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# Diminished neural adaptation during implicit learning in autism

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ABSTRACT

Neuroimaging studies have shown evidence of disrupted neural adaptation during learning in individuals with autism spectrum disorder (ASD) in several types of tasks, potentially stemming from frontal-posterior cortical underconnectivity (Schipul et al., 2012). The aim of the current study was to examine neural adaptations in an implicit learning task that entails participation of frontal and posterior regions. Sixteen high-functioning adults with ASD and sixteen neurotypical control participants were trained on and performed an implicit dot pattern prototype learning task in a functional magnetic resonance imaging (fMRI) session. During the preliminary exposure to the type of implicit prototype learning task later to be used in the scanner, the ASD participants took longer than the neurotypical group to learn the task, demonstrating altered implicit learning in ASD. After equating task structure learning, the two groups' brain activation differed during their learning of a new prototype in the subsequent scanning session. The main findings indicated that neural adaptations in a distributed task network were reduced in the ASD group, relative to the neurotypical group, and were related to ASD symptom severity. Functional connectivity was reduced and did not change as much during learning for the ASD group, and was related to ASD symptom severity. These findings suggest that individuals with ASD show altered neural adaptations during learning, as seen in both activation and functional connectivity measures. This finding suggests why many real-world implicit learning situations may pose special challenges for ASD.



## Introduction

Numerous studies have identified atypical neural processes underlying cognitive task performance in autism spectrum disorder (ASD), yet few have examined the neural mechanisms that function while learning is occurring. Evidence of atypical patterns of brain activation during cognitive task performance in ASD, even in cases where individuals with ASD do not show a behavioral disadvantage, suggest that there may be something qualitatively different in the way individuals with ASD perform such tasks. It is possible that these neural differences arise because individuals with ASD learn in atypical ways (that may or may not be reflected in behavioral performance). Therefore, brain imaging studies of the learning process in ASD may reveal insights into the disorder that are not discernible from behavior alone. The present study aimed to examine neural adaptations in ASD during implicit learning with the goal of identifying neural disruptions in the disorder that may affect behavior in many real-world situations.

There is increasing evidence that brain function consists of networks of regions operating collaboratively, and that communication among brain regions may be disrupted in ASD. One theory posits that brain communication in ASD is impaired particularly between frontal and posterior regions (Just et al., 2004, 2012), based on widespread evidence of reduced anatomical and functional (synchronization) connectivity in ASD (for a review, see Schipul et al., 2011). Because learning typically relies on the integration of a large network of regions throughout the brain, it may be particularly susceptible to disorders of connectivity. Limited communication between distinct brain regions in ASD may impair coordination among these regions during the learning of a novel task, as well as the ability to streamline neural processes necessary to perform the task. In this way, brain underconnectivity may lead to impaired learning in ASD, particularly for learning processes that depend on the integration of a widely distributed task network.

Implicit learning is a type of learning that may be particularly affected and informative to study in ASD. Implicit learning refers to the acquisition of information about the world that arises without an intention to learn or without conscious access to what we know (Perruchet and Pacton, 2006; Reber, 1989), and includes tasks ranging from motor sequence memorization to visual pattern abstraction. Implicit learning is believed to underlie the learning of behaviors in two domains that are diagnostically disrupted in ASD, social interaction and language (Gomez and Gerken, 1999; Lieberman, 2000; Saffran et al., 1997), which may implicate implicit learning in the emergence of core symptoms of

*Abbreviations:* ADI-R, Autism Diagnostic Interview — Revised; ADOS, Autism Diagnostic Observation Schedule; ASD, autism spectrum disorder; MNI, Montreal Neurological Institute; NT, neurotypical individuals; ROI, region of interest.

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ASD. Previous behavioral work has provided mixed evidence of implicit learning abilities in ASD, suggesting possible impairments, discussed below. Finally, because many types of implicit learning rely on distributed cortical networks, they may be impacted by disruptions in brain connectivity. The present study utilized a non-social, non-verbal visuospatial task to isolate neural and behavioral patterns of basic implicit learning in ASD, which should be minimally affected by deficits in social interaction and language. The study investigated the disruption in neural learning mechanisms in autism by examining neural adaptations with a focus on functional connectivity during an implicit learning task.

*Implicit learning in ASD*

Previous behavioral studies of implicit learning in children and adults with ASD have revealed a mixed pattern of results across different types of tasks. Motor sequence reaction time tasks report both intact (Barnes et al., 2008; Brown et al., 2010; Gordon and Stark, 2007; Müller et al., 2004; Nemeth et al., 2010; Travers et al., 2010) and impaired (Gidley Larson and Mostofsky, 2008; Mostofsky et al., 2000) performance. Mixed results have also been reported in artificial grammar tasks (intact: Brown et al., 2010; Klinger et al., 2007; impaired: Klinger et al., 2007) and probabilistic learning (intact: Brown et al., 2010; Solomon et al., 2011; impaired: Scott-Van Zeeland et al., 2010a). Previous studies reported intact behavior in contextual cueing (Brown et al., 2010; Kourkoulou et al., 2011), while a more recent study found intact performance when both spatial and object identity cues were available, but impaired performance when only object cues were provided (Travers et al., 2013).

Visual prototype learning tasks require the participant to abstract a representation of a category based on exposure to multiple exemplars and these tasks have also shown mixed results in ASD. There is evidence of impaired prototype learning in ASD for face stimuli (Gastgeb et al., 2009, 2011b) and cartoon animal stimuli (Klinger and Dawson, 2001; Klinger et al., 2007). However, others have reported a wide range of performance across ASD participants using similar stimuli (Molesworth et al., 2008), suggesting that this is a fragile disruption in ASD. Dot pattern categories are particularly useful stimuli in prototype learning studies, because they can be precisely controlled and are comparably familiar across participant groups. Again, results have been mixed in ASD, with evidence of both intact (Froehlich et al., 2012; Molesworth et al., 2005) and impaired (Church et al., 2010; Gastgeb et al., 2011a; Vladusich et al., 2010) performance relative to neurotypical participants.

Several explanations of the mixed findings of implicit learning abilities in children and adults with ASD have been proposed, including that certain tasks may allow the use of explicit strategies whose execution is closely related to IQ (Klinger et al., 2007; Brown et al., 2010); that individuals with ASD may be able to learn from certain types of cues (e.g., spatial cues), but not others (e.g., object identity, Travers et al., 2013); or that individuals with ASD can learn but may take longer to do so (Vladusich et al., 2010). The present study aimed to reduce such potential confounds by selecting a task that cannot be performed explicitly, equating participant groups on IQ, using spatial stimuli, and training participants to a set learning criterion prior to the scanning session. Furthermore, neuroimaging may indicate disruptions in neural processing during implicit learning in ASD even when behavior appears intact, which may suggest underlying impairments that may affect behavior in more demanding conditions (e.g., increased task difficulty or a shorter learning session). Neuroimaging may also reveal whether implicit or explicit strategies are used as they give rise to activation in different brain regions (i.e., basal ganglia vs. medial temporal lobe, Poldrack et al., 2001).

*Neural adaptations during typical learning*

Typical patterns of activation change during learning have been identified in neurotypical individuals. The predominant adaptation during learning is a decrease in activation throughout the network of association areas involved in the task (for a review, see Kelly and Garavan, 2005), including areas responsible for control processes (Chein and Schneider, 2005). This effect is thought to reflect increased neural efficiency, because the same behavioral performance is achieved with fewer mental resources. Decreases in activation over the course of learning have also been found in sensory processing areas, an effect known as repetition priming (Desimone, 1996). In contrast, activation increases during learning occur in medial temporal and subcortical areas involved in stimulus response mappings (Salimpoor et al., 2010), and have been shown to correlate directly with behavioral performance improvements (Salimpoor et al., 2010). Finally, the synchronization of fMRI-measured activation across different brain regions involved in a task has been shown to increase over the course of learning, resulting in increased functional or effective connectivity (Büchel et al., 1999; Toni et al., 2002). In summary, typical neural adaptations during learning include decreased association area activation, decreased sensory area activation, increased subcortical and medial temporal activation, and increased inter-region synchronization.

*Neural adaptations during learning in ASD*

Few fMRI studies have assessed the neural mechanisms of learning in ASD. The changes in activation patterns during the learning of a complex social task have been shown to be disrupted in ASD relative to neurotypical participants, despite similar behavioral improvements across groups (Schipul et al., 2012). While neurotypical adults demonstrated decreases in activation in association and sensory processing regions and increases in medial temporal and subcortical regions, adults with ASD showed a more unchanging pattern of activation throughout learning, showing only small decreases in sensory processing areas and increases in task-related association areas. Neurotypical participants also showed larger increases in functional connectivity than did the ASD participants. These findings suggest that the neural processes in ASD participants did not adapt over the course of learning in the context of intact behavioral performance. It is unclear if this effect is specific to the social domain or generalizable to other types of learning in ASD.

While no other studies have focused on neural adaptation during learning in ASD, evidence can be found in existing related studies. Adults with ASD were shown to maintain activation in frontal premotor regions during motor sequence learning, while neurotypical adults generally showed decreases in these areas (Müller et al., 2004). ASD adults were shown to have decreased activation in the fusiform gyrus, but not the amygdala, after extended exposure to faces, while neurotypical adults had decreases in both regions (Kleinhans et al., 2009). Facial affect recognition training was associated with increased activation in parietal and occipital regions in adults with ASD (Bölte et al., 2006). In an artificial language study, neurotypical children showed neural sensitivity to the systematicity of artificial language stimuli, as well as increasing activation with extended exposure, while children with ASD showed no distinguishing activity for artificial language compared to random stimuli, nor for extended exposure (Scott-Van Zeeland et al., 2010b). Studies have also shown evidence of atypical neural responses to rewards during learning in children and adults with ASD (Kohls et al., 2013; Schmitz et al., 2008; Scott-Van Zeeland et al., 2010a). Thus, preliminary evidence suggests that neural processes during learning are disrupted in ASD. However, further investigation is necessary to isolate these effects with regard to specific types of learning.

*Aim of the present study*

The aim of the present study was to examine the neural adaptations during implicit learning in ASD. We hypothesized that the ASD group would have disruptions in implicit learning due to effects of underconnectivity on a task requiring a distributed network. We examined changes in brain activation and synchronization occurring over a