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Neural systems mediating decision-making and response inhibition for social and nonsocial stimuli in autism

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ABSTRACT

Autism is marked by impairments in social reciprocity and communication, along with restricted, repetitive and stereotyped behaviors. Prior studies have separately investigated social processing and executive function in autism, but little is known about the brain mechanisms of cognitive control for both emotional and nonemotional stimuli. We used functional magnetic resonance imaging to identify differences in neurocircuitry between individuals with high functioning autism (HFA) and neurotypical controls during two versions of a go/no-go task: emotional (fear and happy faces) and nonemotional (English letters). During the letter task, HFA participants showed hypoactivation in the ventral prefrontal cortex. During the emotion task, happy faces elicited activation in the ventral striatum, nucleus accumbens and anterior amygdala in neurotypical, but not HFA, participants. Response inhibition for fear faces compared with happy faces recruited occipitotemporal regions in HFA, but not neurotypical, participants. In a direct contrast of emotional no-go and letter no-go blocks, HFA participants showed hyperactivation in extrastriate cortex and fusiform gyrus. Accuracy for emotional no-go trials was negatively correlated with activation in fusiform gyrus in the HFA group. These results indicate that autism is associated with abnormal processing in socioemotional brain networks, and support the theory that autism is marked by a social motivational deficit.

1. Introduction

Autism spectrum disorders (ASD) are neurodevelopmental disorders characterized by impairments in social reciprocity, interaction and communication, and restricted/repetitive interests and behaviors. A prominent feature of ASD is an inability to implement socially appropriate behaviors or choose the most fitting behavioral response in a given social situation. Such behavioral flexibility requires the identification of facial expressions, eye movements, and body posture, coupled with the cognitive control mechanisms provided by executive functions (EF) such as planning, monitoring, and inhibiting prepotent responses.

Studies indicate altered functioning within brain regions responsible for socioemotional and EF processes in autism (Dichter and Belger, 2007; Dichter et al., 2009; Kana et al., 2007; Kleinhans et al., 2009; Schmitz et al., 2006; Shafritz et al., 2008), but most have investigated social and emotional aspects of human behavior apart from the cognitive control mechanisms necessary to implement appropriate behaviors. Therefore, little is known about the underlying neural processes that bridge cognitive control mechanisms with emotional processing in ASD. It is also unclear whether social impairments in ASD are related to emotion recognition deficits; some studies document impaired emotional recognition (Ashwin et al., 2006a; Pelphrey et al., 2002; Rump et al., 2009), while others show no impairments (Ashwin et al., 2006b; Corbett et al., 2009; Geurts et al., 2009; Monk et al., 2010; Wang et al., 2004). Previously observed deficits in emotional face recognition may be driven primarily by impairments in rapid decision-making with social stimuli, rather than a deficit in emotion recognition, per se (Clark et al., 2008). Prominent theories explaining emotion recognition deficits in autism invoke hypoactivity in the fusiform gyrus during face processing tasks (Corbett et al., 2009; Pelphrey et al., 2007; Schultz et al., 2000), but not all evidence supports this notion (Duerden et al., 2013; Hadjikhani et al., 2004; Perlman et al., 2011).

Another proposal suggests that a motivational deficit in which social information is not rewarding may underlie social impairments in ASD (Dawson et al., 2005), but limited evidence supports this hypothesis. There is some indication of diminished neural responses in the nucleus accumbens/ventral striatum during the anticipation of social reward (Richey et al., 2014) and during a social reward learning task (Scott-Van

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Zeeland et al., 2010), and in the dorsal striatum during the receipt of social reward (Delmonte et al., 2012). However, other studies have found hypoactivation in these brain regions in ASD during anticipation or receipt of monetary rewards, but not social rewards (Dichter et al., 2012a,b; Kohls et al., 2013).

The current study sought to address these limitations and contradictory findings. We used functional magnetic resonance imaging (fMRI) to examine whether regional brain activation would differ between ASD and control groups during a letter go/no-go task and an emotional go/no-go task. The emotional go/no-go (Hare et al., 2005; Shafritz et al., 2006) examines rapid decision-making coupled with emotion recognition by requiring participants to quickly respond or inhibit responses to faces of varying emotions. Prior work has demonstrated that the dorsal anterior cingulate cortex (ACC) and lateral prefrontal cortex are strongly implicated in nonemotional go/no-go performance, while the pregenual ACC is differentially recruited by specific emotions in emotional go/no-go paradigms (Albert et al., 2012; Shafritz et al., 2006). Moreover, relatively intact emotional go/no-go performance has been observed in ASD (Duerden et al., 2013; Geurts et al., 2009), and any observed deficits on this task may be related to the desire to view emotional faces, rather than a deficit in decision-making regarding these faces (Yerys et al., 2013). Further, no studies have used the go/no-go to examine the neural correlates of decision-making in both emotional and nonemotional contexts in autism. Although prior fMRI work (Duerden et al., 2013) has examined response inhibition for social stimuli in autism, this study lacked a nonemotional control condition crucial for distinguishing cognitive control processes mediating response inhibition in social contexts from those involved in generic response inhibition. Therefore, the current study was designed to examine whether previously observed activation differences during emotional go/no-go tasks in ASD are specific to emotional stimuli or reflect deficits in more domain-general response inhibition.

Based on prevailing literature, we hypothesized that (1) during the letter go/no-go, participants with ASD would show decreased activation compared with controls in EF circuitry; (2) during the emotional go conditions, participants with ASD would also show reduced activation compared with controls in the amygdala (Ashwin et al., 2007; Monk et al., 2010) for fear stimuli relative to happy stimuli, and in the ventral striatum (Hare et al., 2005) for happy stimuli relative to fear stimuli; (3) contrasting fear no-go with happy no-go would yield activation differences in the pregenual ACC (Albert et al., 2012; Shafritz et al., 2006); and (4) for emotional no-go, participants with ASD would show increased activation in fusiform compared with controls (Duerden et al., 2013).

2. Methods

2.1. Subjects

Participants in the autism group were 20 individuals (17 male, 3 female) with High Functioning Autism (HFA), recruited from the Linder Center for Autism and Developmental Disabilities within the North Shore-LIJ Health System. All participants met DSM-IV criteria for either Autistic Disorder ($n = 14$) or Asperger's Disorder ($n = 6$), established through the Autism Diagnostic Interview—Revised (Lord et al., 1994) and the Autism Diagnostic Observation Schedule—Generic (Lord et al., 2000), administered by an experienced psychiatrist (J.B.). Five participants in this group failed to meet motion criteria for fMRI data analysis (see Functional image analysis section) and were excluded from the final sample. Therefore, the final HFA sample consisted of 15 individuals (12 male, 3 female; 11 meeting criteria for Autistic Disorder, 4 meeting criteria for Asperger's Disorder; mean age 18.1 years, age range 13–23). Exclusion criteria were presence of co-morbid mood, anxiety, psychotic, or seizure disorders, or Attention-Deficit/Hyperactivity Disorder, and IQ < 70. IQ scores were obtained using the Wechsler Abbreviated Scale of Intelligence (WASI). Mean (SD) IQ scores for the autism group were: Full-Scale = 101.5 (18.6), Verbal = 105.7 (18.8), and Performance = 103.5 (17.4). Five participants reported no history of medication use. Two reported a history of psychostimulant use, but were free of medication at the time of study. Eight participants were currently using the following medications (numbers in parentheses): citalopram (2); escitalopram (1); alprozolam (1); venlafaxine (1); sertraline (1); aripiprazole (2); clomipramine (1); lithium (1) and guanfacine (1). Based on psychiatric evaluations, symptoms shared with other conditions (such as anxiety or impulsivity) were best attributed to autism rather than independent co-morbid disorders. Hence, medications targeted symptoms related to autism.

Eighteen age- and sex-matched neurotypical control participants (15 male, 3 female) were recruited by advertisement. Three participants in this group failed to meet fMRI motion criteria and were excluded. Therefore, the final control group consisted of 15 individuals (12 male, 3 female; mean age 18.4 years, age range 12–23). All participants in this group were screened through detailed interviews to assure absence of psychiatric, neurological, or developmental disorders. Mean (SD) IQ scores for the control group were: Full-Scale = 115.2 (9.3), Verbal = 118.8 (14.9), and Performance = 108.0 (8.1). Full-Scale IQ scores differed between the autism and control groups ($p < .05$), but this difference was driven by a marginal difference in verbal IQ ($p = .05$); there were no between-group differences in performance IQ ($p = .39$). Considering the characteristic impairment in verbal communication among individuals with autism, the difference in verbal IQ was expected.

All participants (and parents or guardians if applicable) received a complete verbal description of the study. This study was approved by the North Shore-LIJ Institutional Review Board and written informed consent was obtained from all participants or parents (with written assent from participants) as appropriate.

2.2. fMRI task

The task was a block design go/no-go task, using a design similar to our prior work (Shafritz et al., 2006). In the letter version, participants viewed a series of letters and were visually instructed to either respond (by pressing a response button) for all letters that appeared, or respond to all letters except for 'X'. In the emotional version, participants viewed happy, fearful, or neutral faces and were instructed to either press for all faces, or withhold responses specifically for happy or fearful faces. By including the letter task, we could determine whether any between-group activation differences observed during the emotion task were related specifically to the processing of emotional stimuli, or reflected more domain-general inhibitory processes. Letter stimuli were uppercase consonant English letters in bold Courier New font. Emotional face stimuli were twelve male and twelve female Ekman faces (i.e., happy, fearful, and neutral faces from four male and four female actors) from the Pictures of Facial Affect set (www.paulekman.com). Stimuli were presented using E-Prime v1.1.3 (www.pstnet.com) and reverse-projected onto a screen viewed through a mirror located over the participant's head.

In the go condition of the letter task, participants viewed a series of 16 letters (not including 'X') and were visually instructed, "Press for all letters," via an instruction screen (3 s). In the letter no-go condition, participants viewed a series of 16 letters (50% were 'X') and were instructed, "Do not press for 'X'." Fig. 1 depicts sample trials from the task.

In the emotion task, participants viewed happy, fearful, or neutral faces and were instructed to either press for all faces, or withhold responses specifically for happy or fearful faces. To determine the distinct neural circuitry engaged by happy and fearful faces, as well as the neural regions responsible for inhibiting responses for happy and fearful faces, the emotion task was divided into several conditions. During happy,