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Impact of Emotional Processing on Working Memory in Preadolescents with High Autistic and Anxiety Traits

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By

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Abstract

Adolescence is an important neurodevelopmental period that confers both opportunity for positive change, and a risk for emerging psychopathology. In particular, anxiety disorders and autism spectrum disorder (ASD) both cause significant challenges during adolescence that impact individuals throughout their lifespan. Notably, functional impacts of anxiety and ASD are not limited to those who meet diagnostic criteria, and can be present at sub-clinical levels. However, despite high rates of co-morbidity of ASD and anxiety symptomology, the degree to which the neural bases of anxiety are similar or qualitatively different in individuals with and without autistic traits is unknown. One candidate neurobehavioral marker of anxiety is negative stimulus biases in cognition—i.e., prioritized attentional and executive processing of stimuli with a negative valence in individuals with greater anxiety. Utilizing a large neuroimaging repository such as the Adolescent Brain Cognitive Development (ABCD) project allows us to probe these populations independently and in conjunction with enough power to elucidate differences

Specifically, we used the ABCD study—specifically, ABCD's emotional n-back task that uses affective stimuli in a working memory paradigm to probe the neural circuits implicated in negative stimulus bias—to compare negative stimulus bias across 4 well-matched subgroups of 9–10-year-old preadolescents: 1) high anxiety and low autistic traits (ANX; N=54), 2) high autistic traits and low anxiety (AUT; N=48), 3) high anxiety and autistic traits (DUAL; N=51), and 4) low anxiety and low autistic traits (CTRL; N=51). Behaviorally, groups did not significantly differ in the impact of emotional faces on working memory task performance, refuting a long-standing assumption about negative affective biases in cognitive processing in youth with clinically-significant anxiety, however negative threat biases were present more globally. fMRI results revealed subtle differences in neural recruitment, including aberrant recruitment of task-positive brain networks under high versus low cognitive load in clinical groups. Results also revealed potential evidence for a generalized increase in vigilance in preadolescence with anxiety—i.e., an overall increase in blood oxygenation-level dependent (BOLD) activation was present in those with high anxiety across most task-relevant clusters. Despite equivalent behavioral performance across groups, the impact of increasing cognitive load on positive and negative faces showed differential effects of group. Positive faces showed overall increased activation and decreased deactivation across clusters as a factor of anxious whereas negative faces showed no impacts of anxious traits. Autistic traits drove differential recruitment in several networks (dorsal attention, somatomotor, and default networks) in negative but not positive face interactions with cognitive load. Dual groups showed differential activation in both positive and negative cognitive load specific contrasts across multiple networks. This suggests differential neural recruitment may underpin emotional processing interactions with working memory in

preadolescents with elevated anxiety and/or autistic traits, to achieve equivalent behavioral outcomes.

Table of Contents

List of Figures

List of Tables

Introduction

Preadolescence and adolescence represent periods of significant physical, environmental, and neurodevelopmental change (Guyer et al., 2016; Larsen & Luna, 2018; Picci & Scherf, 2015; Silvers, 2022; Sisk & Gee, 2022; Spear, 2013; Uddin, 2021). Many brain systems continue to mature throughout preadolescence and adolescence and thus brain plasticity may be particularly high during this life period due to factors such as synaptic pruning, myelination, and synaptic stabilization (Guyer et al., 2016; Sisk & Gee, 2022; Spear, 2013). There is also a high onset of psychiatric disorders during preadolescence and adolescence—especially mood and anxiety disorders—and the inherent plasticity of this neurodevelopmental stage may lend itself to intervention (Guyer et al., 2016; Kessler et al., 2005; Larsen & Luna, 2018; Paus et al., 2008; Pfeifer & Allen, 2021; Picci & Scherf, 2015; Silvers, 2022; Sisk & Gee, 2022; Spear, 2013). Psychiatric issues in youth often persist into adulthood and have significant impacts on outcomes in social functioning, independence, educational and occupational attainment, and global functioning domains (Larsen & Luna, 2018; Pfeifer & Allen, 2021). Therefore, understanding the mechanisms underpinning affective disturbances in adolescence has the potential to identify precision medicine approaches or identify better neural markers to monitor intervention success.

The field is heretofore lacking a clear delineation of the neural correlates that drive anxiety risk in adolescence. There is also a lack of understanding of the shared and unique mechanisms driving anxiety symptoms transdiagnostically in adolescence with and without a highly comorbid symptom: autistic traits. The current study will focus specifically on negative stimulus biases in cognitive processing—referring to a tendency to prioritize negatively-valenced information in attention and working memory (Bishop, 2008; Monk et

al., 2006; Mueller et al., 2015; Pine, 2007; Roy et al., 2008). Negative stimulus bias has been implicated in the acquisition and maintenance of anxiety in youth (Bar-Haim et al., 2007; Bishop, 2008; Cisler & Koster, 2010), yet the degree to which this represents a transdiagnostic mechanism driving anxiety symptoms across youth with and without comorbid autistic traits has not been determined. In this section, I review anxiety traits in adolescence, as well as comorbid autistic traits. I will then discuss negative stimulus biases in working memory in these populations and outline the motivation and approach for the current study.

Anxiety

Anxiety disorders are one of the most common mental health conditions, with prevalence estimates across the lifespan approaching 30% (Strawn et al., 2021). Anxiety is also one of the earliest appearing disorders, and can emerge early in development and often presents alongside co-morbid mental health challenges (Strawn et al., 2021). Rates of anxiety increase during preadolescence and adolescence and may be driven by increased neural sensitivity to fear stimuli (Guyer et al., 2016; Pfeifer & Allen, 2021). While there are multiple subcategories of anxiety disorders, anxiety can be generally characterized by phasic increases in fear and distress in specific situations (specific phobia, separation anxiety, social anxiety) or persistent feelings of worry about everyday issues and situations (generalized anxiety disorder). Several anxiety disorders—such as generalized anxiety disorder, separation anxiety disorders, and social anxiety—share risk factors, have similar courses, and commonly co-occur and thus are often studied collectively (Strawn et al., 2015, 2021). Anxiety disorders in preadolescence are associated with functional impairment, suicidal ideations and attempts, decreased occupational and educational attainment, and additional

comorbidities (Burris et al., 2019; Strawn et al., 2015, 2021). Therefore, clinically significant anxiety symptoms are common in youth, driving an urgent need to better understand their underlying mechanisms to inform next-generation treatment approaches.

Anxiety and Autistic Traits

Autism Spectrum Disorder (ASD) is frequently comorbid with anxiety. ASD is a neurodevelopmental disorder with core impairments in socio-communication and accompanied by restrictive and repetitive behaviors (American Psychiatric Association et al., 2013; Lord et al., 2018). Recent prevalence observations estimate 1 in 44 children are diagnosed with ASD (Maenner, 2020). Because it is a spectrum disorder, autistic individuals present with a wide range of abilities and the presentation is significantly heterogeneous. Like any spectrum, autistic traits are present in non-clinical populations and may confer risks even in sub-clinical-threshold populations (Lundström et al., 2011; Mandy et al., 2018; Skuse et al., 2009).

The challenges with autistic traits are not restricted to those with diagnosed ASD, and subclinical autistic traits can confer risk for a variety of mental health challenges and functional difficulties across domains (Lundström et al., 2011; Mandy et al., 2018; Skuse et al., 2009). Evidence has shown alterations in brain connectivity associated with both dimensional and categorical conceptualizations of ASD (Elton et al., 2016), highlighting the importance of investigating the neural mechanisms driving autistic traits across the spectrum. Estimates of anxiety in children with ASD vary, but are as high as 89% (Leyfer et al., 2006; Mayes et al., 2011; Strang et al., 2012; White et al., 2009). In comparison, prevalence rates for anxiety disorders for typically developing children tend to vary from approximately 2.2-27% (Costello et al., 2006; van Steensel et al., 2011). van Steensel et al.'s (2011) meta-

analysis put rates of anxiety in ASD as more than twice that of the typically developing population. Gathering evidence for which mechanisms are altered in individuals with high autistic traits can provide not only a better understanding of the etiology of ASD, but may also provide potential treatment targets and markers of treatment-induced change.

Youth are exposed to increasingly complex social situations in educational and social environments throughout preadolescence and adolescence. Critically, this is a time of increasing independence in education, employment, and living situations (Picci & Scherf, 2015; Uddin, 2021). Adults with ASD are frequently less successful in these tasks than those with other developmental disorders (Picci & Scherf, 2015). Additionally, the neural mechanisms associated with preadolescent plasticity may be abnormal in this population, causing an additional challenge (Picci & Scherf, 2015; Uddin, 2021). The trajectory of autistic social traits over late childhood and adolescence is also different for girls and boys, with autistic social traits decreasing for boys and increasing for girls, showing that preadolescence may be a critical time for changes in this population (Mandy et al., 2018) especially since the onset of puberty is associated with a deterioration of functioning in approximately a third of adolescents with ASD (Picci & Scherf, 2015). Given both the inherent neural plasticity and huge differences in developmental trajectories in preadolescence, understanding how neural mechanisms of ASD are impacted and how they can be targeted for treatment is critical.

Co-morbidities such as anxiety have been shown to relate to poorer outcomes in children with ASD (Grondhuis & Aman, 2012; Strang et al., 2012). Though it is widely believed that anxiety is a common and impairing problem for youth with autistic traits (Leyfer et al., 2006; Mayes et al., 2011; Strang et al., 2012; White et al., 2009), there are

persistent open questions about the precise symptoms and underlying mechanisms that constitute this phenotype. These challenges are particularly acute for clinicians evaluating youth with autistic traits who present with symptoms of distress that are inconsistent with traditional anxiety as defined by the Diagnostic and Statistical Manual for Disorders, Fifth Edition (DSM; American Psychiatric Association et al., 2013; Halim et al., 2018; Kerns et al., 2014; Lau et al., 2020; Simpson et al., 2021). Identifying neural markers of anxiety that are similar across both preadolescents with and without comorbid autistic traits therefore holds the potential for better identifying and monitoring anxiety symptoms in youth.

Negative Stimulus Bias in Cognitive Processing

Attention

A large body of research suggests that pediatric anxiety disorders are associated with an attentional bias to negative stimuli—characterized by enhanced attentional orienting to, and difficulties disengaging attention from, potentially harmful stimuli (e.g., facial expressions of anger; Cisler & Koster, 2010). Neural structures associated with attentional biases to negative stimulus include the amygdala, the prefrontal cortex (PFC), the anterior cingulate cortex (ACC), and the orbitofrontal cortex [OFC; (Cisler & Koster, 2010)]. Amygdala and ACC likely play a role in facilitated attention to—and prioritized downstream responses to—potentially threatening stimuli (Bishop, 2008; Tully & Niendam, 2014). In contrast, frontal cortical areas may be related to affective evaluation of prospective threats (OFC), and efforts to regulate or disengage attention (i.e., emotional regulation circuits in ventrolateral PFC; Tully & Niendam, 2014). Neural evidence for negative stimulus bias in attention involves increased amygdala activation and decreased prefrontal activation, but

notably this may be modulated by other factors including perceptual load, task complexity, and stimuli valence of distractors (Cisler & Koster, 2010).

Attentional bias towards negative stimuli has been proposed to be implicated in both development and maintenance of anxiety disorders (Bar-Haim et al., 2007; Bishop, 2008; Cisler & Koster, 2010). Bar-Haim et al.'s (2007) meta-analysis showed significant negative stimulus-bias in anxious children and adults (effect size = 0.45), but not for non-anxious participants. Another finding is that emotionally ambiguous stimuli are more likely to be interpreted negatively (Bar-Haim et al., 2007; Bishop, 2007; Mueller et al., 2015). The finding of attentional biases towards negative stimulus stimuli is well established, but not universal, particularly in children (Bar-Haim et al., 2007; Bishop, 2007; Ehrenreich & Gross, 2002; Puliafico & Kendall, 2006; Shafiee et al., 2008). Dalgleish et al. (2003) found attentional biases for negative stimulus related words depended on task, which might be evidence for some of the aspects of negative stimulus bias, but not all, being altered in an anxious group of children and adolescents. In healthy children and adolescents, high trait anxiety was correlated with attentional bias towards angry faces and increased right dorsolateral and ventrolateral PFC activation in response to angry faces (Telzer et al., 2008). Studies in children have found attentional biases both towards and away from angry faces (Waters et al., 2008, 2010).

Additionally, amygdala activation is heavily implicated in anxiety and negative emotional biases (Bishop, 2007, 2008; Bishop et al., 2007; Pine, 2007; Stout et al., 2017). Amygdala abnormalities in volume, activation, and connectivity have been some of the most replicated results in pediatric anxiety (Strawn et al., 2014, 2015). Aberrant amygdala recruitment in response to emotional faces have frequently been reported in the context of

autistic traits (Costa et al., 2020; Ecker et al., 2015; Kleinhans et al., 2009; Leung et al., 2018; Monk et al., 2010; Picci & Scherf, 2015; Swartz et al., 2013; Weng et al., 2011).

In children with ASD, there has been some evidence of attentional bias away from negative faces (García-Blanco et al., 2017; Ghosn et al., 2019), which is opposite the pattern typically found in typical development. In response to negatively-valenced non-face stimuli, other studies have yielded mixed results, with some indicating a bias towards these stimuli in ASD, a *reduced* bias relative to typical development, or no differences between youth with ASD and typically-developing peers (Bergman et al., 2021; Fan et al., 2020; García-Blanco et al., 2017; Ghosn et al., 2019; Hollocks et al., 2014; May et al., 2015; Moore et al., 2012; Wagner et al., 2020). At the neural level, inconsistent findings on amygdala activation in response to emotional faces in ASD may be driven by an interaction between autistic and anxiety traits: with autistic traits driving amygdala hypoactivation, anxiety traits driving hyperactivation, and comorbidity being associated with a lack of evoked blood oxygenation-level dependent (BOLD) response to emotional face stimuli (Herrington et al., 2016). Overall, conflicting results in both behavioral performance and neural activation leave the question of negative stimulus bias in individuals with high autistic traits open.

At a psychological level: attentional bias to negative stimulus can happen at multiple stages of processing – whether it involves faster initial orienting or difficulty disengaging from the stimulus (Cisler & Koster, 2010; Sahuquillo-Leal et al., 2022). Stage of processing may therefore be one source of inconsistency in the literature on emotional stimulus biases in attention in ASD. Some research has showed initial (orienting) negative stimulus bias in ASD but not typically-developing peers, who conversely showed attentional engagement and maintenance bias towards negative stimuli (Sahuquillo-Leal et al., 2022). Many paradigms

designed to investigate negative stimulus bias look exclusively at initial orienting reaction times, which may not be the only important process (Judah et al., 2013). For example, sustained worry in anxiety and social interaction difficulties (such as during a conversation) in ASD all present on a longer timeframe. The ability to maintain or update emotional faces in working memory may also be impacted differentially by negative stimulus bias, but may do so in different ways in these conditions. For example, multiple studies have found differences in filtering efficiency in anxiety (Moran, 2016; Qi, Chen, et al., 2014; Qi, Ding, et al., 2014; Qi, Zeng, et al., 2014). To probe this, investigations on negative stimulus biases in the maintenance and/or updating of information in working memory are warranted.

Neurodevelopment of Working Memory

Working memory (WM) involves maintenance (keeping the information accessible) and manipulation of a limited amount material that is no longer perceptually present over short time frames. WM improves continuously between childhood and adulthood (Simmonds et al., 2017; Tervo-Clemmens et al., 2022). Developmentally, the same networks support WM in children and adults, and the structural neurodevelopment of frontal and parietal regions throughout childhood and adolescence correlate with improvements in WM longitudinally (Chai et al., 2018). Functional neuroimaging studies suggest longitudinal changes in the recruitment of subcortical, prefrontal, frontal, parietal, and temporal regions during WM processing—suggestive of a maturational shift in WM over the course of preadolescence and adolescence that is predictive of WM task performance (Andre et al., 2016.; Simmonds et al., 2017). Overall, existing studies suggest WM is undergoing a period of considerable neurodevelopmental change throughout preadolescence and adolescence.

Working Memory Alterations in Anxiety

While some studies have found an overall WM impairment in anxiety (Leigh & Hirsch, 2011, Moran, 2016; Visu-Petra et al., 2006, 2014; Vytal et al., 2013), others have found impairments in either verbal (Visu-Petra et al., 2010, 2011) or spatial (Shackman et al., 2006) WM, or deficits that are dependent on characteristics such as complexity or emotion (Edwards et al., 2015; Visu-Petra et al., 2010). Yao et al. (2018) looked at 104 adults and found trait anxiety was negatively associated with WM, particularly for negative (compared to neutral faces). Despite some mixed results, meta-analytic evidence suggests a general impairment in the maintenance and updating of emotional information in WM in youth with anxiety.

Working Memory and Autistic Traits

Results on WM in ASD have been inconsistent and little investigation has probed differences in sub-threshold ASD populations. Significant research has found deficits in visuospatial WM development in children and adolescents with ASD, which persist into adulthood (Barendse et al., 2018; Barnard et al., 2008; Cui et al., 2010; Kercood et al., 2014; Lai et al., 2017; Landa & Goldberg, 2005; Luna et al., 2007; Sinzig et al., 2008; Williams et al., 2005, 2006; Zimmerman et al., 2016) but these findings are not universal (Gardiner et al., 2017; Geurts et al., 2004; Happé et al., 2006). Many studies have found atypical frontal connectivity or reduced activation in adults and adolescents with ASD in working memory tasks, such as decreased frontoparietal or fronto-striatal connectivity and reduced frontal activity in executive functioning tasks in ASD (Barendse et al., 2013; Koshino et al., 2008; Silk et al., 2006; Solomon et al., 2009), even lacking behavioral differences (Urbain et al., 2015).

When specifically looking at the interaction between affective imagery and working memory in individuals with autism or autistic traits, some studies have found that face stimuli results in reduced working memory performance compared to non-face stimuli (Webb et al., 2017). The n-back task is commonly used to probe updating and maintenance processes in working memory, and has been used extensively in both children and adults (Meule, 2017; Yaple & Arsalidou, 2018). N-back tasks utilizing face stimuli in this population have found reduced amygdalar habituation (i.e., less pronounced attenuation of amygdala responses to repeated stimuli) in ASD (Tam et al., 2017) and abnormal fusiform face area activation and connectivity (Koshino et al., 2008). Collectively, these studies suggest that subtle neural activation differences may be present in tasks that probe the intersection of facial and working memory processes. However, few of these studies have looked at valence in stimuli, so further investigation into negative stimuli bias in these tasks is necessary. Given significant heterogeneity in ASD, inconsistent findings are not altogether surprising. Further investigation is needed to examine WM in ASD and see what processes are impaired, to what degree, and for whom.

Working Memory in Co-Morbid Anxiety and Autism

Investigation into how ASD with comorbid anxiety impacts processes such as working memory is ongoing, with little to no research directly exploring the impact of comorbidity on WM. Current investigations often look at executive functioning more globally, subsuming WM. Wallace et al. (2016) found that adults with ASD were impaired in multiple executive functioning domains, in real world behavioral outcomes, with peak deficits in flexibility as well as planning and organization. These results were not associated with age and IQ but were associated with anxiety. Hollocks et al. (2014) found that in

adolescents with ASD, poor executive functioning skills, but not social cognition, were related to anxiety, but not depression. In younger children, aged 3-6, with autism, special interest intensity was associated with deficits in attentional shifting and inhibitory control, but not with reward responsiveness, reward drive, or anxiety (Godfrey et al., 2021). Overall, further investigation into the behavioral and neural impacts of the anxiety and ASD interaction on WM is warranted, as existing studies have yielded inconsistent findings. Additionally, despite evidence for aberrant negative stimulus bias in these populations, no existing studies have investigated how emotional processing effects WM maintenance and updating to produce (or fail to produce) a negative stimulus bias in individuals with co-morbid anxiety *and* autistic traits.

Rationale for the Current Study

Overall, there is significant—albeit inconsistent—evidence for an impact of anxiety and autistic traits on the interaction between emotional processing and working memory. Despite significant co-morbidity of autism and anxiety, few studies have characterized whether the mechanisms driving anxiety symptoms are quantitatively or qualitatively different in this population. For disorders that emerge in youth, it is critical to be able to examine the neural mechanisms that drive mental health challenges during this period of heightened neuroplasticity, in order to capitalize on this neurodevelopmental window to improve treatment outcomes (Ragland & Solomon, 2016). Shared neuroimaging databases with task-based fMRI data are a critical resource for this type of investigation as they allow researchers to collect data on a larger number of participants than would otherwise be possible (Ragland & Solomon, 2016).

There are no prior studies exploring negative stimulus biases in working memory in preadolescence with elevated anxiety, autistic traits, or both. Data from the *Adolescent Brain Cognitive Development* (ABCD; Casey et al., 2018) are particularly well-suited to tackling this topic, as the dataset includes a combination of field-standard clinical assessments of anxiety and sub-clinical autistic traits, as well as an emotional working memory paradigm presented during functional magnetic resonance imaging (fMRI). Data was pulled from the ABCD data archive and screened to include only high-quality neuroimaging and behavioral data. Subgroups from the ABCD study dataset after matching on potentially confounds and screening for data correspond to i) low anxiety and low autistic traits (*N=54*; CTRL), ii) high anxiety with low autistic traits (*N*=56; ANX), iii) high autistic traits with low anxiety (*N*=50; AUT), and iv) high anxiety *and* high autistic traits (*N*=53; DUAL). These groups were matched with respect to age, sex, and general cognitive functioning, and this approach provided us with an unparalleled opportunity to determine the unique and shared variance in the neural and behavioral correlates of negative stimulus bias in working memory across the spectrum of anxiety and autistic traits in adolescence. Specifically, our study had the following two specific aims:

Aim 1: ***To determine whether negative stimuli bias in working memory is a transdiagnostic feature of anxiety across individuals with and without high autistic traits.***

Hypothesis 1 - We hypothesize aberrant negative stimulus modulation of working memory performance and recruitment of prefrontal regions in the anxiety and dual groups relative to control. Specifically, negative faces will enhance emotional modulation, while positive faces will attenuate emotional modulation of task performance and evoked neural responses. We predict increased neural activation but decreased performance (disrupted control) with the

negative stimuli. Whereas we hypothesize the response to positive stimuli will exhibit hypoactivation.

Hypothesis 2 - Altered activation associated with anxiety, such that individuals with high anxiety symptoms will have activation that differs more drastically from the overall group activation patterns.

Aim 2: ***To determine the extent of how negative stimuli modulate working memory performance in the context of aberrant emotional face processing and amygdala activation as a function of anxiety and ASD traits.***

Hypothesis 1 – We hypothesize decreased emotional modulation of face stimuli, across valence, in the ASD and dual groups. We predict altered activation in the amygdala in face stimuli, regardless of valence. We predict the ASD group will show decreased emotional modulation and thus hypoactivation in the amygdala whereas the dual group will show increased emotional modulation, and thus hyperactivation of the amygdala (Herrington et al., 2016).

Methods

Data

The ABCD Project is a multi-site, longitudinal study of development and psychopathology which includes a variety of self and parent report measures as well as magnetic resonance imaging, both structural and functional (Casey et al., 2018). One of its strengths is the recruitment of over 10,000 children (9- and 10-year-olds) at baseline. Additionally, ABCD oversampled for children at risk children, with approximately 42% showing early signs of externalizing and internalizing symptoms (Casey et al., 2018). With

its variety of measures and large sample size, the ABCD project is ideal for exploring neuroimaging questions and ensuring sufficient power to detect effects.

Measures

CBCL

Psychopathology, including symptoms of anxiety, was assessed via the Child Behavior Checklist (CBCL: Achenbach & Rescorla, 2001). The CBCL is a parent rating scale and contains 113 statements concerning child behavior in the past six months and can be used with children ages 6 to 18. Items are on a Likert-type scale with 3 levels.

The CBCL yields a number of different measures. Broadly speaking, there are scales representing internalizing and externalizing problems, derived via factor analysis (Achenbach & Rescorla, 2001; Magyar & Pandolfi, 2017). Six DSM oriented scales can also be obtained, which correspond to the DSM diagnostic categories and were derived via expert consensus (Achenbach & Rescorla, 2001; Magyar & Pandolfi, 2017). Raw scores are transformed into T-scores with higher scores indicating higher impairment. (Achenbach & Rescorla, 2001; Lawson et al., 2015). T scores have an average of 50 (normed on age and gender) and a standard deviation of 10 and scores of 65 on the syndrome and DSM-oriented scales indicate "borderline" concerns and scores of 70 indicate a clinical cutoff (Achenbach & Rescorla, 2001; Gjevik et al., 2015).

Research has shown that the CBCL can discriminate between clinical and non-clinical populations (Achenbach & Rescorla, 2001). The CBCL is widely used, norm referenced, and assesses a wide range of emotional and behavioral problems (Achenbach & Rescorla, 2001; Magyar & Pandolfi, 2017). The DSM scales for affective and anxiety problems have been validated for use in ASD (Magyar & Pandolfi, 2017). Parent scores on

the CBCL are more in line with clinician evaluations using semi-structured interviews for both ASD and typically developing adolescents then self-report scales (Hogeveen et al., 2018).

SRS

ASD traits are assessed via a short version of the social responsiveness questionnaire (SRS; Reiersen et al., 2008). The full version of the SRS is a 65-item questionnaire designed to assess features of ASD from a clinical to a sub-clinical range (Constantino et al., 2000). The shortened version of the SRS administered to the ABCD sample included eleven items, which measure features of social motivation, social cognition, social communication, and restrictive and repetitive behavior (Reiersen et al., 2008).

NIH Toolbox – crystalized and fluid intelligence fully corrected scores

The NIH Toolbox® cognition measures consist of tasks that measure memory, executive functions, attention, working memory, processing speed, and language. It was designed to be usable in longitudinal studies, have good psychometric properties, and be relatively brief. Utilized were corrected T-scores which have a mean of 50 and a standard deviation of 10 and which take into account demographic factors such as gender, education, and race/ethnicity, and which show good test-retest reliability and validity in children (Luciana et al., 2018; Weintraub et al., 2013).

EN-back

The emotional n-back (EN-back; Casey et al., 2018) is a version of the commonly used '*n*-back' WM paradigm that includes positive and negative emotional face stimuli. In the standard *n*-back paradigm, subjects identify over consecutive trials whether the current stimulus matches a stimulus presented *n* trials previously, which probes several domains of

executive control, including maintenance and updating of items in working memory, and inhibition of non-*n* items and premature responses (Chatham et al., 2011). In the EN-back version of this paradigm, emotional (positive, negative, and neutral faces) and non-emotional (place) stimuli are randomly interspersed, with each stimulus category presented under one of 2 cognitive load conditions (0-back, 2-back; Casey et al., 2018). At the neural level, the contrast between the 2-back and 0-back in the *n*-back paradigm–i.e., high versus low executive control demand–reliably yields activation of a core set of frontal, parietal, and striatal brain regions (Tsuchida & Fellows, 2009; Owen et al., 2005). Additionally, the face stimuli used in the EN-back task recruit fronto-amygdalar pathways critical for emotional stimulus reactivity and regulation (Gee et al., 2013; Hare et al., 2008). Therefore, this task is well-suited to probing the recruitment of frontoparietal, frontostriatal, and frontoamygdalar circuits thought to be implicated in negative affect biases in individuals with anxiety or autistic traits.

Groups

We sampled participants with low and high amounts of anxiety symptoms (based on the CBCL) and ASD traits (based on the SRS) to generate 4 groups. Due to an issue with data collected using Phillips scanners in data preprocessing, participants from these scanners were excluded (approximately 13%; Rosenberg et al., 2020). We excluded participants with poor neuroimaging quality or EN-back performance as in prior ABCD studies using this task (Rosenberg et al., 2020). These exclusion criteria included a motion score, a pial overestimate score, a white matter underestimation score, an inhomogeneity score; where all were excluded if rated as >1, which corresponded to moderate/severe. Additionally, if the overall quality control score or the task performance flag indicated either were unacceptable,

these were excluded as well. This resulted in the groups being as follows: high anxiety with low autistic traits (ANX; N=73), high anxiety with high autistic traits (DUAL; N=103), high autistic traits with low anxiety (AUT; N=297), low anxiety and low autistic traits (CTRL; N=1934).

Due to significant group size disparities, as well as concerns about groups matching on potential confounds such as intelligence, age, and gender, cases were matched accordingly. Cases with "NA"s in any of the matching variables (Weintraub et al., 2013; NIH Toolbox, fully normalized scores: crystallized intelligence and fluid intelligence; age and sex) were excluded as well. Then all groups were matched using the R software package 'MatchIt', where matching method was set to nearest neighbor (Ho et al., 2007, 2011), to the smallest group (ANX) resulting in 4 groups of *N*=56 participants. Later neuroimaging analyses led to the exclusion of additional subjects for poor MR signal in key regions-of-interest resulting in poor mask coverage (n=4), an incidental finding that was likely to disrupt brain segmentation and registration (n=1), or EN-back neuroimaging data unavailable on the NIH Data Archive (possibly suggesting they did not complete this task; n=6). Behavioral analysis included only those subjects included in the neuroimaging analyses for consistency, resulting in the final groups of 204 participants: AUT (n= 48), ANX (n=54), DUAL (n=51), and CTRL (n=51). Parent report via the CBCL and SRS aligned reasonably well with clinical diagnosis utilizing the Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Age Children (KSADS; Kaufman et al., 1997), with diagnosed ASD higher in AUT and DUAL groups relative to ANX and CTRL ($\chi^2 = 48.49$, $p < .001$) and diagnosed anxiety disorders higher in ANX and DUAL groups relative to AUT and CTRL ($\chi^2 = 24.12$, $p < .001$).

Table 1 Participant Demographics

Variable	Overall	AUT	ANX	Dual	Ctrl
N	204	48	54	51	51
Age (in months)	120.4 (7.62)	121 (7.67)	121 (7.51)	121 (7.61)	120 (7.86)
Sex (F, M)	76,128	20,28	24,30	13,38	19,32
Race					
White	176	46	44	40	46
Black	24	5	5	7	7
Hispanic	38	4	12	14	8
Asian	10	2	3	1	4
NIH Toolbox					
Fluid	46.37 (10.09)	46.8 (11.0)	46.1 (10.6)	45.8 (9.99)	46.9 (9.01)
Crystalized	53.74 (13.05)	53.5 (12.9)	52.6 (12.9)	54.5 (13.7)	55.6 (12.9)
Clinical					
SRS	17.33 (6.12)	21.5 (3.68)	12.9 (1.11)	23.5 (5.38)	11.9 (1.01)
CBCL	61.41 (9.63)	53.8 (4.28)	68.0 (4.11)	71.0 (6.57)	51.8 (2.74)

Planned Analyses

EN-Back Task Performance

D' scores (i.e., a z-scored metric of hits minus false alarms; a common behavioral measure of target sensitivity that is robust to response biases), accuracy (the rate of correct responses to stimuli during run 1 and run 2), and response times were examined for each cognitive load (2 vs 0 back), stimulus type (positive faces, negative faces, neutral faces, and places), and group (high anxiety traits only, high ASD traits only, dual anxiety/ASD traits, control) condition. The two-way interaction between load and stimulus type was used to index the emotional modulation of executive control. Critically, the three-way interaction determined how emotional modulation of executive control varies as a function of participant group.

Magnetic Resonance Imaging (MRI) Acquisition and Analysis

Image Acquisition.

ABCD scan acquisition parameters were harmonized across 21 sites across the United States using 3-tesla MRI scanners (Siemens Prisma or GE MR750). Participants were trained prior to scanning in a mock MRI with motion capture and feedback. Several strategies were employed real-time to account for head motion including head motion capture images during the T1 (Hagler et al., 2019). Siemens scanners additionally employed additional software, Framewise Integrated Real-Time MRI Monitoring software (Dosenbach et al., 2017) which allowed for real time movement tracking to provide additional data and correction as well as feedback to participants. Acquisition parameters for the T1 anatomical scan were as follows: matrix = 256 × 256; slices = 176 (Siemens), 208 (GE); field of view = 256 × 256; resolution = 1-mm isotropic space; repetition time = 2,500 ms (Siemens, GE); echo time = 2.88 ms (Siemens), 2 ms (GE); flip angle = 8. For the fMRI scans they were: matrix = 90 × 90, slices = 60, field of view = 216 × 216, resolution = 2.4-mm isotropic space, repetition time = 800 ms, echo time = 30 ms, flip angle = 52, multiband factor = 6 (Casey et al., 2018).

Preprocessing.

ABCD data (release 2.0-3.0 minimally preprocessed data) were downloaded with permission from the NIH Data Archive (https://nda.nih.gov/). Anatomical brain images were extracted from the full head image using AFNI's '3dSkullStrip' function (Cox, 1996). The majority of the remaining MRI preprocessing and analysis pipeline was performed using the FMRIB Software Library (FSL). To facilitate subsequent image registration to Montreal Neurological Institute (MNI) standard space, we ensured all anatomical and functional images were in the same orientation as the MNI152 2-mm brain via FSL's 'fslreorient2std'

prior to preprocessing. Distortion correction was performed on functional data using FSL Topup (Jenkinson et al., 2012; Smith et al., 2004). fMRI data were processed by regressing out 24 standard head motion parameters and their derivatives (cf., Satterthwaite et al., 2013), spatial smoothing (5-mm full-width half maximum), temporal filtering (high pass =100), fitting a first-level GLM in native space, and group-level normalization to MNI 2-mm space using a 12-parameter nonlinear registration. Given low number of trials for each condition, modeling correct versus incorrect trials separately would lower the within-subjects power too much to make it possible to get reliable estimates of the task contrasts, especially given high motion during scan (Durnez et al., 2018; Wager & Nichols, 2003).

First-level fMRI Models.

Subject-level volumetric fMRI data were modeled using FMRIB's Local Analysis of Mixed Effects (FLAME; (Woolrich et al., 2004)). Stimulus-locked BOLD responses were modeled as a function of the planned contrasts described by the ABCD analysis team, including: 1) 2 back vs 0 back; 2) Faces (all) vs places; 3) Emotional faces vs neutral faces; 4) Negative faces vs neutral faces; 5) Positive faces vs neutral faces (Hagler et al., 2019). Additionally, we added two novel contrasts to elucidate the neural circuits activated as a function of the positive and negative emotional modulation on trials with high executive control demands: 6) positive 2-back versus neutral 2-back, and 7) negative 2-back versus neutral 2-back, respectively. However, the neutral condition did not represent an ideal baseline, with no significant results for positive or negative faces versus neutral faces, so contrasts 6 and 7 were designed to examine the interaction of load and emotional valence, directly comparing load in positive and negative faces respectively. These evoked BOLD responses were modeled with duration 0, and we accounted for variation in the shape of the

hemodynamic response using the default FMRI Linear Optimal Basis Sets (FLOBS) in FSL (Smith et al., 2004). The default FLOBS set comprises three waveforms: a canonical hemodynamic response function (HRF), and its temporal and dispersion derivatives. For each event, the canonical HRF was orthogonalized to the derivative waveforms, and only the HRF parameter estimates were used in second-level models.

Second-Level fMRI Models.

After run 1 and run 2 were modeled, they were combined at the subject-level utilizing FSL's fixed effects modeling. Since ABCD data was collected across 21 sites, all sites with more than a single participant were grouped using FSL's mixed effects modeling (FLAME 1). Then sites were combined using a simple OLS model to examine overall effects for each contrast. For each contrast, we computed whole-brain activation and deactivation maps across the entire sample controlling for familywise error rate using cluster-extent thresholding ($z>3.1$, $p_{FWE}<0.05$). Due to needing to account for site and limitations of FSL to run multilevel modeling contrasts accounting for both site and group at the same time, Bayesian models were run to compare activation across clinical groupings. This method better accounts for error and avoids issues of over-penalizing found in a massively univariate approach and improves model efficiency (G. Chen et al., 2019). Additionally, Bayesian Multilevel Modelling improves sensitivity for detecting effects at smaller brain regions relative to conventional cluster-extent thresholding (G. Chen et al., 2019). Bayesian modeling comparing groups has also been shown to be superior to t-tests (Kruschke, 2013).

Bayesian Analyses.

Bayesian multi-level modeling (G. Chen et al., 2019) was used to elucidate how significant overall clusters varied from full group results by group membership. Group-level data were modeled using a Bayesian Multilevel Modelling approach using brms v2.16.3 (https://cran.r-project.org/ web/packages/brms/index.html) in R v3.6.3 (https://www.r-project.org). As average framewise displacement (FD) varied between groups, with the control group (mean Ctrl FD = 0.088, versus AUT: t = -2.54 (df = 58.41), p = 0.014, versus Anx: t = -2.09 (df = 74.96), p = 0.040, versus Dual: t = 3.77 (df = 69.854) p < 0.001) having significantly less framewise displacement than all other groups (which did not differ from each other, all p's > .157) average framewise displacement for each subject was included in the multilevel Bayesian model as a random effect. First, mean percent signal change was extracted for each participant based on significant clusters at the whole group level. Second level models were fit in brms with the form:

"Y ~ AUT + ANX + (1 | gr(Subj, dist= \"student\")) + (AUT + ANX + FD | gr(ROI, dist=\"student\"))"

In these models, "Y" corresponds to the percent signal change to a given regressor from the first-level models, the "Subj" term represents the random effect associated with each subject, "FD" represents the framewise displacement for the subjects, and the "ROI" term represents the random effect associated with each cluster. For interaction models, we computed another dummy coded variable to represent membership in the DUAL group and added it to the AUT + ANX terms. We then computed the marginal posterior distributions associated with each cluster for each group. Statistical inferences regarding the credibility of

each cluster encoding a given regressor were made based on the proportion of each distribution that was above. Values less than 0.15 were used to indicate credible evidence for negative encoding of a given regressor, whereas values above 0.85 indicated credible evidence for positive encoding. Models used 4 Markov Chain Monte Carlo (MCMC) chains and with 5,000 iterations per chain, and the convergence criteria was $\hat{R}<1$.

Amygdala Analyses.

To explore the differential impacts of negative stimuli on the amygdala, mean percent signal change in anatomically-defined group-level amygdala masks (via Harvard-Oxford subcortical probabilistic atlas distributed in FSL; Jenkinson et al., 2012; Smith et al., 2004) were extracted for the face versus place and positive versus negative face contrasts. These data were entered into the same Bayesian Analyses used in the previous Aim to examine if BOLD signal was modulated by group.

RESULTS

EN-back Task Performance

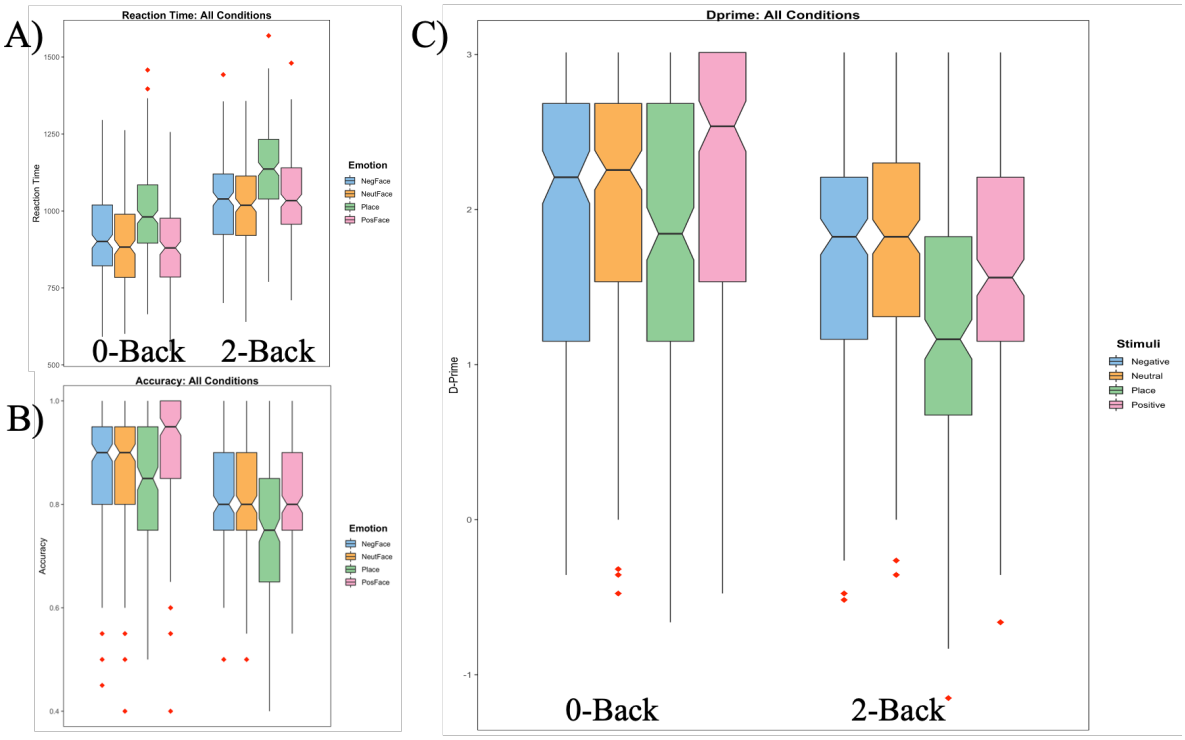

Figure 1 Behavioral Results

(A) Reaction time (RT) was increased for 2-back versus 0-back performance as expected. Overall, place stimuli seemed to evoke the longest reaction times across conditions. (B) Accuracy was near ceiling for the easier condition and seemed to be lowest for place stimuli. (C) d' was higher in 0-back, and seemed to be facilitated for positive faces at low, but not high cognitive load.

Means and standard deviations of all n-back variables are presented in Table 2. Behavioral performance data violated assumptions of normality and homoscedasticity and thus robust inferential tests were used (Field & Wilcox, 2017). Robust 4 (Group: ANX, AUT, DUAL, CTRL) x 4 (Stimulus type: Positive Negative, Neutral, and Place) mixed design (between by within) analysis of variance (ANOVA; Group x Stimuli Type; Field & Wilcox, 2017) were conducted on the difference scores between 2- and 0-back conditions for accuracy, reaction time, and *d'* data using "bwtrim" in R (Field & Wilcox, 2017; R version 3.6.0). Difference scores were used to directly quantify the impact of working memory load

on task performance. Notably, for all significant effects of stimulus or group on difference scores, planned comparisons were used to determine whether they were driven by improved task performance in the low load condition (0-back) or disrupted performance in the high load condition (2-back). Accuracy and *d′* yielded the same results (**Figure 1B-C**), therefore we focused on *d′* given it is commonly used in the literature on this task (Forns et al., 2014; Haatveit et al., 2010; López-Vicente et al., 2016; Nikolin et al., 2021), and is less subject to response bias confounds (i.e., a global tendency to respond 'match' on the task can result in high accuracy via high hit *and* false alarm rates). Planned comparisons were conducted using robust mean comparisons ("yuend"; Field & Wilcox, 2017) when main effects were found for either Group or Stimuli and were conducted to see which groups differed from each other (main effect of group) or which stimuli were different (difference scores for each type of stimuli; main effect of stimuli type).

Reaction Time

Robust ANOVA revealed a main effect of stimuli type (Q = 3.245, p = .025) but not of group (p = .837) and no significant interaction (p = .391; **Figure 1A**). Planned comparisons revealed significantly greater effects of increased working memory load on reaction time to positive faces (Mean RT [M] for positive faces [M_{pos}]=153.05, SD_{pos}=145.11) versus negative faces (M_{neg}=117.64, SD_{neg}=151.13; t_{yuen} = 2.24 (df = 123), p = .027), and versus neutral faces (M_{neu}=127.66, SD_{neu}=150.47; t_{yuen} = 2.44 (df = 123), p = 0.016). There was no difference in the effect of working memory load on reaction time to positive faces versus places (M_{place}=149.35, SD_{place}=150.42; p = .902). In turn, the effect of increased working memory load on decreased reaction time to place stimuli was significantly greater than in response to both negative faces (t_{yuen} = -2.07 (df = 123), p = 0.041) and

neutral faces (t_{yuen} = -2.16 (df = 123), p = 0.032). There were no differences between negative faces and neutral faces (p = .995). Effect sizes (Cohen's d) for significant results ranged from .13 to .15.

d'

Robust 4x4 ANOVA (Group x Stimuli Type) revealed a main effect of stimuli type (Q = 6.411, p = .0005) but not of group (p = .548) and no significant interaction (p = .970; **Figure 1C**). Planned comparisons revealed significantly greater effects of increased working memory load on sensitivity to positive faces (M_{pos}=-0.558, SD_{pos}=1.10) versus negative faces (M_{neg}=-0.254, SD_{neg}=1.09; t_{yuen} = -3.60 (df = 123), p = .0005), and versus neutral faces (M_{neu}=-0.259, SD_{neu}=1.07; t_{yuen} = -3.30 (df = 123), p = 0.001). There was no difference in the effect of working memory load on sensitivity to positive faces versus places (M_{place}=-0.579, SD_{place}=1.21; p = .925). In turn, the effect of increased working memory load on reduced sensitivity to place stimuli was significantly greater than in response to both negative faces (t_{yuen} = 3.08 (df = 123), p = 0.003) and neutral faces (t_{yuen} = 2.72 (df = 123), p = 0.007). There were no differences between negative faces and neutral faces (p = .576). Effect sizes (Cohen's d) for significant results ranged from .2 (neutral faces versus places) to .25 (positive faces versus negative faces). Interestingly, post-hoc tests revealed that the individual conditional means suggested that these difference score effects were driven by enhanced recognition of positive faces in the 0-back load condition relative to negative faces and places ($t \geq 3.57$, $p_{holm} \leq 0.005$), whereas places were associated with greater disruption in the 2-back condition compared to all face conditions ($t \geq 5.16$, $p_{holm} < 0.001$).

Table 2 N-Back Performance

Variable	Overall	AUT	ANX	Dual	Ctrl
Accuracy					

0-back					
Positive Faces	0.89 (0.12)	0.90 (0.12)	0.89 (0.12)	0.88 (0.12)	0.89 (0.13)
Negative Faces	0.86 (0.12)	0.88 (0.09)	0.86 (0.11)	0.85 (0.14)	0.86 (0.11)
Neutral Faces	0.88 (0.11)	0.88 (0.11)	0.87 (0.11)	0.89 (0.10)	0.88 (0.12
Places	0.85 (0.13)	0.84 (0.13)	0.85 (0.14)	0.83 (0.15)	0.87 (0.12)
2-back					
Positive Faces	0.81 (0.11)	0.82 (0.10)	0.79 (0.12)	0.81 (0.10_	0.82 (0.10)
Negative Faces	0.82 (0.10)	0.81 (0.10)	0.83 (0.07)	0.80 (0.11)	0.83 (0.10)
Neutral Faces	0.83 (0.11)	0.83 (0.09)	0.83 (0.11)	0.83 (0.11)	0.85 (0.12)
Places	0.75 (0.12)	0.74 (0.13)	0.75 (0.12)	0.75 (0.11)	0.78 (0.12)
Reaction Time					
0-back					
Positive Faces	890.45 (143.74)	895.91 (155.94)	887.75 (139.44)	897.15 (134.58)	881.46 (148.80)
Negative Faces	914.66 (136.67)	910.98 (138.16)	904.16 (141.62)	942.63 (136.23)	901.26 (130.26)
Neutral Faces	891.67 (139.46)	901.25 (138.15)	908.26 (148.78)	887.56 (139.78)	869.21 (130.79)
Places	987.24 (142.29)	998.04 (161.03)	981.33 (138.90)	998.06 (150.90)	972.53 (118.79)
2-back					
Positive Faces	1043.50 (133.17)	1074.41 (150.78)	1038.02 (141.23)	1043.02 (123.26)	1020.68 (113.19)
Negative Faces	1032.30 (145.91)	1033.03 (151.49)	1036.21 (142.44)	1059.68 (143.80)	1000.10 (144.38)
Neutral Faces	1019.34 (132.74)	1029.49 (122.05)	1020.37 (148.68)	1031.02 (106.92)	996.99 (148.06)
Places	1136.59 (138.08)	1140.49 (141.08)	1147.54 (154.06(	1120.79 (123.63)	1137.14 (133.63)
d'					
0-back					
Positive Faces	2.13 (0.94)	2.25 (0.93)	2.13 (0.95)	2.00 (0.95)	2.13 (0.94)
Negative Faces	1.88 (0.90)	1.98 (0.76)	1.91 (0.85)	1.79 (1.03)	1.86 (0.94)

Neutral Faces	2.04 (0.88)	2.07 (0.85)	1.94 (0.98)	2.09 (0.81)	2.05 (0.88)
Places	1.80 (1.03)	1.80 (0.96)	1.77 (1.09)	1.68 (1.12)	1.94 (0.96)
2-back					
Positive Faces	1.57 (0.79)	1.68 (0.77)	1.49 (0.83)	1.53 (0.77)	1.58 (0.78)
Negative Faces	2.63 (0.79)	1.62 (0.74)	1.74 (0.61)	1.47 (0.93)	1.68 (0.84)
Neutral Faces	1.78 (0.80)	1.71 (0.71)	1.76 (0.80)	1.70 (0.88)	1.92 (0.80)
Places	1.22 (0.84)	1.13 (0.85)	1.86 (0.84)	1.14 (0.75)	1.41 (0.91)

Table 3 N-Back Difference Scores

Variable	Overall	AUT	ANX	Dual	Ctrl
Accuracy					
Positive Faces	-0.08 (0.14)	-0.08 (0.15)	-0.10 (0.14)	-0.06 (0.12)	-0.07 (0.13)
Negative Faces	-0.04 (0.13)	-0.07 (0.11)	-0.03 (0.11)	-0.05 (0.16)	-0.03 (0.13)
Neutral Faces	-0.05 (0.13)	-0.05 (0.15)	-0.05 (0.13)	-0.06 (0.11)	-0.03 (0.14)
Places	-0.09 (0.17)	-0.10 (0.19)	-0.10 (0.16)	-0.09 (0.17)	-0.09 (0.14)
Reaction Time					
Positive Faces	153.05 (145.11)	178.50 (146.36)	150.27 (143.05)	145.87 (160.66)	139.22 (130.29)
Negative Faces	117.64 (151.13)	122.05 (150.15)	132.04 (132.04)	117.05 (166.71)	98.84 (141.11)
Neutral Faces	127.66 (127.66)	128.24 (146.06)	112.11 (148.62)	143.46 (154.99)	127.78 (154.65)
Places	149.35 (150.42)	142.46 (161.24)	166.21 (149.73)	122.73 (152.74)	164.61 (137.88)
d'					
Positive Faces	-0.56 (1.10)	-0.57 (1.14)	-0.64 (1.17)	-0.47 (1.03)	-0.55 (1.08)
Negative Faces	-0.25 (1.09)	-0.36 (1.00)	-0.16 (0.95)	-0.32 (1.31)	-0.18 (1.08)
Neutral Faces	-0.26 (1.07)	-0.35 (1.16)	-0.18 (1.13)	-0.39 (0.98)	-0.13 (1.01)
Places	-0.58 (1.21)	-0.67 (1.36)	-0.58 (1.26)	-0.54 (1.30)	-0.53 (0.94)

Neuroimaging

Across all subjects, whole brain cluster-extent thresholding did not yield any significant differences in the positive versus neutral face contrast, the negative versus neutral face contrast, or the neutral 2-back versus neutral 0-back conditions. Given these contrasts were not of direct relevance to our current hypotheses—and well-known inter-subject variability in the psychological and neural response to 'neutral faces' (Blasi et al., 2009; Hester, 2019)—these contrasts were not included in our subsequent group-wise Bayesian multilevel modeling analyses. Network labels used to contextualize fMRI clusters come from the Schaefer atlas parcellation (Schaefer et al., 2018).

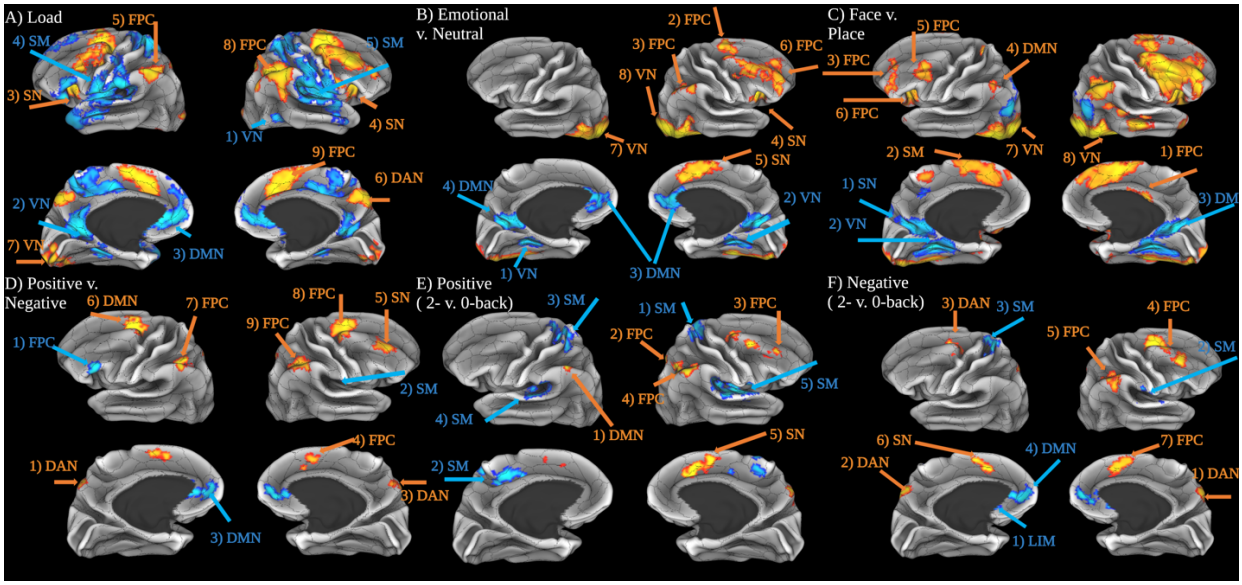

Figure 2 Whole Group Contrasts

(A) Load (*2-back versus 0-back)* Contrast. (B) Emotional versus Neutral Faces Contrast. (C) Faces versus Places Contrast. (D)Positive versus Negative Faces Contrast. (E) *Positive Faces (2-back versus 0-back) Contrast. (F) Negative Faces (2-back versus 0-back) Contrast. All ROIs are labelled according to their network assignment: Frontoparietal Control (FPC), Salience (SN), Dorsal Attention (DAN), Visual (VN), Limbic (LIM), and Somatomotor (SM). Numbers correspond to the index number in their appropriate contrast table. Orange represents positive activation whereas blue represents deactivation. Volumetric analyses projected onto cortical surface maps for visualization.*

Load Contrast

The 2-back versus 0-back contrast was designed to reveal blood oxygenation-level dependent signal changes associated with increased cognitive load (i.e., increased WM demands). Areas classically associated with task-evoked increases in BOLD signal (i.e., 'task-positive networks') demonstrated positive activation in the 2-back relative to the 0-back condition, including: clusters within the frontoparietal control network (peaks in superior frontal gyrus and bilateral supramarginal gyrus, dorsal attention network (dorsocaudal precuneus), salience network (left and right lateral orbitofrontal cortex extending into frontal operculum), visual network (occipital pole), and subcortical regions (cerebellum and brain stem; Figure 2A; Table 4).

Table 4 Peak Cluster Activations for Load Contrast

Pos/Neg	Index	Z - max	MNI Peak	Size	Atlas Label (Peak location)	Network Label
Pos	1	4.44	-6,-32,-18	232	Brain stem	Subcortical
Pos	2	4.26	38,-48,-34	339	Cerebellum	Subcortical
Pos	3	5.16	-30,30,-4	426	Left frontal orbital cortex	Salience
Pos	4	5.23	34,18,10	503	Right frontal operculum cortex	Salience
Pos	5	5.66	-50,-46,48	1295	Left supramarginal gyrus, posterior division	Frontoparietal Control
Pos	6	5.03	10,-60,54	1580	Right precuneus	Dorsal Attention
Pos	7	5.51	-2,-98,-8	2166	Left occipital pole	Visual
Pos	8	6.85	46,-42,38	2440	Right supramarginal gyrus, posterior division	Frontoparietal Control
Pos	9	6.03	22,2,56	7440	Right superior frontal gyrus	Frontoparietal Control
Neg	1	4.44	50,-60,-6	141	Right lateral occipital cortex, inferior division	Visual
Neg	2	4.9	-34,-44,-6	580	Left lingual gyrus	Visual
Neg	3	6.31	-12,40,-8	3024	Left paracingulate gyrus	Default
Neg	4	6.13	-50,-10,14	6351	Left central opercular cortex	Somatomotor

Neg	5	5.97	46,-28,20	12232	Right parietal operculum cortex	Somatomotor

Emotional Faces versus Neutral Faces Contrast

The emotional versus neutral faces contrast probed BOLD changes associated with emotional faces (positive or negative) as compared to neutral faces. Activation increases for emotional faces were found in areas of the frontoparietal control network (superior frontal gyrus and supramarginal gyrus) and visual networks, as well as in the salience (anterior insula and dorsal paracingulate) and visual (inferior lateral occipital cortex, occipital pole, and fusiform cortex) networks. Some areas in the visual network also demonstrated modest deactivations in response to emotional faces (dorsal lateral occipital cortex, lingual gyrus), and robust deactivations associated with emotional relative to neutral faces were observed in the default network (perigenual cingulate cortex, and ventral precuneus). Overall, there was a generally right-lateralized pattern of neural recruitment in response to emotional relative to neutral faces, which aligns with literature on emotional processing (Rossion & Lochy, 2021; Figure 2B; Table 5). Given that this contrast has greater power than splitting emotional faces into positive and negative, finding significant results in this contrast despite a lack of findings in either positive versus neutral or negative versus neutral contrasts is not wholly surprising. When we use other methods to parse out emotional impacts, such as directly comparing positive and negative faces, we also find results, demonstrating that neutral faces being poorly differentiated from negative faces or impacted by other factors (Hester, 2019; Siegel et al., 2018; Wieser et al., 2014) is likely driving a lack of results (such as increased noise) in the lower powered analyses.

Table 5 Peak Cluster Activations for Emotional versus Neutral Faces Contrast

Pos/Neg	Index	Z -max	MNI Peak	Size	Atlas Label (Peak location)	Network Label
Pos	1	4.33	24,-14,-14	144	Right Hippocampus	Subcortical
Pos	2	4.45	20,6,64	326	Right Superior Frontal Gyrus	Frontoparietal Control
Pos	3	4.91	54,-42,48	404	Right Supramarginal Gyrus, posterior division	Frontoparietal Control
Pos	4	5.04	36,20,2	616	Right Insular cortex	Salience
Pos	5	4.88	8,26,40	814	Right Paracingulate gyrus	Salience
Pos	6	5.29	46,48,18	1747	Right Frontal pole	Frontoparietal Control
Pos	7	6.31	-34,-88,-12	2606	Left lateral occipital cortex, inferior division	Visual
Pos	8	6.33	38,-92,-6	3151	Right occipital pole	Visual
Neg	1	4.48	-28,-48,-8	319	Left temporal occipital fusiform cortex	Visual
Neg	2	4.67	24,-40,-10	357	Right lingual gyrus	Visual
Neg	3	5.32	6,42,0	1129	Right cingulate gyrus, anterior division	Default
Neg	4	5.75	-12,-54,20	1780	Left precuneus	Default

Faces versus Places Contrast

This contrast looked at BOLD signal changes in response to face stimuli relative to a common non-face stimulus (places). Activation networks in this contrast were similar to the emotional face versus neutral faces contrast, except more left lateralized. Activation increases for faces were found in frontoparietal control and visual areas (Figure 2C; Table 6).

Table 6 Peak Cluster Activations for Faces versus Places Contrast

Pos/Neg	Index	Z -max	MNI Peak	Size	Atlas Label (Peak location)	Network Label
Pos	1	4.95	6,-18,26	163	Right cingulate gyrus, posterior division	Frontoparietal Control
Pos	2	4.43	-6,-30,62	204	Left precentral gyrus	Somatomotor
Pos	3	4.92	-46,46,0	259	Left frontal pole	Frontoparietal Control

Pos	4	5.44	-58,-64,38	334	Left lateral occipital cortex, superior division	Default
Pos	5	4.76	-48,18,34	385	Left middle frontal gyrus	Frontoparietal Control
Pos	6	5	-28,22,-8	1215	Left insular cortex	Frontoparietal Control
Pos	7	7.03	-42,-88,-4	3425	Left lateral occipital cortex, inferior division	Visual
Pos	8	7.57	30,-94,10	16480	Right occipital pole	Visual
Neg	1	4.72	-6,-32,44	149	Left cingulate gyrus, posterior division	Salience
Neg	2	6.34	-26,-48,-6	1025	Left lingual gyrus	Visual
Neg	3	6.75	22,-56,18	6043	Right precuneus	Default

Positive Faces versus Negative Faces

When contrasting positively versus negatively-valenced faces, several areas within the frontoparietal control and dorsal attention networks responded preferentially to positive faces (superior frontal gyrus, supramarginal gyrus, and right precuneus). In contrast, regions of the control and somatomotor networks along the frontal operculum (inferior frontal gyrus, and central opercular cortex) as well as perigenual cingulate cortex both responded preferentially to negative face stimuli (Figure 2D; Table 7).

Table 7 Peak Cluster Activations for Positive versus Negative Faces Contrast

Pos/Neg	Index	Z -max	MNI Peak	Size	Atlas Label (Peak location)	Network Label
Pos	1	4.48	-10,-70,60	117	Left lateral occipital cortex, superior division	Dorsal Attention
Pos	2	4.89	36,-60,-34	126	Cerebellum	Subcortical
Pos	3	4.65	8,-72,56	229	Right precuneus cortex	Dorsal Attention
Pos	4	4.61	2,30,42	251	Right paracingulate gyrus	Frontoparietal Control

Pos	5	5.41	40,44,28	344	Right frontal pole	Salience
Pos	6	4.72	-24,10,58	350	Left superior frontal gyrus	Default
Pos	7	4.87	-46,-46,48	504	Left supramarginal gyrus, posterior division	Frontoparietal Control
Pos	8	6.03	22,10,58	478	Right superior frontal gyrus	Frontoparietal Control
Pos	9	6.02	46,-46,46	788	Right supramarginal gyrus, posterior division	Frontoparietal Control
Neg	1	4.28	-50,30,12	130	Left inferior frontal gyrus, pars triangularis	Frontoparietal Control
Neg	2	4.52	50,-12,20	225	Right central opercular cortex	Somatomotor
Neg	3	4.66	-2,38,-4	1030	Left cingulate cortex, anterior division	Default

Positive and Negative Faces (2-back) versus (0-back)

Load-dependent responses in task-positive brain networks were observed in response to positive faces (i.e., 2-back positive versus 0-back positive) in a subset of the same brain regions found to be activated / deactivated in the overall cognitive load contrast (Figure 2A,C; Tables 3,7). A highly similar load-dependent scaling of BOLD activity was observed in response to negative faces, except several clusters recruited bilaterally in the negative face 2 versus 0 contrast were right-lateralized in response to positive faces (Figure 2E-F; Tables 8-9).

Table 8 Peak Cluster Activations for Positive Faces: 2- versus 0-back Contrast

Pos/Neg	Index	Z -max	MNI Peak	Size	Atlas Label (Peak location)	Network Label
Pos	1	3.98	-42,-58,58	163	Left lateral occipital cortex, superior division	Default
Pos	2	3.89	38,-62,44	221	Right lateral occipital cortex, superior division	Frontoparietal Control
Pos	3	3.92	50,32,32	256	Right middle frontal gyrus	Frontoparietal Control

Pos	4	3.88	48,-50,50	270	Right angular gyrus	Frontoparietal Control
Pos	5	4.16	12,18,48	598	Right superior frontal gyrus	Salience
Neg	1	4.13	20,-28,64	274	Right precentral gyrus	Somatomotor
Neg	2	4.94	-8,-24,50	434	Left precentral gyrus	Somatomotor
Neg	3	4.35	-24,-32,64	565	Left postcentral gyrus	Somatomotor
Neg	4	5.08	-44,-24,18	748	Left parietal operculum cortex	Somatomotor
Neg	5	4.96	56,-12,8	1533	Right central opercular cortex	Somatomotor

Table 9 Peak Cluster Activations for Negative Faces: 2- versus 0-back Contrast

Pos/Neg	Index	Z -max	MNI Peak	Size	Atlas Label (Peak location)	Network Label
Pos	1	4.31	12,-64,50	149	Right precuneus cortex	Dorsal Attention
Pos	2	4.65	-12,-64,54	213	Left lateral occipital cortex, superior division	Dorsal Attention
Pos	3	5.49	-26,0,42	257	Left middle frontal gyrus	Dorsal Attention
Pos	4	4.7	44,30,32	269	Right middle frontal gyrus	Frontoparietal Control
Pos	5	5.23	50,-40,38	430	Right supramarginal gyrus, posterior division	Frontoparietal Control
Pos	6	4.98	-8,26,38	459	Left paracingulate gyrus	Salience
Pos	7	5.03	26,10,54	693	Right superior frontal gyrus	Frontoparietal Control
Neg	1	4.3	-4,14,-6	181	Left subcallosal cortex	Limbic
Neg	2	3.87	68,-14,16	204	Right postcentral gyrus	Somatomotor
Neg	3	5.13	-26,-24,72	305	Left precentral gyrus	Somatomotor
Neg	4	5.67	-4,48,-10	540	Left frontal medial cortex	Default

Bayesian Group by Condition Contrasts

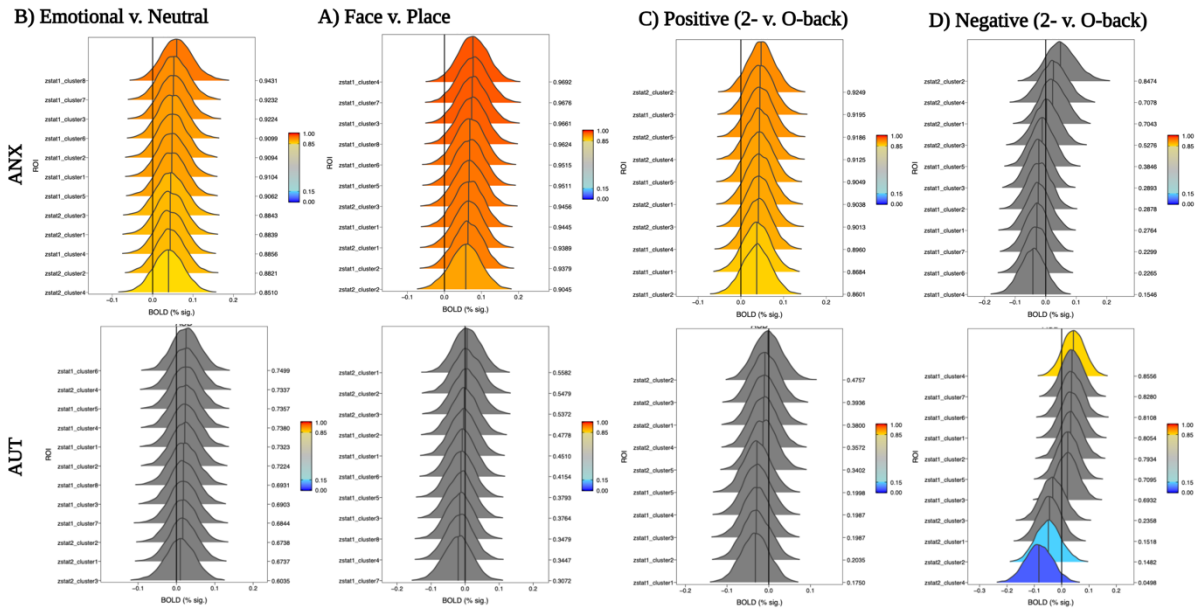

Figure 3 Bayesian Analysis

Bayesian analysis posterior distributions for anxious traits (top row) and autistic traits (bottom row) for main contrasts: emotional versus neutral (A), face versus place (B), positive faces, 2-back versus 0-back (C), and negative faces, 2-back versus 0-back (D). Zstat1 clusters represent areas that demonstrated positive BOLD signal changes, whereas zstat2 clusters represent deactivated clusters, for each contrast. Cluster numbers correspond to the "Index" column in the associated Tables 3-8.

Load Contrast

Autistic traits did not modulate any of the clusters from the Load (i.e., N-Back 2 versus N-Back 0) contrast. Notably, anxiety was associated with aberrant task-evoked responses in the Load contrast, including reduced activation of task-positive clusters anchored in ventrolateral prefrontal cortex, dorsolateral prefrontal cortex, and dorsocaudal precuneus as well as less deactivation of the perigenual cingulate. Individuals both anxiety and autistic traits demonstrated greater global deactivation in both activated and deactivated clusters across networks (with the exception of left paracingulate) in response to the high versus low working memory load conditions.

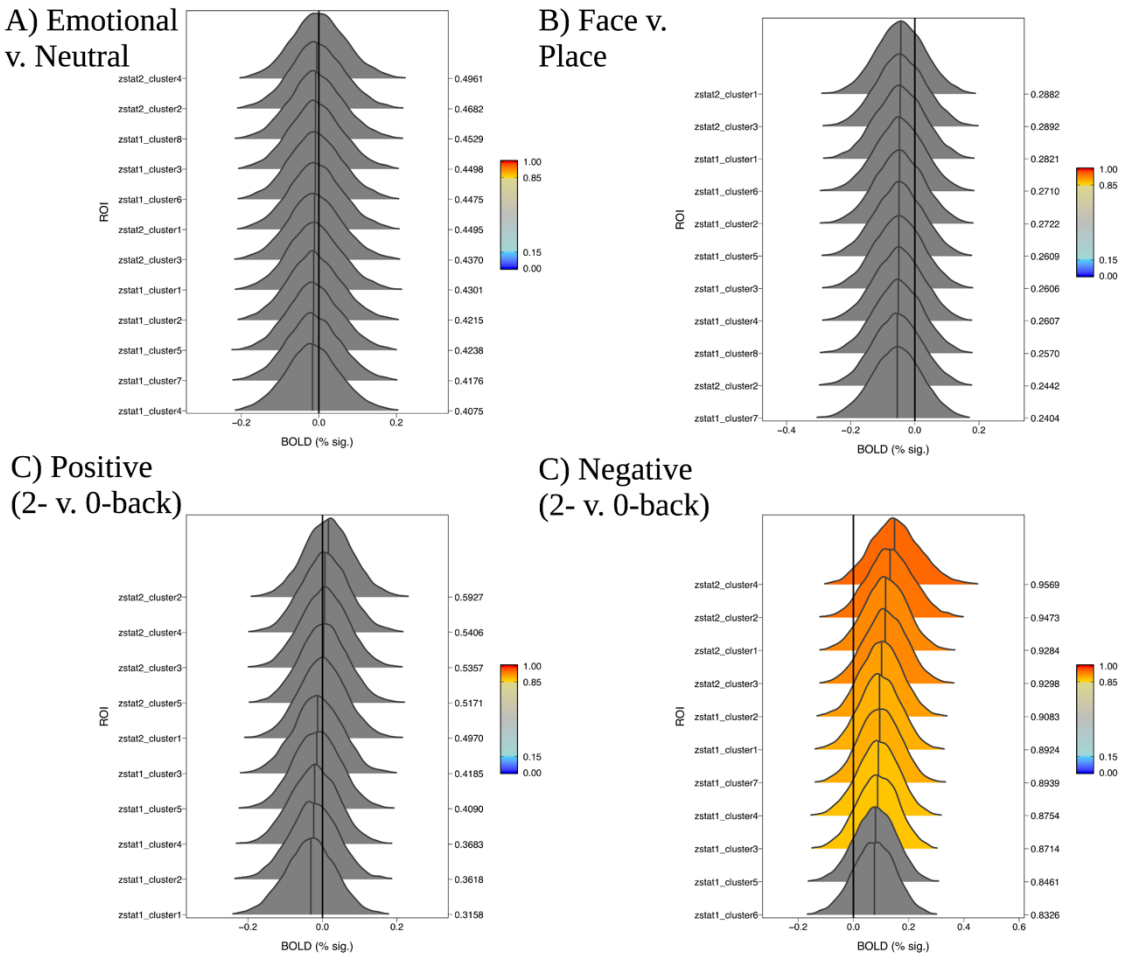

Figure 4 Bayesian Posteriors for Dual Group

Bayesian analysis posterior distributions for Dual group for main contrasts: emotional versus neutral faces (A), face versus place (B), positive faces, 2-back versus 0-back (C), and negative faces, 2-back versus 0-back (D). Zstat1 clusters represent areas that demonstrated positive BOLD signal changes, whereas zstat2 clusters represent deactivated clusters, for each contrast. Cluster numbers correspond to the "Index" column in the associated Tables 3-8.

Emotional Faces versus Neutral Faces Contrast

There were no clusters that showed differential activation as a product of AUT traits. For anxiety, all clusters were significantly more activated, showing both increased activation in activated areas and a decreased deactivation in less-activated areas (Figure 3A). This suggests potentially greater sensitivity to emotion or neural inefficiency in processing

emotion for highly anxious children. There were no significant clusters that showed differential activation for the dual group (Figure 4A).

Faces versus Places Contrast

There were no clusters that showed differential activation as a product of AUT traits. For anxiety, all clusters were significantly more activated, showing both increased activation in activated areas and a decreased deactivation in less-activated areas (Figure 3B). This suggests potentially greater sensitivity to faces or neural inefficiency in processing faces for highly anxious children. The dual group showed no differential activation (Figure 4B).

Positive Faces versus Negative Faces

There were no clusters that showed differential activation as a product of AUT traits. For anxiety, the left anterior cingulate cortex (default network) was less deactivated, however this area anatomically appeared to be the subgenual ACC which is associated with the paralimbic network. For the dual group there was no differential activation.

Positive Faces (2-back) versus Positive Faces (0-back)

There were no clusters that showed differential activation as a product of AUT traits. For anxiety, all clusters were significantly more activated, showing both increased activation in activated areas and a decreased deactivation in less-activated areas (Figure 3C). This suggests potentially greater sensitivity to positive faces or neural inefficiency in processing positive faces for highly anxious children. The dual group showed no differential activation (Figure 4C).

Negative Faces (2-back) versus Negative Faces (0-back)

For AUT traits, the right middle frontal gyrus showed increased activation (dorsal attention network). Additionally, the right postcentral gyrus and left frontal medial cortex we both deactivated to a greater extent in this group (somatomotor and default networks). Overall, the AUT group showed an amplification of the typical pattern, representing a quantitative, but not qualitative activation difference. For anxiety, there were no clusters that showed differential activation (Figure 3D). The dual group showed increased activation in multiple dorsal attention network and frontoparietal control areas. There was also reduced deactivation in all deactivated areas (somatomotor, limbic, and default networks; Figure 4D).

Amygdala Bayesian Analysis

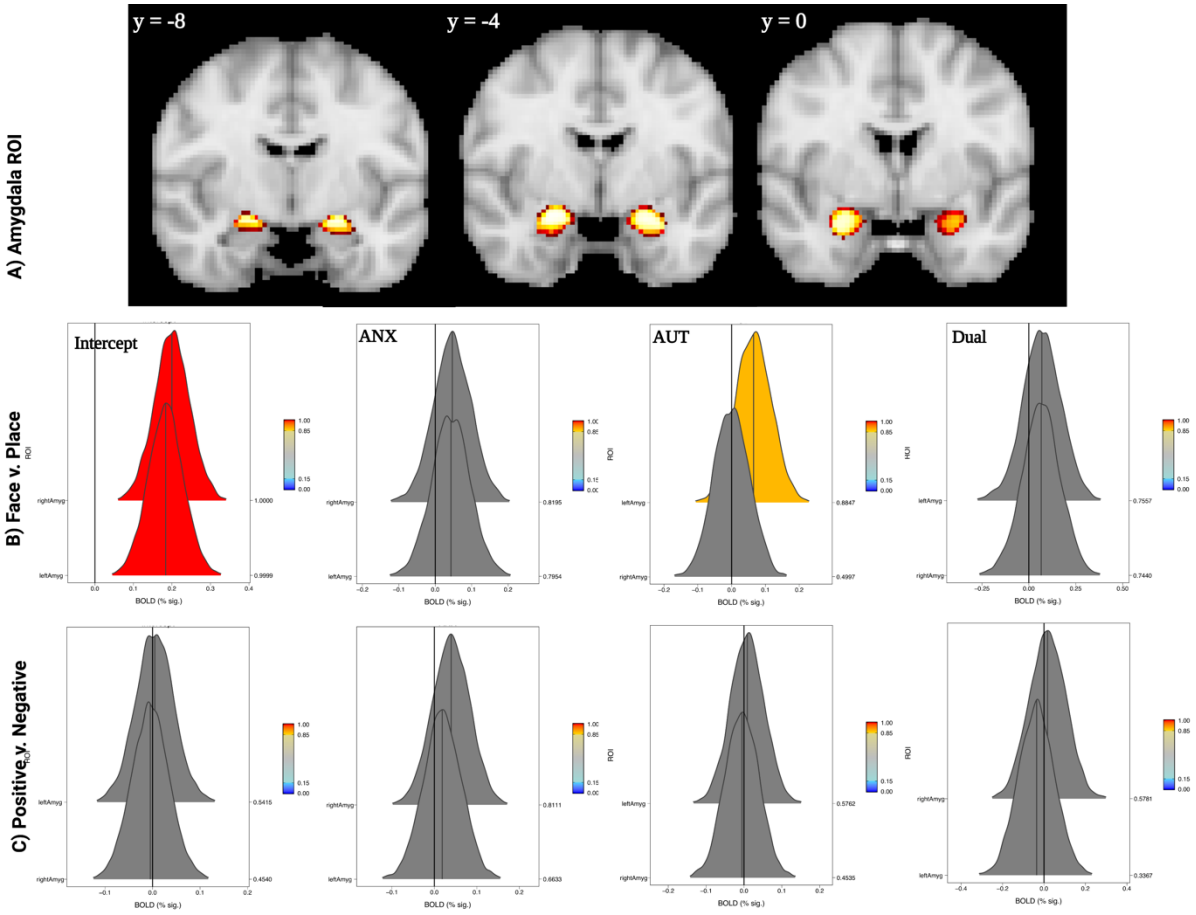

Figure 5 Bayesian Amygdala Analyses

Bayesian amygdala analyses. Amygdala ROI (A), Face versus Place Contrast (B), Positive versus Negative Faces Contrast(C).

Looking at the face versus place contrast, both left and right amygdala were significantly more activated for faces rather than places. There were no differential effects for anxious traits, but the left amygdala showed greater activation as a result of autistic traits.

The positive versus negative contrast showed no significant activation differences either overall or for either group. There were null results for the dual group. This suggests

that the amygdala may be more sensitive to face stimuli in general, but not for differential activation to face stimuli as a function of valence.

Comparison of Results with d' Exclusion Criteria

Despite excluding subjects based on accuracy as recommended by the ABCD team and as done in other studies utilizing this data (Casey et al., 2018; Rosenberg et al., 2020), 6 subjects did not have a *d'* score that was positive over all conditions, perhaps subjects who had a large number of false alarms. We excluded these subjects from the analysis and reran to ensure results were not unduly influenced by these subjects. DICE correlations measure spatial similarity by looking at the overlap of voxels of activated clusters (Bowring et al., 2019; Dice, 1945). This tends to be a very stringent measure of spatial similarity. The correlation ratio measures functional dependence of two variables as a ratio (Roche et al., 1998). These metrics were run using the nipype overlap and similarity metrics (Gorgolewski et al., 2011) between the original contrast and the version with these six subjects excluded. DICE correlations for all contrasts (except emotional versus neutral faces and faces versus places) ranged from 0.71 to 0.91, showing strong spatial correlations between the analysis and showing the results were not driven by these subjects. For all contrasts, the correlation ratio similarity index was above 0.972 showing strong similarity between the analyses.

Behavioral results for *d'* showed similar results as with the full sample, with neither group ($p = 0.476$) nor the group by stimuli interaction ($p = 0.976$) being significant and a significant main effect of stimuli ($p < .001$).

Scanner Effects

Follow-up analyses revealed that the observed group-wise effects were unlikely to be driven by scanner differences. There were no differences in proportions of individuals being scanned on SIEMENS and GE devices across the ASD, ANX, DUAL, and CTRL groups (X^2 = 0.35 (df=3) p = .951), and there was minimal evidence for scanner differences in our main effects models. Accordingly, the results of our group-wise Bayesian models were unlikely to be driven by scanner differences.

How Autistic Traits Impact the Effects of Anxiety

To directly compare the transdiagnostic effects of anxiety, we directly subtracted the posterior estimates of the dual group from the anxious group and examined activations that significantly differed. When we directly contrasted the anxiety traits only and the dual groups, several contrasts showed significant differences in activation between the groups. For load, several deactivated clusters showed greater deactivation in the visual, default, and somatomotor networks. For face versus place, all clusters showed increased deactivation. For negative faces 2-back versus 0-back, all clusters except one activated cluster (right supramarginal gyrus, posterior division, frontoparietal control network) and two deactivated clusters (left subcallosal cortex [limbic network] and right postcentral gyrus [somatomotor network]) showed increased activation. For emotional versus neutral faces, positive versus negative faces, and positive 2-back versus 0-back faces there were no differences (Figure 6A-C).

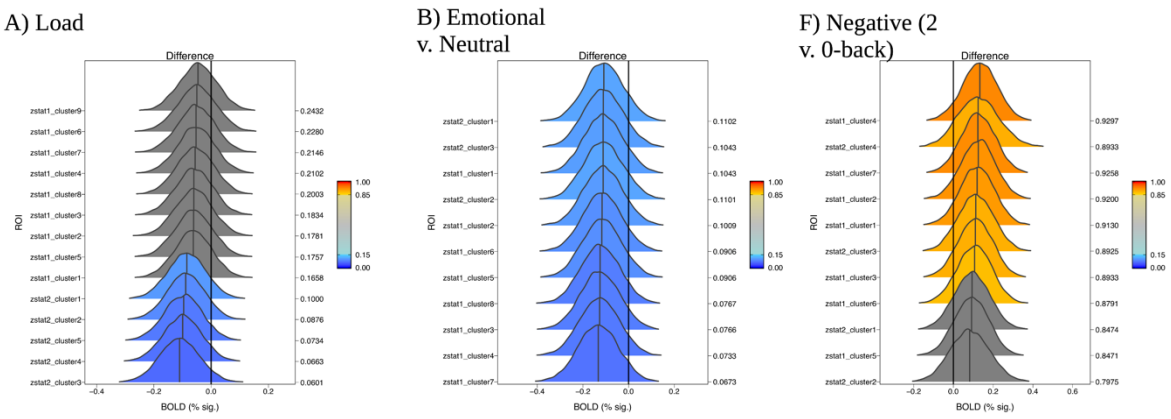

Figure 6 Significant Clusters (ANX - DUAL)

Bayesian analyses of transdiagnostic anxious trait differences. Load Contrast (A), Emotional versus Neutral Faces Contrast (B), Negative Faces (2 back versus 0-back) Contrast (C).

Prevalence Estimates Across Sample

ABCD does not reflect a normal sample as the team oversampled for individuals with both internalizing and externalizing problems (Casey et al., 2018). There are similar rates of high autistic and anxious traits across the sample (Figure 7; ANX = 9.25%, AUT = 8.98%, DUAL = 5.42%) despite ASD being a much lower base rate condition (Maenner et al., 2020; Strawn et al., 2021). The relative similarity in prevalence can be accounted for by the differences in measures used to capture anxious and autistic traits. The CBCL is used for differentiating clinical populations whereas the SRS captures autistic traits rather that ASD diagnosis explicitly (Achenbach & Rescorla, 2001; Constantino et al., 2000, 2004). It has been suggested that more general autistic social traits are normally distributed in the population (Constantino & Todd, 2003; Posserud et al., 2006; Skuse et al., 2009) and the percentage in our sample classified as AUT is similar to the percentage of males scoring above the cut-off on a different social communication measure at this age in a large population cohort (Mandy et al., 2018). The differential domains of impairments in ASD may

be related to different genetic risk factors and each may be normally distributed in the population, including social communication deficits (Happé et al., 2006).

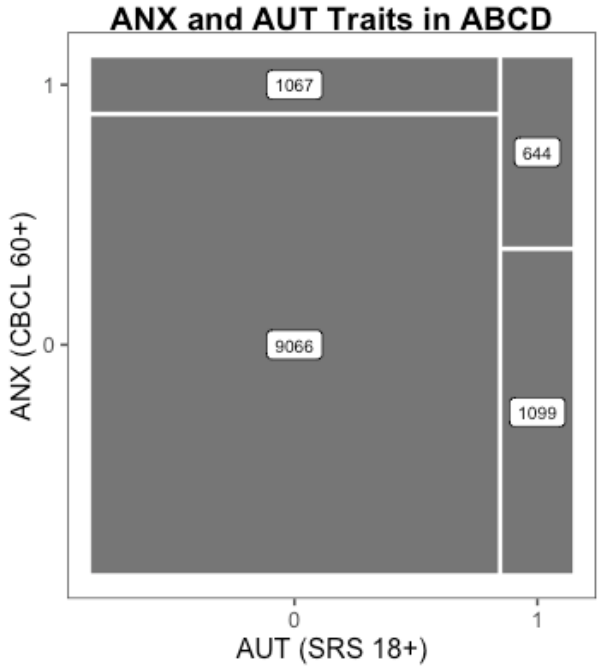

Figure 7 Prevalence of ANX/AUT Traits across entire ABCD sample as defined by SRS and CBCL score

Discussion

There is a broad literature examining potential behavioral and neural correlates of negative stimulus biases in attention in individuals with elevated anxious and autistic traits across the lifespan (Bar-Haim et al., 2007; Bishop, 2007, 2008; Cisler & Koster, 2010; García-Blanco et al., 2017; Sahuquillo-Leal et al., 2022) . However, there is a relative lack of research on how emotional information may be differentially held in working memory in youth with elevated anxiety, elevated autistic traits, or both. The aim of the current study was to begin to fill this gap in the literature. We examined behavioral and neural correlates of negative stimulus biases in working memory in preadolescents with clinically-significant anxiety, autistic traits, or both, using a large set of well-matched youth from the *ABCD* study

dataset. No group differences were observed for reaction time and *d'* outcome measures, failing to yield behavioral evidence of negative stimulus bias in working memory in individuals with elevated anxiety and/or autistic traits. This directly contradicts prior studies suggesting that complex socio-affective biases in cognitive processes like attention and working memory underlie core symptoms of developmental anxiety (Bar-Haim et al., 2007; Bishop, 2008; Cisler & Koster, 2010). Our behavioral data also did not reveal any evidence for reduced processing speed or sensitivity to emotional face stimuli in preadolescents with elevated autistic traits, a commonly held assumption in the literature on social perception in ASD (Halliday et al., 2014; Harms et al., 2010; Webb et al., 2017)**.** However, stepping into the neural data suggested several patterns of aberrant neural recruitment in preadolescents with elevated anxiety and/or autistic traits that likely evidence either compensatory or differential mechanisms underpinning emotional working memory task performance between groups.

fMRI analyses were designed to examine BOLD signal changes in response to emotional processing differences and working memory load differences. These analyses were conducted both at the whole-brain level, as well as focused on a specific *a priori* ROI (amygdala). These analyses were also initially conducted across the entire sample, with follow-up modeling performed to examine how task-relevant brain areas may be differentially recruited in youth with elevated anxiety symptoms and/or autistic traits. Across the whole brain, working memory load (i.e., 2- versus 0-back contrasts) was associated with elevated recruitment of task-positive brain networks including frontoparietal control regions, dorsal attention network regions, and areas of the visual and somatomotor networks, alongside deactivation in task negative default mode areas. Notably, a subset of these same

clusters was similarly recruited across both positive (positive 2-back versus positive 0-back) *and* negative (negative 2-back versus negative 0-back). Working memory load effects were slightly more bilateral in response to negative relative to positive faces, with the latter demonstrating primarily right-lateralized task-related BOLD signal changes.

Overall, group-wise analyses revealed similar whole-brain patterns of neural recruitment across the task, but several noteworthy exceptions. Specifically, individuals with clinically-significant anxiety demonstrated a generalized pattern of enhanced recruitment across both task-positive and task-negative brain areas in several of the contrasts in the current study. There are several prominent models of pediatric anxiety that suggest an enhanced vigilance in anxious individuals when processing novel stimuli that they perceive as potentially threatening (Derakshan et al., 2007; Pine, 2007).

We observed minimal evidence for differential task-related BOLD responses as a function of working memory load in the AUT group. This diverges from existing studies demonstrating aberrant recruitment of frontoparietal control networks during n-back task performance in youth with ASD (Koshino et al., 2005; Vogan et al., 2014) suggesting a potential source of divergence between subclinical autistic traits and youth with clinically-diagnosed ASD.

Group-wise models of stimulus type-evoked fMRI activity (i.e., face > place, emotional face > neutral, and positive > negative face) demonstrated a complex pattern of results suggesting potential mechanisms of differential or compensatory processing of emotional face stimuli in youth with elevated anxiety and/or autistic traits. Notably, comparisons of face versus non-face stimuli showed no differential activation for the AUT group, which runs contrary to our hypothesis (and lots of research) that suggests differences

in facial processing as a core deficit in ASD (Aoki et al., 2015; Costa et al., 2020; Hadjikhani et al., 2007; Kleinhans et al., 2016; Weng et al., 2011). Youth with anxiety—similar to the working memory load contrasts—did demonstrate some patterns of increased activation across clusters in response to face relative to nonface stimuli, providing an additional marker of potentially increased vigilance or potentially reduced neural efficiency in this participant group (Rainer & Miller, 2000). We also observed greater deactivation of perigenual anterior cingulate cortex in participants with increased anxiety symptoms suggesting a potential role for this area in anxious traits during emotional face processing. This is directly in line with existing studies demonstrating aberrant anterior cingulate structure and function in individuals with elevated anxiety and autistic traits (Pillay et al., 2006; Strawn et al., 2014, 2015; Wang et al., 2016) but our lack of a difference for either the DUAL or AUT group for this area contrasts with research that this area is additionally implicated in high autistic traits during emotional processing (Amaral et al., 2008; Hau et al., 2019).

Interestingly, amygdala-specific models suggested this region responded preferentially to faces but was not sensitive to positive versus negative face valence across the full sample. This draws into question research that claims that the amygdala reacts preferentially to valence or negative face stimuli, rather than faces in general (Gamer & Büchel, 2009; Morrison & Salzman, 2010; Scheller et al., 2012; Sergerie et al., 2008; Weng et al., 2011). This contradicted our prediction for valence-based stimulus encoding in the amygdala. However, this finding was compatible with other research has shown that they amygdala responds to faces more broadly (Hennessey et al., 2018; Inagaki et al., 2022; Kale et al., 2019; Murray & Fellows, 2022; Putnam & Chang, 2021; Taubert et al., 2018) or to

social cognition (Fishman et al., 2018; Putnam & Chang, 2021; Putnam & Gothard, 2019; Sato et al., 2019).

Notably, despite amygdala not encoding stimulus valence, we did find evidence for aberrant face-specific recruitment of amygdala in individuals with elevated autistic traits, directly in line with existing studies (Aoki et al., 2015; Hadjikhani et al., 2007; Herrington et al., 2016; Kleinhans et al., 2011, 2016; Leung et al., 2018; Weng et al., 2011). Specifically, we found *increased* recruitment in the left amygdala in response to face stimuli relative to place stimuli in participants with elevated autistic traits. Despite our prediction that amygdala would be hypoactivated in response to face stimuli in those with heightened autistic traits, there are several findings in the literature suggesting that some tasks evoked enhanced amygdala recruitment to emotional faces in ASD (Kliemann et al., 2012; Tanaka & Sung, 2016). One possible source for this discrepancy may be the degree to which individuals with autistic traits or clinical ASD are able to perform at 'normative' levels on the relevant cognitive task. In the majority of prior studies demonstrated amygdalar deactivation in ASD this is coupled with impaired behavioral performance (Pelphrey et al., 2011), whereas on the current task individuals with high autistic traits performed similarly well to individuals with low autistic traits. On such tasks, hyperactivation of the amygdala in response to face stimuli may therefore represent a potential compensatory mechanism for enabling similar behavioral performance in participants with elevated autistic traits.

Historically, the amygdala was seen as the fear center or hub (Deming et al., 2022; Hennessey et al., 2018; LeDoux & Pine, 2016), but is now viewed as a network hub encompassing valence, salience, cognition, reward, and social learning (Deming et al., 2022; Hennessey et al., 2018). The amygdala is implicated in all five Research Domain Criteria

(RDoC) domains (Negative Valence Systems, Positive Valence Systems, Cognitive Systems, Social Processes, and Arousal and Regulatory Systems) and, as such, is an important area to investigate transdiagnostically (Hennessey et al., 2018). One of the strengths of the RDoC criteria is that they can explicitly probe heterogeneity, which can be particularly useful in spectrum conditions such as autism as well as the ability to probe conditions dimensionally (Hennessey et al., 2018). The amygdala and its connectivity with other regions are developing throughout childhood through adolescence making its investigation during this timeframe essential (Hennessey et al., 2018). Some research on the amygdala in comorbid ASD and anxiety, for instance, has suggested that the choice of dimensional or categorical constructs impacts findings (Yarger et al., 2022).

There is a move in neuroscience research away from the definition of circuits associated with discrete emotions, and instead represent affect as valence and arousal combinations (Deming et al., 2022). In this view the amygdala might be better conceptualized by emotion recognition and association with danger cues (Deming et al., 2022). While there was no differential amygdala activation for positive versus negative faces, there were also no differential consequences or impacts of the emotionally valenced stimuli in this paradigm. Therefore, if the view is that the amygdala helps coordinate more of valenced outcomes, this lack of activation could potentially be expected.

Other factors may also impact amygdala reactivity, such as implicit or explicit presentation of stimuli. Chen et al. (2021) found negative correlations to the parietal network with explicit fearful faces but correlations to the prefrontal networks, temporal pole, and hippocampus were stronger with implicit fearful face presentation in individuals with ASD.

One potential implication of our lack of findings for attentional bias towards negative stimuli in anxious groups speaks to treatment. For instance, attention bias modification is a commonly used anxiety treatment in pediatric anxiety (Bar-Haim, 2010; Hang et al., 2021). This treatment is predicated on the idea that such a bias exists, that it is critical for maintaining pediatric anxiety, and that altering this bias alleviates symptoms. If our lack of findings is applicable to a pediatric anxiety clinical sample (and the CBCL has been shown to reliably differentiate clinical samples; Achenbach & Rescorla, 2001; Magyar & Pandolfi, 2017) this suggests a mismatch between current treatment methods and behavioral and neural evidence of purported mechanisms of action that should be further investigated. While recent meta-analyses have demonstrated efficacy of this treatment (Hang et al., 2021), our large sample study found little evidence for this bias this treatment is supposed to modify. This is an avenue for further investigation, both into how to appropriately probe attentional bias in this population, and into this treatment.

Limitations and Future Directions

Due to the nature of the ABCD study, groups were created by looking at high scores on clinical measures of anxiety and autistic traits. However, the prevalence rates of anxiety and autism diagnoses in the ABCD sample do not match the general US population in this age range. In fact, moderate to severe autism was an exclusion criteria for ABCD (Casey et al., 2018; Rosenberg et al., 2020), thereby limiting the generalization of our results to specific anxiety disorders and to a significant portion of the autism spectrum. Future work should collect similar measures on *de novo* data collected from clinically-diagnosed youth with anxiety, ASD, or comorbid anxiety and ASD to determine how the current findings translate to a clinical population.

The finding of a lack of behavioral differences by anxiety, as well as a lack of differentiation between negative and neutral faces, suggests further investigation into the use of this task in children, as it may not be processed the same way as it is in adults. These findings suggest that the facial expressions in this task might not evoke anxiety or emotion in the same ways are not sensitive or appropriate to do so. Our lab plans to follow up on this result in the full sample to further examine the relationship between dimensional anxiety and these results behaviorally and via neuroimaging.

Overall, this is the first study looking at the interaction of working memory and negative stimuli bias in highly anxious and high autistic trait preadolescence. Previous research has highlighted the importance of looking at these clinical conditions both dimensionally and categorically, and this research aligns with RDoC goals of promoting transdiagnostic investigation into multiple domains. Additionally, the neural plasticity, the increase in emerging psychopathology, and the potential for different developmental trajectories for ASD and anxiety inherent in the pre- to adolescent stage, this age range represents a critical target for investigation. Sample size is a strength of this study, as many fMRI studies have samples of under 30-40. This sample, which had each group with over 48 subjects allows us to have more confidence in our results, particularly null results.

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