IMPLICIT LEARNING IN TYPICAL DEVELOPMENT AND CHILDREN WITH

DEVELOPMENTAL DISORDERS

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Implicit Learning in Typical Development and Children with Developmental Disorders

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Abstract

Learning is critical for the typical development of linguistic, social, and motor skills. However, little is known about whether learning develops during childhood or is disrupted in developmental disorders. This dissertation examined associative implicit learning, which occurs unintentionally and enables learning about variability and stability in the environment (e.g., when or where something is likely to occur). Chapter I discussed theories of brain and cognitive development that guided and informed this body of work. In Chapter II, we investigated whether younger children, older children, and adults differed in learning of simple and complex sequence structure (a source of variability in past studies). Results indicated that sequence-specific learning was sensitive age but not to sequence structure; it was reduced in younger than older children and adults for both sequence structures. Chapters III and IV addressed the status of two forms of learning, implicit sequence learning and implicit spatial contextual learning, in children with ADHD, children with ASD, and matched controls. Children with ADHD showed reduced learning on the implicit sequence task, but did not differ from controls
on the implicit spatial learning task. Therefore, results indicated a selective impairment in implicit sequence learning in children with ADHD. In contrast, learning on the implicit sequence learning and implicit spatial contextual learning tasks did not differ between children with ASD and controls, indicating a general sparing of implicit learning in childhood ASD. Chapter V addressed the neural basis of probabilistic implicit sequence learning in children with ASD and controls using functional Magnetic Resonance Imaging (fMRI). Behaviorally intact general skill learning in childhood ASD was reliant upon the same neural networks as controls, whereas behaviorally intact sequence-specific learning in childhood ASD was reliant upon qualitatively different neural networks than controls. Chapter VI discussed the implications of these findings for models of brain and cognitive development in typical childhood development, childhood ADHD, and childhood ASD. The dissertation ends by suggesting that development can be considered in terms of a three-way interactions between developing systems of learning, executive control, and emotional regulation.
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Chapter I:

INTRODUCTION

Throughout middle childhood and into early adolescence, developmental periods spanning ages 6- to 14-years, children gradually acquire a vast array of knowledge and skillful behaviors. Children learn to use increasingly complex grammar and vocabulary when speaking, construct and participate in complex social networks with peers, and develop fine motor skills such as writing and typing. The acquisition of these skills is not supported by a single learning mechanism but by the joint contributions of two systems, one that is effortful and one that occurs unintentionally.

Explicit memory and implicit memory comprise the broadest distinction among forms of memory (Squire & Zola, 1996). Declarative or explicit memory refers to the capacity for conscious recollection of facts and events, whereas non-declarative or implicit memory refers to recollection without intention or awareness (Schacter, 1987; Squire & Zola, 1996). Implicit memory systems can be further subdivided into associative (e.g., procedural or habit learning) and non-associative (e.g., priming or habituation) systems. Associative implicit learning involves the gradual acquisition of information from repeated experience with stimuli or responses that are deterministically (i.e., invariantly) or probabilistically related. Different mechanisms enable learning about temporal and spatial regularities. For example, people can learn the sequential structure of events over time (termed implicit sequence learning) or patterns in the spatial relationships among visual objects (termed implicit spatial contextual learning). These broad distinctions among memory systems belie the multitude of factors that influence the acquisition and expression of learning in adults (e.g., types of subjects, kinds of
events to be remembered, or manipulation of encoding or test conditions, Roediger, 2008). However, they provide a useful framework for thinking about typical development and developmental disorders because the establishment of these memory systems represents an endpoint of typical childhood development.

Association implicit learning has been demonstrated to support the acquisition and development of language (Kuhl, 2004), social intuition (Lieberman, 2000), social cognition (Evans, 2008), and motor skills (Perruchet & Pacton, 2006) throughout childhood. However, little is known about whether the mechanisms that enable implicit learning also develop during this period. Even less is known about the status of implicit learning in children with developmental disorders. Thus, the purpose of this dissertation is to address two critical questions in developmental cognitive neuroscience: 1) What is the developmental trajectory of implicit learning in healthy children? 2) What is the status of implicit learning in children with developmental disorders?

The four studies comprising this dissertation focused on association implicit learning for three reasons. First, less is known about the development of association implicit learning than other forms of learning and memory. Explicit memory (e.g., recognition and recall tests) undergoes substantial development during middle childhood and early adolescence, whereas non-associative implicit memory, (e.g., on habituation tasks) matures within the first few years of life (for review see Anooshian, 1998). Currently, only a handful of studies (De Guise & Lassonde, 2001; Karatekin, Marcus, & White, 2007; Maybery, Taylor, & O'Brien-Malone, 1995; Meulemans, Van der Linden, & Perruchet, 1998; Thomas et al., 2004; Thomas & Nelson, 2001; Vaidya, Hughe, Howard, & Howard, 2007) have examined associative implicit learning during middle
childhood and early adolescence. Critically, these studies have not led to a consensus about the developmental trajectory of associative implicit learning. Second, the neural networks supporting associative implicit learning, which are described in Chapters II – V, have been elucidated through adult brain imaging and lesion studies. An understanding of the neural basis of associative implicit learning in adults can constrain predictions about why certain forms of associative implicit learning might be immature in childhood or impaired in children with developmental disorders.

Finally, little is currently known about the status of associative implicit learning in common developmental disorders, such as Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD). To date, no study has examined associative implicit learning in ADHD and only one study has examined it in ASD (Mostofsky, Goldberg, Landa, & Denckla, 2000). This knowledge is necessary for comprehensive modeling of cognition in each of the disorders. Ultimately, these models may benefit from contrasting the two disorders rather than studying them in parallel, especially if certain impairments of associative learning mechanisms are unique to each.

There is reason to suspect that mechanisms of learning and memory may function atypically in children with ADHD and ASD. Deficits in executive control and emotional regulation occur in ADHD (Nigg & Casey, 2005) and ASD (Bachevalier & Loveland, 2006; Hill, 2004). Theoretical accounts of brain and cognitive development, such as Posner and Rothbart’s (2000), posit that multiple mechanisms of plasticity (i.e., the capacity of the brain to reorganize on the basis of experience) allow executive control and emotional regulation to influence each other bidirectionally during development. This dynamic development is thought to ultimately enable socialization in a culturally
constrained way (Posner & Rothbart, 2007). If adaptive executive control and emotional regulation are developmental consequents of experience-dependent plasticity, then it is possible that impaired executive control and emotional regulation, as seen in children with ADHD and ASD, might be the developmental consequents of atypical experience-dependent plasticity. This evidence leads to the prediction that associative implicit learning, a form of plasticity that is operational in childhood, may be impaired in ADHD and ASD. A contrasting prediction, also grounded in developmental cognitive neuroscience theory, is that while certain forms of plasticity may be disrupted in children with ADHD and ASD, associative implicit learning could be spared because it does not rely on conscious, cognitive control, which has been shown to be impaired in both ADHD and ASD. Together, these predictions suggest that children with ADHD and children with ASD may have similar associative implicit learning profiles, characterized either by general impairment or sparing of learning.

Alternatively, children with ADHD and children with ASD may display unique associative implicit learning “profiles”. One prediction is based on the evidence that a constrained set of neural circuits, namely frontal-striatal and frontal-cerebellar circuits, have been implicated in ADHD, whereas pervasive abnormalities affecting the whole brain (e.g., early whole-brain overgrowth of both gray and white matter, Courchesne et al., 2007), have been implicated in ASD. These findings suggest that forms of associative implicit learning reliant on frontal-striatal and frontal-cerebellar circuits may be selectively impaired in ADHD, whereas multiple forms of associative implicit learning may be impaired in ASD. A second prediction is based on the evidence that children with ASD exhibit a preference for repetition and sameness, a symptom that is not seen in
children with ADHD, who instead show higher tendencies for novelty seeking (Anckarsater et al., 2006). This preference for repetition may be a manifestation of an intact ability to acquire information about invariant features in the environment, which could lead to general sparing of implicit learning in ASD but not ADHD. Thus, there are three possible outcomes regarding the status of associative implicit learning in ADHD and ASD: 1) general impairments in both disorders, 2) general sparing in both disorders, and 3) unique learning “profiles” across disorders.

Behavioral measures may not yield a comprehensive picture of associative implicit learning in developmental disorders. Even if learning were spared in a given developmental disorder, questions would remain regarding the mechanisms that enabled learning. Brain imaging allows for a more sensitive analysis of the neural networks related to cognition. Specifically, the neural correlates of a cognitive function of interest can be examined using functional Magnetic Resonance Imaging (fMRI), a non-invasive brain imaging technique used in children that involves minimal risk when safety guidelines are followed. FMRI indirectly assesses neural activity by measuring changes in the Blood Oxygen Level Dependent (BOLD) signal, a metabolic function closely related to local field potentials (i.e., electrophysiological measures of the average of input signals of a neural population) (Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001). The neural networks supporting cognition can be examined by measuring changes in the BOLD signal across experimental conditions related to a cognitive function of interest. For example, despite spared behavior, children with developmental disorders might display different regional patterns of BOLD signal changes in the service of learning than
controls. This can lead to new hypotheses about neurocognitive mechanisms that may be aberrant in that disorder.

The following outline explains how each chapter of this dissertation has addressed the two questions outlined at the beginning of this chapter, namely: 1) What is the developmental trajectory of implicit learning in healthy children? 2) What is the status of implicit learning in children with developmental disorders?

Chapter II. What influences the developmental trajectory of implicit learning?
The first major goal of this dissertation was to understand what might influence the developmental trajectory of implicit sequence learning. Prior studies have compared children to adolescents and adults on implicit sequence learning tasks yielding mixed findings. While some studies have found that younger children learn less than older children (De Guise & Lassonde, 2001) and adults (Thomas et al., 2004), other studies have found no differences between children, adolescents, and adults (Karatekin, Marcus, & White, 2007; Meulemans, Van der Linden, & Perruchet, 1998; Thomas & Nelson, 2001). However, prior studies (e.g., De Guise & Lassonde, 2001) have not controlled for structural complexity, defined as the temporal lag or proximity between predictive elements within a to-be-learned sequence. This factor has been shown to influence learning in adults (Cleeremans & McClelland, 1991). We therefore examined whether the age at which learning appears mature is influenced by the structural complexity of the to-be-learned sequence. This issue was explored in Chapter II.

Chapters III and IV. What is the status of implicit learning in children with ADHD and children with ASD? The second major goal of this dissertation was to determine the status of two forms of associative implicit learning in children with ADHD
and in children with ASD. While these disorders differ with respect to their diagnostic criteria, behavioral impairments in domains including executive control and emotional regulation occur in both disorders. Typically, the tasks used to measure these cognitive and emotional processes require effortful control of attention. Thus, it is unknown whether associative implicit learning, which occurs without effortful control of attention (Gabrieli, 1998), would also be disrupted. In Chapters III and IV, we examined whether children with ADHD and children with ASD showed deficits in two forms of implicit learning reliant upon dissociable neural circuitry. First, we examined the status of implicit sequence learning, which has been shown in adults to rely on frontal, striatal, and cerebellar networks (Gabrieli, 1998). Second, we examined the status of implicit spatial contextual learning, which has been shown in adults to rely on medial temporal lobe networks (Chun, 2000). The growing cognitive neuroscience literature on ADHD and ASD, reviewed in the introductions of Chapters III and IV, provides a framework for more specific hypotheses. We explore the status of implicit learning in children with ADHD and children with ASD versus matched control children in Chapters III and IV, respectively.

Chapter V. What is the neural basis of implicit sequence learning in typically developing children and children with ASD? Finally, the third goal of this dissertation was to determine the neural networks that support implicit learning in high functioning children with ASD and matched controls. This study was motivated by our findings of spared implicit sequence and spatial contextual learning in ASD (reported in Chapter IV). Because we are exploring a behaviorally intact system, in contrast to many prior fMRI
studies in ASD, group differences in activation cannot be attributed to impaired performance in the ASD group.

Using fMRI, we probed the neural networks supporting learning using a probabilistic implicit sequence learning task (i.e., triplets-learning task, Howard, Howard, Dennis, & Kelly, in press) in high functioning children with ASD and matched controls. We predicted that implicit learning on the triplet-learning task would be intact in children with ASD, based on the spared implicit sequence learning reported in Chapter IV.

Second, we explore two alternative predictions about the neural basis of implicit sequence learning ASD. On the one hand, it is possible that because implicit sequence learning is intact in ASD it would be reliant upon the same neural networks in children with ASD versus matched control children. On the other hand, it is possible that intact implicit sequence learning would be reliant upon atypical cortical and subcortical activation based on evidence of widespread differences in activation on a variety of cognitive, linguistic, and perceptual tasks (Muller, 2007). These predictions are outlined in greater detail in Chapter V.
Chapter II:

Development of implicit sequence learning in late childhood: Does sequence complexity matter?

(This chapter has been submitted for publication as Barnes, KA, Benner, ME, & Vaidya, CJ. Development of implicit sequence learning in late childhood: Does sequence complexity matter?)

While multiple learning mechanisms support the development of linguistic and social skills, their maturational time-courses are not fully known. Learning that occurs unintentionally and without awareness is termed implicit and is known to support acquisition of both non-associative (e.g., habituation to novel stimuli) and associative (e.g., perceptual-motor sequencing) information (Gabrieli, 1998). Associative implicit learning is most commonly measured in the perceptual-motor domain using the Serial Reaction Time (SRT) task (Nissen & Bullemer, 1987), in which participants respond to the location of a stimulus presented in discrete positions via spatially mapped keys. Participants' speed and accuracy improve on blocks in which stimuli follow a repeating sequence and "rebound" (i.e., become slower and less accurate) on blocks in which stimuli occur randomly. Improved performance with practice followed by the “rebound effect” indicates that participants have learned sequence-specific, predictive relationships between repeated stimuli, responses, or both. While non-associative implicit learning is often mature in infancy (Rovee-Collier, 1997), the maturational time-course of associative implicit learning is not fully known.

The developmental trajectory of associative implicit learning has not emerged conclusively from past studies using the SRT task. Two studies suggest that implicit learning is immature in childhood. First, 7- to 11-year-old children showed a smaller
magnitude of learning and acquired sequence-specific information at a slower rate relative to adults (Thomas et al., 2004). Second, 6- to 11-year-old children showed a smaller magnitude of learning relative to 12- to 16-year-old children on an SRT task that required bimanual responding (De Guise & Lassonde, 2001). Together, these studies suggest that implicit sequence learning continues to develop until age 12. In contrast, four studies suggest that implicit learning is mature by age 6-7. First, 6-7-year-olds, 10-11-year-olds, and adults did not differ in magnitude of learning and its maintenance over a one-week-delay (Meulemans, Van der Linden, & Perruchet, 1998). Second, 7-year-olds and 10-year-olds did not differ in magnitude of learning, and some, but not all, 4-year-olds learned on a modified SRT task (Thomas & Nelson, 2001). Third, 8- to 17-year-olds and adults did not differ in oculomotor measures (i.e., mean oculomotor RTs and anticipations) of implicit sequence learning on a manual SRT task (Karatekin, Marcus, & White, 2007). Finally, 6- to 16-year-olds did not differ in magnitude of learning on an SRT task that required unimanual responding (De Guise & Lassonde, 2001). Together, these studies suggest that implicit sequence learning is mature in school age children. This makes the disparate findings difficult to reconcile since similarly aged samples and similar tasks were used across studies.

Mixed findings across studies may result from a failure to control for variables known to influence learning. Adult studies indicate that implicit sequence learning is not a unitary process. Rather, it relies on component processes (e.g., consolidation, automatization) that are supported by distinct neural mechanisms (Doyon & Benali, 2005). To date, only one study has manipulated the learning environment to determine whether the same processes support learning in children and adults. De Guise and
Lassonde (2001) manipulated response characteristics (i.e., bimanual vs. unimanual responses on the SRT task) to determine whether integrating sequential information from two effectors affects the age at which implicit sequence learning appears mature. In the bimanual SRT task, younger children (6- to 11-year-olds) demonstrated smaller magnitudes of learning than older children (12- to 16-year-olds). In contrast, in the unimanual SRT task, younger and older children did not differ in learning on the first hand (either left or right, counterbalanced) or its transfer to the second hand. However, the unimanual sequence was “easier” than the bimanual sequence because first-order transitions (i.e., the relationship between adjacent stimulus pairs) were generally wider (e.g., unimanual: P(A|B) = .33, P(C|B) = 0, P(D|B) = .67; bimanual: P(A|B) = P(C|B) = P(D|B) = .33) and, therefore, more discriminable. Thus, is it possible that the apparent developmental differences in implicit sequence learning by response characteristics may be due to differences in the complexity of the learned sequences.

We examined whether the structural complexity of the to-be-learned sequence underlies developmental differences in implicit sequence learning. Structural complexity is classified based on the number of intervening trials between predictive elements within a sequence: zero-order (some stimuli appear more frequently), first-order (some stimulus-pairs appear more frequently), and second-order (some non-adjacent stimulus-pairs—that is, with another intervening stimulus--appear more frequently). For example, the sequence A-B-A-D-B-C-D-A-C-B-D-C contains second-order regularities but no zero-order or first-order regularities. “A-x-B”, “B-x-D” and D-x-C” occur more frequently than “A-x-A”, “B-x-C”, and “D-x-A”, but all stimuli and adjacent stimulus-pairs occur an equal number of times. Manipulating structural complexity does not influence
perceptual-motor demands because overall performance did not differ for sequences with different structural complexities in studies with adults (Cleeremans & McClelland, 1991; Curran, 1997; Howard et al., 2004; Smith & McDowall, 2004). However, structurally complex sequences with higher-order regularities place higher demands on working memory due to longer temporal lags between to-be-associated predictive elements (Newport & Aslin, 2004). Because working memory is immature in childhood (for review see Gathercole, 1998), higher-order regularities should be more challenging for younger children to learn. No study has compared structural complexity of to-be-learned information within the same children, and therefore, it remains unknown whether structural complexity determines the age at which sequence learning matures in childhood.

In the present study, 7 – 9-year-old children, 10 – 13-year-old children, and college aged adults performed two versions of the SRT task, one with first-order and one with second-order sequence structure. The two tasks differed in the nature of the to-be-learned regularities but not perceptual-motor demands. Further, to eliminate the role of non-associative information in the learned sequences, neither sequence contained zero-order regularities. Thus, our manipulation of sequence structure was designed to maximize sensitivity to differences in associative implicit learning. We predicted developmental differences on the complex second-order task but not the simpler first-order task. Each participant performed both SRT tasks and therefore, any differences in magnitude of learning between the tasks were not confounded by individual differences in perceptual-motor ability. In addition, we used two measures of explicit awareness (i.e., verbal report and familiarity ratings) to determine whether learning was implicit.
First, for the verbal report measure, participants selected amongst 5 sentences describing whether they thought a sequence repeated in the task (e.g., “I am sure there was a pattern, and I know what that pattern was”). This measure assessed knowledge of the repeating sequence that could be used strategically to enhance learning. Second, participants rated the familiarity of the entire sequence and of sequence fragments via rating scales. This measure assessed partial sequence knowledge that would be sufficient to improve performance on sequence blocks relative to random blocks. Multiple measures were included because the familiarity for partial sequences ought to be sensitive to age differences even if children could not verbalize their knowledge of the entire sequence.

Method

Participants

Eighteen younger children (10 males) ranging in age from 7 to 9 years ($M = 8.12$ years, SD = .71) and nineteen older children (10 males) ranging in age from 10 to 13 years ($M = 11.42$ years, SD = 1.07) were recruited from the Washington, DC metropolitan area and were compensated monetarily for their participation. Twenty Georgetown University students (10 males) ranging in age from 18 to 20 years ($M = 18.55$ years, SD = .69) participated for course credit.

Exclusion criteria for children included diagnoses of ADHD and mood disorder indexed by T scores greater than 60 on the Attention Problems Scale and the Anxious/Depressed Scale of the Child Behavior Checklist (Parent Form), respectively. Exclusion criteria for adults included self-report of any past or current neurological or psychological disorder such as ADHD, dyslexia, anxiety disorder, depression, or epilepsy. All participants had full-scale IQ above 85 estimated from the Vocabulary and
Matrix Reasoning subtests of the Weschler Abbreviated Scale of Intelligence (Psychological Corporation, 1999). Full-scale IQ estimates did not differ between younger children \((M = 120.72, SD = 15.98)\), older children \((M = 120.90, SD = 7.02)\), and adults \((M = 124.15, SD = 6.25)\), \(p = .52\).

*Design*

*Implicit sequence learning.* The SRT task was adapted from Smith and McDowall (2004) and consisted of a 3 x 2 x 6 mixed design with Group (younger children, older children, and adults) as a between-subjects factor and Structure (First-order and Second-order) and Block (1 - 6) as within-subjects factors.

*Explicit Awareness.* Verbal report and familiarity ratings were adapted from Smith and McDowall (2004). Verbal report consisted of a 3 x 2 mixed design with Group (younger children, older children, and adults) as a between-subjects factor and Structural Complexity (First-order and Second-order) as a within-subjects factor. Familiarity ratings for 12-item (complete sequence) and 4-item (sequence fragment) sequences consisted of a 3 x 2 mixed design with Group (younger children, older children, and adults) as a between-subjects factor and Trial-type (Foil vs. Target) as a within-subjects factor. Familiarity ratings were not collected after the first task to prevent participants from explicitly searching for any repeating sequences during the second task. Thus, familiarity in First-order and Second-order SRT tasks was assessed between-subjects in each age group; half of the participants performed the First-order task second and the remaining half performed the Second-order task second.
Procedure

Participants were tested on a Dell computer using E-Prime (Psychology Software Tools, www.pstnet.com) and were seated within comfortable reach of the computer. Participants performed the First-order and Second-order tasks within a single session in counterbalanced order and completed 20 practice trials prior to beginning the experiment.

The procedure was the same for the First-order and Second-order tasks. Each trial began with four empty circles displayed horizontally across a screen. Each circle was mapped to a key (“v”, “b”, “n”, and “m” marked with stickers). Participants responded bimanually, using their index and middle fingers. The experimenter confirmed that this was done throughout the task. On each trial, one filled-in circle was presented. A response to the filled-in circle’s location, indicated via keypress, initiated the next trial (i.e., response-to-stimulus interval = 0). Participants were instructed to respond as quickly and accurately as possible. In each task, participants completed 6 blocks of 120 trials. In Blocks 1 and 6, stimulus location was randomly determined with the constraint that it appeared in each location an equal number of times. On Blocks 2 through 5, the stimulus moved in a fixed 12-item sequence that repeated 10 times per block. In the First-order task the sequence was “A-D-A-C-D-B-C-B-A-C-D-B”. In the Second-order task the sequence was “A-B-A-D-B-C-D-A-C-B-D-C”.

Explicit awareness was assessed with verbal report and familiarity ratings. At the end of both the First-order and Second-order tasks participants were read the following five sentences and chose the one that best described the task: a) "I believe that the circle moved randomly and I did not notice any pattern", b) "I believe that the circle may have moved in a pattern, but it is possible that it moved randomly too", c) "I am pretty sure the
circles moved in a pattern, but I’m not sure what the pattern is", d) "I am pretty sure that the circles moved in a pattern, and I think I have identified what the pattern was", or e) "I am sure there was a pattern, and I am sure that I know what the pattern was". Responses were scored numerically from 1 – 5, corresponding to sentences “a”-“e”, respectively. At the end of the second task, participants completed two familiarity measures, evaluating eight 12-item-sequences and twelve 4-item-sequence fragments. Seven of the eight 12-item sequences were novel (foils) and one had occurred in the experiment (target). Six of the twelve 4-item sequences were foils and six were targets. Participants rated each stimulus on a scale of 0 – 100 as having occurred in the experiment. The following rating scale was explained to each participant: a rating of 0 indicated the participant was certain the sequence did not repeat in the experiment, a rating of 50 indicated complete uncertainty about whether or not the sequence appeared in the experiment, and a rating of 100 indicated the participant was certain that the sequence was repeated in the experiment. Participants were encouraged to use any number from 0 to 100.

Results

Percentage of correct responses (accuracy) and mean reaction times (RTs) for correct trials were computed for each participant and analyzed in two dependent measures of learning: (1) General skill learning indexed by differences across Blocks 1 – 5; and (2) Sequence-specific learning indexed by the rebound effect, defined by slower and less accurate performance on Block 6 (random) than Block 5 (sequential).

Effects of Counterbalancing Order

Effects of task order on the two indices of learning, general skill learning and the rebound effect, were examined by testing for Order X Block interactions using repeated
measures ANOVAs with Group (younger children, older children, and adults) and Order (First-order first and Second-order First) as between-subjects factors and Block (1-5 for general skill learning analyses or 5 - 6 for the rebound effect) and Structure (First-order and Second-order) as within-subjects factors. For both RT and accuracy, Order X Block interactions were not significant for either general skill learning (all ps > .19) or the rebound effect (all ps > .14). Thus, counterbalancing order did not influence learning.

Subsequent analyses were performed on data collapsed across counterbalancing order. For the two indices of learning, separate repeated measures ANOVAs were performed with Group (younger children, older children, and adults) as a between-subjects factor and Block (1-5 for general skill learning and 5 and 6 for the rebound effect) and Structure (First-order and Second-order) as within-subjects factors. T-tests were used for examining significant effects of Block (paired t-tests) and Group (unpaired t-tests) using a Bonferroni correction for multiple comparisons, p < .005 for Block and p < .02 for Group. Effect sizes were evaluated using Cohen’s d. Effects most pertinent to our hypothesis are reported. They are main effects of Group (to determine whether there were developmental differences in overall performance) and Block (to determine whether overall performance changed with practice) and interactions of Group X Block (to determine whether there were developmental differences in the extent to which performance changed with practice) and Group X Block X Structure (to determine whether structural complexity impacted developmental differences in learning).

General Skill Learning: Accuracy. Overall accuracy differed between the groups (main effect of Group), F (2, 54) = 6.25, p = .004 (see Table 1). Younger children were less accurate than older children, t (35) = 2.41, p = .02, d = .79, and adults, t (36) = 3.61,
Older children and adults did not differ, \( p = .44, d = .25 \). No other main effects or interactions reached significance (all \( ps > .24 \)). Thus, overall accuracy improved with age, but was insensitive to practice and to sequence structure. Table 1. Mean percent accuracy (standard deviations in parentheses) for the First Order (FO) and Second Order (SO) SRT tasks by Group in each Block.

**Table 1.** Mean percent accuracy (standard deviations in parentheses) for the First Order (FO) and Second Order (SO) SRT tasks by Group in each Block.

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<th>Two Sequence</th>
<th>Three Sequence</th>
<th>Four Sequence</th>
<th>Five Sequence</th>
<th>Six Random</th>
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<td>FO SO</td>
<td>FO SO</td>
<td>FO SO</td>
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</tr>
<tr>
<td>93.6 (5.0)</td>
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<td>94.3 (4.2)</td>
<td>92.4 (7.2)</td>
<td>93.4 (5.2)</td>
<td>92.9 (7.9)</td>
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<tr>
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<td>97.1 (3.0)</td>
<td>95.7 (4.3)</td>
<td>94.4 (10.3)</td>
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**General Skill Learning: RTs.** Overall response speed differed between the groups (main effect of Group), \( F(2, 54) = 62.28, p < .0001 \) (see Figure 1). Younger children were slower to respond than older children, \( t(35) = 6.19, p < .0001, d = 2.02 \), and adults, \( t(36) = 10.48, p < .0001, d = 3.33 \). Older children were slower to respond than adults, \( t(37) = 5.05, p < .0001, d = 1.61 \). No other main effects and interactions reached significance (all \( ps > .08 \)). Thus, similar to accuracy, overall RTs improved with age, but were insensitive to practice and to sequence structure.

**Rebound Effect: Accuracy.** Overall accuracy differed between the groups (main effect of Group), \( F(2, 54) = 3.70, p = .03 \) (see Table 1). Younger children were less accurate than adults, \( t(36) = 2.40, p = .02, d = .77 \). Older children did not differ from younger children, \( p = .06, d = .63 \), or adults, \( p = .59, d = .17 \). Sequence-specific learning was obtained because participants demonstrated a rebound effect (main effect of Block),
F (1, 54) = 4.06, \( p = .05, d = .21 \), responding less accurately on Block 6 than Block 5. The rebound effect differed between age groups (Group x Block interaction), F (2, 54) = 3.80, \( p = .03 \). The magnitude of the rebound effect (Accuracy Block 6 - Accuracy Block 5) was smaller in younger children (\( M = -.63, SD = 2.97 \)) than in adults (\( M = 1.79, SD = 2.39 \)), t (36) = 2.77, \( p = .008, d = .90 \). Older children (\( M = 1.03, SD = 2.87 \)) did not differ from younger children, \( p = .09, d = .57 \), or adults, \( p = .37, d = .29 \). Further, we determined whether each age group demonstrated a significant rebound effect by conducting separate one-way ANOVAs with Block as a within-subjects factor for each group. Adults, F (1, 19) = 11.22, \( p = .003 \), demonstrated a significant rebound effect, whereas older children, \( p = .13 \), and younger children, \( p = .38 \), did not. However, developmental differences in magnitude of the rebound effect did not differ by structural complexity (Group x Block x Structure interaction, \( p = .35 \)). Thus, performance accuracy indicated that sequence learning improved with age regardless of the complexity of sequence structure.
Rebound Effect: RTs. Overall response times differed between the groups (main effect of Group), $F (2, 54) = 63.90, p < .0001$ (see Figure 1). Younger children responded slower than older children, $t (35) = 6.01, p < .0001, d = 1.97$, and adults, $t (36) = 11.08, p < .0001, d = 3.54$. Older children responded slower than adults, $t (37) = 5.26, p < .0001, d = 1.68$. Participants demonstrated a rebound effect (main effect of Block), $F (1, 54) = 37.85, p < .0001, d = .21$, by responding slower on Block 6 than Block 5 (see Figure 1). There were no age differences in the rebound effect (Group x Block interaction), $p = .10$. Therefore, in contrast to the analysis of accuracy, sequence-specific learning indexed by response latencies was insensitive to developmental differences. No other main effects or interactions reached significance (all $ps > .56$). Thus, the manipulation of sequence complexity did not yield developmental differences in sequence-specific learning.

Proportional Measure of Learning for Rebound Effect

Findings for the rebound effect revealed age differences in accuracy but not in response speed. It is likely that overall slower responding in children confounded differences in the magnitude of the rebound effect. Therefore, we examined group differences in the rebound effect on a proportional measure computed for response speed as $[(\text{Block 6} - \text{Block 5}) + (\text{Block 6} + \text{Block 5})]$ (following Cherry & Stadler, 1995;
Proportional learning scores were analyzed in repeated measures ANOVA with Group (younger children, older children, and adults) as a between-subjects factor and Structure (First-order and Second-order) as a within-subjects factor. Proportional learning differed between the groups (main effect of Group), $F(2, 54) = 6.89, p = .002$ (see Figure 2). Magnitude of proportional learning was smaller in younger ($M = .014, SD = .047$) than older children ($M = .051, SD = .033$), $t(35) = 2.77, p = .008, d = .91$, and adults ($M = .069, SD = .054$), $t(36) = 3.29, p = .002, d = 1.09$. Older children and adults did not differ, $p = .24, d = .40$. Further, we determined whether each group demonstrated a significant magnitude of proportional learning by conducting separate $t$-tests on the proportional magnitude of learning for each group. Adults, $t(19) = 5.67, p < .0001$, and older children, $t(18) = 6.72, p < .0001$, demonstrated significant magnitudes of proportional learning, whereas younger children did not, $p = .21$. No other main effects or interactions reached significance (all $ps > .38$). Thus, similar to rebound effects determined by accuracy, the proportional measure of learning for the rebound effect showed age differences regardless of sequence complexity.

**Percentage of Participants Demonstrating the Rebound Effect**

Task performance varied widely, particularly in younger children, raising the possibility that few participants, those with very small or large proportional learning (outliers), were responsible for group differences. Thus, we examined developmental differences in implicit sequence learning without the contribution of outliers by determining whether the number of participants displaying any learning differed by age group. Each participant was classified based upon the proportional measure of learning
for the First-order and Second-order SRT tasks separately —“learners” if it was greater than zero and “non-learners” if it was less than or equal to zero. More adults (First-order: 95%; Second-order: 90%) and older children (First-order: 94.74%; Second-order: 89.47%) were learners than younger children (First-order: 66.66%; Second-order: 50%), First-order: $\chi^2 = 8.12, p = .02$; Second-order: $\chi^2 = 11.05, p = .004$. Thus, developmental differences observed in the frequency analysis were consistent with results from analyses of performance accuracy and proportional response speed.

*Explicit Awareness*

Verbal report scores were computed for each participant separately for the First-order and Second-order SRT tasks. For the 12-item complete sequence recognition test, target familiarity ratings and mean foil familiarity ratings were computed for each participant. For the 4-item sequence fragment recognition test, mean target and mean foil familiarity ratings were computed for each participant. Familiarity ratings for each participant were performed after the second task only and were either for the First-order or the Second-order SRT task only, depending on counterbalancing order. Data were lost for two adults and one older child due to technical malfunction.

Mean verbal report measures were below the cutoff for explicit awareness (i.e., Sentence 4: “I am pretty sure that the circles moved in a pattern, and I think I have identified what the pattern was”) (see Figure 3). A repeated measures ANOVA with Group (younger children, older children, and adults) as a between-subjects factor and Structure (First-order and Second-order) as a within-subjects factor was performed to determine whether there were developmental differences in explicit awareness. Ratings (verbal report) of explicit awareness of sequence structure were higher, but still below
cutoff, for the Second-order than First-order task (main effect of Structure), F (1, 51) = 5.17, p = .03. No other main effect or interaction reached significance (all ps > .48). Thus, there were no developmental differences in verbal report of explicit awareness.

For each SRT task, repeated measures ANOVAs with Group (younger children, older children, and adults) as a between-subjects factor and Trial-type (foil and target) as a within-subjects factor were performed on familiarity ratings separately for the 12-item complete sequences and 4-item sequence fragments. Familiarity ratings for the foil and target did not differ (main effect of Trial-type, all ps > .10). No other main effects or interactions reached significance (all ps > .12). Therefore, there were no developmental differences in familiarity ratings for the repeating sequence.

Finally, we examined whether proportional measures of implicit sequence learning differed by age and explicit awareness. Each participant was classified based on verbal report for the First-order and Second-order SRT tasks separately—“aware” if they selected Sentence 4 or 5 and “unaware” if they selected Sentences 1, 2, or 3. There were no developmental differences in number of participants in each age group classified as aware (First-order: Adults: 28%; Older children: 11%; Younger children: 29%; χ² = 2.08, p = .35; Second-order: Adults: 33%; Older children: 39%; Younger children: 33%; χ² =
Second, proportional measures of learning were analyzed in repeated measures ANOVAs with Group (younger children, older children, and adults) and Awareness (aware, unaware) as between-subjects factors. The main effects of Awareness and Group x Awareness interaction did not reach significance (p > .26). Thus, developmental differences in implicit sequence learning were not the result of explicit awareness.

Discussion

The present study revealed four main findings regarding the development of implicit sequence learning on a bimanual SRT task. First, sequence-specific learning indexed by the rebound effect in accuracy and proportional response speed was reduced in 7- to 9-year-old children relative to older children and adults. However, there were no developmental differences in general perceptual-motor skill acquisition, indexed by practice-related improvement in performance speed. Thus, immature sequence-specific learning in younger children was unlikely to be due to immature perceptual-motor skill learning. Second, the developmental trajectory of implicit sequence learning was not influenced by the complexity of sequence structure because developmental differences were obtained for learned sequences with low (first-order) and high (second-order) structural complexity. Third, overall performance speed was slower in younger children and developmental differences in sequence-specific learning were apparent only upon measuring learning relative to baseline response speed. Differences in overall performance accuracy were less pronounced, and developmental differences in sequence-specific learning were apparent without measuring learning relative to baseline accuracy. Fourth, learning was implicit because participants were unable to verbalize their
knowledge of the learned sequence or rate complete or partial sequences as familiar. In the absence of any explicit awareness of the learned sequences, the observed developmental difference in implicit learning is unlikely due to variable explicit memory for the learned information.

Age differences in performance variability or explicit awareness cannot account for reduced sequence-specific implicit learning in younger children. Differences in magnitude of learning were unlikely due to outliers in any group because age differences were obtained in the percentage of participants showing any learning, regardless of its magnitude. Specifically, fewer younger children than older children and adults demonstrated learning on both first-order and second-order SRT tasks. Thus, the diminished magnitude of learning in the younger children was not due to high inter-individual variability. Overall age differences in speed and accuracy with age could have also impacted the expression of learning. Baseline speed could influence sequence-specific learning because participants could be slower at the end of the task due to fatigue or faster due to eagerness to complete the experiment. However, developmental differences in learning were apparent in proportional response latencies that controlled for differences in baseline speed. Further, reduced implicit sequence learning in younger children was not due to their reduced conscious awareness of the repeated sequence because explicit awareness was at chance in all groups, on probes of verbal report and familiarity ratings. Importantly, there was no relationship between age, verbal report, and implicit sequence learning, as measured by the proportional rebound effect.

Our study is the first to systematically examine whether complexity of sequence structure underlies developmental differences in implicit learning on a SRT task. Our
task design examined only associative information that varied in complexity, first-order or second-order, without inclusion of any non-associative information, zero-order regularities. Contrary to our hypothesis, learning was immature in 7- to 9-year-old children for sequences of not only high but also low structural complexity. Thus, our finding of immature implicit sequence learning in younger children is consistent with two studies (De Guise & Lassonde, 2001 [bimanual condition]; Thomas et al., 2004) but inconsistent with four others (De Guise & Lassonde, 2001 [unimanual condition]; Karatekin et al., 2007; Meulemans et al., 1998; Thomas & Nelson, 2001). While there is no clear resolution of the discrepant findings among these studies, the present findings allow us to eliminate structural complexity of the to-be-learned sequences as an explanatory factor.

A possible explanation of discrepancies in developmental differences across studies is that the extent of practice determines maturity of implicit sequence learning on the bimanual SRT task. Studies that reported reduced learning in younger children had the most sequence repetitions (60 repetitions in Thomas et al., 2004; 80 repetitions in De Guise & Lassonde, 2001 [bimanual condition]). In contrast, studies that found no developmental differences had the fewest sequence repetitions (25 repetitions in Meulemans et al., 1998; 30 repetitions in Karatekin et al., 2007 and Thomas & Nelson, 2001). Our study involved 40 repetitions of the first-order and second-order sequences, placing it squarely between studies finding and failing to find developmental differences. It is possible that the extended practice in our study (relative to 25 repetitions) was sufficient to enhance older children and adults’ ability to use predictive elements of the sequence to guide performance. Thus, greater practice may have enhanced the
expression of learning selectively for older participants. Indeed, studies with adults indicate that the expression of sequence learning in performance can be dissociated from the acquisition of sequence knowledge. For example, participants’ response latencies were modulated by task characteristics (e.g., stimulus context) and performance demands (e.g., inclusion of a secondary task), even though the structural knowledge of sequences they gained was unchanged (Jimenez, Vaquero, & Lupianez, 2006; Willingham, Greenberg, & Thomas, 1997). Future studies ought to manipulate extent of practice systematically in order to determine whether it underlies differences in magnitude of learning.

The present findings of immature implicit sequence learning are in accord with literature highlighting ongoing neural and cognitive development in the years prior to adolescence. Between the ages of 6-9 and 10-12 years, we noted a marked improvement in implicit sequence learning, but learning in older children was not “adult-like”. Despite no significant differences in learning between these two groups, older children’s magnitude of learning was numerically less than adults, suggesting that implicit sequence learning develops through adolescence. What is known about the neural basis of implicit sequence learning supports this idea. Fronto-striatal and fronto-cerebellar circuits are necessary for implicit sequence learning because learning was impaired in adults with degenerative disorders affecting the striatum (Ferraro, Balota, & Connor, 1993; Knopman & Nissen, 1991; Pascual-Leone et al., 1993; Willingham & Koroshetz, 1993) and the cerebellum (Pascual-Leone et al., 1993) that also disrupt their projections to frontal cortex. Implicit sequence learning was also impaired by temporarily disrupting dorsolateral prefrontal cortex function via Transcranial Magnetic Stimulation (Robertson,
Both structural and functional neuroimaging studies indicate that fronto-striatal and fronto-cerebellar circuits do not fully mature until late adolescence (for review see Casey, Tottenham, Liston, & Durston, 2005). Indeed, functional neuroimaging studies indicate that children recruit fronto-striatal circuits during implicit sequence learning to a lesser extent than adults (Thomas et al., 2004). Behaviorally, other cognitive and motor processes (i.e., processing speed, response inhibition and working memory, commonly grouped together as executive functioning) that rely on fronto-striatal and fronto-cerebellar circuits do not fully mature until adolescence (Luna, Garver, Urban, Lazar, & Sweeney, 2004). Whether ongoing maturation in fronto-striatal and fronto-cerebellar circuits results in differential recruitment of these circuits during functional neuroimaging of implicit sequence learning remains to be examined in adolescents.

The present findings extend knowledge about the maturation of associative implicit learning in childhood by elucidating the role of structural complexity of the to-be-learned information. Similar age-related improvements have been observed in other forms of associative learning, of spatial context (Vaidya, Huger, Howard, & Howard, 2007) and covariation (Maybery, Taylor, & O'Brien-Malone, 1995). All these forms of associative learning are insensitive to explicit awareness of the to-be-learned information. Together, these developmental findings contribute to the elaboration of the functional organization of implicit memory systems.
Attention Deficit Hyperactivity Disorder (ADHD) is defined by symptoms of inattention, hyperactivity, and impulsivity that significantly disrupt voluntary control of behavior in cognitive, social, and emotional domains (Barkley, 2005). Indeed, neurocognitive models of ADHD have emphasized executive dysfunction reflected in ineffective inhibitory control of thoughts and actions mediated by atypical development of frontal-striatal-cerebellar circuitry (Barkley, 1997; Castellanos & Tannock, 2002). More recently, however, deficits in non-executive domains have been recognized in ADHD children (Castellanos, Sonuga-Barke, Milham, & Tannock, 2006). One non-executive domain of cognition is our ability to learn from environmental regularities (e.g., when or where events may occur) without intention or conscious awareness, termed implicit learning. Implicit learning comprises multiple neuroanatomically dissociable processes that support acquisition of visual, linguistic, perceptual-motor, and cognitive skills (Gabrieli, 1998). These processes develop gradually and are often immature in late childhood (Thomas et al., 2004; Vaidya, Huger, Howard, & Howard, 2007), the diagnostic age for ADHD. Whether implicit learning processes are intact in ADHD is currently unknown. This knowledge is necessary for specifying comprehensive models of ADHD.
The present study examined two forms of implicit learning known to be neuroanatomically dissociable in adults: implicit sequence learning and implicit spatial contextual learning. Implicit sequence learning involves repeated experience with invariant sequential structure of stimuli, which forms the basis for predicting subsequent responses to contiguous (e.g., Serial Reaction Time [SRT] task, Nissen & Bullemer, 1987) or non-contiguous (e.g., Alternating SRT [ASRT] task, Howard & Howard, 1997) stimuli. On these tasks, subjects respond faster to stimuli whose locations follow a repeating pattern than for stimuli whose locations are randomly determined. Learning is implicit because participants are unable to distinguish between repeated and novel sequences on subsequent recognition measures. Patients with striatal (Smith & McDowall, 2004; Willingham & Koroshetz, 1993) and cerebellar (Pascual-Leone et al., 1993) damage from degenerative disease or stroke show impaired learning on SRT tasks. Neuroimaging studies of sequence learning in healthy subjects reveal frontal involvement in addition to striatal and cerebellar regions (for review see Doyon, 2008). Thus, implicit sequence learning is mediated by frontal-striatal-cerebellar circuitry.

In contrast, implicit learning of spatial contextual information relies on the medial temporal lobes. This form of learning involves repeated experience with invariant spatial relationships, which provide predictive cues that guide visual attention during visual search tasks (e.g., Contextual Cueing [CC] task, Chun & Jiang, 1998). In this task, faster visual search occurs for targets among distractors whose spatial configuration covaries with target location across trials (Chun, 2000). Learning is implicit because participants are unable to distinguish between repeated and novel distractor configurations on subsequent recognition measures. Patients with extensive medial temporal lobe damage
show impaired spatial contextual learning (Chun & Phelps, 1999). Neuroimaging studies of spatial contextual learning in healthy subjects show involvement of hippocampal (Greene, Gross, Elsinger, & Rao, 2007) and surrounding entorhinal/perirhinal cortices (Preston & Gabrieli, 2008). Learning appears to be mediated by those surrounding cortices rather than the hippocampus because damage confined to the hippocampus did not impair learning on the task (Manns & Squire, 2001).

Two lines of evidence predict impaired implicit sequence learning but not spatial contextual learning in ADHD. First, functional and structural neuroanatomical studies in ADHD subjects have found atypical frontal, striatal and cerebellar regions that mediate sequence learning but intact medial temporal regions that mediate spatial contextual learning. Neuroimaging studies revealed reduced activation in frontal and striatal regions during response inhibition (for review see Aron & Poldrack, 2005) and in cerebellar regions during working memory performance (Valera, Faraone, Biederman, Poldrack, & Seidman, 2005) in ADHD relative to control subjects. Further, meta-analysis of structural imaging studies indicated that the most consistent volumetric reductions in ADHD relative to control subjects were in the cerebellum and prefrontal cortex bilaterally and the caudate in the right hemisphere (Valera, Faraone, Murray, & Seidman, 2007). In light of these functional and volumetric abnormalities, any learning processes mediated by those regions ought to also be disrupted in ADHD. The medial temporal lobes, in contrast, did not differ between the groups in that meta-analysis. However, cognitive processes depending critically upon the medial temporal lobes such as recall and recognition memory are intact in ADHD (Denckla, 1996). Thus, there is stronger
neuroanatomical support for predicting impaired implicit learning of sequential than spatial contextual information in ADHD.

Second, behavioral studies have found atypical temporal characteristics of responses in ADHD subjects that may influence sequential but not spatial contextual learning. Specifically, intra-individual response variability was greater in children with ADHD during sustained attention (Johnson et al., 2007; Leth-Steensen, Elbaz, & Douglas, 2000) and inhibition (for review see Lijffijt, Kenemans, Verbaten, & van Engeland, 2005) tasks such that they had a higher proportion of trials with slower responses relative to controls. This performance characteristic ought to impede learning of sequential rather than spatial contextual relationships for the following reason: On SRT or ASRT tasks, the to-be-learned sequence unfolds over time and variable response latencies among trials within a subject will increase the lag between some predictive elements in a sequence. Such variable delays between elements are likely to yield unstable associations within the to-be-learned sequence. Indeed, inducing response variability by design in healthy subjects, by including either an increased (e.g., Frensch, Buchner, & Lin, 1994) or variable (e.g., Howard, Howard, Dennis, & Yankovich, 2007) interval between one trial's response and the next stimulus onset (termed the response-to-stimulus interval), reduced learning on SRT and ASRT tasks. In contrast, on the CC task, the to-be learned predictive relationships among spatial elements occur within each trial and are invariant over time. Therefore, it is unlikely that increased intra-individual response variability would impact learning on the CC task. Thus, based on the temporal characteristics of ADHD subjects’ behavioral responses, one would predict impairment in implicit learning of sequential rather than spatial contextual information.
We examined implicit learning of temporal sequences using the ASRT task (Howard & Howard, 1997) and of spatial context using the CC task (Chun & Jiang, 1998), in children with ADHD versus age-, gender-, and IQ-matched controls. On the ASRT task, participants respond to the location of a visual stimulus by pressing a corresponding key. Unbeknownst to participants, the stimulus location is varied in a fixed sequence involving alternate trials (i.e., item \( n \) predicts item \( n +2 \)); in other words, randomly determined stimulus locations alternate with sequence trials. Context-dependent learning is indexed by faster responses on sequence compared to random trials. On the CC task, participants search for a target (left/right oriented “T”) among distractors (rotated “Ls”) whose spatial configuration is repeated on some trials and novel on others. Context-dependent learning is indexed by faster responses on trials with repeated, rather than novel, distractor configurations. We predicted that children with ADHD would show a selective impairment of implicit learning on the ASRT but not CC task.

Method

Participants

Twenty children with ADHD (15 males) aged 7 to 12 years (\( M = 10.20, SD = 1.61 \)) with normal IQ (\( M = 113.15, SD = 13.60 \)) and twenty control children (16 males) aged 7 to 14 years (\( M = 10.50, SD = 1.82 \)) with normal IQ (\( M = 115.20, SD = 12.78 \)) were recruited from the Washington DC area through advertisements and were paid for participation. The groups did not differ in age (\( p = .58 \)) and IQ (\( p = .63 \)). Informed consent was obtained from parents and assent from children. Data from a subset (n = 14) of control participants was described in Barnes et al. (in press). ADHD diagnosis was
confirmed for DSM-IV criteria using the ADHD Rating Scale (DuPaul, Power, Anastopoulos, & Reid, 1998) and the Behavior Assessment System for Children (BASC) (Reynolds & Kamphaus, 1992) (Hyperactivity-impulsivity: $M = 61.83$, $SD = 10.50$; Attention Problems: $M = 64.00$, $SD = 8.73$). Of the 20 children with ADHD, 13 were diagnosed with ADHD-Combined Subtype and 7 with ADHD-Inattentive Subtype.

Control children were screened for psychiatric conditions with the Child Behavior Checklist (CBCL) (Achenbach, 1991) ($n = 14$, Attention Problems: $M = 50$, $SD = 0$) or the BASC ($n = 7$, Hyperactivity: $M = 42.83$, $SD = 8.08$; Attention Problems: $M = 43.83$, $SD = 3.37$). All children were screened for reading disorder using the Woodcock Johnson Third Edition (III) Letter Word Identification and Word Attack. Children with ADHD were excluded if they had co-morbid neurological or psychiatric disorders or learning disabilities except Oppositional Defiant Disorder ($n = 2$). ADHD children participated following withdrawal of stimulant medications for at least 24 hours (methylphenidate: $n = 8$; dextroamphetamine: $n = 6$); 6 children were unmedicated.

**Design and Stimulus Materials**

**ASRT.** A 2 x 2 x 5 mixed design was used with Group (ADHD vs. Control) as a between-subjects factor and Trial type (Pattern vs. Random) and Epoch (1 – 5) as within-subjects factors.

Each trial began with three empty circles displayed horizontally across a screen (Figure 1, upper portion), each mapped to a keyboard key (“M” and the adjacent symbol keys < and >). On each trial, one circle was filled and remained filled until participants pressed the correct key. The circles remained empty for 120 ms between trials. A pattern was randomly assigned to each participant (either A-r-B-r-C-r or A-r-C-r-B-r, where A,
B, and C denote the left, central and right positions and r denotes a random element, constrained so that all locations appeared with equal frequency). The three-position long pattern repeated throughout the experiment.

CC. A 2 x 2 x 6 mixed design was used with Group (ADHD vs. Control) as a between-subjects factor and Configuration (Repeated vs. Novel) and Epoch (1 – 6) as within-subject factors.

Each trial consisted of a 12-element stimulus array of a single target and 11 distractors presented in white on a gray background (Figure 1, lower portion). The target was a horizontal “T” rotated left or right by 90°, to which subjects responded by pressing a keyboard key (“Z” for left, “/” for right). The distractors were “L”s randomly rotated by 0°, 90°, 180°, or 270°. Arrays were generated by randomly placing the 12 items into cells of an invisible grid (6 rows x 8 columns). Target location was balanced for distance from the screen’s center and screen half (left/right); no target appeared in the four center or corner cells. Every element was randomly repositioned by ± 2 pixels along each axis to avoid colinearity. Each block consisted of 24 trials: 12 unique configurations of distractors.
(Novel) and 12 configurations of distractors that repeated across the experiment (Repeated). Target location, but not orientation (left/right), was fixed for each Repeated configuration. Following the task, 24 configurations (12 Novel, 12 Repeated) were tested for recognition memory.

Procedure

Participants performed the ASRT and CC tasks within a single session in counterbalanced order. Both tasks were self-paced. Participants took short breaks between blocks, approximately every 90 s on the ASRT task and every 60 s on the CC task. Including breaks, total time on the ASRT task ranged from 20 – 25 minutes and total time on the CC task ranged from 30 – 45 minutes. For both tasks, children were instructed to rest their hands over the relevant response keys. The experimenter confirmed that this was done throughout the task.

**ASRT Task.** Stimuli were presented via E-Prime with instructions to press the key that matched the filled-in circle’s location (“M” and the adjacent symbol keys < and >). Participants completed 20 blocks of 60 trials each. Blocks were grouped into 5 epochs of 4 blocks (e.g., Blocks 1 - 4 comprised Epoch 1). Each block began with 8 practice trials and ended with feedback encouraging speed and accuracy. We did not test for the conscious awareness of learned sequences. However, it is unlikely that children would become aware of the regularity in the ASRT task given that college students do not, demonstrated using various assessments of awareness including recognition tests (Howard et al., 2004). Adding these tests would have unacceptably increased testing time.
**CC Task.** Stimuli were presented via Matlab with instructions to locate the “T” as quickly and accurately as possible. Following 24 practice trials, participants completed 30 blocks of 24 trials each. Trials were randomized within blocks. Blocks were grouped into 6 epochs of 5 blocks (e.g., Blocks 1 - 5 comprised Epoch 1). On each trial, a fixation dot appeared for 1 s followed by a stimulus, which remained until a response was made. If no response was made within 6 s, the trial timed-out following an error-tone. Feedback tones were high-pitched for correct responses and low-pitched for errors. The recognition memory test was administered at the end of the 30 blocks. Participants viewed one block of 24 recognition trials and pressed a key for familiar configurations.

**Results**

Percentage of correct responses (accuracy) and median Reaction Times (RTs) for correct trials were computed for each condition and epoch for each participant. Intra-individual variability was examined by computing coefficients of variability (Mean RT/Standard Deviation). Cohen’s $d$ and $\eta^2_p$ effect sizes are reported for t-tests and Analyses of Variance (ANOVAs), respectively.

**ASRT Task**

Accuracy and median RTs and coefficients of variability for correct trials were computed for each participant and were analyzed in separate Group (ADHD vs. Control) X Trial type (Pattern vs. Random) X Epoch (1 – 5) repeated measures ANOVAs. On this task, sequence learning is defined by a Trial type X Epoch interaction, indicating greater sensitivity to sequential information with practice. Analysis of accuracy revealed no significant main effects or interactions except higher accuracy on Pattern than Random trials (main effect of Trial type), $F (1, 38) = 65.14, p < .0001, \eta^2_p = .63$ (all other $ps > .23$,
\(\eta_p^2 < .04\). Overall accuracy was high in both ADHD (Pattern: \(M = 93.62\%\), \(SD = 4.05\); Random: \(M = 91.18\%\), \(SD = 4.33\)) and control (Pattern: \(M = 94.06\%\), \(SD = 3.60\); Random: \(M = 91.28\%\), \(SD = 4.82\)) groups.

Overall RTs did not differ between groups (main effect of Group), \(p = .19\), \(\eta_p^2 = .04\) (Figure 2). Participants exhibited improvement in perceptual-motor skill, as responses were faster with practice (main effect of Epoch), \(F(4, 152) = 13.53\), \(p < .0001\), \(\eta_p^2 = .26\). Overall, participants were sensitive to sequential information, as responses were faster on Pattern than Random trials (main effect of Trial Type), \(F(1, 38) = 40.27\), \(p < .0001\), \(\eta_p^2 = .52\). While overall sequence learning was not significant (Trial type X Epoch interaction), \(p = .11\), \(\eta_p^2 = .05\), it differed between ADHD and control children (Group X Trial Type X Epoch interaction), \(F(4, 152) = 2.89\), \(p = .02\), \(\eta_p^2 = .07\). No other interactions reached significance (all \(ps > .62\), \(\eta_p^2 < .02\)). We examined this three-way interaction in two ways: 1) We determined whether significant sequence learning was obtained in each group with separate Trial type X Epoch ANOVAs; and 2) We determined whether sensitivity to sequential information differed between groups during practice with separate Group X Trial type ANOVAs for each epoch. Sequence learning was significant in control children (Trial type x Epoch interaction), \(F(4, 76) = 2.71\), \(p = .04\), \(\eta_p^2 = .13\), but only marginally so in children with ADHD, \(p = .09\), \(\eta_p^2 = .10\). Further, sensitivity to

![Figure 2: Median response time (in ms) on the ASRT task as a function of epoch and trial type for the ADHD and control groups.](image-url)
sequential information was reduced in ADHD relative to control children at the midpoint of practice, in Epoch 3 (Group x Trial type interaction), $F(1, 38) = 5.52, p = .02, \eta_p^2 = .13$, but not in other epochs ($ps > .11, \eta_p^2 < .07$). Thus, magnitude of implicit sequence learning was reduced in ADHD compared to control children.

Analysis of coefficients of variability did not reveal group differences in intra-individual variability (ADHD: $M = .34, SD = .14$; CON: $M = .34, SD = .23$) as no main effects or interactions reached significance (all $ps > .13, \eta_p^2 < .06$).

**CC Task**

One subject with ADHD was excluded for failure to comply with task instructions. Following Chun & Jiang (1998), trials without a response within 6 s were excluded from analysis. The mean number of trials without a response was small and did not differ between groups (ADHD: $M = 1.37, SD = 1.98$, Control: $M = 1.75, SD = 4.47$, $p = .73, d = .11$).

Accuracy and median RTs and coefficients of variability for correct trials were computed for each participant and were analyzed in separate Group (ADHD vs. Control) X Configuration (Repeated vs. Novel) X Epoch (1 – 6) repeated measures ANOVAs. On this task, spatial contextual learning is defined by a Configuration X Epoch interaction indicating greater sensitivity to repeated spatial context with practice. Accuracy was weakly sensitive to contextual learning, as the Configuration x Epoch interaction was marginally significant, $F(5, 185) = 1.95, p = .09, \eta_p^2 = .05$ (other $ps > .13, \eta_p^2 < .06$); no other main effects or interactions reached significance. Overall accuracy was high in the ADHD (Repeated: $M = 96.39\%$, $SD = 2.27$; Novel: $M = 96.55\%$, $SD = 2.38$) and control (Repeated: $M = 96.79\%$, $SD = 2.35$; Novel: $M = 96.35\%$, $SD = 2.77$) groups.
Analysis of RTs revealed that responses were marginally slower in ADHD than Control children (main effect of Group), $F(1, 37) = 3.05, p = .09, \eta_p^2 = .08$ (Figure 3). Participants exhibited improvement in visual search skill, as responses were faster with practice (main effect of Epoch) $F(5, 185) = 61.11, p < .0001, \eta_p^2 = .62$. While overall responses were faster to Repeated than Novel configurations (main effect of Configuration), $F(1, 37) = 15.84, p = .003, \eta_p^2 = .30$, children exhibited context-dependent learning, as the benefits of repetition increased with practice (Configuration x Epoch interaction), $F(5, 185) = 2.52, p = .03, \eta_p^2 = .06$. No other interactions reached significance (all $ps > .24, \eta_p^2 < .04$). Thus, in contrast to the ASRT task, spatial contextual learning did not differ between groups.

In light of slower visual search in ADHD relative to control children, we determined whether differences in learning were apparent on a measure that expressed learning as a proportion of one’s baseline speed (i.e., Novel – Repeated/Novel calculated per epoch). Proportional learning scores computed for each participant were analyzed in a Group X Epoch ANOVA. Similar to the analysis of median RTs, proportional measures of learning did not differ between groups (Group x Epoch interaction), $p = .22, \eta_p^2 = .04$. Thus, the absence of group differences in learning cannot be attributed to baseline speed differences.
Analysis of coefficients of variability revealed that responses were marginally more variable in ADHD ($M = .45$, $SD = .05$) relative to control ($M = .42$, $SD = .05$) children, $F (1, 37) = 3.15$, $p = .08$, $\eta_p^2 = .08$. No other main effects or interactions reached significance (other $ps > .19$, $\eta_p^2 < .04$).

For the recognition memory test, the percentage of repeated trials correctly identified as old (i.e., Hits) and the percentage of novel trials incorrectly identified as old (i.e., False Alarms) were computed for each participant and analyzed in a Group (ADHD vs. Control) X Trial (Hits vs. False Alarms) repeated measures ANOVA. Overall, the percentage of Hits ($M = 58.33\%$, $SD = 19.44$) was greater than the percentage of False Alarms ($M = 44.14\%$, $SD = 18.83$) (main effect of Trial), $F (1, 35) = 6.23$, $p = .02$, $\eta_p^2 = .15$. However, recognition memory for repeated configurations did not differ between groups (main effect of Group, $p = .13$, $\eta_p^2 = .07$, Group x Trial interaction, $p = .57$, $\eta_p^2 = .01$). Thus, there were no group differences in explicit awareness on the CC task.

Discussion

Two forms of implicit learning were dissociable in children with ADHD and controls: Implicit sequence learning on the ASRT task was reduced in children with ADHD relative to controls. In contrast, implicit spatial contextual learning on the CC task did not differ between children with ADHD and controls. These results suggest a selective implicit sequence learning deficit in childhood ADHD.

The present CC results differ from past studies in that recognition memory for repeated configurations was above chance. Inspection of individual children’s recognition memory data revealed these results were due to superior explicit memory in a subset of control children. Specifically, high recognition accuracy in three control
children (Hits: M = 100.0%, SD = 0; False Alarms: M = 2.78%, SD = 4.81) accounted for the significant difference between Hits and False Alarms (see Appendix). However, the control children with explicit awareness on the CC task did not influence CC learning for the following reasons. First, their CC learning was within the 95% Confidence Interval of the group (see Appendix). Second, most importantly, CC learning and recognition memory for spatial context did not differ between groups regardless of whether the three control participants with high recognition accuracy were included (see Appendix). Thus, superior recognition memory in a subset of control children did not account for the lack of group differences in implicit spatial contextual learning.

Group differences in explicit memory and performance characteristics did not contribute to reduced implicit sequence learning in ADHD children. First, it is unlikely that greater implicit sequence learning in control children was mediated by superior explicit awareness of sequential information. Healthy adult subjects do not usually become aware of sequential elements on the ASRT task because they are non-contiguous (Howard et al., 2004). While we did not directly assess explicit awareness on the ASRT task, recognition memory on the CC task provides an index of children’s explicit memory ability. Recognition memory did not differ statistically between groups but was above chance in three control children as discussed above. Those three control children with superior explicit memory, however, did not inflate the magnitude of ASRT learning because: 1) Reduced implicit sequence learning in ADHD persisted after excluding those three participants and 2) Implicit sequence learning on the ASRT task for those participants was within the 95% confidence interval of the group (see Supplemental Materials). Thus, using the recognition memory data on the CC task as an index of
children’s ability for explicit memory, it appears that superior explicit awareness did not relate to superior implicit sequence learning in controls. Second, reduced implicit sequence learning was not an artifact of atypical perceptual-motor performance in ADHD children. Specifically, there were no group differences in response speed or variability in the ASRT task. Furthermore, atypical perceptual-motor response characteristics do not appear to influence the magnitude of implicit learning because ADHD children’s responses tended to be slower and more variable on the CC task but their learning did not differ from control children. Slower and more variable responses were observed on the CC but not ASRT task, most likely due to the longer inter-stimulus interval (ISI), 1000 ms on the CC task but 120 ms on the ASRT task. Longer ISIs are likely to promote lapses of attention, exacerbating sustained attention problems that are a defining symptom of ADHD. Indeed, increasing the ISI on the Continuous Performance Task led to increasingly impaired target detection in ADHD relative to control children (Borger & van der Meere, 2000).

Reduced sequential but not spatial contextual learning suggests that a learning process dependent upon frontal-striatal-cerebellar circuitry was selectively impaired in ADHD. In light of current models of ADHD, at least two characteristics of that learning process are suggested by the present findings: First, functional and structural pathology of dorsal striatal projections to and from prefrontal and cerebellar regions are thought to underlie impaired executive control of responses in ADHD (Castellanos, Sonuga-Barke, Milham, & Tannock, 2006). Impaired executive response control, however, is unlikely to mediate the observed reduction in implicit sequence learning because learning occurs without conscious awareness and independently of working memory capacity (Gabrieli,
Executive control, however, requires conscious awareness and relies heavily on working memory capacity (Miller & Cohen, 2001). Indeed, the magnitude of ASRT learning in ADHD children in the present study (i.e., sum of the difference between trial types across epochs) did not correlate with parental report of the extent of executive dysfunction (measured using BRIEF Global Executive Composite T scores, M = 65.84, SD = 12.86. $r = -0.01, p = .96$). Further, electrophysiological studies with non-human primates reveal dissociable time courses of neuronal activity during learning and executive control. During associative learning, activity in striatal neurons encodes probabilistic information and their firing rate precedes that of prefrontal neurons (Pasupathy & Miller, 2005), whereas during executive control, activity in prefrontal neurons encodes goal related information and their firing rate precedes that of striatal neurons (Muhammad, Wallis, & Miller, 2006). Thus, impairments in implicit sequence learning and executive control may reflect distinct deficits in bottom-up and top-down frontal-striatal-cerebellar signaling, respectively.

Second, behavioral and neuroimaging studies with ADHD participants have suggested aberrations in temporal processing (Nigg & Casey, 2005). As the to-be-learned sequential information unfolds over time, it is possible that deficits in predicting when an event is likely to occur may underlie the observed reduction in implicit learning. Indeed, children and adolescents with ADHD showed a smaller difference in response speed and reduced cerebellar activation when target stimuli on a Go/No-Go task appeared at an unexpected time rather than at an expected time (Durston et al., 2007). However, this study did not examine whether these differences emerged later in the task, which would indicate impaired learning, or were pervasive throughout the task, which could
indicate an atypical response to novelty. Our study suggests that impaired learning could relate to the reduced response to expectancy violations in ADHD, but it does not exclude the possibility that an atypical response to novel information could also contribute to the results. Further work is needed to disentangle the relationship between learning, temporal processing, and novelty processing in childhood ADHD.

In sum, the present study extends atypical cognition in ADHD children beyond the domain of conscious processes to associative implicit learning. Our findings show a selective impairment in associative implicit learning mediated by frontal-striatal-cerebellar circuits. This selective impairment has also been observed in dyslexia (Howard, Howard, Japikse, & Eden, 2006), another disorder of developmental origin. However, a dissociation between implicit sequence and spatial contextual learning is not ubiquitous to developmental disorders because both forms of learning were spared in Autism Spectrum Disorder (Barnes et al., in press). While ADHD, dyslexia, and Autism Spectrum Disorder differ in their symptomatology, they often share executive dysfunction and temporal processing deficits. Thus, exploring the relationship between impaired frontal-striatal-cerebellar processes (e.g., implicit sequence learning, executive control, and temporal processing) in a broader developmental context may ultimately yield the greatest insight into the neurocognitive basis of disordered development.
Chapter IV:

Intact implicit learning of spatial context and temporal sequences in childhood

Autism Spectrum Disorder

(This chapter has been accepted for publication as Barnes, KA, Howard JH, Jr., Howard DV, Gilloty, L, Kenworthy, L, Gaillard, WD, & Vaidya, CJ. (in press). Neuropsychology.)

The ability to learn environmental regularities (e.g., where or when events may occur) implicitly, without intention or conscious awareness, is posited to support linguistic and motor skill acquisition (Perruchet & Pacton, 2006) and social intuition (Lieberman, 2000). Impairments in these domains characterize children with Autism Spectrum Disorder (ASD) in whom difficulties with social communication accompany repetitive behaviors and restricted interests. Implicit learning of contextual information guides perception of social cues and predicts actions and therefore may mediate atypical cognition in ASD. However, investigation of the integrity of learning processes has not figured centrally in models of cognitive dysfunction in ASD. The present study examined implicit contextual learning in two domains: In the spatial domain, repeated experience with invariant spatial relationships provides predictive cues that guide visual attention during visual search tasks (e.g., Contextual Cueing [CC] task, Chun, 2000). In the perceptual-motor domain, repeated experience with invariant sequential structure of stimuli forms the basis for predicting subsequent responses to contiguous (e.g., Serial Reaction Time [SRT] Task, Nissen & Bullemer, 1987) or non-contiguous (e.g., Alternating SRT [ASRT] task, Howard & Howard, 1997) stimuli. Learning is implicit because participants cannot recollect or recognize the learned spatial context or sequential information. Knowledge of these two forms of implicit learning in ASD is necessary for constraining knowledge about the status of cognition in the disorder.
Examining two forms of implicit learning in ASD provides the opportunity to probe the functional integrity of learning mechanisms shown to be dissociable in adults. Whether functional specialization of memory systems is complete by late childhood is not fully known. Nevertheless, forms of learning that have been dissociated in adults provide a heuristic for systematic examination of memory systems in childhood (see also Berl, Vaidya, & Gaillard, 2006). Spatial contextual learning is hypothesized to involve the medial temporal lobes (i.e., the hippocampus, and entorhinal, perirhinal, and parahippocampal cortices) because learning was reduced in patients with extensive medial temporal lobe lesions (Chun & Phelps, 1999). While hippocampal lesions did not disrupt learning on the CC task (Manns & Squire, 2001), hippocampal involvement was observed using functional brain imaging during CC performance in healthy adults (Greene, Gross, Elsinger, & Rao, 2007). Furthermore, activations also involved lateral frontal and temporal cortices projecting to the medial temporal lobe. Thus, while the necessity of the hippocampus remains to be established, other medial temporal lobe regions and their cortical projections appear to be important for spatial contextual learning.

In contrast to spatial contextual learning, sequence learning is hypothesized to involve striatal circuitry because it is impaired in people with Huntington’s and Parkinson’s disease (Willingham, 1997), which are characterized by degeneration of basal ganglia structures. Functional brain imaging studies also show involvement of the cerebellum and regions projecting to the striatum such as prefrontal and motor cortices in adults on the ASRT and SRT tasks (Fletcher et al., 2005; Rauch et al., 1997; Willingham, Salidis, & Gabrieli, 2002) and in children on the SRT task (Thomas et al., 2004).
dissociations in elderly participants further suggest that implicit spatial contextual and sequence learning are separable. Specifically, Negash et al. (2007) reported reduced CC but not ASRT learning in individuals with Mild Cognitive Impairment, a condition characterized by medial temporal lobe pathology, compared to age-matched controls. In contrast, reduced ASRT but not CC learning was reported in healthy aging (Howard, Howard, Dennis, Yankovich, & Vaidya, 2004), a period characterized by reductions in striatal, cerebellar, and prefrontal volumes with relative sparing of the medial temporal lobes (Raz et al., 2005). Thus, brain imaging and neuropsychological findings suggest that medial temporal and fronto-striatal-cerebellar circuits mediate learning of spatial context and sequential structure, respectively.

Cognitive strengths and weaknesses observed in ASD lead to distinct hypotheses about the status of implicit learning. A strength observed in ASD is a tendency towards superior processing of local information. Relative to controls, participants with ASD are faster at detecting targets embedded in complex visual figures (Jolliffe & Baron-Cohen, 1997) and give fewer context-appropriate pronunciations of homographs (Happé, 1997). The source of this bias, whether due to impaired (Happé, 1999) or unaffected (Mottron, Burack, Iarocci, Belleville, & Enns, 2003; Plaisted, Saksida, Alcantara, & Weisblatt, 2003) global information processing remains unresolved. Nevertheless, those findings suggest that contextual information weakly modulates visual-perceptual and linguistic processing in ASD. Such a bias could reduce contextual encoding, thereby reducing learning dependent on invariant contextual information in ASD, regardless of stimulus domain. Thus, this view hypothesizes reduced learning on both sequence learning and contextual cueing tasks. Consistent with this prediction, sequence learning on the SRT
task was reduced in children with ASD (Mostofsky, Goldberg, Landa, & Denckla, 2000). Alternatively, intact learning on both sequence learning and contextual cueing tasks may be hypothesized in light of one of the core symptoms of ASD, the need for sameness and regularity. The preference for repetition in ASD may promote acquisition of invariant contextual information leading to spared or superior learning of spatial and sequential relationships. Thus, there are reasonable arguments to hypothesize both impaired and intact contextual learning in ASD. The present study tested these hypotheses by examining both learning of spatial context and sequential information in the same children with ASD and matched controls.

We examined implicit learning of spatial context using the CC task and of sequences using the ASRT task, in children with ASD and age, gender, and IQ matched controls. On the CC task, participants search for a target among distractors whose spatial configuration repeats on some trials and is novel on others. Context-dependent learning is indexed by faster responding on trials with repeated than novel distractor configurations. On the ASRT task, participants respond to the location of a visual stimulus by pressing a corresponding key. Unbeknownst to participants, the stimulus location varies in a fixed sequence involving alternate trials (i.e., item \( n \) predicts item \( n +2 \) on these trials); randomly determined stimulus locations alternate with sequence trials. Context-dependent learning is indexed by faster responding on sequence than random trials. The ASRT rather than SRT task was used for two reasons. First, the ASRT task is more resistant to the development of conscious awareness of underlying sequential structure and use of explicit memory strategies during performance. Therefore, differences in explicit memory abilities are less likely to influence sequence learning.
Second, the ASRT task is more sensitive to ongoing learning because performance on sequential and random trials is assessed continuously during learning rather than after learning has occurred. Thus, factors affecting expression of learning such as fatigue are minimized for ASRT than SRT learning.

Method

Participants

Fourteen children with ASD (13 males) aged 8 to 14 years with IQ within the normal range were recruited from Children’s National Medical Center (see Table 1). Ten children with ASD had a diagnosis of Asperger Syndrome; of the four remaining children with ASD, two had a diagnosis of High Functioning Autism and two had a diagnosis of Pervasive Developmental Disorder-Not Otherwise Specified. Fourteen control children (13 males) aged 7 to 14 years with IQ within the normal range were recruited from the Washington, DC area through advertisements. The groups matched for gender, age (ASD: $M = 11.57$, $SD = 1.65$, Controls: $M = 11.00$, $SD = 1.80$, $p = .39$), and IQ (ASD: $M = 110.43$, $SD = 12.59$, Controls: $M = 116.29$, $SD = 13.79$, $p = .25$). All parents or guardians provided informed consent; children provided informed assent and were paid for participation.

Children were diagnosed with ASD by clinicians using DSM-IV-TR criteria (APA, 2000); diagnosis was confirmed by expert opinion of clinicians specializing in ASD (LK, LG) (see Table 1). The Childhood Asperger Syndrome Test (CAST) (Scott, Baron-Cohen, Bolton, & Brayne, 2002) was used to objectively screen for ASD symptoms (cutoff = 15); all participants with ASD were above the ASD cutoff (see Table
1). Additionally, a portion of children with ASD who had clinical evaluations at Children’s National Medical Center received the Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Schedule (ADOS) (Lord et al., 2000; Lord, Rutter, & Le Couteur, 1994). Seven children received both ADI-R and ADOS, three children ADOS only, one child ADI-R only, and 3 children neither ADI-R nor ADOS. All ADOS Social Domain Summary Scores ($M = 8.60$, Range = 4 – 13, Cutoff = 4) and all but one of the ADOS Communication Domain Summary Scores ($M = 3.60$, Range = 1 – 8, Cutoff = 2) were above the ASD cutoff. Restricted and Repetitive Behavioral Domain Summary Scores were consistent with Lord et al.’s (2000) scores ($M = 3.00$, Range = 2 – 4, No Cutoff). ADI scores were above the Autism cutoff (Reciprocal Social Interaction: $M = 21.12$, Range = 18 – 25, Cutoff = 10; Communication: $M = 19.25$, Range = 14 – 24, Cutoff = 8; Restricted and Repetitive Behaviors: $M = 8.62$, Range = 5 – 12, Cutoff = 3). Exclusion criteria included other neurological disorders (e.g., epilepsy), IQ < 85, or use of anti-psychotic medications. Medications could not be withdrawn in 10 children with ASD who participated on anti-depressants (9), stimulants (3), non-stimulants (i.e., Strattera) (1), or Valproic Acid (1); 4 children were unmedicated. Control children were screened for ASD using the CAST (Scott et al., 2002) and psychiatric conditions (e.g., Attention Problems) using the Child Behavior Checklist (Achenbach, 1991). Children completed the subtests of the Woodcock Johnson III Diagnostic Reading Battery to screen for reading disorder. No control participants had any neurological or psychiatric conditions, including ASD. Unpaired t-tests confirmed that symptoms on the CAST were higher in ASD than control participants (ASD: $M = 19.71$, $SD = 4.20$; Controls: $M = 5.00$, $SD = 3.19$, $t (26) = 10.45$, $p < .0001$).
Table 1. ASD Participant Demographics

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<th>Gender</th>
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Note. FSIQ = Full-Scale IQ determined by WISC-III or WASI. CAST = Childhood Asperger Syndrome Rating Scale Score (ASD diagnosis suggested by scores higher than 15). Diagnosis: ASP = Asperger Syndrome, HFA = High-functioning Autism, PDD = Pervasive Developmental Disorder Not Otherwise Specified. All children with a diagnosis of ASP had normal onset of language and normal adaptive functioning. CC Learning: faster RTs to Repeated than Novel configurations in the last epoch. ASRT Learning: faster RTs to Pattern than Random trials in the last epoch. S3’s CAST score was one point below cutoff, but this participant met criteria for ASD on the ADI/ADOS.

CC Task.

Design and Stimulus Materials. A 2 x 2 x 6 mixed design was used with Group (ASD vs. Control) as a between-subjects factor and Configuration (Repeated vs. Novel) and Epoch (1 - 6) as within-subject factors.

Each trial consisted of a 12-element stimulus array of a single target and 11 distractors presented in white on a gray background (Figure 1, upper portion). The target was a horizontal “T” rotated left or right by 90°, to which subjects responded by pressing a keyboard key (“z” for left, “/” for right). The distractors were “L”s randomly rotated by 0°, 90°, 180°, or 270°. Arrays were generated by randomly placing the 12 items into cells of an invisible grid (6 rows x 8 columns). Target location was balanced for distance
from the screen’s center and screen half (left/right); no targets appeared in the four center or corner cells. Every element was randomly repositioned by +/-2 pixels along each axis to avoid colinearity. Each block consisted of 24 trials: 12 unique configurations of distractors (Novel) and 12 configurations of distractors that repeated across the experiment (Repeated). Target location, but not orientation (left/right), was fixed for each Repeated configuration.

Procedure. Stimuli were presented via Matlab with instructions to locate the ‘T’ as quickly and accurately as possible. Following 24 practice trials, participants completed 30 blocks of 24 trials each. Trials were randomized within blocks. Blocks were grouped into 6 epochs of 5 blocks (e.g., Blocks 1 - 5 comprised Epoch 1). On each trial, a fixation dot appeared for 1 second followed by a stimulus, which remained until a response was made. If no response was made within 6 seconds, the trial timed-out following an error-tone. Feedback tones were high-pitched for correct responses and low-pitched for errors. Following the task, 24 configurations (12 Novel, 12 Repeated) were presented for recognition memory; participants pressed a key for familiar configurations.
**ASRT Task**

*Design and Stimulus Materials.* A 2 x 2 x 5 mixed design was used with Group (ASD vs. Control) as a between-subjects factor and Trial type (Pattern vs. Random) and Epoch (1 - 5) as within-subjects factors.

Each trial began with three empty circles displayed horizontally across a screen (Figure 1, lower portion), mapped to a keyboard key (“M” and the adjoining symbol keys < and >). On each trial, one circle filled in and remained filled until participants pressed the correct key. The circles remained empty for 120 ms between trials. One of two patterns was randomly assigned to each participant (either A-r-B-r-C or A-r-C-r-B-r, where A, B, and C denote the left, central, and right positions and r denotes a random element, constrained so that all locations appeared with equal frequency). The three-position long pattern repeated throughout the experiment.

*Procedure.* Stimuli were presented via E-Prime with instructions to press the key that matched the filled-in circle’s location (“M” and the adjoining symbol keys < and > on a keyboard). Participants completed 20 blocks of 60 trials each. Blocks were grouped into 5 epochs of 4 blocks (e.g., Blocks 1 - 4 comprised Epoch 1). Each block began with 8 practice trials and ended with feedback encouraging speed and accuracy. Conscious awareness for learned sequences is commonly tested subjectively with questions such as “Did you notice any regularity in the way the stimulus moved?” We did not include such a test because metacognitive immaturity in childhood often results in unreliable introspective reports (Kuhn, 2000).
**General Procedure**

Participants performed the CC and ASRT tasks within a single session in counterbalanced order. Both tasks were self-paced. Participants took short breaks between blocks, approximately every 60 s on the CC task and every 90 s on the ASRT task. Including breaks, total time on the CC task ranged from 30 – 45 minutes and total time on the ASRT task ranged from 20 – 25 minutes. For both tasks, children were instructed to rest their hands over the relevant response keys during the experiment. The experimenter confirmed that this was done throughout the task.

**Results**

Trials with Reaction Times (RTs) that were three or more standard deviations from the mean were excluded. The percentage of excluded trials did not differ between groups (CC: ASD: $M = 1.00\%, SD = .73$, Control: $M = .81\%, SD = .54$, $p = .45$, $d = .30$; ASRT: ASD: $M = 1.15\%, SD = .49$, Control: $M = 1.27\%, SD = .63$; $p = .56$, $d = .21$). Based on past research using the CC task (Chun & Jiang, 1998), trials without a response within 6 seconds were excluded (Total trials - ASD = 11; Controls = 5). Cohen’s $d$ and $\eta_p^2$ effect sizes are reported for t-tests and ANOVAs, respectively.

**CC Task**

Percentage of correct responses (accuracy) and mean RTs for correct trials were computed for each participant and were analyzed in Group (ASD vs. Control) X Configuration (Repeated vs. Novel) X Epoch (1 - 6) repeated measures Analyses of Variance (ANOVAs) (Figure 2). Analysis of accuracy revealed no significant main effects or interactions except a trend for higher accuracy for Repeated than Novel configurations (main effect of Configuration), $F (1, 26) = 3.89, p = .06$, $\eta_p^2 = .13$ (other
Overall accuracy was high (ASD: $M = 97.58\%, SD = 1.88$; Control: $M = 97.03\%, SD = 2.31$).

Analysis of RTs revealed that responses were slower in ASD than Control children (main effect of Group), $F (1, 26) = 5.20, p < .03, \eta_p^2 = .17$. Participants exhibited learning of visual search skill because responses were faster with practice (main effect of Epoch), $F (5, 130) = 43.57, p < .0001, \eta_p^2 = .63$. While overall responses were faster to Repeated than Novel configurations (main effect of Configuration), $F (1, 26) = 17.95, p < .0001, \eta_p^2 = .41$, children exhibited context-dependent learning because the benefits of repetition increased with practice (Configuration X Epoch interaction), $F (5, 130) = 3.25, p = .008, \eta_p^2 = .11$. Magnitude of learning did not differ between groups (Group X Epoch X Configuration interaction, $p = .95, \eta_p^2 = .01$). No other interactions reached significance (all $ps > .14, \eta_p^2 < .06$).

In light of slower visual search in ASD relative to control children, we determined whether differences in magnitude of learning were apparent on a measure that equated speed by expressing learning as a proportion of one’s baseline speed (i.e., Novel – Repeated/ Novel, calculated per epoch). Proportional learning scores computed for each participant were analyzed in a Group X Epoch ANOVA. The main effect of Group and

\[ \text{Figure 2. Mean response time (in seconds) on the CC task as a function of epoch and type of configuration for ASD and control groups.} \]
the Group x Epoch interaction were not significant ($ps > .43, \eta_p^2 < .02$) indicating that measures of proportional learning did not differ between ASD and Control children. Thus, the absence of group differences in learning was not an artifact of speed differences because group differences were not observed after equating for response speed.

For the recognition memory test, d-prime scores [$z$(hits) $- z$(false alarms)] were computed for each participant. One-sample t-tests indicated that d-prime scores did not differ from chance in ASD ($M = .75$, $SD = 1.50$, $p = .11$) and Control ($M = .28$, $SD = 1.41$, $p = .54$) children. Further, an unpaired t-test indicated that d-prime scores did not differ between groups ($p = .44$, $d = .32$). Thus, participants were unable to consciously recognize the repeated configurations.

**ASRT Task**

Percentage of correct responses (accuracy) and mean RTs for correct trials were computed for each participant and were analyzed in Group (ASD vs. Control) X Trial Type (Pattern vs. Random) X Epoch (1-5) repeated measures ANOVAs (Figure 3). Accuracy did not differ between ASD ($M = 92.25\%$, $SD = 3.48$) and Control ($M = 93.37\%$, $SD = 3.08$) participants (main effect of Group, $p = .38$, $\eta_p^2 = .03$). Participants were more accurate on Pattern than Random trials (main effect of Trial type), $F (1, 26) = 36.40$, $p < .0001$, $\eta_p^2 = .58$, and accuracy increased with practice (main effect of Epoch), $F (4, 104) = 2.42$, $p < .05$, $\eta_p^2 = .09$. No interactions reached significance (all $ps > .17$, $\eta_p^2 < .06$).

Overall RTs did not differ between groups (main effect of Group, $p = .90$, $\eta_p^2 = .001$). Participants exhibited perceptual-motor skill learning because responses were faster with practice (main effect of Epoch), $F (4, 104) = 6.59$, $p < .0001$, $\eta_p^2 = .20$. 

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While overall responses were faster to Pattern than Random trials (main effect of Trial type), $F(1, 26) = 32.13, p < .0001, \eta^2_p = .55$, children exhibited sequence learning because the benefits of repetition increased with practice (Trial type X Epoch interaction), $F(4, 104) = 3.72, p = .007, \eta^2_p = .13$.

Group differences in learning were suggested by a Group X Epoch X Trial type interaction, $F(4, 104) = 2.53, p < .05, \eta^2_p = .09$. No other interactions reached significance (all $ps > .26, \eta^2_p < .05$). We examined the three-way interaction for effects of Group (with Epoch X Trial type ANOVAs for each group) and Epoch (with Group X Trial type ANOVAs for each epoch). Each group exhibited sequence learning because the Epoch X Trial type interaction reached significance (ASD: $F(4, 52) = 2.60, p < .05, \eta^2_p = .17$; Control: $F(4, 52) = 3.60, p = .01, \eta^2_p = .22$).

Sequence learning marginally differed between groups in Epoch 5 (Group x Trial Type interaction, $F(1, 26) = 3.84, p = .06, \eta^2_p = .13$, but not in Epochs 1-4 (all $ps > .11, \eta^2_p < .10$). Planned comparisons indicated that the difference between Pattern and Random trials was larger in ASD than Control participants in Epoch 5, $t(26) = 1.96, p = .06, d = .74$ (other Epochs $ps > .11, d < .63$). Thus, ASD but not control children continued to show learning into the last epoch.
It is possible that group differences in magnitude of learning emerged because the ASD group’s response speed appeared to improve to a greater extent than did controls’. We therefore determined whether differences in magnitude of learning were apparent on a measure that equated speed by expressing learning as a proportion of one’s baseline speed (i.e., Random – Pattern/Random, calculated per epoch). Proportional learning scores computed for each participant were analyzed in a Group X Epoch ANOVA. Overall measures of proportional learning did not differ between ASD and control children (main effect of Group), $p = .41, \eta_p^2 = .03$. Group differences in learning were suggested by a significant Group x Epoch interaction, $F (4, 104) = 2.47, p < .05, \eta_p^2 = .09$. We examined this interaction to determine whether each group demonstrated learning (with one-way ANOVAs for each group) and whether magnitude of learning differed between the two groups (with unpaired t-tests for each Epoch). Each group exhibited sequence learning because the main effect of Epoch was significant (ASD: $F (4, 52) = 3.07, p = .02, \eta_p^2 = .19$; CON: $F (4, 52) = 3.28, p = .02, \eta_p^2 = .20$). Unpaired t-tests revealed that proportional magnitude of learning was larger in ASD than Control children in Epoch 5, $t (26) = 1.99, p = .06, d = .75$ (all other $ps > .17, d < .54$). Thus, group differences in learning persisted after controlling for baseline differences in response speed.

Discussion

Two forms of implicit learning, for spatial context and perceptual-motor sequences, did not differ between high-functioning children with ASD and controls. For spatial contextual learning, learning on the CC task did not differ between groups despite slower visual search performance in ASD relative to control children. For sequential
learning, while baseline ASRT performance did not differ between the groups, expression of learning was more prolonged in ASD than control children. Recognition memory for spatial configurations did not differ between groups, and therefore, differences in explicit memory ability are unlikely to account for the observed findings on the CC task. Explicit memory for sequences on the ASRT task was not tested.

In a disorder characterized by impaired functioning in multiple behavioral domains, spared learning abilities have important implications for future research and treatment. Nonetheless, accepting the null hypothesis requires caution and we consider several alternative explanations: First, it is possible that our measures lacked sensitivity to detect group differences in learning. However, previous studies have found reduced magnitude of learning on the ASRT task in healthy aging (Howard & Howard, 1997; Howard et al., 2004) and dyslexia (Howard, Howard, Japikse, & Eden, 2006) and on the CC task in childhood (Vaidya, Huger, Howard, & Howard, 2007) and Mild Cognitive Impairment (Negash et al., 2007), suggesting that these tasks are sensitive to group differences in learning. Second, small sample size could result in reduced statistical power, thereby reducing our ability to detect group differences in learning. Effect size for a group difference in total magnitude of learning (sum of the difference between trial types across epochs) was moderate for the ASRT task ($d = .43$) and small for the CC task ($d = .16$); the larger effect size for the ASRT task reflects greater rather than reduced learning in ASD relative to control children. The power to detect these effect sizes is low (ASRT: .17 - .25; CC task: .06 - .08). Over 70 subjects would be needed for group differences of the obtained effect sizes to be significant at $\alpha = .05$ with Power = .80. Third, similar ASRT learning in the two groups may result from differential explicit
awareness for sequential information between the two groups. In past studies using a variety of recognition measures, adult participants did not develop explicit awareness on the CC and ASRT tasks (Chun & Jiang, 2003; Song, Howard, & Howard, 2007). While CC recognition was at chance in the present study, the influence of explicit awareness on the ASRT task cannot be conclusively ruled out because it was not measured. Fourth, there were subjects in the ASD group who did not demonstrate learning in the last epoch (see Table 1), suggesting that there may be some children with ASD who showed impaired implicit learning. However, lack of implicit learning on the last epoch at the individual level is not unusual because it was apparent in some control children (ASRT task: 5/14; CC task: 1/14).

While considering our observation of lack of group differences, it is important to note that several characteristics of our sample constrain interpretation and generalization of the present findings. First, IQ was matched across groups, and therefore, the present findings are limited to intellectually high-functioning children with ASD. Second, the present findings are limited to Asperger Syndrome, the diagnosis for 10 out of the 14 children with ASD. It is also important to note that neither ADOS nor ADI scores were available on 3 children with ASD. Third, the present findings extend primarily to males with ASD because only 1 female was included in the ASD sample. Fourth, only two children with ASD were left-handed. Although hand-assignment for the tasks was not changed for these participants, exclusion of their data from analyses did not influence the results. Fifth, psychotropic medications that could not be withheld during testing in some children could have influenced learning. Four of these children were on medications for attention problems that are most likely to influence learning. However, magnitude of
learning did not differ between children medicated for attentional problems, unmedicated children with ASD, and controls on either task (unpaired t-tests, all $p_s > .31$). Further, magnitude of learning for these children was within 95% confidence intervals for mean magnitude of learning in control children for each task. Sixth, differences in fatigue did not appear to influence the results because both groups responded faster as epochs progressed. Faster performance, particularly on random/novel trials, is inconsistent with fatigued performance. Thus, the present findings most directly extend to right-handed, intellectually high-functioning males diagnosed with Asperger Syndrome.

Despite no group differences in implicit spatial contextual learning, the ASD group’s performance differed from controls in two ways. First, overall response speed on the CC task was slower in children with ASD than controls, a finding that is inconsistent with reports of superior visual search in ASD (O’Riordan, Plaisted, Driver, & Baron-Cohen, 2001; Plaisted, O’Riordan, & Baron-Cohen, 1998). Superior visual search in ASD has been posited to arise from weak central coherence (Happé, 1999) or a preference for visual details (O’Riordan et al., 2001). However, past studies have noted that superiority in ASD may not extend to all visual search tasks (Kenworthy, Black, Wallace, Ahluvalia, Wagner, & Sirian, 2005; Kleinhans, Akshoomoff, & Delis, 2005). Our finding of slower visual search in ASD is consistent with at least one previous study examining visual search for a target letter (“T” or “F”) surrounded by similar distractors (letters that were halfway between “T”s and “F”s; Edgin & Pennington, 2005). The present CC task also requires searching for a target (“T”) among similar distractors (“L”). In the present task, targets were rotated and the response required an orientation judgment for the long arm of the “T” (left/right). This added perceptual demand may have made
visual search more effortful, enhancing the task’s sensitivity to group differences. Thus, slower performance on tasks requiring visual search in ASD may be more apparent under certain experimental conditions. Slower visual search in children with ASD was not due to general motor impairments because baseline response speed on the ASRT task did not differ between groups. Task-selectivity of performance differences suggests that slower visual search in ASD reflects atypical properties of spatial attention, possibly mediated by oculomotor dysfunction (Sweeney, Takarae, Macmillan, Luna & Minshew, 2004) rather than perceptual-motor dysfunction. However, motivation levels could have also differed across tasks.

Second, learning on the ASRT task did not differ between the groups but its expression was more prolonged in ASD than control children. Studies with adults indicate that the expression of sequence learning in performance can be dissociated from the acquisition of sequence knowledge. For example, participants’ response latencies were modulated by task characteristics (e.g., stimulus context) and performance demands (e.g., inclusion of a secondary task), even though the structural knowledge of sequences they gained was unchanged (Jiminez, Vaquero, & Lupianez, 2006; Willingham, Greenberg, & Thomas, 1997). It is possible that prolonged expression of sequence learning in ASD reflects cognitive inflexibility that is known to characterize the ASD phenotype (Hill, 2004). Cognitive inflexibility may promote expression of learning pertaining to invariant stimulus-response contingencies, due to an inability to discard the adopted task set. Indeed, the tendency for more expression of sequence learning was observed in another psychiatric condition that is characterized by stereotypical behaviors and cognitive inflexibility, Obsessive-Compulsive Disorder. Patients with Obsessive-
Compulsive Disorder showed numerically, albeit not statistically, greater SRT improvement relative to controls (Rauch et al., 1997). Small sample size in the present study precludes examination of the relation between magnitude of sequence learning and cognitive inflexibility in ASD. However, this hypothesis can be tested in future studies.

Unimpaired learning of a complex sequential structure (i.e., involving 2\textsuperscript{nd} order regularity) in children with ASD is surprising in light of impaired learning of a simpler sequential structure on the SRT task (i.e., containing zero-order regularity where some positions occur more frequently than others) (Mostofsky et al., 2000). Two factors could have contributed to these differences: First, characteristics of performance differed between the groups in Mostofsky et al.’s study. Overall response speed was slower in ASD than control children perhaps due to motor impairments that are common in ASD. Thus, non-mnemonic aspects of SRT performance may have reduced the expression of learning in Mostofsky et al.’s ASD participants. Second, ASD is characterized by highly heterogeneous symptom expression. Perhaps differences in findings between the studies simply reflect distinct cohorts of children with ASD. Our sample consisted primarily of children diagnosed with Asperger Syndrome (10/14) whereas Mostofsky et al.’s participants were diagnosed with high-functioning autism. Among the 4 non-Asperger children in the present study, learning was not below the 95\% confidence interval in any child for the ASRT task but was below the 95\% confidence interval in 2 children (1 with HFA, 1 with PDD-NOS) for the CC task. Thus, future studies that compare ASD cohorts are needed to clarify the extent of sparing or impairment in implicit learning.

These results provide new knowledge about the functional integrity of neural systems that subserve implicit learning in ASD. First, the finding that children with ASD
did not differ from controls in spatial contextual learning suggests preservation of at least one mnemonic process supported by the medial temporal lobes. Volumetric and histological studies have noted differences between individuals with ASD and controls in the hippocampus (Raymond, Bauman, & Kemper, 1996; Salmond et al., 2005; Schumann et al., 2004). Spatial contextual learning appears to rely on cortical regions surrounding the hippocampus because it was intact in amnesic patients with lesions restricted to the hippocampus (Manns & Squire, 2001). These surrounding cortices were also involved in learning of hierarchical relations among elements on a transitive inference task in monkeys (Buckmaster, Eichenbaum, Amaral, Suzuki, & Rapp, 2004;). These findings suggest that medial temporal cortices are involved in relational organization of spatial information. It would be useful to examine whether these cortical areas develop typically in ASD.

Second, the finding that sequence learning in ASD did not differ from controls suggests spared frontal-striatal-cerebellar function. No consistent finding has emerged from volumetric studies of frontal-striatal-cerebellar structures in ASD (Brambilla et al., 2003) as both larger and smaller volumes have been reported. While there is agreement that these structures are involved in sequence learning and that their maturation supports its development (Thomas et al., 2004), the specific contribution of each structure is not fully known even in intact sequence learning. Functional imaging in ASD adults showed that despite comparable sequence learning with controls, activation was reduced in prefrontal cortex and increased in premotor cortex (Müller, Cauich, Rubio, Mizuno, & Courchesne, 2004). Thus, involvement of different cortical regions in adults with ASD and matched controls may support intact sequence learning in ASD. However,
participants learned the sequence explicitly rather than implicitly in Muller et al.’s study. Prefrontal involvement in sequence learning appears to depend upon the extent of explicit awareness of sequential structure in both SRT and ASRT tasks (Fletcher et al., 2005; Willingham et al., 2002). The present finding of intact ASRT learning in childhood ASD provides a basis for investigating the nature of frontal-striatal-cerebellar involvement that characterizes preserved learning.

In sum, the present findings indicate that two dissociable forms of learning, of spatial context and perceptual-motor sequences, were intact in ASD children with a diagnosis of Asperger syndrome. If the present findings are replicated in future studies, they could be harnessed for treatment purposes. Future research could study interventions that encourage children to focus on the degree to which social cues and contextual information co-occur and how that relates to the status of implicit learning. Further, findings from the ASRT task suggest that ASD may promote longer expression of learning based upon invariant sequential information. Functional imaging studies of sequence learning are required to elucidate the neural basis of the current findings. The ASRT task is an optimal probe for those studies because it taps a well-operationalized learning mechanism that is rooted in frontal-striatal-cerebellar anatomy.
Autism Spectrum Disorder (ASD) is a developmental disorder recently estimated to affect 1 in 150 children by the CDC (Kuehn, 2007). Although genetic factors are thought to underlie ASD (Abrahams & Geschwind, 2008), there is currently no biological marker for the disorder. Thus, diagnosis is based on a triad of behavioral symptoms: qualitative impairments in social interaction and communication, and restricted, repetitive, and stereotyped patterns of behavior, interest, and activities (APA, 2000).

Current neurocognitive models have primarily addressed ASD symptomatology in two ways, either positing core deficits in symptomatic domains (e.g., theory of mind, Baron-Cohen, Leslie, & Frith, 1985) or in lower-level processes (e.g., executive function, Hill, 2004) or perceptual processing biases (Happe, 1999) that might underlie symptom development. These models rely heavily on evidence from studies examining processes that are under conscious, cognitive control. However, social cognition (Evans, 2008) and language (Kuhl, 2004) are dual process systems, meaning a combination of “slow, deliberative, and conscious” and “fast, unconscious, and automatic” processes enable adaptive behavior. For example, social intuitions, a social cognitive process impaired in ASD (Frith, 2001), are “takes into account nonconsciously generated information, gathered from experience” (Lieberman, 2000, p 110). Comprehensive models of
neurocognition in ASD must begin to address the status of fast, unconscious, and automatic processes.

Behaviorally, one form of unconscious, automatic processing that occurs over the span of minutes, termed implicit sequence learning, has been shown to be intact in high functioning children with ASD. Implicit sequence learning enables learning about environmental regularities (e.g., where or when an event is likely to occur) and occurs unintentionally and without conscious awareness of what is learned. Learning is commonly measured in the perceptual-motor domain using tasks that involve repeated experience with invariant sequential structure of stimuli, which forms the basis for predicting subsequent responses to stimuli (e.g., Serial Reaction Time [SRT] task, Nissen & Bullemer, 1987). Behaviorally, two components of implicit learning were intact in high functioning children with ASD on an SRT task involving an alternating, repeated sequence (Barnes et al., in press, but see Mostofsky, Goldberg, Landa, & Denckla, 2000). Children with ASD and age-, IQ-, and gender-matched controls did not differ in general skill learning, indexed by overall faster responding with practice, or sequence-specific learning, indexed by faster responding for stimuli whose locations follow a repeating pattern than for stimuli whose locations are randomly determined. Thus, there is evidence that fast, unconscious, and automatic processes such as implicit sequence learning are intact in ASD.

Spared implicit sequence learning in ASD is surprising in light of widespread abnormalities of brain structure and function in the frontal, striatal, and cerebellar networks shown to support learning in adults (for reviews see Brambilla et al., 2003; Muller, 2007). In adults, implicit sequence learning is dependent upon these networks
because learning is impaired in individuals with damage to the prefrontal cortex (Gomez Beldarrain, Grafman, Pascual-Leone, & Garcia-Monco, 1999) and the striatum and cerebellum from degenerative disease or stroke (for review see Doyon, 2008). Functional neuroimaging studies in healthy adults confirm that these and additional cortical regions, including inferior parietal lobule, Supplementary Motor Area (SMA), and anterior cingulate cortex, are involved in implicit sequence learning because activation in these regions is greater for repeated than novel sequences of events (for review see Hazeltine & Ivry, 2002).

There are several predictions that can be made about the neural networks that might support behaviorally intact implicit sequence learning in children with ASD. On the one hand it is possible that because behavioral measures of implicit sequence learning do not differ between children with ASD versus controls, activation of the frontal, striatal, and cerebellar networks that support learning would not differ between children with ASD and controls. Alternatively, behaviorally intact implicit sequence learning in ASD could be supported by differential recruitment of these networks. This prediction is supported by fMRI studies revealing atypical cortical and subcortical activation when performance was intact on tasks measuring processes such as perceptual processing (Lee et al., 2007), visual-motor sequence learning (Muller, Cauich, Rubio, Mizuno, & Courchesne, 2004; Muller, Kleinhans, Kemmotsu, Pierce, & Courchesne, 2003), and components of executive control (Schmitz et al., 2006). Finally, it is possible that the two forms of implicit learning (i.e., general skill learning and sequence specific learning) show differences in the extent to which they rely on common or different neural networks across groups. Thus, a third prediction is that common networks support general skill
learning in ASD and controls, whereas qualitatively different networks support sequence-specific learning in ASD versus controls, or vice versa.

In the present study we used a modified version of a triplet-learning task (Howard, Howard, Dennis, & Kelly, in press) to examine probabilistic implicit sequence learning in 7–12-year-old children with ASD and matched controls. In this task, children were presented with displays comprising three sequential stimuli, two cues and one target, and responded to the target’s location via keypress. Unbeknownst to participants, the location of the first cue predicted the target appearing in one location on 80% of trials (High Probability condition) and in another location on 20% of trials (Low Probability condition). Importantly, learning on the Triplets Learning Task occurs implicitly and without resulting conscious awareness of the probabilistic structure embedded in the task in adults (Howard, Howard, Dennis, & Kelly, in press).

We implemented the triplet-learning task in an event-related fMRI paradigm to separately examine the two forms of learning described above (i.e., general skill learning and sequence-specific learning). First, we examined general skill learning by looking for regions showing linear changes (i.e., increases and decreases) in task-related activation over the duration of the scan for the task (i.e., all High and Low Probability trials) compared to our baseline condition (i.e., fixation on a cross hair). This approach has been successfully implemented in other studies examining dynamic changes in activation during learning (e.g., probabilistic feedback learning on the weather prediction task, Poldrack et al., 2001). Second, we examined sequence-specific learning by looking for regions showing different responses to High versus Low Probability trials. This allows us to look at regions showing a greater response for expected sequences of events (i.e.,
High Probability > Low Probability) and for regions showing a greater response for unexpected sequences of events (i.e., Low Probability > High Probability), with closely matched perceptual-motor demands across conditions. We used these complimentary approaches to determine whether children with ASD rely on the same neural networks as controls during general skill learning and sequence-specific learning on the triplet-learning task. Finally, if contrasts revealed group differences in activation during learning, we probed whether activation for those contrasts related to individual differences in symptom expression in children with ASD, as measured on the Autism Diagnostic Interview-Revised. This allowed us to determine whether recruitment of atypical neural networks to support implicit sequence learning was more pronounced in individuals with greater symptom expression.

Method

Participants

Thirteen children with ASD, recruited from the Center for Autism Spectrum Disorders at Children's National Medical Center, and thirteen control children, recruited from the Washington, DC metropolitan area, participated in the study (see Table 1). Five additional children with ASD were scanned but excluded from analysis due to excessive motion (n = 1), noncompliance with task instructions (n = 1), or scanner artifact (n = 3). Along with parental consent, all participants gave assent and were compensated monetarily for participation. All participants were 7 – 12 years old, with full scale IQ above 85, and without history of seizure disorder, current antipsychotic or neuroleptic medication, and metal implants or braces. The groups were matched for gender (p = .62), age (p = .38), and Full Scale IQ (p = .63). Three children with ASD and one control
were left-handed; no special accommodations were made for these children. Two children with ASD withheld stimulant medications (i.e., methylphenidate and dexmethylphenidate) for 24 h prior to participation; the remaining 11 children were unmedicated. Thus, no child was prescribed anti-depressant or anti-anxiety medications that are commonly used for managing ASD symptoms.

ASD diagnosis was based on DSM-IV criteria by a pediatric neuropsychologist (L.K.) and confirmed for 12 children using the Autism Diagnostic Interview-Revised (ADI-R) (Lord, Rutter, & Le Couteur, 1994) and Autism Diagnostic Observation Schedule (ADOS) (Lord et al., 2000). Of the 13 children with ASD, 1 was diagnosed with autistic disorder, 7 were diagnosed with Asperger disorder, and 6 were diagnosed with Pervasive Developmental Disorder, Not Otherwise Specified. Control children were screened for history of neurological and psychiatric conditions by interview and for attentional and emotional problems by the Behavior Assessment System for Children (BASC) (Reynolds & Kamphaus, 1992).

**Table 1. Participant Demographics**

<table>
<thead>
<tr>
<th>Group</th>
<th>Age</th>
<th># Male</th>
<th>FSIQ</th>
<th>ADI Social</th>
<th>ADI Comm</th>
<th>ADI Rep</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD</td>
<td>9.48 (1.66)</td>
<td>11</td>
<td>117.25 (19.31)</td>
<td>15.25 (6.81)</td>
<td>12.25 (5.61)</td>
<td>5.5 (2.61)</td>
</tr>
<tr>
<td>Control</td>
<td>9.98 (1.17)</td>
<td>10</td>
<td>120.60 (12.83)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Note: FSIQ = Full-Scale IQ determined by WISC-III or WASI. ADI Social = ADI Reciprocal Social Interaction. ADI Comm = ADI Communication. ADI Rep = ADI Restricted and Repetitive Behaviors.  

**Task Procedure**

Stimuli were generated using E-Prime viewed via a MRI-compatible projector with a mirror affixed to the headcoil. Head movement was minimized using foam cushions placed between the participant’s head and the coil.
Participants performed three 6:20 min runs of the triplet-learning task. Trials were presented in a rapid event-related design. A pseudorandomized trial presentation order and jittered fixation (henceforth, Null condition) was fixed across participants and optimized for efficiency using OptSeq2 (Dale, 1999). Null trial duration ranged from .5 s – 6 s (M = 1.36, SD = 1.05). Each run comprised 135 trials: 108 High Probability trials and 27 Low Probability Trials.

The stimulus display was composed of three open circles, presented horizontally. Each trial comprised three events, which occurred when one of the open circles filled in either red or green (see Figure 1). Two red “cues” and one green “target” were displayed on each trial. Each trial lasted 2 s and involved presentation of the First Cue for 200 ms, an open circle for 250 ms, the Second Cue for 200 ms, an open circle for 250 ms, the Target for 850 ms, and finally an open circle for 250 ms. Participants were instructed to press one of three optical buttons held in the right hand that corresponded to the location of the Target circle as quickly and accurately as possible.
Unbeknownst to participants, there was a probabilistic relationship between the First Cue and Target such that location of the First Cue predicted that the Target would appear in one location on 80% of the trials (High Probability trials) and in another location on 20% of the trials (Low Probability trials). The location of the Second Cue was not predictive of the Target location, and the location of Cues and Targets were counterbalanced across trials. Thus, a non-adjacent or second-order regularity was embedded within the task.

Eighteen (out of a possible 27 [i.e., 3 locations x 3 events]) triplets were presented. Of these, each of the 9 High Probability triplets occurred with a probability of .0888 (9 x .0888 = .8), whereas each of the 9 Low Probability triplets occurred with a probability of .0222 (9 x .0222 = .2).

fMRI Methods

Imaging Procedure. A high-resolution sagittal T1-weighted scan was acquired on a Siemens Trio 3.0T MRI scanner using a 3D MPRAGE sequence with a scan time of 7:23 min and the following parameters: TR = 2300 ms, TE = 2.94 ms, 256x256 mm FOV, 160 mm slab with 1 mm thick slices, 256x256x160 matrix (effective resolution is 1.0 mm$^3$), 1 excitation, and a 9° flip angle. Functional images were acquired on the same scanner using a T2*-sensitive gradient echo pulse sequence with the following parameters: TR = 2500 ms, TE = 30 ms, 256x256 mm FOV, 64x64 acquisition matrix, and a 90° flip angle. Forty-two 3.7mm thick slices were acquired descending in the transverse plan for 154 time points for each run (the first 2 TRs were included for signal stabilization and discarded from analysis).
Data Analysis. Images from the first two runs were included in the fMRI analyses. The third run was discarded due to extensive motion but was included in the behavioral analysis. Using SPM5 (Wellcome Department of Cognitive Neurology, London), the first two functional runs were concatenated, and images were corrected for motion and differences in slice acquisition time to the middle slice. Images were then normalized into standard space and interpolated to 2 x 2 x 2 mm cubic voxels using an EPI template. Normalized images were spatially smoothed (8 mm full-width at half-maximum Gaussian kernel) to ameliorate differences in intersubject localization.

For each participant, head motion was computed as the mean of the absolute value of translation in each plane (x, y, and z) across scans. Motion was within 4 mm in each plane for all participants. Unpaired t-tests revealed that mean translation in the x- (ASD: M = .42 mm, SD = .27; CON: M = .36 mm, SD = .49) and y- (ASD: M = .42 mm, SD = .26, CON: M = .36 mm, SD = .26) planes did not differ between ASD and control children (ps > .42). However, mean translation in the z-plane was marginally higher in ASD (M = 1.59 mm, SD = .85) than control (M = 1.15 mm, SD = .91) children (p = .08). Motion parameters were therefore included as covariates of no interest in the analysis of individual subject’s data to ensure that marginally greater motion in the ASD than control group did not unduly influence the results.

fMRI Analysis: First Level Analysis. Two different models were fit for each participant. The first model assessed changes in activation related to general perceptual-motor skill learning (henceforth, General Skill Learning). The second model assessed encoding of probabilistic sequential information (henceforth, Sequence-specific Learning). For both models, fMRI responses for conditions of interest were modeled by
a canonical hemodynamic response function and its temporal derivative. For both models, there were seven conditions of no interest: Error (consisting of all incorrect High and Low Probability trials) and 6 motion parameters (corresponding to translation and rotation in the x-, y-, and z- planes).

The General Skill Learning model consisted of 3 conditions of interest: Task (consisting of all correct High and Low Probability trials), Task, defined as a first order (i.e., linear) Time x Condition interaction for the Task condition, and Null. For each participant, two activation maps were generated identifying regions that increased linearly with practice (Task > Null contrast) and decreased linearly with practice (Null > Task contrast).

The Sequence-specific Learning model consisted of three conditions of interest: High Probability (consisting of all correct High Probability Trials), Low Probability (consisting of correct Low Probability Trials), and Null. For each participant, two activation maps were generated identifying regions that were more responsive to expected events (High > Low Probability contrast) and to unexpected events (Low > High Probability contrast).

*Second Level fMRI Analysis.* For the General Skill Learning analysis, second level analysis consisted of separate one-way Analyses of Variance (ANOVAs) for the two contrasts (i.e., Task > Null and Null > Task) with Group (ASD vs. CON) as a between-subjects factor. For the Sequence-specific Learning analysis, second level analysis consisted of separate one-way ANOVAs for the two contrasts (i.e., High > Low Probability and Low > High Probability) with Group (ASD vs. CON) as between-subjects factors.
For both the General Skill Learning and Sequence-specific Learning ANOVAs, two tests were conducted using random effects models. First, each contrast was tested collapsed across groups to determine regions consistently activated overall (height threshold: \( p < .005 \), spatial extent threshold = 10 voxels). Second, a Main Effect of Group was tested for each contrast only within those regions showing overall activation for that contrast (inclusive mask, height threshold: \( p < .05 \)) to determine regions whose activation differed between groups (height threshold: \( p < .005 \), spatial extent threshold = 10 voxels). Finally, post-hoc tests were conducted on regions showing a Main Effect of Group to determine which group showed greater activation, ASD or Control.

*Correlation Analysis.* If any of the ANOVAs yielded group differences in learning-related activation, we conducted separate whole brain, voxel-wise correlations on the contrasts from that analysis and measures of parental report of symptom expression in three domains as measured by the ADI-R: Social Interaction, Communication, and Repetitive Behaviors. Due to the exploratory nature of these correlations, a more stringent threshold was applied (height threshold: \( p < .001 \), spatial extent threshold = 10 voxels).

**Results**

*Behavioral Results*

Percentage of correct responses (accuracy) and median reaction times (RTs) for correct trials were computed for each Run and Trial type for each participant. Overall accuracy was above 75% for all participants, and was high for both ASD (\( M = 89.75\% \), \( SD = 7.38 \)) and Control (\( M = 94.87\% \), \( SD = 4.16 \)) children. An unpaired t-test revealed that accuracy was marginally higher in Control than ASD children, \( t(21) = 2.02, p = .06 \).
To examine learning, median RTs were analyzed in a Group (ASD vs. Control) X Run (1 – 3) X Trial type (High Probability vs. Low Probability) repeated measures ANOVA with Group as a between-subjects factor and Run and Trial type as within-subjects factors. Overall median RTs did not differ between ASD (M = 532.57; SD = 112.62) and Control (M = 513.92; SD = 54.48) children (main effect of Group), p = .62 (see Figure 2). Participants exhibited improvement in perceptual-motor skill, indicated by faster responses with practice (main effect of Run), F (2, 42) = 35.22, p < .0001. Participants were sensitive to probabilistic sequence information, indicated by faster responses to High versus Low Probability trials (main effect of Trial type), F (1, 21) = 4.79, p = .04. There were no group differences in learning because no interactions with Group reached significance (ps > .42).

**fMRI Results**

For each contrast, significant activations are listed in Tables 2 – 5 by anatomy, Brodmann area (BA), Talairach coordinates (transferred from MNI using mni2tal algorithm) of peak maximum for the cluster, Z-score, volume in mm³.

**General Skill Learning.** ASD and control groups did not differ in regional involvement during the course of general skill learning because the Main Effect of Group
was not significant for either the Task\textsubscript{AI} > Null or the Null > Task\textsubscript{AI} contrasts. Overall activation in the Task\textsubscript{AI} > Null contrast revealed increases in a bilateral fronto-parieto-striatal network over time (see Table 2). Specifically, increasing activation was seen in right inferior frontal gyrus (BA 44), right caudate and bilateral putamen, and in bilateral inferior parietal cortex (BA 40). Increasing activation was also seen in sensorimotor regions, including left premotor cortex (BA 6) and postcentral gyrus (BA 3). Additional increasing activations were seen in the right superior temporal gyrus (BA 22) and the left insula.

**Table 2.** Regions showing increasing activation during general skill learning (Task\textsubscript{AI} > Null).

<table>
<thead>
<tr>
<th>Region of Activation</th>
<th>BA</th>
<th>Talairach Coordinates</th>
<th>Volume (mm\textsuperscript{3})</th>
<th>Z Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caudate</td>
<td>-</td>
<td>18 10 11</td>
<td>372</td>
<td>3.24</td>
</tr>
<tr>
<td>Inferior Frontal Gyrus</td>
<td>44</td>
<td>61 9 29</td>
<td>102</td>
<td>3.11</td>
</tr>
<tr>
<td>Putamen</td>
<td>-</td>
<td>-16 8 9</td>
<td>80</td>
<td>3.21</td>
</tr>
<tr>
<td>Putamen</td>
<td>-</td>
<td>18 7 -7</td>
<td>95</td>
<td>3.25</td>
</tr>
<tr>
<td>Insula</td>
<td>-</td>
<td>-38 0 7</td>
<td>46</td>
<td>2.99</td>
</tr>
<tr>
<td>Superior Temporal Gyrus</td>
<td>22</td>
<td>65 -3 11</td>
<td>55</td>
<td>3.05</td>
</tr>
<tr>
<td>Superior Frontal Gyrus</td>
<td>6</td>
<td>-22 -8 63</td>
<td>25</td>
<td>3.28</td>
</tr>
<tr>
<td>Postcentral Gyrus</td>
<td>3</td>
<td>-42 -24 62</td>
<td>29</td>
<td>3.25</td>
</tr>
<tr>
<td>Inferior Parietal Lobule</td>
<td>40</td>
<td>50 -34 57</td>
<td>44</td>
<td>2.93</td>
</tr>
<tr>
<td>Inferior Parietal Lobule</td>
<td>40</td>
<td>59 -37 33</td>
<td>337</td>
<td>3.80</td>
</tr>
<tr>
<td><strong>CON&gt;ASD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ASD&gt;CON</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Overall activation in the Null > Task contrast revealed decreases in a premotor-occipital network over time (see Table 3). Specifically, decreasing activation was seen in left premotor cortex (BAs 6 and 8- anterior to the region showing linear increases in activation) and ventral portions of occipital cortex, bilaterally (BAs 18, 19, and 37). Decreasing activation was also seen in right supramarginal gyrus (BA 40) and bilateral posterior cingulate cortex (BAs 24 and 31).

**Table 3.** Regions showing decreasing activation during general skill learning (Null > Task<sub>3T</sub>)

<table>
<thead>
<tr>
<th>Region of Activation</th>
<th>BA</th>
<th>Talairach Coordinates</th>
<th>Volume (mm&lt;sup&gt;3&lt;/sup&gt;)</th>
<th>Z Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior Frontal Gyrus</td>
<td>8</td>
<td>-22 30 50</td>
<td>21</td>
<td>2.96</td>
</tr>
<tr>
<td>Middle Frontal Gyrus</td>
<td>6</td>
<td>-18 18 54</td>
<td>15</td>
<td>3.04</td>
</tr>
<tr>
<td>Cingulate Gyrus</td>
<td>24</td>
<td>-12 -10 30</td>
<td>21</td>
<td>3.02</td>
</tr>
<tr>
<td>Caudate Body</td>
<td></td>
<td>-24 -26 29</td>
<td>119</td>
<td>3.28</td>
</tr>
<tr>
<td>Cingulate Gyrus</td>
<td>31</td>
<td>18 -29 33</td>
<td>48</td>
<td>3.42</td>
</tr>
<tr>
<td>Cingulate Gyrus</td>
<td>31</td>
<td>-18 -43 32</td>
<td>16</td>
<td>2.88</td>
</tr>
<tr>
<td>Fusiform Gyrus</td>
<td>37</td>
<td>-32 -47 -8</td>
<td>18</td>
<td>2.75</td>
</tr>
<tr>
<td>Supramarginal Gyrus</td>
<td>40</td>
<td>44 -58 36</td>
<td>95</td>
<td>3.23</td>
</tr>
<tr>
<td>Fusiform Gyrus</td>
<td>19</td>
<td>-36 -70 -8</td>
<td>297</td>
<td>3.50</td>
</tr>
<tr>
<td>Middle Occipital Gyrus</td>
<td>19</td>
<td>32 -81 8</td>
<td>1973</td>
<td>4.38</td>
</tr>
<tr>
<td>Lingual Gyrus</td>
<td>18</td>
<td>-8 -90 -4</td>
<td>72</td>
<td>2.99</td>
</tr>
<tr>
<td>Inferior Occipital Gyrus</td>
<td>18</td>
<td>-24 -94 16</td>
<td>363</td>
<td>3.44</td>
</tr>
</tbody>
</table>

**CON>ASD**

None

**ASD>CON**

None

*Sequence-specific Learning.* ASD and control groups differed in regional involvement in the response to expected and unexpected events because the Main Effect of Group for both the High > Low Probability and the Low > High Probability contrasts yielded significant activations.
Overall activation in the High > Low Probability contrast was restricted to the right hemisphere, in motor (BA 4), temporal (BA 21), and insular cortices (see Table 4). Group differences in the response to expected events were seen in left middle frontal gyrus (BA 6) and the angular gyrus, bilaterally (BA 39), with greater activation in those regions in control than ASD children. Thus, the response to expected events was characterized by overall activation of motor, temporal, and insular cortex, and by increased activation in frontal and angular cortices in control than ASD participants.

**Table 4.** Regions showing greater activation for expected events during sequence-specific learning (High > Low Probability)

<table>
<thead>
<tr>
<th>Region of Activation</th>
<th>BA</th>
<th>Talairach Coordinates</th>
<th>Volume (mm$^3$)</th>
<th>Z Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precentral Gyrus</td>
<td>4</td>
<td>62 -3 22</td>
<td>15</td>
<td>3.09</td>
</tr>
<tr>
<td>Insula</td>
<td>-</td>
<td>36 -18 12</td>
<td>14</td>
<td>2.90</td>
</tr>
<tr>
<td>Middle Temporal Gyrus</td>
<td>39</td>
<td>55 -67 10</td>
<td>16</td>
<td>3.10</td>
</tr>
<tr>
<td><strong>CON&gt;ASD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle Frontal Gyrus</td>
<td>6</td>
<td>-26 13 50</td>
<td>20</td>
<td>3.06</td>
</tr>
<tr>
<td>Angular Gyrus</td>
<td>39</td>
<td>-48 -71 24</td>
<td>68</td>
<td>3.97</td>
</tr>
<tr>
<td>Angular Gyrus</td>
<td>39</td>
<td>50 -70 27</td>
<td>14</td>
<td>3.21</td>
</tr>
<tr>
<td><strong>ASD&gt;CON</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Overall activation in the Low > High Probability contrast was seen in diffuse cortical and medial temporal lobe regions. Specifically, a greater response to unexpected events was seen in right orbitofrontal cortex (BA 11), left anterior cingulate cortex (BA 24), bilateral insula, the right superior (BA 7) and inferior parietal (BA 40) cortices, left occipital cortex (BAs 18 and 19), and bilateral medial temporal lobes (left parahippocampal gyrus [BA 27] and right hippocampus). Group differences in the response to unexpected events were seen in right premotor cortex (BA 6), left inferior
parietal lobule (40) and bilateral caudate, with greater activation in those regions in ASD than control children. Thus, the response to unexpected events was characterized by widespread cortical and medial temporal lobe activation, and by increased activation in fronto-parietal and striatal regions in ASD than control participants.

**Table 5.** Regions showing greater activation for unexpected events during sequence-specific learning (Low > High Probability)

<table>
<thead>
<tr>
<th>Region of Activation</th>
<th>BA</th>
<th>Talairach Coordinates</th>
<th>Volume (mm$^3$)</th>
<th>Z Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orbitofrontal Gyrus</td>
<td>11</td>
<td>26 31 -3</td>
<td>15</td>
<td>3.24</td>
</tr>
<tr>
<td>Cingulate Gyrus</td>
<td>24</td>
<td>-8 27 -1</td>
<td>42</td>
<td>3.33</td>
</tr>
<tr>
<td>Insula</td>
<td></td>
<td>-22 21 3</td>
<td>12</td>
<td>3.19</td>
</tr>
<tr>
<td>Superior Frontal Gyrus</td>
<td>6</td>
<td>22 13 62</td>
<td>62</td>
<td>4.11</td>
</tr>
<tr>
<td>Middle Temporal Gyrus</td>
<td>21</td>
<td>48 3 -17</td>
<td>20</td>
<td>2.91</td>
</tr>
<tr>
<td>Insula</td>
<td></td>
<td>38 5 22</td>
<td>29</td>
<td>3.48</td>
</tr>
<tr>
<td>Hippocampus</td>
<td></td>
<td>34 -26 -5</td>
<td>108</td>
<td>3.46</td>
</tr>
<tr>
<td>Parahippocampal Gyrus</td>
<td>27</td>
<td>-26 -29 -5</td>
<td>28</td>
<td>3.10</td>
</tr>
<tr>
<td>Inferior Parietal Lobule</td>
<td>40</td>
<td>59 -38 48</td>
<td>114</td>
<td>3.55</td>
</tr>
<tr>
<td>Superior Parietal Lobule</td>
<td>7</td>
<td>24 -61 64</td>
<td>34</td>
<td>3.44</td>
</tr>
<tr>
<td>Fusiform Gyrus</td>
<td>19</td>
<td>-28 -82 -6</td>
<td>10</td>
<td>2.98</td>
</tr>
<tr>
<td>Lingual Gyrus</td>
<td>18</td>
<td>-14 -87 -1</td>
<td>36</td>
<td>3.17</td>
</tr>
</tbody>
</table>

**CON>ASD**

| None                          |    |                        |                |         |

**ASD>CON**

| Caudate                       |    | -18 21 -4              | 98             | 3.92    |
| Caudate                       |    | 10 19 -3              | 13             | 3.46    |
| Superior Frontal Gyrus        | 6   | 22 13 58              | 22             | 3.30    |
| Inferior Parietal Lobule      | 40  | 61 -43 43             | 19             | 3.21    |

**Correlations.** Based on group differences in activation during sequence-specific learning, we examined the extent to which symptom expression in social interaction, communication, and repetitive behaviors domains positively related to activity in the High > Low Probability and Low > High Probability contrasts in the ASD group only.
Greater response to expected events (i.e., High > Low Probability) in the cerebellum correlated with expression of repetitive behavior symptoms. In contrast, greater response to unexpected events (i.e., Low > High Probability) correlated with each of the three symptom domains in different cortical regions. Specifically, greater activation in left motor cortex (BA 4) was associated with increased social symptom expression, activation in left prefrontal (BA 10), left lateral sensorimotor (BA 2) and medial parietal (BA 7) cortex was associated with increased repetitive behavior symptom expression, and activation in right temporal pole (BA 38) and right angular gyrus (BA 39) was associated with increased communication symptom expression. These findings suggest that the atypical recruitment of cortical regions during unexpected events was more pronounced for individuals with higher symptom expression.

Table 6. Regions showing positive correlations between ADI-R Repetitive Behaviors (ADI-Rep), Social Interaction (ADI-Social), and ADI-Communication (ADI-Comm) symptom expression and activation during sequence-specific learning for ASD children

<table>
<thead>
<tr>
<th>Region of Activation</th>
<th>BA</th>
<th>Talairach Coordinates</th>
<th>Volume (mm$^3$)</th>
<th>Z Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High &gt; Low x ADI-Rep</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebellum</td>
<td>-</td>
<td>22</td>
<td>56</td>
<td>36</td>
</tr>
<tr>
<td><strong>Low &gt; High x ADI-Rep</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle Frontal Gyrus</td>
<td>46</td>
<td>-36</td>
<td>42</td>
<td>16</td>
</tr>
<tr>
<td>Postcentral Gyrus</td>
<td>2</td>
<td>-50</td>
<td>-29</td>
<td>40</td>
</tr>
<tr>
<td>Precuneus</td>
<td>7</td>
<td>12</td>
<td>-54</td>
<td>52</td>
</tr>
<tr>
<td><strong>Low&gt;High x ADI-Social</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precentral Gyrus</td>
<td>4</td>
<td>-12</td>
<td>-24</td>
<td>66</td>
</tr>
<tr>
<td><strong>Low &gt; High x ADI-Comm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior Temporal Gyrus</td>
<td>38</td>
<td>32</td>
<td>16</td>
<td>-29</td>
</tr>
<tr>
<td>Angular Gyrus</td>
<td>39</td>
<td>55</td>
<td>-62</td>
<td>33</td>
</tr>
</tbody>
</table>
Discussion

The present study revealed four main findings about implicit sequence learning in childhood ASD. First, implicit sequence learning on the Triplet Learning Task was intact in high functioning ASD because learning did not differ between children with ASD and controls. Second, the neural networks supporting general skill learning did not differ between children with ASD and controls; learning was characterized by overall increases in activation of frontal, parietal, and striatal structures and by overall decreases in activation of occipital structures. Third, sequence-specific learning of probabilistic information differed such that control children showed a greater response than children with ASD to expected sequences of events in frontal and parietal networks, whereas children with ASD showed a greater response to unexpected sequences of events than controls in frontal, parietal, and striatal networks. Finally, the qualitatively different response during sequence-specific learning related to ASD symptom expression because greater cortical activation for unexpected sequences of events was associated with parental report of ASD symptom expression on the ADI-R.

Group differences in behavior cannot account for the functional neuroimaging results. First, individual differences in learning were unlikely to have obscured possible group differences in the neural basis of general skill learning because the majority of participants with ASD and controls demonstrated learning, defined as faster responses to High Probability than Low Probability trials (ASD: 12/13, CON: 8/11). Further, the number of participants demonstrating learning did not differ by group ($\chi^2 = 1.65, p = .20$). Second, differences in sequence-specific learning were not the result of either impaired or superior learning in ASD because there were no group differences in
response speed measures of learning. This finding is consistent with one prior report of intact implicit sequence learning in ASD (Barnes et al., in press, but see Mostofsky et al. 2000). Third, overall accuracy was marginally worse in ASD than control participants, but this is unlikely to have affected the fMRI results for two reasons: 1) overall accuracy was high for all participants (> 75%), indicating that all participants were engaged in the behavioral task and 2) error trials were excluded from the conditions of interest and were explicitly modeled as a condition of no interest. Thus, any variance associated with error trials was accounted for in the general linear model. Therefore, it is unlikely that behavioral characteristics of ASD and control participants unduly influenced the common networks supporting general skill learning and the qualitatively different networks supporting sequence-specific learning.

Overall, general skill learning was characterized by both increases and decreases in cortical and subcortical activation. These changes took place during the “early”, “fast”, or “initial” stages of implicit sequence learning, which happen over the course of minutes and do not involve offline consolidation (Doyon & Benali, 2005). Only a handful of studies have examined changes in activation during implicit sequence learning within that period (as opposed to comparing early stages of learning to later stages of learning occurring after extended practice, consolidation, or both), and they did not report evidence of changes in task-related activation during the fMRI session (Daselaar, Rombouts, Veltman, Raaijmakers, & Jonker, 2003; Thomas et al., 2004). Thus, general skill learning results are discussed in light of the behavioral changes seen during the task. First, increases in frontal, parietal, and striatal networks coincided with faster response speed with practice. It is possible that increases in activation relate to the creation of
stimulus-response mappings in the service of faster performance. Such a process would require integrating or binding information, processes supported by frontal, parietal, and striatal networks for tasks under conscious, cognitive control (e.g., Prabhakaran et al., 2000). Similarly, decreases in premotor, posterior cingulate, and occipital may reflect initial contributions to stimulus-response mapping that are not essential once the task becomes learned.

The absence of group differences in general skill learning contrasts with a report of atypical cortical activation in individuals with ASD on another visual-motor learning task. Specifically, adults and an adolescent with autism showed less activation in prefrontal cortex and more activation in sensorimotor and premotor cortices than controls later in learning (Muller, Cauich, Rubio, Mizuno, & Courchesne, 2004). It is unlikely that low statistical power prevented the detection of group differences in general skill learning in the present study because there was sufficient statistical power to detect group differences in sequence specific learning. Rather, the behavioral task used and participant age might explain the inconsistent findings across studies. First, the behavioral task used might have engaged different learning mechanisms across studies. Muller and colleagues’ task required participants to learn a deterministic (i.e., involving a fixed, invariant sequence order) visual-motor sequence, which often result in spontaneous conscious awareness of the repeating sequence. Thus, results might have differed if implicit and explicit modes of learning, which rely upon distinct neural networks (e.g., Willingham, Salidis, & Gabrieli, 2002), were measured across studies. Second, it is possible that group differences in general skill learning only emerge later in development. Muller et al.’s participants were older (age range: 15 – 41 years) than participants in the
present study (age range: 7 – 12 years). Fundamental components of both tasks (e.g.,
saccades to visual targets (Luna, Garver, Urban, Lazar, & Sweeney, 2004) continue to
mature throughout middle childhood and early adolescence. Any comparison of results
across these studies must be made cautiously in light of these differences.

Qualitative differences in premotor cortex, inferior parietal lobule, and caudate
activation during sequence-specific learning can be interpreted in two ways. One
interpretation comes from the temperament literature. According to this framework,
learning in ASD and controls could rely on common learning mechanisms, but
temperamental biases may modulate the response to familiar or novel sequences of
events. A child’s experience of positive affect in mildly novel situations is a characteristic
of temperament that varies across typically developing children (Derryberry & Rothbart,
1997) and may be less common in toddlers with ASD (Zwaigenbaum et al., 2005). It is
possible that once an event is identified as novel or rare in a probabilistic learning
paradigm, children with low positive affect in mildly novel situations may react
differently from children with high positive affect. The present pattern of results could
have emerged if more individuals with low positive affect comprised the ASD group than
the control group. However, this hypothesis cannot be directly addressed because
temperament measures were not collected in this study.

Second, it is possible that qualitative differences during sequence-specific
learning are the result of group differences in underlying learning processes. For
example, a run of Low Probability trials occurring consecutively may have triggered one
group to update representations about the distribution of probability within the task. If
the groups differ in how they update probabilistic representations throughout the task,
and in whether unexpected or expected events are at the heart of reactive processes such as updating, then qualitative differences in the response to probabilistic information might emerge. However, this cannot be concluded from the present study because the cue and target periods were integrated into one trial, organized on the basis of their probabilistic structure. Accordingly, the hemodynamic response functions of these two cognitive processes are indistinguishable. This can be circumvented by treating cues and targets as separate events in an event-related fMRI design and modeling their hemodynamic response functions separately, an approach that has successfully been employed in reward learning paradigms to examine anticipatory and reactive processing (Behrens, Woolrich, Walton, & Rushworth, 2007). Applying this approach to the study of implicit sequence learning could yield more fine-grained information about the nature of these processes in children with ASD and controls.

Regardless of which account explains the qualitative differences in sequence-specific learning in ASD, activation was restricted to a circumscribed set of regions: premotor cortex, inferior parietal lobules and caudate. These regions are commonly activated in fMRI studies of implicit sequence learning. Specifically, adults showed greater activation in these regions for blocks where the stimulus follows a repeated sequence than blocks where the stimulus changes randomly (e.g., Bischoff-Grethe, Martin, Mao, & Berns, 2001; Grafton, Hazeltine, & Ivry, 1995; Rauch et al., 1997; Willingham, Salidis, & Gabrieli, 2002). This is consistent with the present data for control children, characterized by greater activation for High Probability than Low Probability trials in these regions. The precise contribution of these regions to sequence-specific learning is uncertain. Given known functions of these structures in other
cognitive domains, one could speculate that premotor activation could contribute to motor planning (Picard & Strick, 2001), inferior parietal activation could contribute to spatial and attentional processing (Husain & Nachev, 2007), and striatal activation could contribute to encoding probabilistic information (Schultz, 2006). Accordingly, manipulating or studying such processes in, for example, the context of motor planning, could yield greater insight into the mechanisms underlying the qualitative differences in sequence-specific learning in children with ASD and controls.

The present study is the first investigation of implicit sequence learning in childhood ASD, and much remains to be learned about what mechanisms might underlie the present results. Nevertheless, this study has addressed significant gaps in the literature on the cognitive neuroscience of ASD. First, we examined neurocognition in a relatively unstudied age range. To date, there have only been two published fMRI studies examining preadolescent children (Lee et al., 2007; Pierce & Redcay, 2008). Second, to the best of our knowledge, this study is the first to use fMRI in a population of children with ASD who were not currently taking psychotropic medication during the scanning session. This eliminates the potential confound that any group differences in activation may be attributable to medication effects. Third, our use of a behavioral task that has been shown to be intact in children with high functioning ASD limits the potential confound of group differences in activation being attributable to performance differences. Finally, our focus on processes that operate outside of conscious, cognitive control has expanded our understanding of neurocognition in ASD. This has yielded new hypothesis about the nature of learning and memory that can be explore through future studies.
CHAPTER IV:

GENERAL DISCUSSION

This dissertation began by outlining two critical questions in developmental cognitive neuroscience: 1) What is the developmental trajectory of implicit learning in typically developing children? 2) What is the status of implicit learning in children with developmental disorders? What follows are summaries of how the results of Chapters II-V addressed those questions.

1. Implicit sequence learning had a protracted developmental trajectory and was immature in middle childhood, regardless of the complexity of the to-be-learned sequence.

2. Children with ADHD and ASD showed unique implicit learning “profiles” relative to matched controls.
   a. Children with ADHD showed a selective implicit sequence learning deficit; implicit spatial contextual learning was spared.
   b. Implicit sequence and spatial contextual learning were spared in children with ASD.

3. In children with ASD, behaviorally intact general skill learning was reliant upon the same neural networks as control children, whereas behaviorally intact sequence-specific learning was reliant upon qualitatively different neural networks than control children.

Overall, this dissertation provides a more comprehensive picture of neurocognition in typical development and children with developmental disorders because it focuses on processes that operate outside of conscious, cognitive control.
However, the most thought-provoking questions from both the layman and the scientist regard how these experimentally gleaned results might broadly inform the study of brain and cognitive development.

One limitation of this research is raised before discussing these issues. This set of studies focused exclusively on middle childhood and early adolescence. While this may have reduced variability due to age-related differences in these studies, it limits the extent to which conclusions can be made about other developmental periods. Karmiloff-Smith and colleagues (2003) have outlined several reasons why such comparisons are flawed in the study of developmental disorders. First, compensatory mechanisms may develop to address early behavioral deficits. This could result in the amelioration of early behavioral deficits at a later stage in development. Second, the development of compensatory mechanisms to address one deficient system may adversely impact the development of previously unimpaired systems. This could result in later impairments of a previously unimpaired system. Accordingly, any claims regarding impaired or spared cognitive functions must be restricted to the developmental period under investigation or be investigated using a longitudinal approach. A longitudinal approach was not within the scope of this dissertation, but it marks an important future direction for studies examining the status of associative implicit learning in childhood development. Caution is used when addressing how the findings of this dissertation broadly inform the study of brain and cognitive development.

_How do the present findings impact theories of typical brain and cognitive development?_ Posner and Rothbart’s (2000) model situates experience-dependent plasticity at the interface between developing systems of executive control and emotional
regulation. However, our results suggest that at least one form of plasticity, implicit sequence learning, matures during middle childhood. The present body of work does not provide direct evidence as to what underlies the age-related improvement in behavioral measures of implicit sequence learning. It could be that children and adults differ in their sensitivity to sequential structure of events or in their ability to convey that information to motor systems in the service of faster performance. This remains to be determined by future studies. However, changes in either system would suggest that the brain’s capacity to reorganize on the basis of experience varies with age. The implication is that plasticity is a changing process during development. Accordingly, Posner and Rothbart’s framework could be modified to indicate that successful brain and cognitive development is the result of three-way interactions between developing mechanisms of plasticity, executive control, and emotional regulation.

Nigg and Casey (2005) have outlined one way in which an interaction between implicit sequence learning and executive control could occur in typical development and childhood ADHD. They speculate that if a child’s basic assumptions about the environment are either inaccurate or less salient from disruptions in basic learning mechanisms, then violations of assumptions will be less likely to be detected. This is consistent with our finding of reduced implicit sequence learning in childhood ADHD. Nigg and Casey further speculate that impaired learning would limit the extent to which a child could identify situations where top-down control was needed. This has important implications for the development of executive control, which improves with training (Diamond, Barnett, Thomas, & Munro, 2007). If children with ADHD fail to identify the situations that require top-down control and do not engage executive control
appropriately, then they will have less “natural” training and could develop a relatively weak executive control system. This model is consistent with the original approach outlined by Posner and Rothbart where plasticity influences the development of executive control.

Nigg and Casey’s model does not provide an example of how the development of executive control could influence the development of plasticity (e.g., implicit sequence learning), though they speculate that interactions between learning and executive control are likely bidirectional. One possibility is that such an interaction could take place via Hebbian learning mechanisms. Hebbian learning broadly refers to changes in synaptic strength that occur if a synapse is active when a post-synaptic neuron is active (Hebb, 1949); to use an aphorism from neuroscience courses, “neurons that fire together, wire together”. In typical development, the coactivation of frontal, striatal, and cerebellar networks during the development of executive control could have the unintended consequence of strengthening the same circuits that support implicit sequence learning, leading to behavioral improvements in learning with age. In ADHD, the weakly developing executive control system could fail to engage Hebbian learning mechanisms which act on frontal, striatal, and cerebellar networks to the same extent as control children. This could result in weaker connections between regions necessary for implicit sequence learning, and potentially lead to relative reductions in implicit sequence learning in children with ADHD relative to controls.

Possible bidirectional interactions between emotional regulation and implicit sequence learning are suggested by the present findings and broader literature on childhood ASD. Parental report indicates that toddlers with early signs of ASD have
decreased expression of positive affect in non-threatening or mildly novel situations at 12-months than toddlers without early indications of ASD and low-risk control children (Zwaigenbaum et al., 2005). Other studies have reported reduced novelty seeking in adults with ASD (Anckarsater et al., 2006; Soderstrom, Rastam, & Gillberg, 2002). This suggests that individuals with ASD may be less likely to experience pleasure from novel situations throughout the lifespan. Children with ASD may be less likely to seek out novel situations, as has been documented for typically developing children who display this temperamental trait (Derryberry & Rothbart, 1997) and consistent with a core ASD symptom (i.e., restricted, repetitive, and stereotyped patterns of behaviors, interests and activities (APA, 2000).

Children with ASD could identify, and ultimately try to avoid, novel situations by relying on associative implicit learning. This body of work has demonstrated that associative implicit learning is behaviorally intact in childhood ASD. Children with ASD could use this intact form of learning in childhood to detect violations in the expected sequences of events, which might cue the onset of a novel situation. However, detecting and avoiding novel situations may unintentionally have an adverse effect on the development of emotional regulation. In general, novel situations are entered without knowledge about the emotional response the situation will elicit (i.e., the situation could turn out to be pleasant or unpleasant). Experiencing negative affect in novel situations may force children to develop a repertoire of emotional regulation strategies (e.g., negative affect while playing with a new toy that makes an unexpected, frightening noise may be mitigated by focusing attention on the impending end of the noise). If children with ASD avoid novel situations, they may develop weaker emotional regulation systems
and avoid future novel situations that might elicit difficult-to-regulate negative affect. As a compensatory strategy, children with ASD may rely more heavily on cues that signal the onset of an unexpected sequence of events so that novel situations can be avoided. This might increase the response to unexpected than expected events in ASD, a pattern seen in this body of work. Future studies examining the interactive development of these systems in younger children with ASD could test these predictions.

How do the present findings impact models of disordered brain and cognitive development? Most models of ADHD and ASD have focused on describing the development of processes that are under conscious, cognitive control. (Nigg and Casey’s 2005 article is a notable exception.) The present body of work suggests this narrow focus has yielded an incomplete picture of neurocognition in these disorders.

This sentiment is echoed in recent theoretical accounts highlighting the failings of “core deficit” accounts. For example, Happe, Ronald, and Plomin (2006) suggested that the search for a core deficit in ASD ought to be abandoned in favor of an approach that considers the relationship between cognitive function, genetic factors, and symptom domains. Similarly, Castellanos et al. (2006) reviewed the research in ADHD that documented deficits beyond the domain of response inhibition and concluded that a broader framework was needed to encompass the evidence of behavioral and neural abnormalities in multiple neurocognitive domains. Castellanos et al. (2006) presented an alternative framework, the “multiple pathways model”, which highlights interactions between deficits in the so-called “hot” (e.g., delay aversion on the Choice Delay task) and “cool” (e.g., response inhibition on the Stop Signal Task) executive functions. While this model is an improvement relative to others positing a core deficit in a single component
of executive control, it may need to be updated in light of evidence that processes that fall outside the domain of executive control are also impaired in childhood ADHD.

Both papers suggest that heterogeneity across individuals with ASD or ADHD can be addressed by studying variability along separate symptom or neurocognitive domains and from studying the interactions between symptom or neurocognitive domains in development. However, the scenarios outlined above highlight the ways in which these issues are more complicated in developmental disorders. Variability in symptom expression and neurocognitive processing changes as a function of age and experience. Studying heterogeneity in symptom or neurocognitive domains in a developmental context is challenging and could potentially reveal mechanisms of convergence (i.e., children with a certain set of symptoms become more similar over time) and divergence (i.e., children with a certain set of symptoms become less similar over time). Future studies can examine developmental changes in the heterogeneity of symptom expression and neurocognitive function to yield a clear picture of principles that might influence brain and cognitive development in children with developmental disorders.
REFERENCES


Appendix

Supplemental Materials from Chapter II

Impact of high recognition accuracy on implicit learning. To assess the extent to which the three Control children with high recognition accuracy affected the ASRT and CC task results, we excluded these children and re-analyzed accuracy, RTs, coefficients of variability, and recognition. Excluding these three control children did not change the major findings regarding the impaired implicit sequence learning on the ASRT task (Group x Epoch x Trial type interaction for RTs: $p = .01$), the absence of group differences in implicit spatial context learning (Group x Epoch x Configuration interaction for RTs: $p = .39$) and the absence of group differences in explicit awareness (Group x Trial interaction for recognition: $p = .28$). Only the statistical significance of the following analyses differed after excluding these children: For the recognition analysis, the previously significant difference Hits and False Alarms (main effect of Recognition Response) became non-significant ($p = .15$). For analysis of accuracy on the CC task, the previous trend for a Configuration x Epoch interaction became non-significant ($p = .20$). For analysis of median RTs on the CC task, the previous significant Configuration x Epoch interaction became a trend ($p = .07$). For coefficients of variability on the CC task, the previous trend for a main effect of Group became significant ($p = .04$). For coefficients of variability on the ASRT task, the previously non-significant Epoch x Group interaction became a trend ($p = .08$) and the previously non-significant main effect of Trial Type became significant ($p = .05$).

Implicit spatial contextual learning in children with high and low recognition accuracy.

To determine whether the 3 Control children with high recognition accuracy on the CC
task displayed greater implicit spatial contextual learning than the remaining Control children with low recognition accuracy, we computed 95% Confidence Intervals for the mean magnitude of CC learning (i.e., the sum of the difference between configurations across epochs). Magnitude of learning for the high recognition accuracy children \((M = .28, SD = .40)\) was within 95% Confidence Intervals of the mean magnitude of CC learning for low recognition accuracy children \((CI = .27 \pm .11)\).

*Implicit sequence learning in children with high and low recognition accuracy.* To determine whether the 3 Control children with high recognition accuracy on the CC task displayed greater implicit sequence learning than the remaining Control children with low recognition accuracy, we computed 95% Confidence Intervals for the mean magnitude of ASRT learning (i.e., sum of the difference between trial types across epochs). Magnitude of learning for the high recognition accuracy children \((M = 85.83, SD = 27.26)\) was within 95% Confidence Intervals of the mean magnitude of ASRT learning for low recognition accuracy children \((CI = 65.33 \pm 28.08)\).
Footnotes

1 Separate ANOVAs were conducted for First-order and Second-order tasks because ratings were not available for each participant for both tasks as familiarity was assessed following completion of the second task only (see Methods).

2 The one study to require unimanual responding (De Guise & Lassonde, 2001) also involved a transfer condition, and its results are therefore difficult to incorporate due to the manipulation of an additional variable. Participants had 40 repetitions and then transferred to the other hand for 40 repetitions for a total of 80 repetitions.

3 A linear model was selected based on the nature of the relationship between mean RT and time in the present study. Specifically, we used a second-order polynomial regression to test whether mean RT (for all correct trials) was better predicted by linear and quadratic Time functions (measured as time at stimulus onset in seconds). Overall, the model was significant ($R^2 = .299$). The linear relationship between mean RT and time was significant ($\beta = -.718, p < .0001$), whereas the quadratic relationship between mean RT and time was not ($\beta = .18, p = .27$). Thus, response speed improved with practice linearly. We therefore used a linear function to model parametric changes in task-related activity over time.