) preprocessing pipeline has been shown to retain more data (trials and subjects) than other standardized pipelines [e.g., The Maryland Analysis of Developmental EEG (MADE)] without negatively impacting known ERP effects (Desjardins et al., 2020).

The data were first separated into 1 second non-overlapping time windows. For each time window, the voltage variance across each channel was calculated (a 20% trimmed mean was used). Channels were flagged as unreliable if they had a z-score six times greater than the voltage variance across all channels. Time-periods (i.e., the 1 second time windows) were considered unreliable if more than 10% of the channels were identified as having extreme voltage variances. Finally, any channels that were flagged in more than 20% of the time-periods were considered unreliable throughout the recording.

The data were re-referenced to an interpolated average of 19 sites, excluding flagged channels. The data were filtered with a 1 Hz high pass and 30 Hz low pass filter given that cortical activity would not be expected to exceed 30 Hz. After this step, the data were again checked for the same issues reported above: (1) channels that are unreliable within a given time-period, (2) time-periods that are unreliable, (3) and channels that are unreliable throughout the recording. Specifically, any channels that were unlike its neighbouring channels (e.g., had a low correlation with channels around it), were flagged. A channel was flagged as unreliable if it had a z-score that was 2.326 times greater than the mean of the 20% trimmed distribution of correlation coefficients. Time-periods were considered unreliable if more than 10% of the channels within the window were flagged as unreliable. Any individual channels that were flagged in more than 10% of time-periods were considered unreliable across the entire recording. Bridged

channels (i.e., channels that are highly correlated with invariable signal) were identified after dividing the average maximum correlation by the standard deviation of the distribution of correlation coefficients. Channels that had a positive z-score that was eight times greater than the 40% trimmed distribution of coefficients were flagged as bridged channels.

# **Pre-Processing (Components)**

After pre-processing the channel data, all data that had not been flagged as unreliable was concatenated back into continuous data. These data were then submitted to an initial Adaptive Mixture of Independent Component Analysis (AMICA) to identify different components of the EEG data (e.g., heart rate components, eye blink components, cortical components etc.). This process helps to separate brain activity (neural components) from non-neural activity (e.g., muscle movement).

During this procedure, the data were windowed into 1 second time epochs.

Unreliable components were detected by comparing each individual component to the variance among all components. Components were flagged if they had a z-score that was 2.326 times greater than the trimmed mean. Time-periods that had more than 10% of its components flagged were considered unreliable. The data were then concatenated into the continuous time course and submitted to three simultaneous AMICA decompositions to assess whether components were replicable (i.e., is muscle movement consistently being classified as muscle movement when the process is repeated multiple times). The procedure above for identifying unreliable components (within 1 second epochs) was completed again using the continuous time series data. Next, a dipole (which identifies the position and orientation for the distribution of positive and negative voltages) was fit

using the dipfit plugin in Matlab (Oostenveld, Fries, Maris, & Schoffelen, 2011). Components with a dipole fit residual variance greater than 15% were flagged. Finally, components were classified using the ICMARC plugin. This process assesses each component against a crowd-sourced database to identify activation consistent with five different categories: eye blinks, neural, heart, lateral eye movements, muscle contamination, and mixed signal.

After pre-processing, a manual quality control review was completed to ensure that the decisions made during pre-processing were appropriate. This procedure was completed by one trained research assistant who assessed the accuracy of the independent component classifications. For example, the research assistant would identify whether cortical components were correctly distinguished from non-cortical components (e.g., muscle, eye blinks, etc.) based on topographical projection, continuous activation, dipole fit and power spectrum profile. Thus, the quality control review involved using the independent components to help with artifact correction.

## **EEG** post-processing

EEG data were then segmented into single trials and time-locked to the onset of No-go responses from the Go/No-go task. A final quality check was completed to identify (and remove) channels that had extreme voltage fluctuations (+/-50 mV). Channels that were removed during pre-processing were interpolated (i.e., rebuilt using the remaining channel data) to the full montage of 103 channels (96 scalp, 7 exogenous) using spherical spline. The current study used fronto-central midline sites (FCz: electrodes A8 and B8 on our montage) to identify the ERN. Response-locked epochs

were baseline corrected at -600 to -400. Participants with less than six error trials were removed from the analysis (Olvet & Hajcak, 2009).

## Plan of Analysis

Latent class analysis (LCA) was conducted using Mplus 7 (Muthén & Muthén, 2012). We used Mplus Automation (Hallquist & Wiley, 2018), a package in R (R Core Team, 2019), to automate the LCA and extract the model parameters from Mplus. The three dysregulation, three sensitivity to threat, and four impulsivity items were used as latent class indicators in order to explore whether different groups of individuals could be identified based on their responses to these items. To determine the number of groups that were best represented by the data, four criteria were considered: 1) interpretability of the classes, 2) Bayesian information criterion (BIC), such that smaller values of BIC indicate a better fit model, 3) significance of the Lo-Mendell-Rubin (LMR) significance value once non-significance is reached, the number of classes prior to non-significance is defined as the appropriate number, and 4) average latent class conditional probabilities are close to 1.00 (Nylund, Asparouhov, & Muthén, 2007). Entropy (an index of confidence that individuals belong to the correct class and that adequate separation between latent classes exist) also was examined; scores >.80 are good but there is no set cut-off criterion for entropy (Jung & Wickrama, 2008).

Once groups were identified, we investigated what factors (risk behaviors, social anxiety, age, pubertal status, sex, and parental education) predict group membership (see Table 4.1 for means, standard deviations, and correlations among study variables).

Specifically, we ran a multinomial logistic regression with group status as the dependent variable and all of the factors were entered simultaneously as the independent variables.

We also tested what factors (risk behaviors, social anxiety, age, pubertal status, sex, and parental education) predict the conditional probability of group membership (e.g., does risk taking predict whether individuals have a greater probability of being in a group with higher levels of impulsivity and higher levels of dysregulation?).

Table 4.1. Means, standard deviations, and correlations

| Variable              | M     | SD   | 1     | 2     | 3     | 4     | 5     | 6     | 7     | 8  |
|-----------------------|-------|------|-------|-------|-------|-------|-------|-------|-------|----|
| 1. ST                 | 2.58  | 0.71 |       |       |       |       |       |       |       |    |
| 2. DYS                | 2.19  | 0.75 | .50** |       |       |       |       |       |       |    |
| 3. Imp                | 1.93  | 0.61 | .17** | .36** |       |       |       |       |       |    |
| 4. Risk<br>Taking     | 1.43  | 0.46 | 05    | .09** | .25** |       |       |       |       |    |
| 5. Anxiety            | 1.95  | 0.66 | .39** | .44** | .17** | .03   |       |       |       |    |
| 6. Age                | 11.65 | 1.75 | .17** | .13** | .19** | .15** | .08** |       |       |    |
| 7. Pubertal<br>Status | 2.07  | 0.87 | .26** | .21** | .17** | .14** | .15** | .73** |       |    |
| 8. Sex                | 1.50  | 0.50 | .25** | .06*  | 16**  | 12**  | .17** | .06*  | .28** |    |
| 9. Parental Education | 4.12  | 0.75 | .02   | 11**  | 14**  | 01    | 14**  | .01   | 03    | 03 |

*Note.* M and SD are used to represent mean and standard deviation, respectively. ST= Sensitivity to threat, DYS= emotion dysregulation, IMP= impulsivity. \* indicates p < .05. \*\* indicates p < .01.

To investigate class differences on the ERN, we used STATSLAB, an open-source toolbox that implements robust statistics for analysis of EEG data (Campopiano, van Noordt, & Segalowitz, 2018). This software allows for testing using percentile bootstrap and trimmed means, a technique that is robust to distribution characteristics such as skew, outliers, uneven tails, and various model assumption violations (see Wilcox, 2017).

In STATSLAB, single trial data for our channels were extracted and averaged together. For each subject, the single trial data were resampled, with replacement, to generate a surrogate sampling distribution. The 20% trimmed mean was taken across trials, at each time point (i.e., removing the most extreme voltages at each time point), to generate a robust bootstrapped ERP. This process was repeated for each group and the difference between groups taken. Iterating this process of resampling, trimming, and scoring the difference wave was performed 1,000 times to generate a distribution of differences between conditions (see Campopiano et al., 2018 for details). The 95% confidence interval was obtained to test significant differences between ERP waveforms for each group.

#### Results

Q1: Using latent class analysis, are there distinct groups of individuals who vary in emotion dysregulation, sensitivity to threat, and impulsivity? The LCA was conducted for 1-6 classes. Four classes was chosen as the best solution (see Table 4.2). There was a decrease in BIC from 3 classes to 4 classes. Further, the 4-class solution had an entropy value above .80 and average latent class posterior probabilities were close to 1. The LMR was significant at 5 classes, but no longer significant for 6 classes. The 5th

class, however, only contained 48 participants (3.7 % of the sample) and added little value to the interpretability of the groups. Therefore, a 4-class solution was chosen (see Figure 4.1). The classes were labeled as follows: (1)

HighDysregulation/HighThreatSensitivity/LowModImpulsivity (14.6% of the sample) – hereafter labeled the <code>High\_Dysregulation/ThreatSensitivity</code> group, given that the high levels of dysregulation and threat sensitivity indicators clearly distinguish this group from the other groups, (2) ModDysregulation/ModThreatSensitivity/HighImpulsivity (11.4% of the sample) – labeled <code>ModDysregulation/HighImpulsivity</code> group, as this group is the only group with moderate dysregulation and high levels of impulsivity, (3) LowModDsyregulation/ModThreatSensitivity/LowModImpulsivity (57.6% of the sample) – labelled <code>LowMod</code> (normative) group, given that over 50% of the sample is in this group, and (4) LowDysregulation/LowThreatSensitivity/LowImpulsivity (16.4% of the sample) – labeled the <code>Low</code> group, given their low scores on all indicators (see Table 4.3 for group differences on the indicators).

Table 4.2. Latent class analysis (LCA) fit indices.

| Number of<br>Classes | BIC      | Entropy | Conditional<br>Probabilities | LMR <i>p</i> -value |
|----------------------|----------|---------|------------------------------|---------------------|
| 2 Classes            | 29943.77 | 0.771   | 0.918-0.945                  | 0.0000              |
| 3 Classes            | 29064.62 | 0.829   | 0.898-0.937                  | 0.0097              |
| 4 Classes            | 28477.85 | 0.851   | 0.847-0.945                  | 0.0033              |
| 5 Classes            | 28121.68 | 0.850   | 0.855-0.935                  | 0.0038              |
| 6 Classes            | 27842.06 | 0.843   | 0.827-0.926                  | 0.2636              |

*Note*. BIC = Bayesian information criterion. LMR = Lo-Mendell-Rubin.

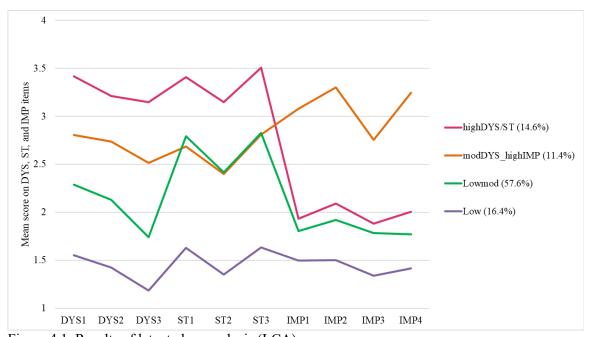


Figure 4.1. Results of latent class analysis (LCA).

Note. DYS= Emotion dysregulation item, ST = Sensitivity to threat item, IMP = Impulsivity Item. highDYS/ST = High\_Dysregulation/ThreatSensitivity group; modDYS\_highIMP = ModDysregulation/HighImpulsivity group. Percentages in brackets indicate the percent of the sample in each group.

Table 4.3. Group means on latent class indicators.

| _    | Low                | LowMod             | ModDysregulation/<br>HighImpulsivity | High_Dysregulation/<br>ThreatSensitivity |
|------|--------------------|--------------------|--------------------------------------|--|
| DYS1 | 1.554 <sub>d</sub> | 2.288 <sub>c</sub> | $2.805_{b}$                          | 3.417 <sub>a</sub>                       |
| DYS2 | $1.422_d$          | 2.131 <sub>c</sub> | $2.739_{b}$                          | 3.211 <sub>a</sub>                       |
| DYS3 | 1.183 <sub>d</sub> | 1.742 <sub>c</sub> | 2.516 <sub>b</sub>                   | 3.149 <sub>a</sub>                       |
| ST1  | 1.629 <sub>c</sub> | 2.791 <sub>b</sub> | $2.688_{b}$                          | $3.407_a$                                |
| ST2  | 1.350 <sub>c</sub> | $2.417_{b}$        | $2.397_{b}$                          | $3.146_{a}$                              |
| ST3  | 1.632 <sub>c</sub> | $2.825_{b}$        | $2.810_{b}$                          | $3.506_a$                                |
| IMP1 | 1.499 <sub>c</sub> | $1.804_{b}$        | $3.080_a$                            | $1.934_b$                                |
| IMP2 | 1.502 <sub>d</sub> | 1.921 <sub>c</sub> | 3.299 <sub>a</sub>                   | $2.093_{b}$                              |
| IMP3 | $1.340_{\rm c}$    | $1.784_{b}$        | 2.752a                               | 1.881 <sub>b</sub>                       |
| IMP4 | 1.415 <sub>d</sub> | 1.772 <sub>c</sub> | 3.248 <sub>a</sub>                   | 2.007 <sub>b</sub>                       |

*Note*. DYS= Emotion dysregulation item, ST = Sensitivity to threat item, IMP = Impulsivity Item. Significant differences across groups are represented by letter subscripts that do not match (across rows), non-significant differences are represented by matching letter subscripts.

Q2a: What factors predict group membership? In order to investigate what factors (risk taking, social anxiety, age, pubertal status, sex, and parental education) predict group membership, we ran three multinomial logistic regressions where we changed the reference category each time (the low group was the reference group in the first analysis, the lowmod (normative) group was the reference category for the second analysis, and the ModDysregulation/HighImpulsivity group was the reference category for the third analysis; see Tables 4.4-4.6 for complete model results).

The overall model was significant  $\chi 2(18) = 361.231$ , p < .001. Risk taking [ $\chi 2(3) = 26.98$ , p < .001], social anxiety [ $\chi 2(3) = 178.919$ , p < .001], pubertal status [ $\chi 2(3) = 178.919$ , p < .001], pubertal status [ $\chi 2(3) = 178.919$ ]

27.490, p < .001], sex [ $\chi 2(3) = 17.170$ , p < .001], and parental education [ $\chi 2(3) = 15.686$ , p = .001] significantly differentiated among the classes. Age [ $\chi 2(3) = 2.591$ , p = .459] was not a significant predictor of class membership.

*Risk taking*. The ModDysregulation/HighImpulsivity group had greater odds of engaging in risk behaviors than the Low group (OR = 2.776, p < .001), the LowMod (normative) group (OR = 2.403, p < .001), and the High\_Dysregulation/ThreatSensitivity group (OR = 2.040, p = .001).

Social Anxiety. Compared to the Low group, individuals with higher social anxiety had greater odds of being in the LowMod (normative) group (OR = 2.882, p < .001), the ModDysregulation/HighImpulsivity group (OR = 5.401, p < .001), and the High\_Dysregulation/ThreatSensitivity group (OR = 9.993, p < .001). Those with greater social anxiety also had greater odds of being in the ModDysregulation/HighImpulsivity group (OR = 1.874, p < .001) and the High\_Dysregulation/ThreatSensitivity group (OR = 3.467, p < .001) compared to the LowMod (normative) group. Higher social anxiety was also associated with greater odds of being in the High\_Dysregulation/ThreatSensitivity group compared to the ModDysregulation/HighImpulsivity group (OR = 1.850, p < .001).

Pubertal Development. Participants with greater pubertal development had higher odds of being in the LowMod (OR = 1.554, p = .005), ModDysregulation/
HighImpulsivity (OR = 2.384, p < .001), and High\_Dysregulation/ThreatSensitivity (OR = 2.600, p < .001) groups compared to the Low group. Participants with greater pubertal development also had greater odds of being in the ModDysregulation/HighImpulsivity (OR = 1.534, p = .012) and High\_Dysregulation/ThreatSensitivity (OR = 1.673, p < .001) compared to the LowMod (normative) group.

Sex. Females had greater odds than males of being in the Low (OR = 1.673, p = .044), LowMod (normative group; OR = 2.216, p < .001) and High\_Dysregulation/
ThreatSensitivity (OR = 2.370, p < .001) groups compared to the ModDysregulation/
HighImpulsivity group.

*Parental education*. Individuals with higher parental education had greater odds of being in the Low group (OR = 1.499, p = .008), LowMod (normative; OR = 1.637, p < .001), and High\_Dysregulation/ThreatSensitivity (OR = 1.496, p = .008), compared to the ModDysregulation/HighImpulsivity group.

Table 4.4. Multinomial Logistic Regression (Comparison Group: Low)

| Group          | Variable        | В     | SE   | OR   | p.value | conf.low | conf.high |
|----------------|-----------------|-------|------|------|---------|----------|-----------|
| LowMod         | Risk_Taking     | 0.14  | 0.20 | 1.16 | 0.48    | 0.78     | 1.72      |
|                | Anxiety         | 1.06  | 0.17 | 2.88 | 0.00*** | 2.06     | 4.04      |
|                | Age             | 0.10  | 0.07 | 1.11 | 0.15    | 0.96     | 1.27      |
|                | Pubertal_Status | 0.44  | 0.16 | 1.55 | 0.01**  | 1.14     | 2.12      |
|                | Sex             | 0.28  | 0.17 | 1.32 | 0.10    | 0.95     | 1.85      |
|                | Parent_Educ.    | 0.09  | 0.11 | 1.09 | 0.42    | 0.88     | 1.35      |
| ModDYS/HighIMP | Risk_Taking     | 1.02  | 0.24 | 2.78 | 0.00*** | 1.73     | 4.46      |
|                | Anxiety         | 1.69  | 0.21 | 5.40 | 0.00*** | 3.58     | 8.16      |
|                | Age             | 0.06  | 0.10 | 1.06 | 0.53    | 0.88     | 1.29      |
|                | Pubertal_Status | 0.87  | 0.22 | 2.38 | 0.00*** | 1.56     | 3.64      |
|                | Sex             | -0.52 | 0.26 | 0.60 | 0.04*   | 0.36     | 0.99      |
|                | Parent_Educ.    | -0.40 | 0.15 | 0.67 | 0.01**  | 0.49     | 0.90      |
| HighDYS/HighST | Risk_Taking     | 0.31  | 0.26 | 1.36 | 0.24    | 0.82     | 2.26      |
|                | Anxiety         | 2.30  | 0.21 | 9.99 | 0.00*** | 6.68     | 14.95     |
|                | Age             | 0.04  | 0.09 | 1.04 | 0.68    | 0.86     | 1.25      |
|                | Pubertal_Status | 0.96  | 0.21 | 2.60 | 0.00*** | 1.74     | 3.89      |
|                | Sex             | 0.35  | 0.24 | 1.42 | 0.15    | 0.88     | 2.28      |
|                | Parent_Educ.    | -0.00 | 0.15 | 1.00 | 0.99    | 0.74     | 1.34      |

Note. ModDYS/HighIMP = ModDysregulation/HighImpulsivity group; HighDYS/HighST= High\_Dysregulation/ThreatSensitivity group; Parent\_Educ.= Parental education. SE = Standard error; OR = Odds Ratio; conf.low = lower bound confidence interval; conf.high= higher bound confidence interval.

Table 4.5. Multinomial Logistic Regression (Comparison Group: LowMod)

| Group          | Variable        | В     | SE   | OR   | p.value | conf.low | conf.high |
|----------------|-----------------|-------|------|------|---------|----------|-----------|
| Low            | Risk_Taking     | -0.14 | 0.20 | 0.87 | 0.48    | 0.58     | 1.29      |
|                | Anxiety         | -1.06 | 0.17 | 0.35 | 0.00*** | 0.25     | 0.49      |
|                | Age             | -0.10 | 0.07 | 0.90 | 0.15    | 0.79     | 1.04      |
|                | Pubertal_Status | -0.44 | 0.16 | 0.64 | 0.01**  | 0.47     | 0.88      |
|                | Sex             | -0.28 | 0.17 | 0.76 | 0.10    | 0.54     | 1.06      |
|                | Parental_Educ.  | -0.09 | 0.11 | 0.92 | 0.42    | 0.74     | 1.13      |
| ModDYS/HighIMP | Risk_Taking     | 0.88  | 0.18 | 2.40 | 0.00*** | 1.70     | 3.39      |
|                | Anxiety         | 0.63  | 0.14 | 1.87 | 0.00*** | 1.42     | 2.48      |
|                | Age             | -0.04 | 0.08 | 0.96 | 0.61    | 0.82     | 1.12      |
|                | Pubertal_Status | 0.43  | 0.17 | 1.53 | 0.01*   | 1.10     | 2.14      |
|                | Sex             | -0.80 | 0.21 | 0.45 | 0.00*** | 0.30     | 0.69      |
|                | Parental_Educ.  | -0.49 | 0.13 | 0.61 | 0.00*** | 0.48     | 0.78      |
| HighDYS/HighST | Risk_Taking     | 0.16  | 0.19 | 1.18 | 0.40    | 0.81     | 1.72      |
|                | Anxiety         | 1.24  | 0.13 | 3.47 | 0.00*** | 2.69     | 4.48      |
|                | Age             | -0.06 | 0.07 | 0.94 | 0.39    | 0.81     | 1.08      |
|                | Pubertal_Status | 0.51  | 0.15 | 1.67 | 0.00*** | 1.24     | 2.26      |
|                | Sex             | 0.07  | 0.20 | 1.07 | 0.73    | 0.73     | 1.57      |
|                | Parental_Educ.  | -0.09 | 0.12 | 0.91 | 0.45    | 0.72     | 1.16      |

Note: *Note*. ModDYS/HighIMP = ModDysregulation/HighImpulsivity group; HighDYS/HighST= High\_Dysregulation/ThreatSensitivity group; Parent\_Educ.= Parental education. SE = Standard error; OR = Odds Ratio; conf.low = lower bound confidence interval; conf.high= higher bound confidence interval.

Table 4.6. Multinomial Logistic Regression (Comparison Group: ModDYS/HighIMP)

| Group          | Variable        | В     | SE   | OR   | p.value | conf.low | conf.high |
|----------------|-----------------|-------|------|------|---------|----------|-----------|
| Low            | Risk_Taking     | -1.02 | 0.24 | 0.36 | 0.00*** | 0.22     | 0.58      |
|                | Anxiety         | -1.69 | 0.21 | 0.19 | 0.00*** | 0.12     | 0.28      |
|                | Age             | -0.06 | 0.10 | 0.94 | 0.53    | 0.78     | 1.14      |
|                | Pubertal_Status | -0.87 | 0.22 | 0.42 | 0.00*** | 0.28     | 0.64      |
|                | Sex             | 0.52  | 0.26 | 1.67 | 0.04*   | 1.01     | 2.77      |
|                | Parental_Educ.  | 0.40  | 0.15 | 1.50 | 0.01**  | 1.11     | 2.02      |
| LowMod         | Risk_Taking     | -0.88 | 0.18 | 0.42 | 0.00*** | 0.29     | 0.59      |
|                | Anxiety         | -0.63 | 0.14 | 0.53 | 0.00*** | 0.40     | 0.71      |
|                | Age             | 0.04  | 0.08 | 1.04 | 0.61    | 0.89     | 1.21      |
|                | Pubertal_Status | -0.43 | 0.17 | 0.65 | 0.01*   | 0.47     | 0.91      |
|                | Sex             | 0.80  | 0.21 | 2.22 | 0.00*** | 1.45     | 3.38      |
|                | Parental_Educ.  | 0.49  | 0.13 | 1.64 | 0.00*** | 1.28     | 2.09      |
| HighDYS/HighST | Risk_Taking     | -0.71 | 0.22 | 0.49 | 0.00**  | 0.32     | 0.76      |
|                | Anxiety         | 0.62  | 0.16 | 1.85 | 0.00*** | 1.35     | 2.54      |
|                | Age             | -0.02 | 0.09 | 0.98 | 0.81    | 0.81     | 1.18      |
|                | Pubertal_Status | 0.09  | 0.20 | 1.09 | 0.67    | 0.73     | 1.62      |
|                | Sex             | 0.86  | 0.26 | 2.37 | 0.00*** | 1.43     | 3.93      |
|                | Parental_Educ.  | 0.40  | 0.15 | 1.50 | 0.01**  | 1.11     | 2.02      |

Note. ModDYS/HighIMP = ModDysregulation/HighImpulsivity group; HighDYS/HighST= High\_Dysregulation/ThreatSensitivity group; Parent\_Educ.= Parental education. SE = Standard error; OR = Odds Ratio; conf.low = lower bound confidence interval; conf.high= higher bound confidence interval.

Q2b: What factors are associated with the conditional probabilities of group membership? We also ran a follow up analysis to assess whether our study variables predict the *probability* of group membership (a continuous measure). To do this, we ran four linear regressions (one for each group's conditional probabilities). The probability of group membership was included as the dependent variable and the study variables (risk behaviors, social anxiety, age, pubertal status, sex, and parental education) were entered as the independent variables.

Low group. The overall model was significant, F(6,1303) = 27.645, p < .001. Lower social anxiety (B = -.241, SE = .014, p < .001) and less advanced pubertal status (B = -.142, SE = .016, p < .001) predicted greater probability of being in the low group.

LowMod group. The overall model was significant, F(6,1303) = 7.202, p < .001. Lower social anxiety (B = -.122, SE = .019, p < .001), lower risk taking (B = -.083, SE = .026, p = .003), higher parental education (B = .061, SE = .016, p = .026), and female status (B = .059, SE = .026, p = .047) predicted greater probability of being in the LowMod group.

 $ModDysregulation/HighImpulsivity\ group$ . The overall model was significant, F(6,1303) = 16.623, p < .001. Higher social anxiety (B = .098, SE = .012, p < .001), higher risk taking (B = .165, SE = .018, p < .001), lower parental education (B = -.111, SE = .011, p < .001), male status (B = -.111, SE = .017, p < .001), and more advanced pubertal status (B = .090, SE = .014, p = .031) predicted greater probability of being in the ModDysregulation/HighImpulsivity group.

 $High\_Dysregulation/ThreatSensitivity\ group$ . The overall model was significant,  $F(6,1303) = 39.889,\ p < .001$ . Higher social anxiety ( $B = .337,\ SE = .013,\ p < .001$ ) and more advanced pubertal status ( $B = -.149,\ SE = .015,\ p < .001$ ) predicted greater probability of being in the High\_Dysregulation/ThreatSensitivity group.

Q3: Do groups show different neural activation on the ERN during an inhibitory control task? We investigated group differences on the ERN during an inhibitory control task. Results are presented in Figure 4.2. The High\_Dysregulation/ThreatSensitivity group had the largest ERN, while the ModDysregulation/HighImpulsivity group had the smallest ERN; the Low and LowMod

groups did not differ on their ERN (see Figure 4.2). Of note, the groups did not differ on reaction time, F(3, 431) = 2.413, p = .066, or on the number of errors they committed, F(3, 431) = 1.907, p = .128, during the go/no-go task.

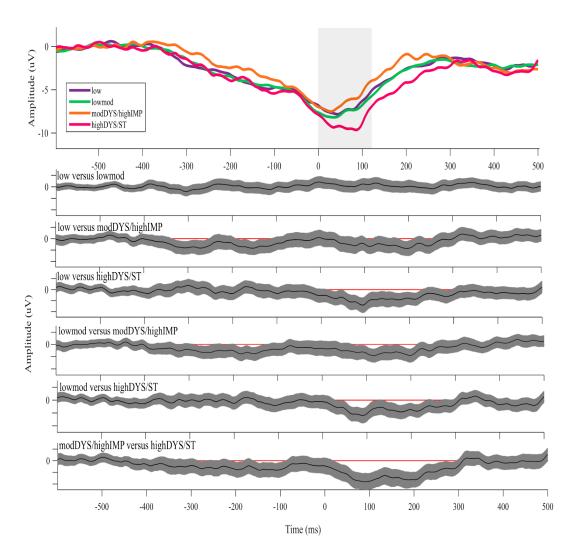


Figure 4.2. Waveforms show the ERN for all groups. *Note*. Bottom panels show the 95% bootstrapped confidence intervals for the pairwise comparison for each group. Confidence intervals that do not overlap with the zero line (red) depict a significant difference at that time point. highDYS/ST = High\_Dysregulation/ ThreatSensitivity group; modDYS highIMP = ModDysregulation/ HighImpulsivity group

### **Discussion**

Adolescence often has been suggested to be a sensitive period of development, characterized by the onset of both internalizing problems (e.g., social anxiety; Beesdo et al., 2009) and externalizing problems (risk taking; Casey et al., 2008; Casey & Caudle, 2013; Dahl, 2004; Ernst, 2014). Several factors may help to differentiate youth who are more likely to have anxiety problems (e.g., threat sensitivity and emotion dysregulation) and youth with risk-taking problems (e.g., impulsivity and emotion dysregulation). The current study examined whether there are distinct groups of individuals who vary on their levels of emotion dysregulation, impulsivity, and sensitivity to threat. At the same time, we were interested in differences between groups on both self-report measures (risk taking, social anxiety, age, pubertal status, parental education, and sex) and the error-related negativity.

We identified four groups with differential levels of emotion dysregulation, impulsivity and sensitivity to threat: (1) a group with high emotion dysregulation, high sensitivity to threat, and low/moderate impulsivity (labeled the <code>High\_Dysregulation/ThreatSensitivity</code> group; 14.6% of the sample) (2) a group with moderate emotion dysregulation, moderate sensitivity to threat, and high impulsivity (labeled <code>ModDysregulation/HighImpulsivity</code> group; 11.4% of the sample) (3) a group with low/moderate emotion dysregulation, moderate sensitivity to threat, and low/moderate impulsivity (labeled the <code>LowMod group</code>; 57.6% of the sample) and (4) a group with low emotion dysregulation, low sensitivity to threat, and low impulsivity (labeled the <code>Low group</code>; 16.4% of the sample). Given that over 50% of the sample was part of the <code>LowMod</code> group, our results suggest that it is common for children and

adolescents to experience low/moderate levels of both emotion dysregulation and impulsivity in combination with moderate sensitivity to threat.

Of interest, our results support neurodevelopmental imbalance models that suggest that adolescents may be a sensitive period of development. Specifically, individuals with more advanced pubertal development had greater odds than those with lower pubertal development of being in the <code>High\_Dysregulation/ThreatSensitivity</code> and <code>ModDysregulation/HighImpulsivity</code> groups. In other words, adolescents (those with greater pubertal development) were most likely to be part of the two groups with the highest dysregulation and high scores on either sensitivity to threat or impulsivity. We did not find, however, that age was a significant predictor of group membership. Thus, when pubertal status and age were included in the same model, age did not explain any additional variance that was not already captured by pubertal status. This result is in line with previous research and the imbalance model which highlights that pubertal status may be a more sensitive marker for adolescent sensitivity than age (e.g., Heffer & Willoughby, 2020; van den Bos et al., 2014).

We also found important individual differences that may help distinguish between the two groups that adolescents are most likely to be a part of – the *ModDysregulation/ HighImpulsivity* and the *High\_Dysregulation/ThreatSensitivity groups*. For example, the *ModDysregulation/HighImpulsivity* group engaged in the most risk behaviors, were more 
likely to be male, and had lower parental education than the other groups. In contrast, the *High\_Dysregulation/ThreatSensitivity* group had the greatest levels of social anxiety 
compared to all other groups. Our results remained consistent when we used conditional 
probabilities of group membership (a continuous measure of how likely an individual is

to be part of each group)— notably, more advanced pubertal development and greater risk taking predicted higher probabilities of being in the *ModDysregulation/ HighImpulsivity group*, while more advanced pubertal development and greater social anxiety predicted higher probabilities of being in the

High Dysregulation/ThreatSensitivity group.

Our results suggest that adolescents have different profiles of impulsivity, sensitivity to threat, and emotion dysregulation that may contribute to whether they are more likely to display social anxiety or risk taking. Indeed, researchers interested in adolescent risk taking may need to target adolescents with moderate dysregulation and high impulsivity; males and individuals with lower parental education also may be particularly likely to be part of this group. In contrast, researchers interested in social anxiety may benefit from identifying adolescents who have high dysregulation in combination with high sensitivity to threat.

A critical component of our study was to identify neural differences between the groups. Specifically, we used the ERN, a neural measure of performance monitoring. Previous research has found that a larger ERN is associated with greater motivation to avoid errors (e.g., Hajcak & Foti, 2008; Meyer et al., 2017). We found that the <code>High\_Dysregulation/ThreatSensitivity</code> group had the largest ERN, while the <code>ModDysregulation/HighImpulsivity</code> group had the smallest ERN. Thus, when individuals have high dysregulation and high sensitivity to threat, they may be particularly motivated to avoid making mistakes. In contrast, individuals who have moderate dysregulation, but high impulsivity may be less concerned with monitoring their performance. Indeed, one of the hallmarks of impulsivity is acting without thinking, which in combination with

lower top-down control may contribute to this group having poorer performance monitoring. As a result, this group may be less bothered by (or take less notice of) making mistakes during the task, compared to groups with lower scores on impulsivity and dysregulation.

Our study has a number of strengths, including a large sample of children and adolescents, the use of a person-centered approach to isolate distinct groups, and the use of multiple methods (e.g., self-report and EEG), this study is not without limitations. First, we did not include the full scale for our core measures (emotion dysregulation, sensitivity to threat, and impulsivity). As the data were part of a larger study assessing a wide range of constructs, it was not feasible to include every item from each scale due to time constraints. Of note, however, the alpha for these measures were above .80, demonstrating good reliability (Cronbach, 1951). Second, causal inference cannot be concluded from our study. For example, we did not test whether having a profile of high dysregulation and high sensitivity to threat *causes* social anxiety, given the concurrent nature of this study. Finally, there are likely other factors that play a role in adolescents' sensitivity to emotion processing that were not included in this study (e.g., sensation seeking, peer presence).

Nonetheless, our study has important implications for adolescent development. Indeed, adolescents are more likely to be in the groups with greater dysregulation; at the same time there are differences in whether they have greater impulsivity or sensitivity to threat. Individual differences in emotion dysregulation, sensitivity to threat, and impulsivity are associated with differential outcomes. Specifically, high dysregulation in combination with high sensitivity to threat was associated with social anxiety, while

moderate dysregulation combined with high impulsivity was associated with risk taking. It is imperative that researchers continue to investigate individual differences among adolescents. Our results highlight that not all adolescents are highly sensitive to threat, just as not all adolescents are highly impulsive. Therefore, sensitivity to emotional processing during adolescence may not be homogenous or display a universal profile. Finally, the ERN may be a potential biomarker to help distinguish between the different profiles of adolescents. Critically, this neural indicator could potentially help predict later development of internalizing or externalizing problems (e.g., social anxiety and/or risk taking) at younger ages (e.g., before children are able to self-report issues with anxiety).

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### **CHAPTER 6: GENERAL DISCUSSION**

Adolescence is thought to be a sensitive period of development, characterized by the onset of internalizing problems such as anxiety (Beesdo et al., 2009). Sensitivity to threat, a heightened responsiveness to aversive situations, has been suggested to be a precursor to anxiety, highlighting the importance of understanding sensitivity to threat among children and adolescents. Theories of adolescent brain development indicate that adolescents may be particularly reactive to emotionally arousing situations (e.g., threats) compared to other age groups (e.g., Casey, 2015; Somerville & Casey, 2010; Steinberg, 2008). Thus, the purpose of this dissertation was to investigate the development of sensitivity to threat among children and adolescents. A variety of methods were used to address my research questions, including self-report, EEG data, longitudinal analyses, and multiple indicators of development (pubertal status, age). Overall, the four studies of my dissertation largely support the notion that adolescents have heightened sensitivity to threat compared to children. Critically, I also found evidence that *consistency* (across time and situation) is an important marker to help detect which youth are most at risk.

Study 1 of my dissertation examined whether adolescents, compared to children, have greater neural sensitivity to negative feedback. In this study, I also examined whether this neural sensitivity was linked to worry— an anxiety-related construct. Using both age and pubertal status, this study showed that for both children and adolescents, worriers have heightened neural activation to negative feedback than nonworriers. This difference, however, was smaller among the adolescents (i.e., adolescent nonworriers also had heightened neural activation to negative feedback). Thus, the results of Study 1

indicate that adolescents in general (even those who self-report low levels of worry) are sensitive to emotionally salient events, such as receiving negative feedback.

Given that Study 1 was concurrent, in Study 2 I examined whether children and adolescents differ in their longitudinal trajectories of sensitivity to threat. I also investigated whether these trajectories were associated with frontal asymmetry (a neural indicator associated with avoidance motivations). Using a latent class growth curve analysis, I identified three distinct trajectory groups: (1) high-stable sensitivity to threat (i.e., consistent sensitivity to threat over *time*), (2) moderate-increasing sensitivity to threat and (3) low-stable sensitivity to threat. Of interest, individuals with more advanced pubertal development (but not age) had greater odds of being part of the high-stable sensitivity to threat group. Additionally, the high-stable sensitivity to threat group had greater right frontal asymmetry activation (i.e., greater neural avoidance motivation) than the other two groups.

In Study 3, I extended this work to examine consistency across threatening *situations*. Results revealed that youth who self-report higher levels of sensitivity to threat had consistently higher neural activation to threatening situations (receiving negative feedback, making mistakes, viewing angry faces). I did not find, however, that adolescents (i.e., individuals with more advanced pubertal status or older age) had consistently higher neural activation to these threatening situations compared to children. An explanation of why this may be the case is offered below.

While Studies 1 through 3 investigated whether adolescence is a period of heightened sensitivity to threat, Study 4 of my dissertation sought to extend this research by investigating individual differences among adolescents. Indeed, while my main focus

has been on understanding whether adolescence is a time of heightened sensitivity to threat, which has been linked to internalizing problems (e.g., anxiety), adolescence also is considered the onset of many externalizing problems (such as risk taking; Casey & Caudle, 2013; Casey et al., 2008; Dahl, 2004; Ernst, 2014). Thus, in this study, my goal was to identify distinct groups of youth who are at risk for anxiety and/or risk taking. Using a latent class analysis, I found that youth who reported high sensitivity to threat in combination with emotion dysregulation had higher anxiety and a larger ERN (i.e., a neural marker associated with motivation to avoid errors) compared to their peers. At the same time, youth who reported the highest levels of impulsivity in combination with emotion dysregulation engaged in greater risk taking and had a smaller ERN.

Importantly, adolescents compared to children were more likely to be in these two groups most at risk for anxiety or risk taking.

Several themes emerged from these studies. First, adolescence appears to be a sensitive period for heightened sensitivity to threat, and notably, puberty is an important developmental marker that may be more sensitive to capturing these differences compared to age. Second, *consistency* (across both time and situation) may be an important indicator associated with increased risk of anxiety-related problems. Finally, neural activation, as measured by EEG, can help differentiate youth with the greatest levels of self-reported sensitivity to threat. Each of these themes will be discussed below.

# Heightened sensitivity to threat during adolescence

The studies of my dissertation largely support the suggestion that adolescence is a sensitive period for heightened reactivity to threats. According to theories of adolescent brain development, adolescence is a time of reorganization of neural circuitry (e.g.,

Casey, 2015; Somerville & Casey, 2010; Steinberg, 2008). The interconnections within the brain's mesolimbic dopamine system are thought to strengthen during this age period (Haber & Knutson, 2010; Sgambato-Faure et al., 2016). This system, which includes highly interconnected nodes in the frontal cortex and basal ganglia, is thought to be important in processing emotionally salient stimuli (Haber & Knutson, 2010; Sgambato-Faure et al., 2016). Further, interactions among the ventral striatum, prefrontal cortex, and other nodes (e.g., the amygdala and insula; Haber & Knutson, 2010; Marchand, 2010; Palminteri et al., 2012; Samanez-Larkin et al., 2008) are thought to broadly orchestrate a range of goal-directed behaviors guided by motivational value (e.g., threats). In line with this idea, adolescents show exaggerated reactivity in nodes within this system when processing aversive cues, compared to other age groups (Galván & McGlennen, 2013; Guyer et al., 2008; Hare et al., 2008). Thus, research investigating adolescent brain development has shown that adolescents may be more responsive to aversive cues than other age groups. The findings from my dissertation support this neurodevelopmental work.

The studies from my dissertation also show that pubertal development, as opposed to age, may be a better developmental marker to capture differences in sensitivity to threat. For example, in Study 1, the results indicate that when developmental groups were defined by pubertal status, adolescents in general (those with more advanced pubertal status) and children (those with less advanced pubertal status) with high worry had longer reaction times after receiving loss feedback compared to win feedback compared to the children nonworriers. This finding is directly in line with our ERP results for Study 1 (i.e., that adolescents in general and child worriers had higher neural sensitivity to

negative feedback than child nonworriers). When groups were defined by grade status, this behavioral finding was not significant. In Study 2, I found that individuals with more advanced pubertal development had greater odds of being part of the high-stable sensitivity to threat group (i.e., high consistency over time) compared to the other groups— age was not a significant predictor in this model. Together, these findings suggest that pubertal status captured more variance in sensitivity to threat (both neural sensitivity and self-reported sensitivity to threats) compared to age. This finding is consistent with other work showing that pubertal status is a better marker of sensitivity to social evaluation than age (e.g., van den Bos et al., 2014).

While my studies largely find support for adolescence as a period of heightened sensitivity to threat, Study 4 of my dissertation found that there are individual differences in this threat sensitivity among adolescence. For example, although adolescents were more likely than children to be in subgroups characterized by heightened sensitivity to threat in combination with emotion dysregulation, they were also more likely than children to be in another subgroup characterized by lower levels of sensitivity to threat yet higher impulsivity and emotion dysregulation. These results highlight that not all adolescents are highly sensitive to threat, just as not all adolescents are highly impulsive. It is important to not make general claims that *all adolescents* are sensitive to threat and therefore at risk for anxiety.

Importantly, Study 3 of my dissertation did not support the claim that adolescents are more sensitive to threats than children. In this study, neither age nor pubertal status was associated with having consistently higher neural activation to threatening situations. This finding was surprising and did not align with my expectation that adolescents would

show more consistent sensitivity. Other studies (including Study 1 of my dissertation), however, have shown that *children* also can have heightened neural activation in response to different threatening situations (e.g., Chong & Meyer, 2019; O'Toole et al., 2013). Indeed, as I found in Study 1, children with high levels of worry have heightened neural activation to negative feedback. Thus, both children and adolescents who have consistently heightened neural sensitivity to different types of threats may be particularly vulnerable.

If we are to consider adolescence as a developmental period marked by heightened sensitivity to threat, it is important to understand why some children also are showing this pattern of results. Moffit's (1993, 2006) prominent developmental theory may offer some explanation to help disentangle these results. Although Moffitt's theory is centered around antisocial behavior, the developmental pathways she suggests are likely relevant for a wide range of behaviors. Moffitt argues that there are several developmental pathways that can help explain different patterns of behavior across the lifespan. The first pathway (referred to as life-course persistent) encompasses a small group of youth who consistently engage in problematic behavior throughout childhood, adolescence, and adulthood. In contrast, the second pathway (referred to as adolescent-limited) includes a group of youth who have adjustment issues *only* during adolescence (see also Patterson & Yoerger, 1993, 1997, Weisner & Silbereisen, 2003).

Moffitt hypothesized that the sources contributing to these problematic behaviors may differ across these groups. For example, the life-course persistent group is thought to engage in problematic behavior due to biological or temperamental factors as well as other early environmental factors (e.g., poor parenting). The adolescent-limited group,

however, is thought to engage in problematic behaviors mainly due to factors that may be 'limited' to or more prominent in adolescence, such as the asynchrony in maturation of different brain systems (as highlighted by the imbalance model), susceptibility to peer influence, etc. In other words, this theory highlights that there likely are some individuals who will have poor adjustment across their entire life (and this may be linked to temperament or personality traits), while for others, heightened issues may be limited to the developmental period of adolescence.

This theory is relevant for my results, as I found that adolescents in general seem to show heightened sensitivity to threat, and thus, for the majority of these individuals, demonstrate an adolescent-limited trajectory. In other words, these adolescents may have heightened sensitivity to threat because it is a relatively normative experience during this age period and not because they necessarily are at risk for anxiety. At the same time, in Study 3 of my dissertation there was a small group (of both children and adolescents) who consistently had high neural activation across a variety of different tasks. This group may be more in line with a life-course persistent trajectory, given that this group was not unique to adolescence and reflects a small group who have the highest levels of threat sensitivity.

# Consistency of sensitivity to threats

Consistency of sensitivity to threat is an important theme throughout my dissertation. Indeed, several of my studies have shown that youth with *consistently high* sensitivity to threat were most at risk for anxiety-related problems (e.g., avoidance motivations). This is critical, as not all youth who are sensitive to threat go on to develop anxiety (Degnan & Fox, 2007); thus, understanding what factors predict which youth are

at a heightened risk is necessary to aid in preventative measures. Across both time and task, I found that youth with more consistent sensitivity to threat were most at risk for anxiety-related problems.

An important contribution from my studies is that sensitivity to threat (at least to some extent) appears to be normative across development. Consistency, however, seems to be an important marker to differentiate non-normative from normative sensitivity to threat. Indeed, in Study 2, only 14% of the sample had consistently *low* sensitivity to threat across three years. This low percentage indicates that the majority of the sample was either in the moderate increasing group (54.3% of the sample) or consistently high group (31.7% of the sample). Thus, only a small subsample of children and adolescents appear to have low sensitivity to threat over time. This idea is echoed in Study 3, where I found that 11.8% of participants had consistently high neural activation to all three tasks, 34.8% of participants had high neural activation to two out of three tasks, 41.6% of participants had high neural activation to one out of three tasks, and 11.8% of participants had low neural activation on all three tasks. In other words, only 11.8% of the sample did not have high activation to any threatening situations. Taken together, these two studies highlight that sensitivity to threat is not uncommon among children and adolescents. At the same time, however, while sensitivity to *some* threats is normative, it is uncommon for youth to be consistently sensitive to threats across time or situations and, importantly, these youth appear to be most at risk.

Across both Study 2 and Study 3, I found that consistency was an important factor associated with the highest levels of threat sensitivity. At the same time, it is interesting to consider why adolescents were more likely than children to self-report consistent

sensitivity to threat across time (Study 2), but they were not more likely to have consistently high neural activation to threats across situations (Study 3). Descriptively, the pattern of results in Study 3 was consistent with Study 2 – the high consistent sensitivity to threat group contained youth with more advanced pubertal development and older age than the other groups; however, this result was not significant. One potential explanation for this difference between Study 2 and Study 3 is that when I calculated an average score of sensitivity to threat using the self-report BIS measure, individuals who respond quite differently to the BIS items can end up with the same score. For example, an individual who responds 'often' to all three questions (scored as a 3 on the Likert scale) would have an identical mean to someone who responds to two of these situations with 'almost always' (scored as a 4) but the third as 'never' (scored as a 1). Thus, individuals in the high stable sensitivity to threat group (i.e., consistently sensitive across time) in Study 2 may not be consistently sensitive across situations, which was the case in Study 3.

To test this idea, I recreated my groups from Study 2 to assess whether adolescents compared to children were more likely to self-report consistently high sensitivity across time *and* situation (i.e., would they consistently report above the mean on all three questions of BIS across all three years). When I recreated these groups, only a small percentage of youth (~ 15%) self-reported that they were consistently sensitive to all three questions across all three years. This percentage is similar to the 12% of youth found in Study 3 who were consistently sensitive to threats across task. However, in contrast to Study 3, but consistent with my original Study 2 results, adolescents still were more likely to be in the consistently high group compared to the group with inconsistent

sensitivity to threat and consistently low sensitivity to threat over time. Thus, the fact that the groups from Study 2 were created differently than the groups from Study 3 (i.e., that Study 2 did not take into account different situations), is not a feasible explanation for the fact that adolescents did not differ from children in Study 3. An alternative potential explanation is that in Study 3, the groups were created based on neural activation. In all of my other studies, the groups were created based on self-report data. When selfreporting their sensitivity to threat, children and adolescents have to subjectively decide how frequently they experience these situations. For example, they have to reflect on whether they experience these situations 'never', 'sometimes', 'often' or 'almost always', whereas in Study 3 the groups were created based on neural responses during the tasks, removing any subjective interpretations. The results clearly indicate that adolescents selfreport higher levels of sensitivity to threat than children, perhaps because adolescents are hypervigilant or more reactive to these types of situations in their daily lives. When they self-report these experiences, they are able to consider a variety of different contexts where they might face these aversive situations (e.g., making mistakes in school in front of their peers versus at home in front of their parents); the computer tasks, however, are limited to only one specific context for each of the aversive situations and do not involve any peer evaluations (a context that is particularly salient to adolescents).

# Sensitivity to threat and neural indicators

Across a wide range of neural indicators, the four studies of my dissertation show that EEG data is sensitive to detect differences in sensitivity to threat among children and adolescents. Indeed, my dissertation used four *different* EEG indicators associated with different types of threats. In Study 1, the P3 successfully differentiated youth who pay

more attention to negative feedback. In Study 2, right frontal asymmetry characterized the group with consistently high sensitivity to threat over time. In Study 3, the P3 to negative feedback, the ERN to making mistakes, and the N170 to angry faces together differentiated youth who self-reported the highest levels of sensitivity to threat. Finally, in Study 4, the ERN helped to differentiate youth who had high levels of sensitivity to threat in combination with emotion dysregulation – a group who had the highest levels of anxiety. Thus, across all of my studies, these different neural indicators were useful markers to identify youth who have heightened sensitivity to threat.

Importantly, the neural indicators used in my dissertation could be used in younger children to identify those most at risk for the later development of anxiety. For example, if young children have difficulty responding to some self-reported measures (e.g., very young children may have trouble understanding the word 'criticism'); we could use these EEG indicators to help identify which children are potentially most at risk for anxiety-related problems. In other words, we could identify the children who *consistently* show:

1) a heightened P3 when being told they lose points during a game, 2) a larger ERN when making mistakes during a task, 3) a larger N170 when viewing angry faces, or 4) greater right frontal asymmetry during rest. My results show that investigating neural consistency may be a promising way to identify even young children, potentially even those who are unable to fully express their threat sensitivity.

#### **Limitations and Future Directions**

The four studies of my dissertation have important strengths, including large sample sizes, multiple methods (e.g., longitudinal analyses, self-report, EEG), and multiple different neural indicators. These studies, however, are not without limitations.

First, several of the measures in my studies did not include the full scale. For example, sensitivity to threat was measured using three items from the Behavioral Inhibition Scale. As the data were part of a larger study assessing a wide range of constructs, it was not feasible to include every item from each scale. Of note, however, the alpha for the measure used in my studies demonstrated good reliability.

Second, the measure of sensitivity to threat (BIS) used in my dissertation was created in accordance with the original RST; however, this theory has undergone revisions since the creation of the BIS scale (Gray & McNaughton, 2000). One of the main changes to the theory is that anxiety and fear are now thought to be more distinct constructs. In the revision, fear is thought to elicits a fight/flight/or freeze reaction when escape or avoidance of a threat is the primary motivation. Anxiety, on the other hand, is thought to involve sustained hypervigilance and negatively-biased risk assessment during goal conflict (e.g., when approaching a potential threat). Further, the revisions to this theory also suggest that different brain regions may be more active during anxiety (e.g., septal-hippocampal system) compared to fear (e.g., amygdala, periaqueductal gray). The revision also highlights that anxiolytic drugs that are effective at reducing symptoms of anxiety (risk assessment) were not effective at reducing symptoms of fear (panic and avoidance). Taken together, the revision to the RST suggests that fear and anxiety are distinct and separable constructs. The measure of sensitivity to threat used in my dissertation (the BIS), however, did not include the two negatively-phrased items capturing 'fear' ("If I think something bad is going to happen, I rarely experience fear or nervousness"; "I have very few fears compared to my friends) and therefore reflects a general measure of threat sensitivity.

Of note, my colleagues and I conducted a study investigating whether the two negatively-phrased fear questions of the BIS are only distinct due to measurement structure (i.e., because they are the only negatively-phrased questions in the BIS) or if the two items represent a separable construct of fear, in line with the revised RST (Heffer et al., 2021). Students filled out the original BIS questionnaire as well as two additional items where we rephrased the two fear questions to be positively-worded ("I have a lot of fears compared to other students"; "If I think something bad is about to happen, I get scared or nervous"). We found that children and adolescents had difficulty understanding the negatively-phrased questions, and the two items only formed a distinct construct (fear) as a result of the measurement structure. When the questions were modified to be positively phrased, the best model was when all items loaded onto an overall sensitivity to threat factor, not separate fear and anxiety factors. Although the revised theory calls for a separation between fear and anxiety, these constructs may be difficult to tease apart in a survey. As an example, we often use words referring to fear ('scared') and anxiety ('worried') interchangeably (e.g., "I was worried about making a mistake" versus "I was scared to make a mistake"). Future research would benefit from further investigating whether the results presented in my dissertation are specific to general sensitivity to threat, or whether they are replicated when using a revised measure of the Reinforcement Sensitivity Theory (i.e., a measure that was designed to assess differences between approach/avoidance conflict and fear).

Third, given that the EEG indicators were not measured at every time point, I was unable to assess temporal order (e.g., whether greater neural activation to threats leads to greater self-reported sensitivity to threat and/or whether greater self-reported sensitivity

to threat leads to greater neural sensitivity). Future longitudinal research would benefit from investigating both self-report measures and neural activation at each time point to assess how these indicators together may change across time.

# **Conclusions**

Taken together, my dissertation offers a collection of studies that used multiple methods (self-report, EEG, longitudinal design) and tasks (BART; go/no-go; face processing) to gain a holistic understanding of the development of sensitivity to threat among children and adolescents. My work shows that adolescence (especially when defined by pubertal status) may be a normative period for sensitivity to threat. Not all youth who are sensitive to threat, however, go on to develop anxiety; thus, my findings perhaps emphasize an adolescent-limited pathway of development. Consistency may be an important way to help identify youth who may be most at risk for anxiety-related problems. Overall, advancing our understanding of sensitivity to threat during childhood and adolescence may be an important way to identify youth most at risk for anxiety.

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