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Early event-related potentials to emotional faces differ for adults with autism spectrum disorder and by serotonin transporter genotype

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HIGHLIGHTS

- Adults with autism spectrum disorder exhibit a different pattern of neural activation (EPN) when encoding and recognizing facial expressions than neurotypical adults.
- Short serotonin transporter allele (*SLC6A4*) carriers have reduced neural responses (P1) during early sensory attention to facial expressions compared to long allele carriers.
- The N170, VPP and EPN, but not the P1, are influenced by emotional expressions and the EPN is the earliest component modulated by open mouths in neurotypical adults.

ABSTRACT

Objective: To test differences in neural sensitivity to facial expressions, including expressions with open versus closed mouths, exhibited by (1) adults with autism spectrum disorder (ASD) compared to neurotypical adults, and by (2) short versus long serotonin transporter allele (*SLC6A4*) carriers.
Methods: Event related potentials (ERPs) to happy, fearful, and neutral expressions were collected from neurotypical adults ($n = 25$) and adults with ASD ($n = 27$)–of whom 32 had short and 13 had homozygous long *SLC6A4* alleles.
Results: In the neurotypical group, we confirmed that the N170, VPP and EPN, but not the P1, were influenced by emotional expressions, and determined the EPN was the earliest component modulated by open mouth. Compared to the neurotypical group, individuals with ASD exhibited differences in EPN amplitude in response to open versus closed mouths and in hemispheric distribution. Across groups, short serotonin transporter allele carriers had reduced P1 amplitude compared to long allele carriers.
Conclusions: Individuals with ASD exhibited a different pattern of neural response when encoding and recognizing facial expressions at the EPN component. Across groups, *SLC6A4* allele type modulated early sensory attention at the P1.
Significance: These results provide insight into the nature of early responses to emotional information according to genetic variation and clinical condition.

1. Introduction

Processing of emotional stimuli involves early stage perception, the generation and awareness of physiological responses to emotional cues, and cognitive and semantic categorization. A number of factors influence emotional processing including genetic background and experiences. There is evidence that individual emotional responses are modulated by genotype (e.g., Bevilacqua

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and Goldman, 2011), which interacts with a lifetime of environmental experiences (e.g., Caspi et al., 2003). In this study we investigated the impact of two conditions: (1) autism spectrum disorder (ASD) and (2) length-based allelic variants of the serotonin transporter gene, *SLC6A4*, on early stage attention and perception of emotional information conveyed by faces. ASD is likely a condition in which both genetic background and experiences are impacted by a variety of factors, whereas *SLC6A4* allele length likely confers a more specific genetic and environmental impact. We examined whether the profiles of these conditions could be distinguished by their neural responses during initial attention and perception of emotional cues on faces given that both ASD and *SLC6A4* are associated with behavioral and neural differences in emotional responding. Understanding the early perceptual processing in adults with ASD and *SLC6A4* allele variants using event related potentials (ERPs) adds to existing knowledge about neural function and provides more precise clinical understanding of how breakdowns in emotional processing might occur. Moreover, this study provides the foundation for examining the specific role of *SLC6A4* allele variants within ASD, because converging evidence including apparent differences in transmission of *SLC6A4* allele length as a function of ASD status (e.g., Devlin et al., 2005; Guhathakurta et al., 2008; Kistner-Griffin et al., 2011; Wassink et al., 2007; but see Huang and Santangalo, 2008) and higher observed whole blood serotonin levels (e.g., Schain and Freedman, 1961; see also Cook and Leventhal, 1996 for review) implicates serotonin in ASD.

1.1. Emotion processing and neural differentiation

Early-stage ERPs (see Table 1) are sensitive to differences in emotional expressions, particularly negative expressions. Investigating these components provides important clues about early differences in attention, perception and discrimination of faces and the emotions they convey. We examined early ERP components reported for a passive viewing task that used the MacBrain Face stimulus set (Tottenham et al., 2009): the P1, Vertex Positive Potential/N170, and Early Posterior Negativity (Smith et al., 2013). Each component represents an aspect of early attention or perception that may be modulated by viewing emotional cues, particularly negative emotions, with minimal task demands.

The P1 is thought to reflect early selective attention and sensory processing of visual stimuli (Hillyard et al., 1973; Olofsson et al., 2008) and is sensitive to first order configural information contained in faces (Boutsen et al., 2006; Mercure et al., 2008). Recent work demonstrates that the P1 may be sensitive to negative emotional expressions (Luo et al., 2010; Rellecke et al., 2012), particularly when attended by the fovea (Eimer and Holmes, 2007; Wijers and Banis, 2012). This attentional modulation of the P1 component is thought to be due to extrastriate generators that are sensitive to threat-related, fearful stimuli (Wijers and Banis, 2012).

Next are the N170 and Vertex Positive Potential (VPP), which occur during the same time window and may share underlying neural mechanisms within the occipito-temporal cortex including the middle temporal gyrus and fusiform gyrus (Joyce and Rossion, 2005). The N170 is sensitive to faces and more negative fluctuations in N170 amplitude are observed over the right hemisphere for faces relative to other stimuli (Bentin et al., 1996). The N170 also appears sensitive to basic stimulus characteristics (Thierry et al., 2007; but see Bentin et al., 2007). There is some evidence that the N170 is enhanced for faces with emotional expressions relative to neutral faces (Blau et al., 2007; Righart and de Gelder, 2008), particularly negative expressions such as anger, fear and sadness (Batty and Taylor, 2003; Williams et al., 2006), but these effects have not been detected consistently (Eimer and Holmes, 2007; Eimer et al., 2003; Rellecke et al., 2013). The VPP is thought to reflect attention and the differences in attention to emotional versus neutral expressions (Luo et al., 2010). The VPP is included in the current investigation because more consistent effects of emotion have been detected for the VPP than the N170, perhaps due to greater sensitivity of the VPP to frontal contributors.

Table 1
Early stage event-related potentials associated with emotion processing.

Component	Window and leads	Role in processing
P1	60–130 ms; medial-occipital	Early selective attention and sensory processing; detecting configural face information
N170	150–180 ms; lateral-occipital and posterior temporal	Preliminary perceptual encoding of faces underlying categorization; possibly sensitive to negative expressions
VPP	150–180 ms; central midline	Attention; detecting emotional versus neutral expressions
EPN	200–350 ms; temporal occipital	Perceptual attention; encoding and recognizing positive and negative facial expressions

Finally, the Early Posterior Negativity (EPN), an enhanced negative-tending amplitude, appears to differ robustly in response to both negative and positive emotions relative to neutral expressions (Foti et al., 2009; Holmes et al., 2009; Rellecke et al., 2011; Schacht and Sommer, 2009; Schupp et al., 2004). The EPN is thought to reflect the perceptual attention underlying coding and recognition of facial expressions in the occipital and temporal cortex (Bradley et al., 2007; Rellecke et al., 2011; Schacht and Sommer, 2009; Schupp et al., 2003, 2004, 2006).

One aspect of neural responding to emotional faces that has not been systematically investigated is the impact of open versus closed mouths. Behaviorally, open mouths influence early processing of facial expressions. The ability to use information from particular features even when faces are shown for less than 150 ms suggests that holistic cues about expression may be available pre-attentively (Scheller et al., 2012). Additionally, open-mouthed faces enhance visual search (Horstmann et al., 2012), suggesting that teeth provide a salient perceptual cue. Varying degrees of teeth and gums are revealed in different facial expressions (Walter et al., 2014) and are linked to the naturalness of expressions (Korb et al., 2014; Van Der Geld et al., 2008), thus the appearance of teeth may be confounded with certain expressions. As well, critical information used to discriminate emotion varies by expression with more information about happiness conveyed by the mouth and more information about fear conveyed by the eyes as reflected in the scanning patterns of neurotypical adults (Eisenbarth and Alpers, 2011). In the context of early ERP components, the presence of open versus closed mouths may influence attention via different degrees of visual contrast between teeth and gums as well as perception of key facial information that underlies subsequent discrimination of emotions. Indeed, due to perceptual differences of "toothiness," the MacBrain stimuli used in the current study have open versus closed mouth versions of each facial expression and validation revealed enhanced accuracy for identification of expressions with open mouths (Tottenham et al., 2009).

1.2. Emotion processing in ASD

Emotional processing, a core component of the social communication system is disrupted in a number of mental health disorders in adults, including autism spectrum disorders (ASD). One hallmark of ASD is reduced social and emotional reciprocity, including reduced or inappropriate responses to the expressions of others and inappropriate or diminished responses to emotional situations