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Difficulties with multi-sensory fear conditioning in individuals with autism spectrum disorder

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ABSTRACT

Background: Classical conditioning represents a fundamental aspect of learning, allowing us to infer relationships between coinciding events in our environment. However, recent evidence has suggested this fundamental form of learning may be compromised in individuals with autism spectrum disorder (ASD). The present study utilized galvanic skin responses to examine classical conditioning in individuals with ASD across sensory modalities.
Method: Fifteen individuals diagnosed with ASD and 16 age-, gender-, and IQ-matched individuals with typical development participated in this study. Using a differential fear conditioning paradigm, participants were presented with a series of colors and sounds. A subset of these colors and sounds was paired with an aversive loud noise. Learning the contingency between the color and/or sound and the aversive noise was measured by changes in skin conductance. Following this task, an explicit-knowledge test probed participant's awareness of these contingencies.
Results: Results indicated that individuals with ASD had a general impairment in fear conditioning compared to individuals with typical development. Additionally, participants with ASD who showed greater explicit awareness of the contingencies showed conditioned responses more similar to participants with typical development.
Conclusions: Implications for theories of the neurobiological mechanisms associated with learning and social impairments in ASD are discussed.

1. Introduction

Autism spectrum disorder (ASD) is a developmental disorder with core symptoms consisting of impairments in social communication and the presence of restrictive interests and repetitive behaviors (American Psychiatric Association, 2013). Our understanding of the social and communication impairments of ASD have largely stemmed from deficits in social and

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emotional processing. These accounts suggest that difficulties in processing emotional information like faces (Adolphs, Sears, & Piven, 2001; Shultz, 2005) or understanding the mental states of others (e.g., theory of mind, Baron-Cohen, 1997) give rise to atypical social behaviors in ASD. However, some authors have argued that another fundamental feature of the ASD phenotype lies in the ability to relate emotional experiences to environmental stimuli. That is, it may not be simply the experience or perception of emotion that is impaired in ASD (e.g., fear) but rather the ability to learn to associate emotional significance to environmental stimuli (Hobson, 1989; Kanner, 1943; Mundy & Sigman, 1989). One way to investigate this is through the use of classical fear conditioning paradigms.

In a traditional classical fear conditioning paradigm, a relatively neutral stimulus, such as a red light (i.e., the conditioned stimulus, CS), is paired with an aversive stimulus such as a loud sound (i.e., the unconditioned stimulus, UCS). Following several pairings of the CS with the UCS, participants begin to learn that presentation of the CS predicts the presentation of the UCS (e.g., the red light predicts the loud sound). Learning is usually assessed by whether participants show a startle or conditioned response (CR) to the CS in the absence of, or prior to, presentation of the UCS. This response is typically measured through galvanic skin response (GSR) or eye-blink magnitude (Knight, Smith, Stein, & Helmstetter, 1999; Knight, Nguyen, & Bandettini, 2003).

Studies of classical fear conditioning in ASD have indicated patterns of both impaired learning (Gaigg & Bowler, 2007; South, Newton, & Chamberlain, 2012), intact learning (Bernier, Dawson, Panagiotides, & Webb, 2005; South, Larson, White, Dana, & Crowley, 2011), and, in one instance, more rapid learning compared to age and IQ-matched individuals with typical development (see Sears, Finn, & Steinmetz, 1994). However, several methodological differences seem to underlie the conflicting patterns of results. Studies finding intact or more rapid conditioning in ASD have measured eye-blink response to a CS which was reinforced on every trial (i.e., 100% reinforcement schedule) and did not include a neutral stimulus (Bernier et al., 2005; Sears et al., 1994). Eye-blink conditioning is known to rely upon cerebellar and limbic system pathways (Steinmetz, Tracy, & Green, 2001), suggesting these pathways may be intact in ASD.

In contrast, studies of differential classical fear conditioning have measured associative learning by comparing changes in the skin conductance response (SCR) to a CS relative to one or more neutral stimuli. This type of conditioning has been linked to amygdala, hippocampal, and prefrontal brain regions (Jarrell, Gentile, Romanski, McCabe, & Schneiderman, 1987; LaBar, LeDoux, Spencer, & Phelps, 1995; Morris, Friston, & Dolan, 1997; Sehlmeyer et al., 2009). Studies of differential conditioning in ASD have found both impaired (Gaigg & Bowler, 2007; South et al., 2012) and intact associative learning (South et al., 2011). The different results may be attributable to an interaction between task complexity and associated brain regions linked to the fear response. For instance, Gaigg and Bowler suggested that the relative complexity of their paradigm may have contributed to the difficulty of the ASD group associating the CS with the UCS. Importantly, the term "complexity" related to differential fear conditioning is defined as a less obvious association between the CS and UCS, an association that can be obscured by the use of multiple neutral stimuli and/or a partial reinforcement schedule (Gaigg & Bowler, 2007). The complexity of the Gaigg and Bowler (2007) paradigm contrasts with a relatively "simple" differential fear conditioning paradigm that involves learning of a simple one-to-one association (i.e., one CS paired with one UCS). For instance, in a similar study by South et al. (2011), using one CS and one neutral stimulus, they demonstrated comparable associative learning between individuals with ASD and individuals with typical development. Because differential fear conditioning paradigms require greater communication between cortical and subcortical brain regions (Jarrell et al., 1987; Morris et al., 1997), poor connectivity between these brain regions in individuals with ASD (Belmonte et al., 2004; Just, Cherkassky, Keller, & Minshew, 2004; Just, Cherkassky, Keller, Kana, & Minshew, 2007; Kana, Keller, Cherkassky, Minshew, & Just, 2006; Minshew & Williams, 2007) may be one explanation why more complex differential conditioning paradigms resulted in poorer learning. That is, learning the association between a visual CS and an auditory UCS when inter-mixed with multiple neutral stimuli may result in poorer learning in ASD for two reasons: (1) learning the association between the CS and UCS requires coordination between visual, auditory, and subcortical brain regions, and (2) discriminating between threatening (i.e., CS) and safe/neutral stimuli requires additional information from pre-frontal brain regions.

Finally, learning in a classical fear conditioning paradigm may also be related to the degree to which individuals are consciously aware of the relation between conditioned and unconditioned stimuli. While it is true that both eye-blink and differential fear conditioning tasks can occur in the presence or absence of explicit awareness (Clark & Squire, 1999; Knight et al., 2003; LaBar et al., 1995; Weike, Schupp, & Hamm, 2007), activation of brain regions associated with explicit processing (e.g., medial temporal lobes; MTL) is less common in eye-blink conditioning tasks (see 'delay conditioning' in Clark, Manns, & Squire, 2002). In contrast, differential fear conditioning is associated with activations in the prefrontal cortex (PFC) and the hippocampus (HC), suggesting that explicit awareness may play a more important role in this type of learning. As a result, differential fear conditioning provides an opportunity to examine the relation between explicit awareness and conditioning in individuals with ASD.

The current study sought to extend previous evidence of impaired classical fear conditioning in ASD using complex presentations. Specifically, the current study used trials with a visual CS (colored square) paired with an auditory UCS (loud tone) and an auditory CS (musical note) paired with an auditory UCS (loud tone), along with two visual and two auditory neutral stimuli. Conditioning was measured as changes in SCRs to stimuli previously paired with the loud sound. Because this was a more complex learning task relative to the simple one CS to one UCS pairing, it was predicted that individuals with ASD would demonstrate poorer classical fear conditioning across modalities (visual CS paired with auditory UCS). That is, individuals with ASD would demonstrate a smaller conditioned response compared to individuals with typical development. However, because less cortical to sub-cortical communication may be required to learn an association within a modality (i.e.,