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Evoked Responses to Affective Stimuli as a Marker for Reward System Dysfunction in Adolescents with Autism Spectrum Disorder (ASD)

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Evoked Responses to Affective Stimuli as a Marker for Reward System Dysfunction in Adolescents with Autism Spectrum Disorder (ASD)

by

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Abstract

The core symptoms of autism spectrum disorder (ASD) may be related to atypical engagement of the brain's reward system. We investigated whether visual reinforcers, images depicting restricted interests, are processed abnormally in ASD, as a marker for reward system dysfunction. We collected electroencephalography (EEG) while 20 ASD and 20 typically developing (TD) control participants, aged 14-20, performed a visual target detection task. We evaluated differences in the late positive potential (LPP), a marker for emotional processing, as well as trial-to-trial variability in the visual P1 response, which may indicate 'noisier' processing of visual reinforcers. We found greater LPP amplitude for high- and low-interest images, relative to neutral, with no significant group difference. In contrast, for the P1, we found overall greater amplitude and amplitude-variability in the ASD group that did not differentiate between conditions. This study provides new insight into processing of visual reinforcers in ASD.

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List of Abbreviations

ABA- Applied Behavior Analysis

ADOS- Autism Diagnostic Observation Schedule

ANOVA-Analysis of Variance

AS- Asperger's Syndrome

ASD- Autism Spectrum Disorder

BOLD- Blood-Oxygen-Level Dependent

CSD- Current Source Density

EEG-Electroencephalography

ERP – Event Related Potential

fMRI- Functional Magnetic Resonance Imaging

IAPS- International Affective Picture System

ICA – Independent Component Analysis

LPP- Late Positive Potential

SEM- Standard Error Mean

SPSS- Statistical Package for the Social Sciences

SRS- Social Responsiveness Scale

VEPs- Visual Evoked Potentials

WASI- Wechsler Abbreviated Scale of Intelligence

Chapter 1: Introduction

1.1 Overview

Autism spectrum disorder (ASD) is a multi-faceted neurodevelopmental disorder characterized by impaired communication, difficulties in social interactions, repetitive motor behaviors and restricted interests (DSM-V). In addition to these primary deficits, ASD is comprised of secondary symptoms such as atypical sensory and motor functioning (Larson & Mostofsky, 2008), reduced adaptability to sudden environmental changes (Nicpon, Doobay, & Assouline, 2010) and general cognitive impairments affecting executive function (Hill, 2004) and attention (Allen & Courchesne, 2001). The presence of comorbid conditions such as anxiety disorders, attention deficit hyperactivity disorder (ADHD), depression and intellectual disabilities are also common among people with ASD (Leyfer et al., 2006; Simonoff et al., 2008; Matson & Shoemaker, 2009). In 2014, the prevalence of ASD was estimated to affect 1 in 68 children, with males five times more likely than females to be diagnosed (CDC, 2014). A major challenge of studying ASD is the heterogeneous nature of the disorder; ASD is defined along a spectrum due to the vast range in symptomatic severity.

Some theories of ASD posit abnormalities in the function of the brain's reward system (Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2012). It has further been suggested that brain responses to sensory stimuli are noisier in ASD (Dinstein et al., 2012; Dawson et al., 1998), which we hypothesize may affect the neural representation of stimulus value, with consequences for neural processing of rewards. The project outlined in this thesis will investigate both affective processing of, and trial-to-trial variability in evoked responses to, visually presented reinforcers. In the background I will review

theories of ASD relevant to this thesis, the brain's reward system and evidence for abnormal functioning of the reward system in ASD, differences in visual processing as well as provide an overview of electroencephalography (EEG) for measurement of visual evoked potentials.

1.2 Links between the social reward and imbalance theories of ASD

The underlying etiology of ASD symptoms has not yet been identified, however several theories have been proposed (as examples, see Baron-Cohen, 2002,Baron-Cohen, Leslie, & Frith, 1985; Rubenstein and Merzenich, 2003; Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2012; McPartland et al., 2012). For the purpose of this thesis we will focus on two recently developed theories of ASD: the social motivation theory, and imbalance in synaptic excitation/inhibition in neural systems.

The social-reward, or social motivation, theory of ASD suggests that reduced orienting towards social stimuli may reflect disruptions in the brain's ability to designate reward to social stimuli (Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2012; McPartland et al., 2012). This theory is well supported by evidence showing that individuals with ASD tend to show a diminished attentional response to social stimuli as shown by difficulties establishing joint attention and deficits in neural responses to social rewards (Dawson et al., 2004; Scott Van-Zeeland et., 2010). Importantly, several lines of evidence suggest that potential abnormalities in the brain's reward system extend beyond social processing. For example, in addition to finding social stimuli to be relatively less rewarding than TD controls, individuals with ASD have intense, idiosyncratic interests which are much more rewarding than hobbies/interests are for TD controls (G. S. Dichter, Damiano, & Allen,

2012). Additionally, studies on neural processing of reward have revealed abnormalities in response to various kinds of non-social reinforcers (e.g., monetary reward) with some studies reporting hyper-responsiveness to circumscribed interests (Scott- Van Zeeland et al. 2010; Cascio et al., 2014).

Another suggested neural mechanism leading to ASD symptoms, proposed by Rubenstein and Merzenich (2003), is a global impairment in brain functioning. Specifically, they state that increased levels of excitation or a reduction in inhibition may lead to impairments in sensory, cognitive, social and emotional systems. Disproportionately high levels of excitation may contribute to the high levels of clinically apparent seizures found in individuals with ASD, due to unstable neural networks (Rubenstein & Merzenich, 2003). This may also lead to more variable brain responses to stimuli in general, because the balance of excitation and inhibition is necessary to regulate the timing and amplitude of neural response. Rubenstein & Merzenich (2003) state that ASD should be looked at from the perspective of generally defective neural systems in order to further understand the complexities of the disorder.

In this thesis we will explore a link between these two theories and test the hypothesis that more variable neural responses to visual stimuli may relate to atypical processing of visual reinforcers.

1.3 The Reward System

The reward system refers to a set of brain structures that are activated by a rewarding or reinforcing stimulus (Thorndike, 1933). The brain regions involved in the anticipation and receipt of reward include the substantia nigra (SN) and ventral tegmental

area (VTA), which direct dopaminergic projections to nucleus accumbens (NAc), the striatum and frontal cortex (Kandel *et al.,* 2000). Rewarding or reinforcing stimuli modulate action-based associative learning (Thorndike, 1933). Reward learning is a process in which a particular behavior is directly strengthened or weakened by the consequence that follows it. That is, the co-occurrence of a particular stimulus and reward will increase the associative strength between these stimuli over time (Rescorla & Wagner, 1972)**.**

1.4 Visual reinforcers

Neuroimaging studies investigating reward circuitry often use visual reinforcers (e.g., pictures of an object a person likes), as they are simple to use in a laboratory setting. The viewing of visual stimuli does not require movement; therefore visual stimuli are also well suited to EEG experiments where artifacts can be created in the context of movement. Previous studies have indicated that visual stimuli can act as effective rewards. Blatter and Schultz (2006) investigated whether different types of visual stimuli (still or moving images) had a rewarding effect during an operant task. The results indicated that both types of visual stimuli elicited approach behavior, suggesting that visual stimuli can act as positive reinforcers. Knutson et al. (2000) also used visual stimuli to invoke anticipation of monetary reward, punishment or no consequences during a reaction time task. The results showed significant activation in striatal and mesial forebrain regions in trials consisting of monetary rewards and punishments. Hence, their study shows that visual stimuli (i.e. pictures of money, not actual money) can be used to activate brain structures involved in the reward system (Knutson *et al.,* 2000). A functional magnetic resonance imaging (fMRI) study by Lebreton et al. (2009) had participants rate either the pleasantness (explicit task) or age (distractive task) of different types of visual stimuli (faces, houses or paintings).

Their findings revealed activation in regions associated with reward system processing, such as the ventromedial prefrontal cortex as well as the ventral striatum, when participants viewed stimuli they rated as more pleasant. Further, this finding was independent of the task (explicit rating or pleasantness vs. rating of age). This study further supports the idea that visual stimuli can elicit valuation signals in the brain automatically and act as effective rewards. Visual stimuli are an excellent choice for reinforcers in ASD specifically, as they can assist researchers and educators in communicating with children who may be non-verbal or struggle to comprehend language (Rao & Gagie, 2006).Visual stimuli are encouraged as learning tools for children with ASD as they attract and engage attention (Rao & Gagie, 2006).

1.5 Evidence for abnormal reward system function in ASD

How can we account for reduced social motivation in the context of abnormal reward system functioning?

It has been suggested that the core symptoms of ASD may be explained through abnormal functioning of the reward system (G. Dichter & Adolphs, 2012). Social motivational models of ASD propose that deficits in social interactions are related to reduced social motivation, which presents as a lack of attending to social stimuli (Chevallier et al., 2012). Previous literature exploring social interaction impairments in ASD have revealed widespread deficits ranging from atypical face processing, difficulties establishing joint attention and lack of responsiveness to social rewards (Dawson et al., 2012; Chevallier *et al.,* 2012). Dawson et al. (1998) proposed that because social stimuli (e.g., facial expressions) are complex and variable, children with ASD might have

difficulties processing these stimuli and therefore will not naturally pursue them. On the other hand, typically developing children thrive on social stimuli as shown, for example, by increased pupillary dilation responses to happy faces and direct gaze (Sepeta et al., 2012). An ERP study by Webb et al. (2006) explored face processing in children with ASD compared to both typically developing children as well as a cohort of children with developmental delays while viewing social (faces) and non-social (object) stimuli. The study examined the N170 potential, which is associated with the neural processing of facial stimuli. Their findings showed that children with ASD showed an atypical N170 response with significantly faster responses to object stimuli compared to facial stimuli. Riby and Hancock (2009) conducted an eye-tracking study to investigate whether ASD and TD participants vary in visual attention to different types of social stimuli: scrambled pictures containing faces and pictures of scenes with embedded faces. Their findings indicated that ASD participants showed shorter face fixation compared to typically developing controls across both picture types. Other research has shown various aspects of face processing to be abnormal in ASD, including memory for facial identity, gaze processing and recognition of facial expressions. (Golarai, Grill-Spector, & Reiss, 2006; Riby & Hancock, 2009).

Social rules of engagement are acquired through direct observation and imitation (Scott-Van Zeeland et al., 2010). Early onset of social impairments in ASD has vast consequences that deprive children of these social engagement experiences, which may lead to lifelong delays in social cognition development (Chevallier et al., 2012). Presently, reduced attending to social stimuli at an early age has been used as a predictor of ASD diagnoses later in life (Dawson et al., 2004). Retrospective studies of 1st birthday home videotapes revealed that 1 year-old infants later diagnosed with ASD oriented less to people

and failed at establishing joint attention when compared to age-matched typically developing controls (Osterling & Dawson, 1994; Osterling, Dawson, & Munson, 2002). The lack of social motivation in ASD has been attributed to decreased feelings of pleasure experienced during social engagements (G. Dichter & Adolphs, 2012). Therefore, reduced orienting to social stimuli in ASD may be related to reduced motivation as well as reward value (Chevallier et al., 2012).

Is there evidence for a more widespread reward system deficit?

An important question is whether this motivational deficit is specific to the processing of social stimuli or a widespread deficit affecting all stimulus-reward associations (Lin, Rangel, & Adolphs, 2012). Neuroimaging studies have looked at both social and non-social reward processing in ASD (G. S. Dichter et al., 2012; Scott-Van Zeeland et al., 2010). Scott-Van Zeeland et al. (2010) found that children with ASD exhibited general impairments in reward learning to both social and monetary stimuli. However, the neural responses measured with fMRI showed a more pronounced reduction in response to social stimuli. Dawson et al. (1998) compared children with ASD to children with Down syndrome as well as typically developing controls in their ability to respond to social stimuli and non-social stimuli. The results indicated that children with ASD failed to orient to both social and non-social stimuli compared to the two other groups, but the failure was more pronounced for social stimuli (Dawson, Meltzoff, Osterling, Rinaldi, & Brown, 1998). These results suggest that both social and non-social stimuli are affected, but social stimuli especially may be less rewarding for children with ASD compared to typically developing (TD) children, and those with Down's syndrome. Perhaps focusing our understanding of ASD from the perspective of widespread rather than socially-related

atypical reward processing will help us further understand the complexities underlying this disorder.

Is it possible to account for restricted interests in the context of abnormal reward system functioning?

Children with ASD often have idiosyncratic interests that are highly engaging (G. Dichter & Adolphs, 2012). These restricted interests can manifest as typical age-appropriate hobbies (e.g. an expert on a local sports team) or obscure hobbies (e.g. an expert on different models of fans). Autobiographical reports from high-functioning individuals with ASD describe restricted interests with a positive connotation (Mercier, Mottron, & Belleville, 2000).

There are various theories to support the claim that restricted interests provide a source of pleasure and reward for individuals with ASD. Restricted interests have been proposed as a coping mechanism for individuals with ASD, in that the expression of a particular interest may provide comfort and relief in the presence of a stressor (Klin et al., 2007). The perceptual reinforcement hypothesis proposes that children with ASD participate in restricted interests as they have learned through interaction that it provides a source of intrinsic reinforcement (Lovaas, Newsom, & Hickman, 1987). Lastly, the arousal theory states that children with ASD engage in restricted interests or repetitive motor behaviours as their sensory input may be over or under-aroused (Kern et al., 1982)

Recent work has found greater blood-oxygen-level dependent (BOLD) response in both the left anterior insula and anterior cingulate cortex in ASD participants as compared to controls while viewing one's own personalized interests versus others interests (Cascio

et al., 2014). Sasson and Touchstone (2014) compared visual attention shifts in children with ASD and typically developing children while viewing social stimuli paired with object stimuli either related or unrelated to their circumscribed interests (CI). The two groups were found to be similar in their visual attention to social stimuli paired with objects unrelated to their CI (N. Sasson & Touchstone, 2014). However, ASD children showed a large reduction in visual attention to social stimuli when paired with objects related to their CI (N. Sasson & Touchstone, 2014). The authors propose that social attention in ASD may be modulated by the salience of the competing object stimuli. Another neuroimaging study by Dichter et al. (2012) showed decreased nucleus accumbens activation in response to monetary rewards in ASD participants. However, an intact response was observed when presented with a broad category of autism-relevant objects (trains and gadgets). This study proposes that ASD is characterized by reduced activation in reward circuitry in response to monetary rewards but an intact response to autism-relevant object images (G. S. Dichter et al., 2012). Taken together, neuroimaging findings suggest that restricted interests may be attributed to functional abnormalities in the brain's reward system (Joseph et al., 2013; Dichter and Adolphs, 2012).

Why this specific pattern of object CIs combined with social aversion?

Previous literature suggests that ASD may be better interpreted as a disorder arising from generalized impairments as opposed to specific deficits (Milne, 2011). Specifically, ASD has been proposed as a general disorder of neural processing, in which neural responses might be more "noisy" or variable (Dinstein et al., 2012). These "noisier" neural responses may account for the sensory sensitivities often present in ASD. Perhaps noisier sensory processing can account for the social deficits in ASD due to the inherent

unpredictability of social stimuli, which are by nature complex and variable (Dawson et al., 1998). Specifically, atypical sensory processing may distort one's perception of the environment in ASD. The complexity and unpredictability of social stimuli may explain why children with ASD often do not naturally pursue them, but instead engage in repetitive circumscribed interests which generate more predictable neural responses (Dinstein et al., 2012).

1.6 Atypical sensory perception in ASD may contribute to abnormal reward processing

In addition to the core diagnostic features of ASD, atypical sensory perception is recognized as part of the ASD phenotype (Milne, Scope, Pascalis, Buckley, & Makeig, 2009). As rewards in the environment are perceived through sensory systems, abnormalities in sensory processing could have consequences for neural representations of reward value. Previous studies suggest that in ASD there is greater trial-to-trial variability in evoked visual responses. Dinstein et al. (2010) reported that individuals with ASD had more variable fMRI responses in both motor and visual brain regions during the execution and viewing of hand movements. Further support by Milne (2011) showed more variable EEG responses in ASD participants during the viewing of high-frequency Gabor patches. Lastly, Dinstein et al.(2012) investigated evoked cortical responses using fMRI in auditory, visual and somatosensory systems in individuals with ASD compared to typically developing controls. The results indicated that within-subject trial-by-trial response variability was significantly larger for individuals with ASD.

Visual perception differences in individuals with ASD have also been found in the balance between local and global processing (Flevaris & Murray, 2014). Previous studies have revealed that individuals with ASD exhibit enhanced "local" processing (increased focus on detail) and reduced "global" processing (viewing an overall image as a whole) when compared to typically developing controls (Dakin & Frith, 2005). Simply, individuals with ASD show a processing bias for local detail and fail to integrate elements to form "the big picture" (Dakin and Frith, 2005). Overall, the underlying neural mechanisms causing these deficits in global processing are unknown.

1.7 EEG and ERPs

Electroencephalography (EEG) is a non-invasive and relatively inexpensive technique that detects electrical activity of large, synchronously firing populations of neurons using small, flat electrodes attached to the scalp. Specifically, the EEG detects post-synaptic potentials generated by synchronously firing populations of neurons. EEG has high temporal resolution and can be used to assess neurological functioning during, or in absence of, overt task performance. EEG has relatively poor spatial resolution but is well suited to measuring signals from the cortical surface. EEG primarily measures neurophysiological changes related to postsynaptic activity in the neocortex.

EEG researchers often measure event-related potentials (ERPs), which are small electrical discharges generated in response to a specific event or stimulus (Blackwood & Muir, 1990). Specifically, ERPs are averaged EEG responses that are time-locked to a particular stimulus or event. ERP experimental designs allow researchers to investigate sensory and cognitive processing with millisecond precision (Light et al., 2010). For this

study we have focused on two ERPs associated with visual processing: P1 and LPP. The use of ERPs allows us to investigate aspects such as amplitude, latency and trial-to-trial variability. At the time of a peak in the ERP both the amplitude and latency can be measured and contribute different information. Amplitude measures reflect synchronous neural activity in the brain region were the potential originates, where more or less synchronous activity results in a larger or smaller (respectively) ERP amplitude. Latency measures reflect cortical information processing, whereby a longer latency indicates delayed processing of a particular stimulus or event. As the ERP component approaches its peak latency, more and more post-synaptic potentials occur spontaneously, until the peak is reached. After the peak, a decrease in synchronous activity occurs and the peak levels off. Therefore, latency measures the time point at which the highest level of synchronous activity is reached.

P1 Component

Previous studies investigating the processing of visual stimuli have revealed two main components which are categorized as visual evoked potentials (VEPs): C1 and P1 (Fu, Fedota, Greenwood, & Parasuraman, 2010). Both components are evoked within the visual cortices of the brain. The first visual cortical response, C1 originates in the striate cortex and is insensitive to attention (Clark, Fan, & Hillyard, 1994). The earliest attentional response to visual stimuli is found in the later visual P1 component, which originates in the extrastriate cortex (Clark et al., 1994). The P1 component is a positive-going deflection that peaks between 100ms and 150ms after stimulus onset (Smith, Cacioppo, Larsen, & Chartrand, 2003). Specifically, the P1 deflection is the result of neural activity in the extrastriate cortex. As attention is allocated to visual stimuli, extrastriate neurons are

recruited to process the stimulus and the P1 amplitude increases (Smith et al., 2003). Therefore, the P1 magnitude or latency is influenced by attentional response to the onset of visual stimuli. For this study we have focused on the P1 component, in order to replicate Milne et al. (2011), which solely examined P1 amplitude and latency in response to a high spatial frequency Gabor patch stimulus – and extend their findings to more complex visual stimuli.

LPP Component

An important feature observed in ERPs evoked by emotional stimuli is the late positive potential (LPP), which is depicted by an amplitude increase for pleasant and unpleasant stimuli relative to neutral stimuli (Liu, Huang, McGinnis-Deweese, Keil, & Ding, 2012). In affective picture viewing, the LPP starts around 300-400ms after picture onset and is sustained for the duration of image presentation (Schupp et al., 2000). Specifically, the LPP is modulated by the emotional intensity of a stimulus. Previous studies have shown that LPP amplitude can vary based on the affective valence (pleasant-unpleasant) as well as arousal levels of the picture content (Schupp et al., 2009; Liu et al., 2012). Weinberg & Hajcak (2010) found arousing neutral pictures (e.g., images including people) generated a larger LPP compared to less arousing neutral pictures (e.g., images without people). Previous studies have indicated that the LPP elicited while viewing emotional stimuli compared to neutral stimuli is a stable, replicable finding (Pastor et al., 2008). Codispoti, Ferrari, & Bradley (2006) found that affective differentiation in the LPP does not change despite multiple repetitions of the same pleasant, neutral, and unpleasant stimuli. Overall, the LPP is a stable electrophysiological marker of emotional perception in humans (Liu et al., 2012).

1.8 Experimental Rationale

Several lines of evidence, including social deficits and circumscribed interests, suggest abnormalities in reward system functioning in ASD. The goal for this project was to investigate whether visual reinforcers are processed abnormally in ASD, in terms of both signal amplitude/latency and trial-to-trial variability, as markers for reward system dysfunction. To explore potential abnormalities in the way that images of rewarding stimuli are processed in ASD, we collected EEG from 20 individuals with ASD and 20 typically developing (TD) control participants, aged 14-20. Participants completed a visual target detection task in which they were presented with a set of images along with intermittent targets, to which they responded to with a button press. The task was chosen to replicate previous findings of greater intra-individual variability in visual evoked responses (Milne, 2011), while introducing variation in the value of presented visual stimuli. We selected images that were related to each participant's interests to ensure that our stimuli could act as visual reinforcers for every participant. We did not use social stimuli (attractive faces) or money as visual reinforcers because although these stimuli are known to engage the reward system in TD participants (Bray & O'Doherty, 2007; Knutson et al., 2000), they may not engage a similar response in participants with ASD (Scott-Van Zeeland 2010; Dichter et al. 2012). The image sets presented to each participant were customized to include images of things that person likes and dislikes. In this way each image set included high-interest and low-interest images. Analyses focused on amplitude and variability in P1 responses, and amplitude of the LPP, in participants with ASD relative to TD controls.

1.9 Hypotheses

Group differences in ERP amplitude

1.We expect the late positive potential (LPP) amplitude to increase for high- and low-interest images relative to neutral images across both groups. However, we anticipate greater amplitude for high-interest pictures in ASD participants as compared to TD controls.

Group differences in ERP intra-individual variability

2. We expect to reproduce findings from Milne et al. (2009 and 2011) showing increased intra-individual variability in P1 response to the Gabor patch in ASD, and extend this finding to images of complex scenes.

3. We expect intra-individual variability in P1 to be modulated by image value, with lower variability in both groups for high and low, relative to neutral images.

Chapter 2: Methods

2.1 Participants

We collected EEG data from 20 individuals with ASD (4 female) and 20 typically developing (TD) control participants (4 female), aged 14-20. Participants were matched by gender, age and non-verbal IQ. Non-verbal IQ scores were not significantly different between groups *Table 1*. Participants were recruited through clinical services, schools, as well as posters placed at University campuses, coffee shops, community centers and local libraries. ASD participants with a history of traumatic brain injuries or seizure disorders were excluded from this study. TD participants with a history of psychiatric or neurological disorders were excluded from this study. All participants were right-handed, with normal or corrected-to-normal vision. Participants under 18 years of age provided assent, and written consent was obtained from a parent or guardian. For participants over 18 years of age, written consent was obtained.

The Autism Diagnostic Observation Schedule (ADOS-2) was administered to assess and confirm participant's diagnosis. 17 ASD participants included in this study exceeded clinical cutoffs for ASD diagnosis. One ASD participant was removed from our sample, as he did not meet clinical cutoffs on the ADOS. Finally, we do not yet have ADOS scores for two participants due to timing constraints. We have included them in our sample, as results remained the same with the inclusion or exclusion of these participants. Therefore, a total of 19 ASD participants were included in this study. In addition, the Social Responsiveness Scale (SRS-2) was administered to obtain scores for social impairments, as well as quantify symptom severity in both ASD and TD participants. Lastly, intellectual ability was

measured with the Wechsler Abbreviated Scale of Intelligence (WASI-2). Participant demographics are shown in *Table 1*. All procedures complied with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2) as approved by the University of Calgary Research Ethics Board.

2.2 Stimuli

During the task used in this study, participants viewed a series of images. The image stimuli presented included a Gabor patch, Target (zebra picture), High-interest images, Low-interest images and Neutral images *(Figure 1)*. In total there were 100 Gabor patch trials, 50 Target image trials, 100 High-interest image trials, 100 Low-interest image trials and 100 Neutral image trials. At a viewing distance of 80cm the stimuli subtended 11.60° x 7.75° of visual angle. Stimuli were centrally presented at a size of 600 x400 pixels on a 24-inch monitor (HP lp2475w), which refreshed at 59 Hz.

The Gabor patch and Target image matched those used by Milne et al. (2009). The Gabor patch was created using MATLAB (The Mathworks, Inc.), and presented in a diagonal (45°) orientation with a spatial frequency of 8 cycles/degree.

Neutral images were selected from the International Affective Picture System (IAPS) database (Lang, Bradley, & Cuthbert, 1999). These images were kept the same across all participants and were selected based on database ratings of valence and arousal. The ratings for the IAPS images were obtained from a group of 100 college students at the University of Florida (approximately 1:1 ratio of males to females). Images were scored on a 9-point rating scale across three separate dimensions: arousal, dominance and valence; 1 indicates a low rating on each dimension (i.e., low arousal, low dominance and low

pleasure) whereas a 9 indicates a high rating on each dimension (i.e., high arousal, high dominance and high pleasure). Images that were neutrally rated (4.5-5) on measures of arousal and valence were selected for this study.

The high and low-interest image sets for each participant were tailored to include his or her likes and dislikes. Before participants (ASD and TD) came in for the study, they were asked to submit a list of items they like and dislike. We asked for particular items that can be easily pictured, such as: favourite TV shows, animals, sports, foods they dislike, movies they dislike etc. Based on these lists we searched for pictures online and generated a picture inventory customized to include both high and low interest images for each participant.

To ensure that there was minimal variation in low-level stimulus properties across images, the SHINE toolbox for MATLAB (http://www.mapageweb.umontreal.ca/gosselif/SHINE/) was used to match low-level properties of the images (i.e. mean luminance). An X-Rite photometer (Danaher Company., Grand Rapids, Michigan, U.S.A.) was used to measure mean luminance and SD luminance for a subset of the stimuli to ensure that SHINE toolbox matching was successful. The SHINE program was specified to output images with a mean luminance of 127d/m^2 and standard deviation of 30cd/m^2. The mean luminance and SD luminance of images were then verified with the X-Rite photometer. The photometer was placed on the desktop monitor and luminance measurements were taken from the centre of each image. This validation check was completed on a random subset of 10 images per participant to verify the SHINE toolbox matching was successful.

2.3 Image Validation

As we created customized image sets of high- and low-interest images based on reported likes and dislikes, we included a measure to capture individual differences in the relative liking of our stimuli as well as to ensure the high- and low-interest categories we defined were appropriate for each subject. After the task, participants viewed pairs of images from a random subset of 108 stimuli and indicated which one they preferred to ensure that high-interest images were in fact perceived as interesting compared to low-interest images. This subset of stimuli included 36 high-interest images, 36 low-interest images and 36 neutral images. In total, 54 trials of 108 paired stimuli were presented. Participants were asked to select an image out of the pair based on the question "What do you like more?" Specifically, high-interest images were paired with neutral images, low-interest images were paired with neutral images and high-interest images were paired with low-interest images. Paired choice data were imported into SPSS, and analyzed using one and two-sample t-tests. One-sample t-tests were performed on each of the three pairings against a chance level of 50% for each group. Following this, choice behaviour between the diagnostic groups was compared with a set of two-sample t-tests.

We also asked for an explicit rating of 10 high and 10 low-interest stimuli from the same subset of images by asking participants "How pleasant do you find this picture from 1 (very unpleasant) to 7 (very pleasant)?". Parametric data were imported into SPSS, and analyzed using a repeated measures ANOVA with picture type (High- and Low interest) as a within subject factor and group as a between subjects factor. This analysis was followed by post-hoc paired t-tests.

2.4 Procedure

Prior to testing, each participant performed a practice run to familiarize him or herself with the task. The practice run included a random set of images (2 target images and 8 non-target images) that were kept the same across all participants and ran for approximately 30 seconds. The actual task was structured as two runs of 9 minutes each. A trial involved centrally presenting one image for 500ms. Participants responded only to the Target image, and were instructed to press a button as quickly as possible whenever they saw the Target image. A jittered intertrial interval (ITI) was generated randomly between 500 and 1000ms following each stimulus. A white fixation cross measuring (0.2° by 0.2°) remained in the center of the screen for the duration of the task. Participants were asked to maintain fixation and limit their blink frequency while completing the task. In total, the run time was approximately 18 minutes or 9 minutes per run. A visual representation of the task can be seen in *Figure 2*.

2.5 Data Recording and Pre-Processing

Participants were seated in an electrically shielded, soundproof chamber during EEG acquisition. 64 channel EEG data was continuously recorded with an EasyCap configured according to the 10/20 positioning system, referenced to Cz using the Brain Vision actiCHamp system (Brain Vision LLC). Impedance levels were kept at under 17kOhms throughout the duration of the recording. During data pre-processing, data was band-passed filtered at 0.1-55Hz, digitized at a 500Hz-sampling rate and then re-referenced to a common average. Prior to re-referencing, data were visually inspected to determine whether the interpolation of noisy channels was required. Noisy channels were then

removed from the data prior to re-referencing so as to not introduce excessive noise into the common average. The continuous data were then segmented into 1200ms epochs with a 200ms pre-stimulus baseline to 1000ms post-stimulus onset. These epochs were then visually inspected and noisy epochs were removed from the dataset. Following this, we performed noise removal using independent component analysis (ICA) on the epoched data using EEGLAB software (Delorme and Makeig, 2004, http://www.sccn.ucsd.edu/eeglab). Components consisting of blinks and horizontal eye movements were removed from the dataset. Trials that included stimulus onsets followed by correct responses (i.e.: Target image followed by button press / all other images followed by no button press) were binned according to stimulus type (High, Low, Neutral, Gabor and Target). Therefore, any false alarms or button responses to non-targets were not analyzed further.

2.6 LPP analysis

LPP analysis was conducted to determine whether there are group and condition differences in ERP amplitude for High-interest, Low-interest and Neutral images. ERPLAB toolbox (http://erpinfo.org/erplab), a program integrated within the EEGLAB software was used for pre-processing and analyzing LPP data. First, clean epoched EEG data were loaded into EEGLAB and averaged across trials. Following this data were re-referenced to the average of the two mastoid electrodes (TP9 and TP10). Specifically, data were re-referenced to the mean of the mastoid electrodes (ch_REF (TP9+TP10/2)). This second re-referencing step was performed, as commonly in LPP literature, data are converted offline to an average mastoid reference. We then generated a Grand Average ERP for both diagnostic groups. These Grand Averaged ERPs were used to assess mean amplitudes between 400-700ms post-stimulus for each condition (High, Low and Neutral) as well as

electrode sites. Our analyses focused on midline electrode scalp sites: central (Cz), frontal (Fz) and posterior (Pz) (Schupp et al., 2000). Amplitude data were imported into SPSS, and analyzed using a repeated measures ANOVA with condition (High-interest, Low-interest and Neutral) as a within subject factor and group as a between subjects factor. Post-hoc paired t-tests were then performed to compare High- and Low-interest relative to Neutral for each group individually. To ensure that the family-wise error rate was maintained at α=0.05 we used the Bonferroni correction ($\alpha/_{\text{number of comparisons}}$ (0.05/4)= 0.0125). Following this, two sample t-tests were performed to compare conditions (High, Low and Neutral) between diagnostic groups.

2.7 Variability analysis

Variability analysis of the P1 response was conducted to determine whether there are group differences in ERP intra-individual variability. We looked at two measures associated with the P1 response: amplitude and latency. The P1 amplitude was determined by the peak amplitude between 100 and 170ms; P1 latency was determined by the time of the peak relative to stimulus onset (Milne, 2011). Two methods were used by Milne (2011) to measure intra-individual variability associated with the P1: current source density (CSD) and ICA. For this study we chose to use ICA with dipole fitting to measure levels of intra-individual variability. The data used for these analyses were re-referenced to a common average. First, we loaded in each subject's cleaned epoched data containing all conditions into EEGLAB. Components were visualized and the component(s) that contributed most strongly to the P1 response were noted and used in further analyses. Following this, the ICA weightings for each condition were exported for further analyses.

In order to ensure that P1 components were generated from the occipital region, as assumed, spatial components were entered into a dipole source localization. DIPFIT (http://sccn.ucsd.edu/wiki/A08: _DIPFIT) is a plugin in EEGLAB that estimates equivalent dipole locations of independent component scalp maps. Specifically, DIPFIT applies inverse modeling techniques to a spherical head model (co-registered to the MNI brain). For this analysis each subject's cleaned epoched data containing all conditions was loaded into EEGLAB and run through DIPFIT to obtain the location of the symmetric dipole (x talairach, y talairach, z talairach) as well as the residual variance (%), dipole position and dipole moment. These values were then used to determine how the overall dipole fits each condition. Each condition was then run through the DIPFIT protocol (manual co-registration to the standard head model and coarse-grained fitting). Following this we performed interactive fine-grained fitting which allowed us to fit the dipole to the component(s) that contributed most strongly to the P1 response containing all conditions. The fine-grained fitting parameter then generates a residual variance (%) that can be used to determine how well each condition fits the overall dipole. Rejection threshold (RV%) was set to 15% to ensure the best-fitting components were selected for further analyses (Milne, 2011). Output RV% for both diagnostic groups across all conditions (High, Low, Neutral and Gabor) were well below our rejection threshold of 15%, suggesting our model was explaining the majority of the variance as well as consistent dipole fitting across both groups.

For each subject and condition, the mean amplitude and latency, as well as the standard deviation of amplitude and latency, for the P1 independent component were obtained. These data were imported into SPSS, and analyzed using repeated measures

ANOVAs with condition (High, Low, Neutral and Gabor) as a within subject factor and group as a between subjects factor. Following this, sets of two sample t-tests were performed to compare conditions (High, Low, Neutral and Gabor) between diagnostic groups. To ensure that the family-wise error rate was maintained at $\alpha=0.05$ we used the Bonferroni correction ($\alpha/_{\text{number of comparisons}}(0.05/4)= 0.0125$).

Table 1.

Participant Demographics: Our groups were age- and gender-matched. Prior to the task three measures were collected from participants: ADOS-2 (ASD participants only), SRS-2 and WASI-2.

	ASD *N=19* *4 females* *14-20 years old*	*TD* *N=20* *4 females* *14-20 years old*	*t- and p-values*
ADOS-2			
Mean	13		
SD	3.80		
Range	7-18		
SRS-2 SCORE			
Mean	74.93	56.29	t(37)>1,p=0.000
SD	6.29	2.36	
Range	66-87	53-60	
WASI-2 SCORE			
Mean	104.1	112.7	
SD	20.35	14.16	t(37)<1, p=0.203
Range	63-132	92-150	

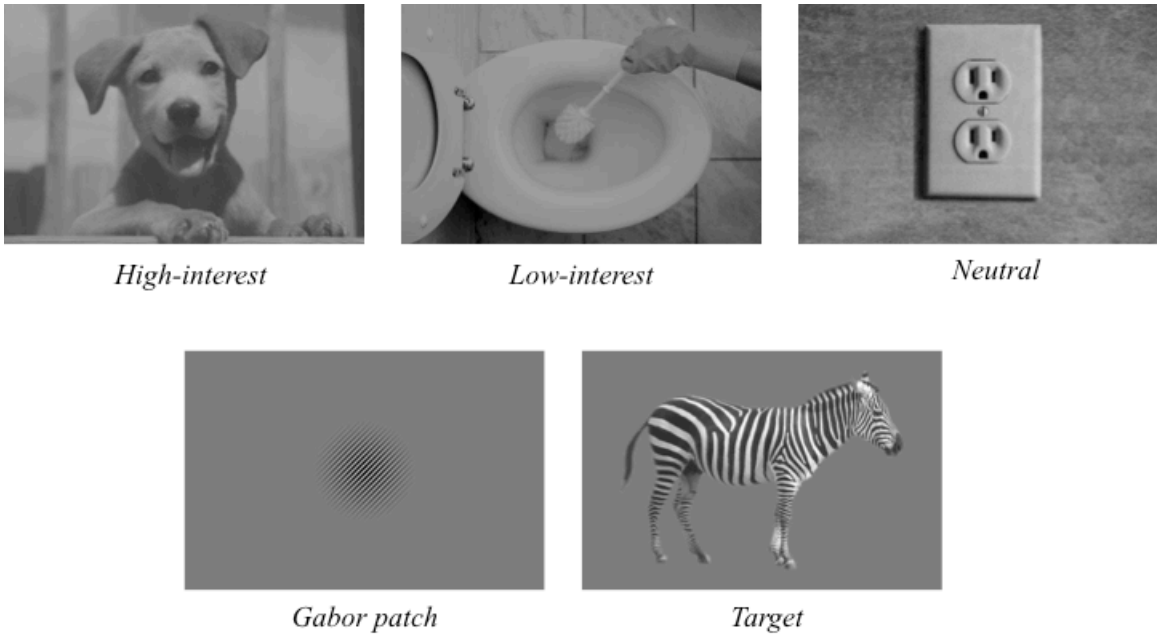

Figure 1. Visual representation of stimuli used in this study

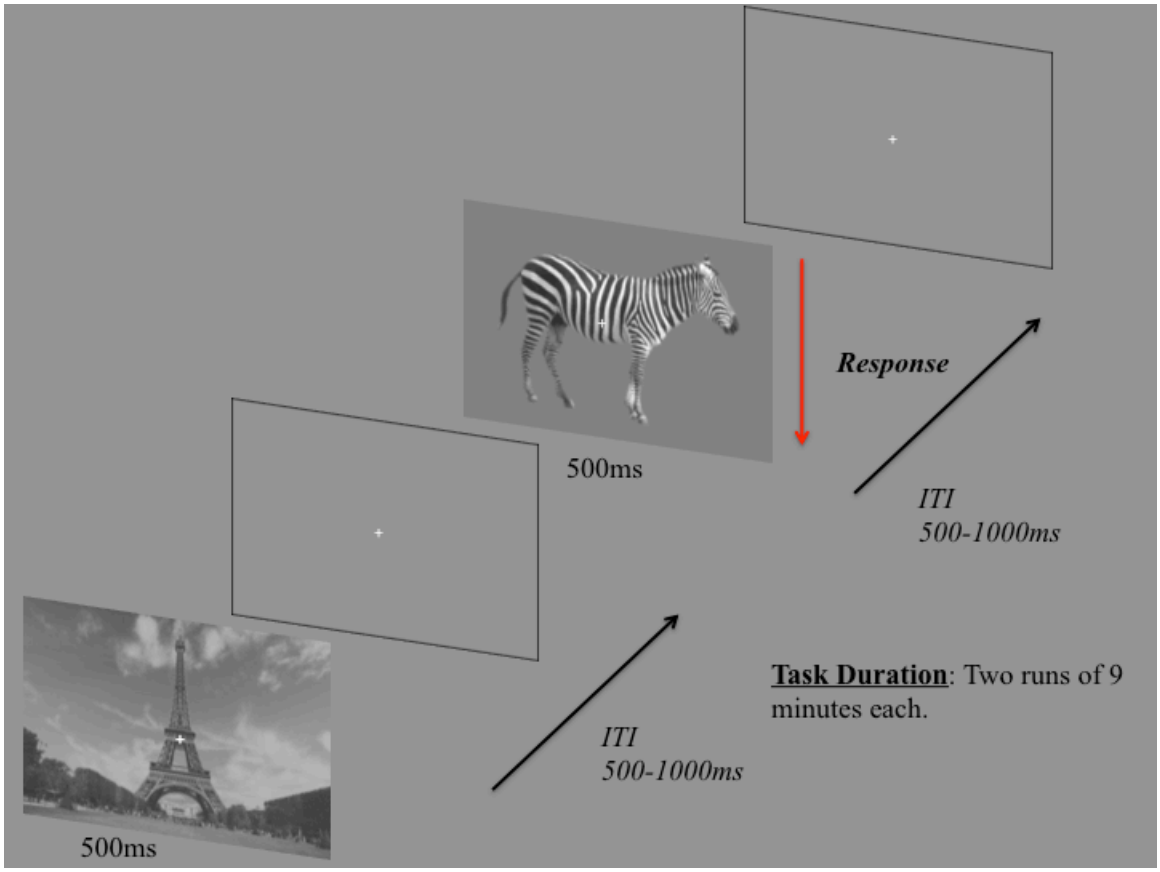

Figure 2. Visual representation of the task. Our task was structured as two runs of 9 minutes each. Images were centrally presented for 500ms. A white fixation cross remained in the center of the screen for the duration of the task. Participants responded only to the Target image (picture of zebra).

Chapter 3: Results

3.1 Reaction Times, Target Detection Accuracy and Epoch Comparisons

Two-sample t-tests were performed to compare reaction times to the Target image between diagnostic groups. We found no significant difference between diagnostic groups for reaction times (*ASD mean= 531.2, SD=62.49, TD mean= 528.9, SD= 58.71);* t(37)= *-0.321,*p=0.821.Two-sample t-tests were performed to compare target detection accuracy between diagnostic groups *(ASD mean target accuracy = 88.8%, TD mean target accuracy= 89.5%),* t(37)= *-0.328,* p=0.745. We found no significant difference between diagnostic groups for target detection accuracy. To ensure variability effects are not related to differences in epoch numbers across conditions and between diagnostic groups, two-sample t-tests were performed which revealed no significant differences in epoch numbers between groups *Table 2*.

Table 2.

Mean and SD values for number of epochs across all 4 conditions. Rightmost column shows results of two-sample t-tests comparing epoch numbers between groups.

	ASD	TD	ASD vs. TD
High	*mean= 178.82, SD=10.87*	*mean=182.13, SD= 9.71*	t(37)= -0.918, p=0.813
Low	*mean= 177.59, SD=8.40*	*mean=179.40, SD= 11.09*	t(37)= -0.525, p=0.536
Neutral	*mean= 178.24, SD=10.44*	*mean=180.20, SD= 11.19*	t(37)= -0.514, p=0.546
Gabor	*mean= 179.29, SD=12.51*	*mean=180.60, SD= 11.53*	t(37)= -0.306, p=0.716

3.2 Behavioural Results

In this study we created customized image sets of high- and low-interest images based on reported likes and dislikes. After the task, participants viewed pairs of images and indicated which image they preferred with a button press; three types of pairs were presented high vs. neutral, high vs. low and low vs. neutral. One-sample planned t-test comparisons were performed on each of the three pairings against a chance level of 50% for each group. All one-sample t-tests performed on each group individually indicated that both diagnostic groups were selecting significantly above chance in the direction that we hypothesized (high > neutral > low) (*Table 3;Figure 3).* Following this, we compared choice behaviour between groups with a set of two-sample t-tests. These indicated no significant differences between diagnostic groups in image preference behaviour *Table 3*.

Table 3.

One-sample t-test results for the three types of pairs against a chance level of 50% for each group. Rightmost column shows results of two-sample t-tests comparing choice behaviour between groups.

	ASD	TD	ASD vs. TD
High> Low	t(18)=64.268,p=0.000	t(19)=57.717,p=0.000	t(37)= 0.381, p=0.706
High> Neutral	t(18)=25.875,p=0.000	t(19)=19.030,p=0.000	t(37)= -0.239, p=0.812
Neutral> Low	t(18)=6.617,p=0.000	t(19)=6.573,p=0.000	t(37)= -0.688, p=0.497

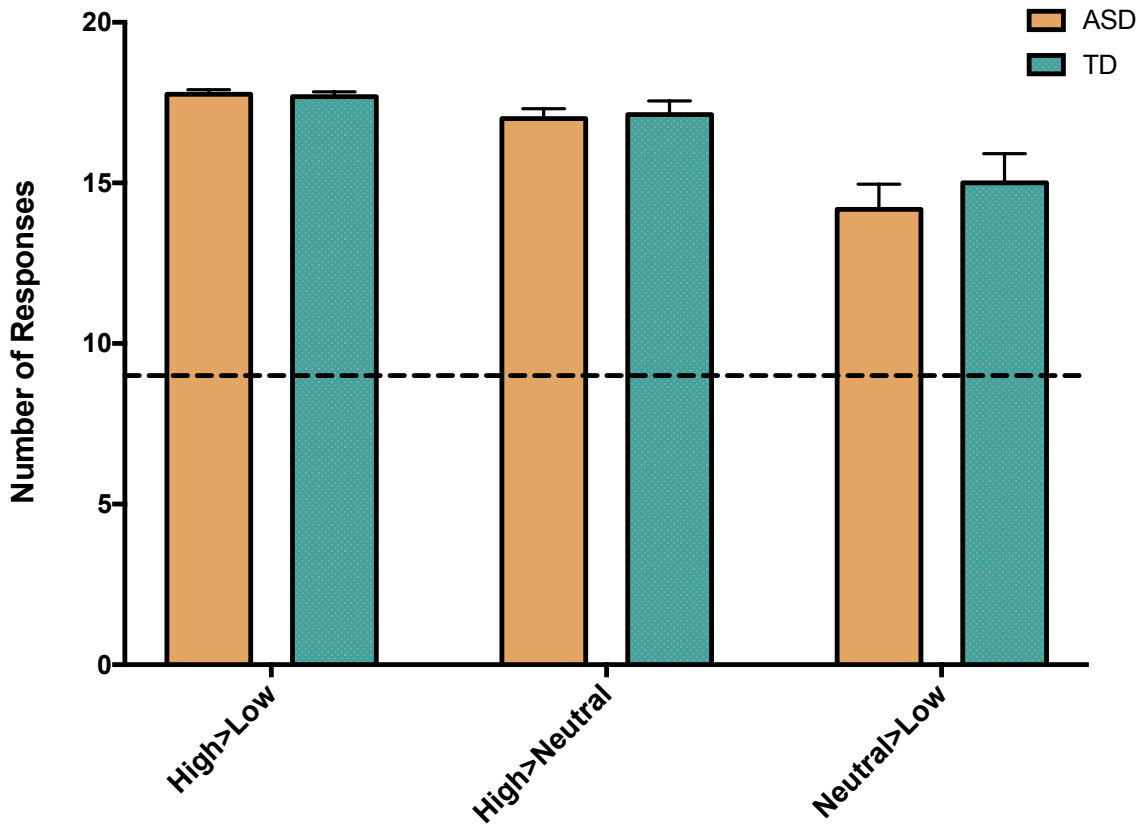

Figure 3. Paired picture choices in ASD and TD participants for the three types of image pairs presented: high vs. low, high vs. neutral and low vs. neutral against a chance level of 50% (indicated by dotted line). Error bars represent standard error of the mean (SEM).

Following the paired picture task, subjects were asked to explicitly rate a subset of 10 high and 10 low-interest images based on the question "How pleasant do you find this picture from 1 (very unpleasant) to 7 (very pleasant)?". Repeated measures ANOVA performed on the parametric rating data showed a significant main effect of picture type [(F(1,37)=372.906, p=0.000)]. Post-hoc paired t-tests indicated that both diagnostic groups rated high-interest images (*ASD mean= 6.31 SD= 0.44, TD mean=6.17, SD=0.54)* significantly higher than low-interest images (*ASD mean= 2.49, SD=0.97, TD mean=2.54, SD= 0.77); t(18)= 12.395, p=0.000 and t(19)= 16.096,p=0.000 for ASD and TD respectively (Figure 4).* We found no significant main effect of diagnostic group [(F(1,37)=0.104, p=0.750)] or picture type by diagnostic group interaction [F(1,37)=0.234,p=0.632)].

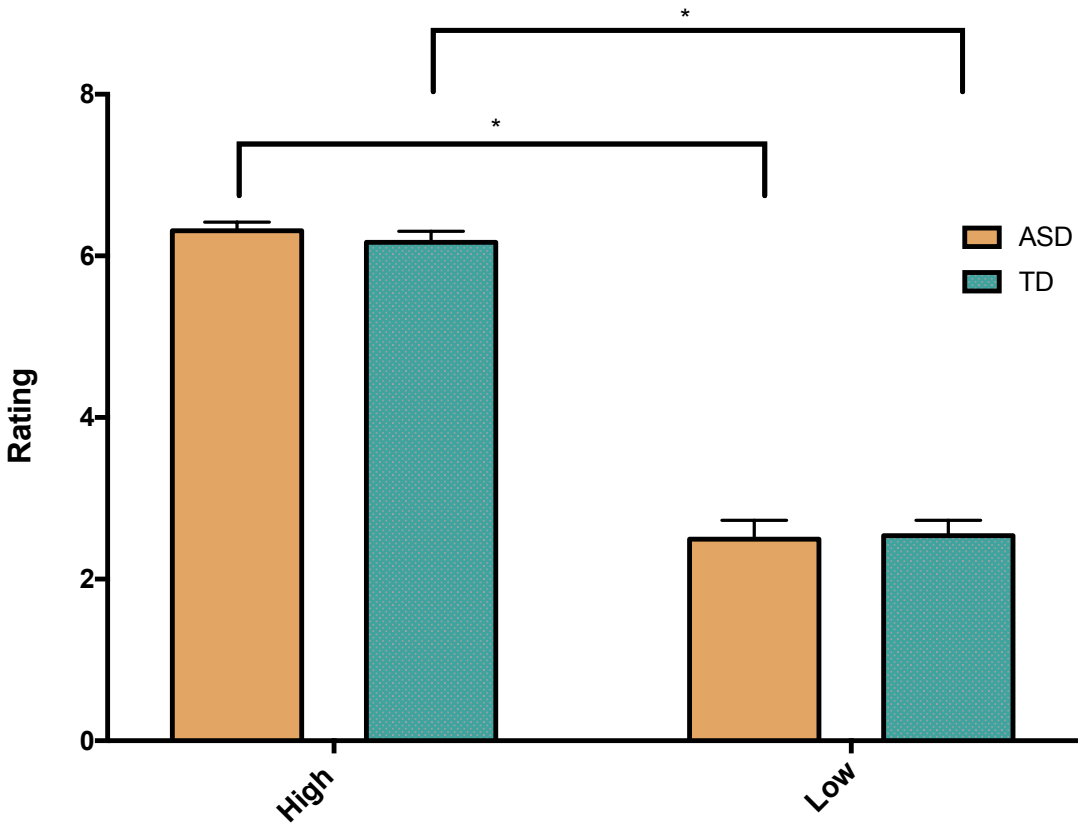

Figure 4. Parametric rating of high- and low-interest images in ASD and TD participants.

** Indicates a significant difference at α=0.05*. Error bars represent SEM.*

3.3 LPP Results

LPP results are based on data from three midline electrodes: Cz, Fz and Pz as these locations showed robust LPP responses *(Figure 5).* LPP amplitudes between 400 and 700ms were calculated and averaged across these midline scalp electrodes. Repeated measures ANOVA showed a significant effect of condition (High, Low and Neutral) [(F (1,115)=35.206, p=0.000)]. This effect was driven by a larger LPP amplitude during the High- and Low-interest, relative to the Neutral condition *(Figure 5).* We did not, however, find a significant main effect of diagnostic group [(F (1,115)=0.136, p=0.713)] or a condition by diagnostic group interaction [(F (1,115)= 2.400,p=0.105)]. Following this, paired t-tests were performed to compare High- and Low-interest relative to Neutral for each group individually. Paired t-tests indicated that for both diagnostic groups, high-interest amplitudes (*ASD mean= -4.72 SD= 5.16, TD mean=-4.00, SD=4.28)* were significantly higher compared to neutral amplitudes (*ASD mean= -5.75, SD=4.56, TD mean= -5.81, SD= 3.80); t(56)= 3.456, p=0.001 and t(59)= 5.736,p=0.000 for ASD and TD respectively.* Paired t-tests indicated that for both diagnostic groups low-interest amplitudes (*ASD mean= -4.81 SD= 4.88, TD mean=-4.50, SD= 3.78)* were significantly higher compared to neutral amplitudes*; t(56)= 5.019, p=0.000 and t(59)= 6.471,p=0.000 for ASD and TD respectively.*

Finally, two sample t-tests were performed to compare conditions (High, Low and Neutral) between diagnostic groups. Despite no significant main effect of group we conducted these analyses as we had a priori hypotheses about group differences in some conditions and not others. Specifically, we anticipated greater amplitude for high-interest images in ASD participants as compared to TD controls. These indicated no significant

differences between diagnostic groups for any condition: High ($p=0.454$), Low ($p=0.727$) and Neutral ($p=0.942$). This suggests that TD and ASD individuals show a similar modulation of the LPP in response to High- and Low interest, relative to Neutral, visual stimuli.

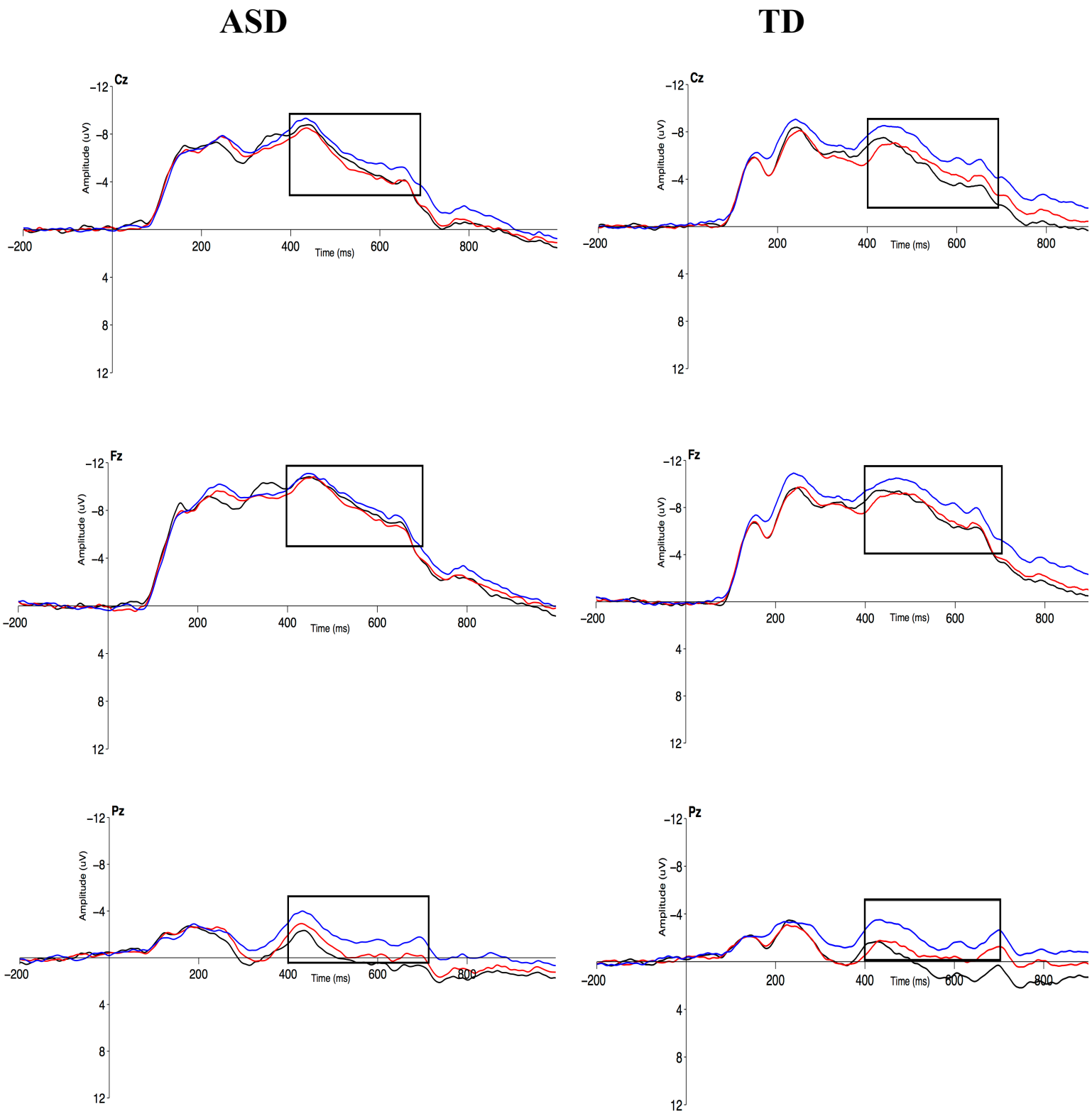

Figure 5. LPP amplitudes for our three electrode sites: Cz, Fz and Pz for both diagnostic groups: ASD and TD. Amplitudes between 400 and 700ms were calculated and averaged across these midline scalp electrodes for statistical analyses. Boxes indicate measurement window for the LPP.

3.4 P1 Amplitude Results: Mean and Variability

The results in this section along with the next section (3.5 P1 Latency and Variability Results) include 19 ASD and 19 TD participants. One TD subject was removed prior to analyses on the basis that a single P1 peak could not be reliably identified within the designated time window.

Mean P1 Amplitude

First we examined effects of group and condition on the amplitude of the P1 response. Repeated measures ANOVA showed a significant effect of condition (High, Low, Neutral and Gabor) [(F (1,36)= 8.694, p=0.000)] as well as a significant main effect of diagnostic group [(F (1,36)= 4.580, p=0.041)]. The condition effect was driven by larger P1 amplitudes during the High, Low and Neutral conditions relative to the Gabor condition *(Figure 6a).* This finding was confirmed with two sample t-tests pooling across the two groups, comparing High, Low and Neutral relative to the Gabor, p=0.034. The group effect was driven by larger P1 amplitudes in the ASD group. We did not, however, find a significant condition by diagnostic group interaction [(F (1,36)= 1.625, p=0.198)]. Two sample t-tests were performed to compare conditions between diagnostic groups. Following correction for multiple comparisons, there is a significant difference between diagnostic groups only for Low images (p=0.008). This effect was driven by larger P1 amplitudes in ASD participants compared to TD controls. The Gabor condition was at trend level following multiple comparisons (p= 0.031). We did not find a significant difference for the High (p=0.147) or Neutral (p=0.096) conditions.

SD P1 Amplitude

Next, to assess differences in trial-to-trial variability, effects of group and condition on the standard deviation of the P1 response were assessed. Repeated measures ANOVA showed a significant effect of condition (High, Low, Neutral and Gabor) [(F (1,36)= 5.927, p=0.001)] as well as a significant main effect of diagnostic group [(F (1,36)= 4.437, p=0.044)]. The condition effect was driven by a larger SD of the P1 amplitude during the High, Low and Neutral conditions relative to the Gabor condition *(Figure 6b)*. This finding was confirmed with two sample t-tests pooling across the two groups, comparing High, Low and Neutral relative to the Gabor, p=0.029. The group effect was driven by larger SD of the P1 amplitudes in the ASD group. We did not, however, find a significant condition by diagnostic group interaction [(F (1,36)= 0.448, p=0.719)]. Two sample t-tests were performed to compare conditions (High, Low, Neutral and Gabor) between diagnostic groups. Following correction for multiple comparisons, only the Low condition (p=0.035) is at trend level. This effect was driven by significantly larger SD of P1 amplitudes in ASD participants compared to TD controls. However, we did not find a significant difference for the High (p=0.109), Neutral (p=0.060) or Gabor (p=0.126) conditions.

3.5 P1 Latency Results: Mean and Variability

Mean P1 Latency

Repeated measures ANOVA did not indicate a significant effect of condition (High, Low, Neutral and Gabor) [(F (1,36)= 1.865, p=0.147)], diagnostic group [(F (1,36)= 3.608, p=0.067)] or condition by diagnostic group interaction [(F (1,36)= 1.662, p=0.186)] *(Figure 6c).* Two sample t-tests were performed to compare conditions (High, Low, Neutral and Gabor) between diagnostic groups. Despite no significant main effect of group we conducted these analyses as the trend approached significance. Following correction for multiple comparisons, both High (p=0.05) and Low conditions (p=0.039) are at trend level. This effect was driven by significantly larger P1 latencies in ASD participants compared to TD controls. We did not find a significant difference for the Neutral (p=0.320) or Gabor (p=0.596) conditions.

SD P1 Latency

Repeated measures ANOVA showed a significant effect of condition (High, Low, Neutral and Gabor) [(F (1,36)= 3.391, p=0.021)] as well as a significant main effect of diagnostic group [(F (1,36)= 4.220, p=0.049)]. The condition effect was driven by a lower SD of the P1 latencies during the High, Low and Neutral conditions relative to the Gabor condition *(Figure 6d)*. This finding was confirmed with two sample t-tests pooling across the two groups, comparing High, Low and Neutral relative to the Gabor, p=0.05. The group effect was driven by larger SD of the P1 latencies in the TD group. We did not, however, find a significant condition by diagnostic group interaction [(F (1,36)= 2.153, p=0.099)]. Two sample t-tests were performed to compare conditions (High, Low, Neutral and Gabor) between diagnostic groups. Following correction for multiple comparisons, only the Low condition (p=0.013) is at trend level. This effect was driven by significantly larger SD of P1 latencies in TD participants compared to the ASD group. We did not find a significant difference for the High (p=0.136), Neutral (p=0.128) or Gabor (p=0.582) conditions.

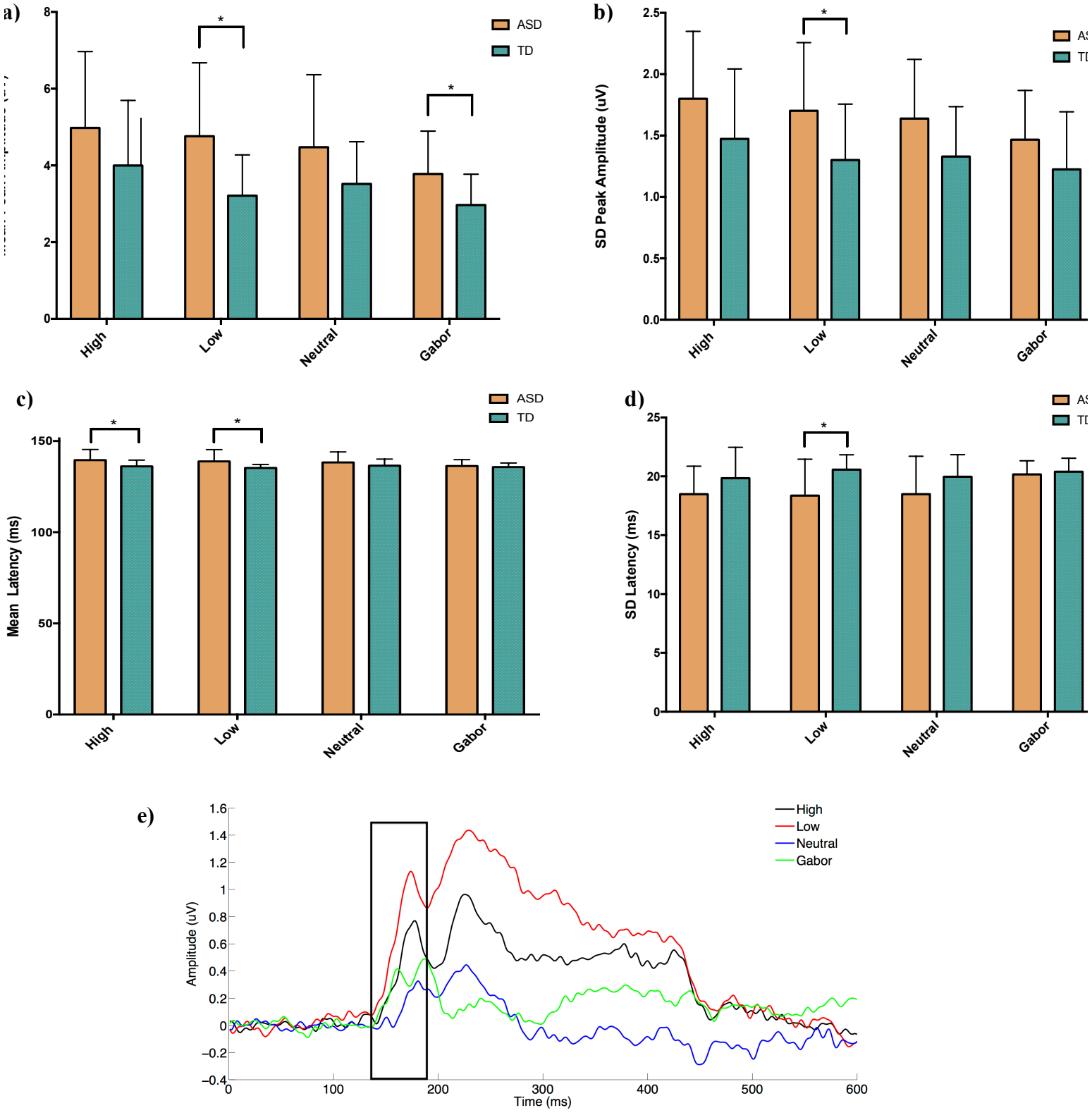

*Figure 6. a) Mean P1 amplitudes for ASD and TD. b) SD peak P1 amplitudes for ASD and TD. c) Mean P1 latency for ASD and TD. d) SD peak P1 latency for ASD and TD. e) A visual representation of a component fitted in space and time. Box indicates P1 waveforms across all 4 conditions (High, Low, Neutral and Gabor) for an ASD participant. * Means p<0.05 uncorrected.*

Chapter 4: Discussion

The goal for this study was to investigate whether visual reinforcers are processed abnormally in ASD, in terms of both signal amplitude/latency and trial-to-trial variability, as markers for reward system dysfunction. We created customized image sets of high- and low-interest images based on reported likes and dislikes. We included two behavioural measures to ensure our image categories were accurately representing individuals' likes and dislikes. We found no significant differences between diagnostic groups in image preference behaviour. We found that there were condition effects in the LPP, a marker for emotional processing, but no group effects. In contrast, for the P1, we found overall greater amplitude and amplitude-variability in the ASD group that did not differentiate between conditions. Lastly, P1 latency results did not show a significant effect of condition or diagnostic group. However, variability measures of P1 latency indicated lower SD to the Gabor condition across groups, as well as more variability overall in the TD group.

4.1 Behavioural Data

We confirmed that individualized stimulus sets showed appropriate relative levels of liking to our participants (high > neutral > low). Simply, both diagnostic groups were more likely to select a high-interest image over a low-interest image or a neutral image over a low-interest image based on the question "What do you like more?" Therefore, we can conclude that our image categories were appropriately defined and targeted individuals' likes and dislikes. There were no significant differences between diagnostic groups in image preference behaviour. Similarly, parametric rating data indicated that both diagnostic groups rated high-interest images significantly higher than low-interest images. These

results further support that our image selection accurately targeted individuals' likes and dislikes, with no significant main effect of diagnostic group.

Our findings replicate previous studies that have explored image rating in ASD and TD groups. Lin et al. (2012) asked both ASD and TD participants to provide valence ratings as part of a study investigating reward-learning of social and monetary rewards. They found no significant differences in valence ratings between diagnostic groups. Another study asked ASD and TD adult participants to provide arousal and valence ratings for different types of visual stimuli (Circumscribed interest (CI) object images, non-CI object images and social images) (N. J. Sasson, Dichter, & Bodfish , 2012). Their findings indicated no significant differences in arousal ratings between diagnostic groups for any image type. However, ASD participants had significantly higher valence ratings compared to TD controls for CI-object images, as well as significantly lower valence ratings for social images. A major limitation of this study is that CI object images were selected based on listings of common CI objects in children. Therefore, these images may not have accurately represented CI of their adult sample. Together these studies suggest that participants with ASD are able to provide valence ratings reflecting their preferences, and that their image preferences are distinct from TD participants.

Here, we did not find any group differences in ratings for stimuli related to TD or ASD adolescents' interests. The lack of group differences could be attributed to a wide variety of factors. First, it is possible that there truly are not any differences in value of the images between the groups. For both groups, the images were selected based on likes and dislikes, and similar to ASD, TD adolescents also have hobbies and interests that they find motivating and engaging. However, it is also possible that the visual properties of image

stimuli, such as colour vs. gray-scale, may impact image rating. Perhaps having coloured as opposed to gray-scale stimuli would have led to differences in ratings of stimuli related to personalized interests. We also note that an image depicting an interest is not the same as interacting with it. Therefore, a group difference in liking of the stimuli may exist but it is just not evident based on image rating. Finally, we might have ceiling effects for our rating data, wherein the ratings for high-interest images might be masking a potential group difference.

4.2 LPP responses during affective picture viewing in ASD and TD participants

LPP results indicated a significant main effect of condition, driven by a larger LPP amplitude during the High- and Low-interest, relative to Neutral conditions. This finding replicates previous neuroimaging studies that have explored affective picture viewing. During simultaneous EEG and fMRI recordings, Liu et al. (2012) found that relative to neutral images, pleasant and unpleasant images elicited a larger LPP amplitude. An EEG study by Schupp et al. (2000) found that emotional visual stimuli evoked a significantly larger LPP amplitude compared to neutral visual stimuli.

We did not, however, find a significant main effect of diagnostic group or a condition by diagnostic group interaction. We anticipated greater amplitude for high-interest pictures in ASD participants as compared to TD controls. This hypothesis stemmed from previous literature suggesting that idiosyncratic interests may be related to abnormalities in the brain's reward system in ASD (G. S. Dichter et al., 2012). Furthermore, theories such as the perceptual reinforcement theory (Lovaas et al., 1987), that proposes that restricted interests provide a source of pleasure and reward for

individuals with ASD, led us to expect enhanced LPP responses in ASD participants relative to TD controls while viewing personalized interests.

Recent work by Benning et al. (2016) investigated the LPP response in ASD and TD participants to different types of visual stimuli: social (smiling faces) and non-social stimuli (images of common restricted interests in ASD) during an EEG recording. Their findings indicated smaller LPP amplitudes in response to social stimuli in the ASD group. However, larger LPP amplitudes were evoked in the ASD group in response to non-social stimuli relating to common ASD interests (i.e. electronics and trains). Similar to our study, they found no group differences in subjective ratings of the image stimuli. However, a limitation of this study is that non-social stimuli were not customized image sets but rather a collection of common restricted interests in ASD (electronics and trains). As for their subjective ratings, one would then expect ratings to be lower for non-social stimuli in the TD group compared to the ASD group given that these images may reflect obscure and not age-appropriate interests. This makes their findings of group differences in LPP amplitude challenging to interpret.

Our finding that TD and ASD individuals show a similar modulation of the LPP in response to High- and Low-interest, relative to Neutral visual stimuli suggests that distributed emotional processing of these complex stimuli is relatively intact in ASD. Moreover, relative to Benning et al. (2016) our findings suggest that if pictures are matched in behavioral ratings of valence between groups, modulation of the LPP amplitude is not different in ASD.

Despite no group differences in LPP amplitude for high-interest pictures, this does not suggest that atypical affective responses are non-existent in ASD. Previous studies clearly indicate differences in reward network responses in ASD participants relative to TD controls (Cascio et al., 2014; Dichter et al., 2012). Together with our findings this work suggests that atypical affective responses may be specific to task context and type of stimuli (social/ non-social, simple vs. complex images), which could be explored in future studies. Also notably, the LPP is not solely modulated by emotional intensity but also attention and motivational significance (Schupp et al., 2000). Specifically, an EEG study by Schupp et al. (2000) found that pleasant and unpleasant stimuli engage attentional processes that led to an enhanced LPP response, which was found to be directly related to the motivational significance of the stimuli.

4.3 P1 Amplitude Results: Mean and Variability

P1 amplitude results indicated a significant main effect of condition, driven by larger P1 amplitudes during the High, Low and Neutral conditions relative to the Gabor condition. This finding replicates previous neuroimaging studies that have explored whether non-spatial visual properties can influence the resulting P1 amplitude. A literature review by Taylor (2002) on non-spatial attentional effects on P1 indicates that stimulus type (simple vs. complex) can impact the resulting P1 amplitude. Our condition effect may be related to the differences in complexity between High, Low and Neutral images relative to the Gabor patch. The High, Low and Neutral image sets consisted of complex scenes (landscapes, animals, people playing sports) whereas the Gabor patch is composed of sinusoidal gratings.

We also found a significant main effect of diagnostic group. This effect was driven by larger P1 amplitudes in the ASD group compared to TD controls. The earliest attentional response to the onset of visual stimuli is found in the P1 component (Clark et al., 1994). As attention is allocated to visual stimuli, extrastriate neurons are recruited to process the stimulus and the P1 amplitude increases (Smith et al., 2003). Therefore, the P1 response is influenced by attentional responses to the onset of visual stimuli. Our group effect may be related to different levels of attention allocated to the visual stimuli, though we note that there were no group differences in accuracy for detecting the target. Nonetheless, this was a very simple task (accuracy close to ceiling) and it is possible that our ASD participants were more engaged throughout the task, resulting in enhanced P1 responses. Direct comparisons between conditions and diagnostic groups revealed a significant difference between groups for Low-interest images. This effect was driven by significantly larger P1 amplitudes in ASD participants compared to TD controls. In addition, the Gabor condition was at trend level following multiple comparisons. These findings could be attributed to variations in attentional responses to Low-interest images and the Gabor patch in ASD and TD participants. Alternatively, these findings may also be related to atypical visual processing in ASD as shown by enhanced low level visual perception or to deficits in global processing (Dakin & Frith, 2005).

To assess differences in trial-to-trial variability, effects of group and condition on the standard deviation (SD) of the P1 amplitude were analyzed. Our P1 trial-to-trial variability results indicated a significant main effect of condition, driven by a larger SD of the P1 amplitude during the High, Low and Neutral conditions relative to the Gabor condition. This condition effect in SD of the P1 response is likely also related to the

differences in complexity between High, Low and Neutral images relative to the Gabor patch. Variations in the size of stimuli can impact the resulting P1 amplitude (Taylor, 2002). For our study we ensured that size and luminance measures were consistent across stimulus categories. However, levels of complexity varied across stimulus categories. High, Low and Neutral images were primarily complex scenes whereas the Gabor patch was simplistic in comparison *(Figure 1)*.

We also found a significant main effect of diagnostic group in SD of the P1, which was larger in the ASD group. This finding replicates previous neuroimaging studies that have explored levels of intra-individual variability in ASD. Dinstein et al. (2010) reported that individuals with ASD had more variable fMRI responses in both motor and visual brain regions during the execution and viewing of hand movements. Further support by Milne (2011) showed more variable EEG responses in ASD participants during the viewing of high-frequency Gabor patches. We expected to reproduce findings from Milne et al. (2009 and 2011) showing increased intra-individual variability in P1 response to the Gabor patch in ASD, and extend this finding to images of complex scenes. Despite our pre-planned comparison of the Gabor patch between diagnostic groups not indicating a significant difference in trial-to-trial variability, we did find an overall higher level of trial-to-trial variability in the ASD participants compared to TD controls across stimulus conditions.

Our finding of increased EEG variability in ASD participants provides evidence for increased neural "noise" (Sannita, 2006). These "noisier" neural responses may account for the sensory sensitivities often present in ASD. These findings of increased neural noise in ASD lends further support to Rubenstein & Merzenich (2003) theory that ASD results from

a signaling imbalance between excitation and inhibition in sensory, social and emotional systems. Lastly, this finding provides support to our hypothesis that nosier sensory stimuli in ASD may affect the neural representation of stimulus value, with consequences for downstream processing of visual reinforcers.

4.4 P1 Latency Results: Mean and Variability

Our P1 latency results did not show a significant effect of condition or diagnostic group. We performed two sample t-tests to compare conditions between diagnostic groups. Despite no significant main effect of group we conducted these analyses as the trend approached significance ($p=0.067$). Direct comparisons between conditions and diagnostic groups revealed both High and Low conditions were at trend level following multiple comparisons. This effect was driven by significantly larger P1 latencies in ASD participants compared to TD controls. The P1 response in ASD has primarily been explored in the context of atypical face processing. Our trend-level finding of larger P1 latencies in High and Low conditions replicates previous neuroimaging studies investigating the P1 response while viewing facial stimuli. An EEG study by O'Connor, Hamm, & Kirk, (2005) investigated emotional expression processing in children (mean age= 11.2 years) and adults (mean age= 24.8 years) with Asperger's syndrome (AS) compared to age- and gender-matched TD controls. Participants viewed facial stimuli depicting five basic expressions (angry, happy, neutral, sad and scary) and were asked to verbalize the emotion expressed following each stimulus. The results indicated delayed P1 latencies to all expressions of facial stimuli in AS adult participants compared to TD controls. Interestingly, this finding was not observed in AS and TD children which they attribute to incomplete development of neural generators associated with the P1 component. As for the Neutral and Gabor

conditions future work is needed to full understand the P1 latency response to simple and complex visual stimuli

To assess differences in trial-to-trial variability, effects of group and condition on the standard deviation (SD) of the P1 latency were analyzed. Our P1 trial-to-trial variability results indicated a significant main effect of condition, driven by a lower SD of the P1 latencies during the High, Low and Neutral conditions relative to the Gabor condition. This condition effect in SD of the P1 latency is likely related to the differences in complexity between High, Low and Neutral images relative to the Gabor patch. We also found a significant main effect of diagnostic group in SD of the P1 latency, which was larger in the TD group. This finding is contrary to the findings of Milne (2011) and to our hypothesis, as it suggests that latency is less variable in the ASD group, relative to TD. In addition, we analyzed High, Low and Neutral together and found no group differences. In this case, both the condition and group effects were unexpected and will require further investigation.

4.5 Implications

This study helps us gain insight into the complexity and heterogeneity of ASD through looking at both affective neural responses and intra-participant variability in early sensory responses. The goal for this study was to investigate whether visual reinforcers are processed abnormally in ASD, in terms of both signal amplitude/latency and trial-to-trial variability, as markers for reward system dysfunction. Our replication of the Milne finding of increased trial-to-trial variability in P1 amplitude suggests that ASD is characterized by increased levels of neural noise. Increased variability in neural activity could be the underlying cause of many features of ASD such as atypical sensory functioning. Our P1

amplitude finding is in line with the theory by Rubenstein & Merzenich (2003) that ASD results from a signaling imbalance between excitation and inhibition in sensory, social and emotional systems. Lastly, our findings provide support to our hypothesis that nosier sensory stimuli in ASD may affect the neural representation of stimulus value, with consequences for downstream processing of visual reinforcers. In addition, our finding of increased P1 amplitude variability in ASD may provide indirect support to the social motivation theory in that there may be disruptions in the brain's reward system in ASD. Though we did not specifically explore responses to social stimuli, we see increased variability in P1 amplitude to various other kinds of reinforcers including circumscribed interests. This lends further support to the Dinstein et al. (2012) study, which proposed that ASD should be viewed as a general disorder of neural processing, in which neural responses might be more "noisy" or variable. Our finding of increased variability in P1 latency in TD participants was unexpected, which motivates us to further explore the P1 response in ASD. We believe that this result may be spurious as it is also unexpected that the Gabor patch stimulus would show greater trial-to-trial variability in latency response than picture stimuli. This may be the result of a processing error and we therefore do not discuss further the implications of this result. Importantly, this study shows the importance of task context and type of stimuli as this could play a key role in atypical affective responses seen in previous studies. Future research into understanding dysfunction of the reward system in ASD is critical as behavioral treatment approaches such as applied behavior analysis (ABA) typically rely on reinforcement learning.

4.6 Limitations

A challenge of studying ASD is the heterogeneous nature of the disorder; ASD is defined along a spectrum due to the vast range in symptomatic severity. Our ASD sample was primarily composed of high-functioning individuals on the spectrum. Our task is very simple (accuracy close to ceiling) but requires participants to remain still and engaged for about 20 minutes. With a lower-functioning group we may have struggled with task completion as well as potentially less useable data due to excessive movement. Therefore, a limitation is whether our findings would extend to a lower-functioning cohort.

We created customized image sets of high- and low-interest images based on reported likes and dislikes. We included two behavioural measures to capture individual differences in the relative liking of our stimuli as well as to ensure that our image categories were appropriately defined. Participants provided ratings for a subset of 10 high- and 10 low-interest images. Our results indicated that both diagnostic groups rated high-interest images significantly higher than low-interest images. However, unexpectedly, we did not find any group differences in image ratings. This lack of group difference might represent ceiling effects in our rating data, wherein high ratings for high-interest images might be masking a potential group difference. However, a limitation for us is we are unable to tease out whether this is a true ceiling effect or there is no group difference in liking of the images.

4.7 Future Directions

A future aim of this project is to further explore our P1 latency findings. As mentioned our finding is contrary to the findings of Milne (2011) and to our hypothesis

suggesting that latency is less variable in the ASD group, relative to TD controls. Our plan is to explore the data on an individual level and use scatterplots to visualize the data and see if there is a trend across ASD and TD participants. Secondly, we plan to analyze each task block separately to see how consistent participants were across the two blocks. Despite very high target detection accuracy ratings across both groups we believe this may be an interesting avenue to further explore our P1 findings.

We intend to use scores from the SRS-2 measure to quantify symptom severity in ASD participants. This assessment measures aspects such as: Social Awareness, Social Cognition, Social Motivation, Social Communication as well as Restricted Interests and Repetitive Behaviours. Perhaps if we reduced our sample size to include only ASD participants with an overall score of 76 or above (severe range) with their age- and gender-matched controls may led to our hypothesis of group differences in LPP amplitude for high-interest pictures in ASD vs. TD controls.

To further explore the LPP in ASD vs. TD participants I would redesign our task to include social stimuli (facial expressions), CI-object images, neutral images and our target image (picture of zebra). The social stimuli would include 5 facial expressions: angry, happy, neutral, sad and scared. The CI-object images would be customized for each subject to include high-interest images. The neutral image set would match the set used in this study and be composed of IAPS images neutrally rated on measures of arousal and valence. Lastly, the target image would be our only response requirement to keep participants engaged throughout the task. As for the results I would anticipate a larger LPP amplitude for CI-object images in ASD participants vs. TD controls. However, I would expect a smaller LPP amplitude for social stimuli in ASD participants compared to TD controls to

replicate the findings of Benning et al.(2016). This finding would support the social motivation theory of ASD, which suggests that individuals on the spectrum have abnormalities in the brain's reward system for designating reward to social stimuli. Furthermore, a finding of larger LPP amplitudes in ASD participants to CI-object images would suggest that restricted interests may also be attributed to functional abnormalities in the brain's reward system.

Lastly, I think it would be interesting to develop a task that uses more engaging/interactive stimuli as opposed to images depicting an interest. These stimuli would be short film clips of interests (i.e. a train moving along tracks or a clip from a favourite movie). Following task completion ASD and TD participants would complete our two behavioural measures. Previous research has shown that moving stimuli can act as effective rewards (Blatter & Schultz, 2006). Perhaps the use of more interactive stimuli would lead to group differences in our behavioural results. We noted that an image depicting an interest is not the same as interacting with it. These new stimuli would again not be the same as interacting with an interest but given that they are more engaging they may reveal a group difference.

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Appendix: Image Sources

Figure 1.

High-interest: http://powellong.com/data/wallpapers/73/WDF_1184280.jpg

Low-interest: http://www.dweho.com/wp-content/uploads/2016/09/nettoyer-toilettes.jpg

Figure 2

High-interest (Eiffel Tower): http://vietkings.org/userfiles/Effel%20Tower.jpg