Procedural and Declarative Memory in Children with Developmental Disorders of Language and Literacy

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Abstract

The procedural deficit hypothesis (PDH) posits that a range of language, cognitive and motor impairments associated with specific language impairment (SLI) and developmental dyslexia (DD) may be explained by an underlying domain-general dysfunction of the procedural memory system. In contrast, declarative memory is hypothesized to remain intact and to play a compensatory role in the two disorders. The studies in the present thesis were designed to test this hypothesis.

Study I examined non-language procedural memory, specifically implicit sequence learning, in children with SLI. It was shown that children with poor performance on tests of grammar were impaired at consolidation of procedural memory compared to children with normal grammar. These findings support the PDH and are line with previous studies suggesting a link between grammar processing and procedural memory.

In Study II, the same implicit sequence learning paradigm was used to test procedural memory in children with DD. The DD group showed a learning profile that was similar to that of children with SLI in Study I, with a significant impairment emerging late in learning, after extended practice and including an overnight interval. Further analyses suggested that the DD impairment may not be related to overnight consolidation but to the effects of further practice beyond the initial practice session. In contrast to the predictions of the PDH, the sequence learning deficit was unrelated to phonological processing skills as assessed with a nonword repetition task.

Study III examined declarative memory in DD. The performance of the DD group was found to be not only intact, but even enhanced, compared to that of the control children. The results encourage further studies on the potential of declarative memory to compensate for the reading problems in DD.

In sum, the results lend partial support for the PDH and suggest further refinements to the theory. Collectively, the studies emphasize the importance of going beyond a narrow focus on language learning and memory functions in the characterization of the two disorders. Such a broader cognitive, motor and language approach may inform the development of future clinical and pedagogical assessment and intervention practices for SLI and DD.

Keywords: Specific Language Impairment, Developmental Dyslexia, Procedural memory, Declarative memory, Implicit sequence learning

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To Lova and Elina
This thesis is based on the following papers, which are referred to in the text by their Roman numerals.


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<th>Acronym</th>
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<tr>
<td>ADHD</td>
<td>Attention deficit hyperactivity disorder</td>
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<tr>
<td>ASRT task</td>
<td>Alternating serial reaction time task. Task used for testing procedural memory in the present thesis.</td>
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<td>DA</td>
<td>Dopamine</td>
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<td>DD</td>
<td>Developmental dyslexia</td>
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<tr>
<td>DecLearn</td>
<td>Task used for testing declarative memory in the present thesis.</td>
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<td>DP-model</td>
<td>Declarative/procedural model</td>
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<tr>
<td>GPe</td>
<td>Globus pallidus pars externa</td>
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<td>GPi</td>
<td>Globus pallidus pars interna</td>
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<td>LComp</td>
<td>Language composite score</td>
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<tr>
<td>MTL</td>
<td>Medial temporal lobe</td>
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<td>PDH</td>
<td>Procedural deficit hypothesis</td>
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<tr>
<td>RT</td>
<td>Reaction time</td>
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<tr>
<td>PIQ</td>
<td>Performance IQ</td>
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<td>SLI</td>
<td>Specific language impairment</td>
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<td>SLP</td>
<td>Speech-language pathology</td>
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<tr>
<td>SRT task</td>
<td>Serial reaction time task. Commonly used task for testing procedural memory.</td>
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<td>TD</td>
<td>Typically developing</td>
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Introduction

The overall aim of the work described in this thesis was to test a novel explanatory account of specific language impairment (SLI) and developmental dyslexia (DD). The procedural memory deficit hypothesis (Nicolson & Fawcett, 2007; Nicolson, Fawcett, & Dean, 2001; Ullman & Pierpont, 2005) makes a set of specific and falsifiable predictions about memory functions in these disorders. It therefore serves well as a scientific platform for furthering our understanding of cognitive and linguistic strengths and weaknesses associated with these conditions.

Developmental disorders of language and literacy

Specific language impairment

Specific language impairment refers to a developmental condition in which a child has poor expressive and/or receptive language skills, relative to typically developing children, for no apparent reason (Bishop, 1997; Leonard, 1998). The diagnostic criteria of SLI are largely exclusionary, emphasizing that the language problems occur in the context of otherwise normal development, and thus cannot be explained by factors such as environmental deprivation, hearing loss or mental retardation.

Specific language impairment is a heterogeneous condition, and the pattern of impairment may vary substantially between affected children. Most children present with impaired production and comprehension of complex grammatical structures, and with phonological and vocabulary deficits (Bishop, 1997, 2006; Conti-Ramsden, Botting, & Faragher, 2001; Leonard, 1998). The prevalence of the disorder has been estimated to be about 7% of children (Tomblin et al., 1997). However, prevalence numbers will depend on the exact diagnostic criteria used, as well as the specific cutoff selected to distinguish impaired from normal performance (Bishop, 2006).

Among the many different theories that have been offered to explain SLI, two broad competing perspectives can be distinguished. Within one perspective, the underlying deficit is hypothesized to be specific to the domain of language while leaving non-language functions largely intact. Two examples of theories within this perspective are the proposal that children with SLI have a selective deficit in establishing structural relationships such as
agreement (Clahsen, 1989), and the “extended optional infinitive” account (Rice, Wexler, & Cleave, 1995; Rice, Wexler, & Redmond, 1999) which suggests that children with SLI have a delayed maturation of a dedicated linguistic component that is implicated in marking of finite verb phrases.

Within the second broad theoretical perspective, it is recognized that many children with SLI have co-occurring deficits outside the domain of language, including of working memory (Gathercole & Baddeley, 1990; Montgomery, 1995; Vugs, Cuperus, Hendriks, & Verhoeven, 2013), attention (McGrath et al., 2008; Tirosh & Cohen, 1998), rapid temporal processing (Tallal & Piercy, 1973a, 1973b; Tallal, 1990; Tallal, Miller & Fitch, 1993) and motor functions (Bishop, 2002a; Hill, 2001). Accordingly, several theories have been developed with the aim of accounting for both language and non-language impairments by a domain-general underlying deficit (Leonard, 1998).

One such framework posits that a range of the language and non-language deficits may be accounted for by a limited cognitive processing capacity, such as a reduced processing rate (Kail, 1994; Leonard, McGregor, & Allen, 1992; Miller, Kail, Leonard, & Tumblin, 2001; Norbury, Bishop, & Briscoe, 2001). Others propose a more specific domain-general impairment, such as a perceptual or temporal processing impairment, particularly of briefly presented stimuli or rapidly presented sequences of items (Tallal & Piercy, 1973a, 1973b; Tallal, 1990; Tallal, Miller & Fitch, 1993), or a dysfunction of phonological perception and processing (Joanisse & Seidenberg, 1998) or of verbal working memory (Gathercole & Baddeley, 1990) that may indirectly lead to the observed language impairments.

Developmental dyslexia

Developmental dyslexia (DD) is characterized by unexpected difficulties with literacy development in the context of otherwise typical intellectual skills and educational opportunities (Lyon, Shaywitz, & Shaywitz, 2003). The disorder has been estimated to affect about 5-10% of children (Shaywitz, Shaywitz, Fletcher, & Escobar, 1990), although, as for SLI, prevalence numbers will depend on diagnostic criteria and selected cutoffs (Catts & Kamhi, 2005). Children with DD typically have difficulties with written word recognition and phonological decoding (using letter-sound mapping knowledge to decode novel words; Bishop & Snowling, 2004; Catts & Kamhi, 2005).

According to the “simple view of reading” (Hoover & Gough, 1990), successful reading depends on two sets of underlying cognitive/linguistic skills; word recognition and listening comprehension. It follows that impaired reading can be the result of any or both of these underlying skills. If decoding and written word recognition is impaired, reading will suffer for obvious reasons. In cases where decoding and word recognition is normal, compre-
hension of what is read will nevertheless be impaired as long as oral language comprehension is poor. Children with DD have specific difficulties with word recognition and are thus argued to be distinct from children who have mixed reading impairment (word reading + comprehension problems) and from children who mainly have comprehension problems (so called ‘‘poor comprehenders’’; Bishop & Snowling, 2004; Catts, Adlof, Hogan, & Weismer, 2005).

Theories of dyslexia span a wide range of suggested underlying deficits. In brief, a shift from visually based explanations (Morgan, 1896) to a language based view of the disorder, took place in the 1970s-1980s (e.g. Frith, 1985; for a review, see Handler and colleagues, 2011). Today, there is widespread consensus that the underlying deficit in DD is related to phonological processing, at least for a majority of cases (Catts & Kamhi, 2005; Frith, 1985; Goswami, 2000, 2008; Lundberg, 1998; Snowling, 2000). Numerous studies have shown that DD is associated with impaired phonological processing skills, including deficits in phonological awareness, nonword repetition and rapid serial naming (Vellutino, Fletcher, Snowling, & Scanlon, 2004). A causal role for phonological skills in learning to read has been suggested by studies in which preschool training in phonological awareness was shown to facilitate later reading and writing development (e.g. Lundberg, Frost and Petersen, 1988).

However, while phonological impairments are indeed found in an overwhelming majority of studies of DD (Ramus & Ahissar, 2012), other impairments, which are not easily explained by a specific phonological deficit, are also commonly reported. These include impairments of working memory (Smith-Spark & Fisk, 2007; Swanson, Xinhua, & Jerman, 2009), executive functions (Brosnan et al., 2002), motor function (Nicolson, Fawcett, & Dean, 2001), implicit sequence learning (Howard, Howard, Japikse, & Eden, 2006; Jimenez-Fernandez, Vaquero, Jimenez, & Defior, 2011; Vicari, Marrotta, Menghia, Molinari, & Petrosini, 2003), artificial grammar learning (Pavlidou, Williams, & Kelly, 2009) as well as problems with other aspects of language that appear to be primary in nature (i.e. not only a consequence of impaired reading; Lyytinen et al., 2004; Snowling, Gallagher, & Frith, 2003; Wimmer & Schurz, 2010).

Moreover, studies of children at family risk for DD have shown that those in the at-risk group who went on to have reading problems at 8 years of age did not show a selective phonological deficit in preschool but rather presented with a widespread pattern of language delay including below-normal syntactic and vocabulary knowledge, in addition to phonological problems. Interestingly, at-risk children who had within-normal range reading skills at age 8 also presented with some phonological problems (such as poor non-word decoding skills), but they did so in the context of normal syntactic and semantic development (Gallagher, Frith, & Snowling, 2000; Snowling, Gallagher, & Frith, 2003; Snowling, Muter, & Carroll, 2007). In line with
such findings, Wimmer and colleagues showed that phonological tasks (specifically assessing phonological awareness, rapid automatic naming and phonological short term memory) had only limited predictive power on reading and writing ability in German children from regular classrooms (Wimmer & Schurz, 2010). Further evidence against the notion that phonological deficits are sufficient to cause severe reading impairment comes from studies of children with speech sound disorder (SSD; a type of language impairment that primarily affects phonological development) who sometimes have intact reading development (Pennington & Bishop, 2009).

It has been suggested that phonological processing impairments may constitute an endophenotype that is related to an increased risk for DD. However, additional deficits may have to be present in order for reading to be seriously impaired. According to this double-deficit hypothesis (Wolf & Bowers, 1999), children who have specific deficits in only one area may be able to master the reading task at a normal pace by relying on compensatory mechanisms. In the presence of impairments in more than one area of language, however, such alternative routes may not be possible.

Points on a continuum or distinct disorders?
The obvious similarities and overlap between the SLI and DD have led some to argue that the two conditions are best treated as variants of the same developmental language disorder, differing mainly in severity (Kamhi & Catts, 1986). Others refer to the fact that not all children with SLI show the phonological decoding problems, that are the cardinal feature of dyslexia, as an argument for treating the disorders as distinct conditions (Bishop & Snowling, 2004; Bishop, McDonald, Bird, & Hayiou-Thomas, 2009; Catts et al., 2005). On this view, children with “SLI-only” are characterized by semantic and syntactic impairments and mild or within-normal range phonological processing skills, especially rapid naming (Bishop et al., 2009; Bishop & Snowling, 2004). In contrast, children with DD have mainly phonological problems, often in conjunction with subtle semantic and/or syntactic difficulties. On this view, cases of co-occurrence are characterized by deficits in all three domains (semantics, syntax and phonology; Bishop & Snowling, 2004; Catts et al., 2005; Ramus, Marshall, Rosen, & van der Lely, 2013)

Patterns of co-occurrence
It has been estimated that about 50% of children diagnosed with SLI in preschool go on to have reading impairments in school-age (Catts, Fey, Tomblin, & Zhang, 2002). However, as seen from the simple view of reading (Hoover & Gough, 1990), co-morbidity will depend on how reading ability is defined. Even though evidence suggests that phonological decoding
and word recognition (i.e. DD criteria) may sometimes be spared in SLI (Bishop et al., 2009), syntactic and semantic problems will nevertheless impair reading comprehension (Bishop & Snowling, 2004).

In addition, both SLI and DD are highly co-morbid with other developmental disorders such as attention deficit hyperactivity disorder (ADHD) and developmental co-ordination disorder (DCD; Asberg, Kopp, Berg-Kelly, & Gillberg, 2010; Hill, 2001; Iversen, Berg, Ellertsen, & Tonnesen, 2005; Yoshimasu et al., 2010). Subtle (i.e. “sub-diagnostic”) deficits of attention and motor skill appear to be even more common (Nicolson & Fawcett, 2011). Indeed, it has been suggested that 40-91% of children with SLI have varying degrees of problems in gross and/or fine motor skills (Hill, 2001; Rechetnikov & Maitra, 2009).

Importantly, co-morbidity patterns may be affected by sample selection. For example, a more widespread pattern of difficulties, including motor and attention problems, may be more likely to lead to parental and pedagogical concern, and thus to a clinic referral, compared to more specific deficits. Accordingly, it has been shown that clinic-referred samples display higher co-morbidity rates, as well as substantially higher boys: girls ratios, compared to research-identified samples (Pennington & Bishop, 2009).

Etiological factors

The fact that both SLI and DD tend to run in families has encouraged research into potential genetic explanations for the two disorders. Studies of monozygotic versus dizygotic twins have yielded heritability estimates (proportion of explained variance attributable to genetic variables) for SLI ranging from .5 to .75 for school-aged children (Bishop, 2002b). Notably, different genes have been linked to specific aspects of language, in particular to nonword repetition (Bishop, 2006; Bishop & Hayiou-Thomas, 2008) and to grammatical impairments (Bishop, 2006). Heritability estimates for DD are largely similar to those for SLI (Astrom, Wadsworth, Olson, Willcutt, & DeFries, 2011; Harlaar, Spinath, Dale, & Plomin, 2005).

Evidence suggests that at least some of the genes that have been associated with the two disorders may be involved in the regulation of early neuronal migration. One such gene is *KIAA0319*, which has been associated with both SLI and DD (Newbury et al., 2011; Rice, Smith, & Gayán, 2009), as well as with variation in reading ability in the normal population (Darki, Peyrard-Janvid, Matsson, Kere, & Klingberg, 2012). Experimental animal studies have shown that interference with (knocking down) this gene leads to focal disruption of neuronal migration in the form of ectopias and heteropias (Peschansky et al., 2010), similar to those linked to dyslexia in a series of studies by Galaburda and colleagues (Galaburda, LoTurco, Ramus, Fitch, & Rosen, 2006; Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985; Humphreys, Kaufmann, & Galaburda, 1990).
Importantly, although there appears to be allelic variants that influence cognitive and linguistic functions, the independent effects of these variants are typically small. This suggests that the etiology of both SLI and DD is multifactorial in nature. That is, the specific allelic variants for which associations have been found may have a detrimental effect on language and reading ability only when they occur together with certain other genetic and environmental factors (Bishop, 2006, 2009; Pennington, 2006; Pennington & Bishop, 2009).

The procedural memory deficit hypothesis

As previously discussed, the pattern of wide-ranging impairments observed in SLI and DD has encouraged attempts to provide unitary explanations for the disorders that may account for both the language and non-language deficits in the form of a domain-general underlying deficit. One influential theoretical view, which is the focus of the present thesis, posits that the underlying deficit in both SLI and DD is caused by a dysfunction in a cortico-striato-cerebellar procedural memory brain network involved in the acquisition and processing of motor and cognitive skills. Within this framework, the impaired procedural memory system is contrasted with an intact medial temporal lobe-based declarative memory network hypothesized to play a compensatory role in the two disorders (Nicolson & Fawcett, 2007; Nicolson et al., 2001; Ullman & Pierpont, 2005). Before introducing the procedural memory deficit hypothesis (PDH) in detail, a brief overview of the procedural and declarative memory systems will be given.

Memory systems

The PDH framework builds on a widely accepted current theory which holds that different forms of learning and memory are subserved by distinct brain networks (Squire, 2004). Memory can be divided into different categories based on both a temporal scale (i.e. how long the information is retained) and a qualitative scale (i.e. what type of information is being kept in memory).

Sensory memory encodes vast amounts of information (only a small subset of which we may be aware of) and lasts for about 500 ms (visual sensory memory) up to a few seconds (auditory sensory memory). Short-term memory (including working memory) can retain information up to a few minutes and is occupied by our often intentional efforts to remember specific information for a particular purpose (e.g. look up a telephone number and keep it in mind long enough to dial it; Gazzaniga, Ivry, & Mangun, 2009). The capacity of working memory has been estimated to be about 5-9 items
(Baddeley & Hitch, 1974), but see Olsson and Poom (2005) and Li, Cowan, and Saults (2013) for a different view.

Long-term memory (which is the focus of this thesis) differs from the previous categories by being limitless, in principle, with respect to both the amount of information that can be acquired and the time scale for which it can be retained. Long-term memory is commonly divided into declarative (sometimes referred to as explicit) memory which is commonly defined as memory that is available to awareness and non-declarative (or implicit) memory which is not available to awareness (Squire, 2004; but see Henke, 2010, for an alternative conceptualization of memory systems based on processes rather than the awareness criterion).

![Figure 1](image_url). Declarative and non-declarative memory systems. The figure indicates the brain structures thought to be especially important for each type of declarative and non-declarative memory. Reprinted from Neurobiology of Learning and Memory, 8(3), Squire, L. Memory systems of the brain: A brief history and current perspective, 171-177.47, Copyright (2004), with permission from Elsevier.
The procedural memory system

The procedural memory system is one of several brain systems involved in the implicit/non-declarative acquisition, consolidation and use of knowledge (Gabrieli, 1998; Squire & Zola, 1996; Willingham, Salidis, & Gabrieli, 2002; see Figure 1). Although previously considered to be important mainly for motor functions (such as learning how to ride a bicycle), it is becoming increasingly clear that this system also underlies a range of perceptual, cognitive and linguistic skills.

A large literature suggests that the procedural memory system plays a crucial role in the learning and computation of rules and sequences (Aldridge & Berridge, 1998; Knowlton, Mangels, & Squire, 1996; Poldrack, Prabhakaran, Seger, & Gabrieli, 1999; Saint-Cyr, Taylor, & Lang, 1988; Willingham et al., 2002). This system has also been shown to be involved in many other cognitive functions, including statistical learning (Karuza, Newport, Aslin, Starling, Tivarus, & Bavelier, 2013; McNealy, Mazziotta, & Dapretto, 2010; Saffran, Aslin, & Newport, 1996), probabilistic classification learning (Poldrack et al., 2001; Poldrack & Rodriguez, 2004), reinforcement learning (Frank, Seeberger, & O’Reilly, 2004), working memory (Dahlin, Neely, Larsson, Backman, & Nyberg, 2008; McNab & Klingberg, 2008) and retrieval from declarative memory (e.g. lexical retrieval; Ullman, 2004). In addition, accumulating evidence indicates that the procedural memory system is involved in aspects of grammar learning and processing, across syntax, morphology and phonology (Conway & Pisoni, 2008; Christiansen, Conway & O’mnis, 2012; Dominey, Hoen, Blanc, & Lelekova-Boissard, 2003; Petersson, Hagort & Folia, 2012; Sambin, Teichmann, de Diego Balague, Giavazzi, Sportiche, Schlenker, Bachoud-Lévi, 2010; Teichmann, Dupoux, Kouider, & Bachoud-Levi, 2006; Ullman, 2001b, 2004; Ullman & Pierpont, 2005).

Procedural memory relies on a network of brain structures in which circuits connecting the cortex with the (dorsal) striatum in the basal ganglia (i.e. corticostriatal circuits) play a crucial role. The basal ganglia are a set of interconnected sub-cortical structures which include the striatum, globus pallidus (external and internal parts), substantia nigra and sub-thalamic nucleus (Alexander, DeLong, & Strick, 1986; Middleton & Strick, 2000).

Originally, Alexander and colleagues described five distinct corticostriatal circuits (Alexander, Mahlon, DeLong, & Strick, 1986) but three circuits have been suggested to capture the main segregation (Joel & Weiner, 2000). Roughly, the motor circuit connects motor regions of the frontal cortex (primary, supplementary and premotor cortices) with the putamen (sometimes referred to as the sensorimotor striatum). Projections from association cortices, such as the dorsolateral prefrontal and posterior parietal cortex, to the caudate nucleus (associative striatum) constitute the associative circuit (the associative circuit is sometimes described as consisting of two distinct loops,
the executive loop and the visual loop; Seger & Spiering, 2011). The *limbic* circuit consists of projections from the orbitofrontal and cingulate cortex, and from the amygdala and hippocampus, to the ventral (or limbic) striatum. Evidence suggests that procedural memory may primarily involve the dorsal motor and associative subcompartments of the striatum (putamen and caudate nucleus; Poldrack et al., 2005; Uddén, Folia, & Petersson, 2010) whereas the ventral (limbic) subcompartment appears to be more strongly linked to aspects of declarative memory (Cervenka, Backman, Cselényi, Halldin, & Farde, 2008). It was originally posited that the corticostriatal circuits were functionally independent. However, this view has yielded to one by which a certain amount of integration of information processing across circuits is necessary for optimal cognitive performance (Haber & Calzavara, 2009).

![Diagram of the procedural memory system](https://example.com/diagram.png)

**Figure 2.** A simplified scheme of the procedural memory system. The figure is adapted from Frank et al., 2011; Gerfen and Surmeier, 2011, and Martinu and Monchi, 2013. GPe = external part of the globus pallidus; GPI = internal part of the globus pallidus; DN = dentate nucleus. Solid arrows represent excitatory projections and dotted arrows represent inhibitory projections.
All circuits include back-projections from the striatum to the site of cortical origin. The circuits project from the striatum to the internal part of the globus pallidus (GPi) via the direct and indirect pathways, and then from the GPi to the thalamus, and from the thalamus back to the cortex (Figure 2). The indirect pathway takes a detour to the GPi via the external part of the globus pallidus (GPe) and the subthalamic nucleus. All projections from the striatum as well as from the GPe and GPi are inhibitory; that is, they suppress activity in their targets. By contrast, all projections from the cortex and the thalamus are excitatory, and thus promote activity in their targets.

The GPi is tonically active, which means that it constantly sends inhibitory signals to the thalamus. The direct and indirect pathways have crucial roles in modulating this “default” inhibitory output by either inhibiting (direct pathway from the striatum to the GPi) or disinhibiting (indirect pathway from striatum via the GPe and subthalamic nucleus to the GPi) the inhibitory output from the GPi to the thalamus. Simply put, because the direct pathway (sometimes referred to as the “Go” pathway) inhibits inhibitory signals to the thalamus it will result in a lack of inhibition on the thalamus, which is then free to send excitatory output back to the cortex. Thus, the end result is a release of “desired” behaviours. The indirect (or “NoGo”) pathway, by contrast, suppresses behaviour by disinhibiting inhibitory signals to the thalamus.

The balance between the direct and indirect pathways, and thus the net effect of basal ganglia output, is modulated by dopaminergic projections from the substantia nigra pars compacta to the striatum. Imbalances in the dopaminergic system are associated with motor and cognitive impairments and with diseases such as Parkinson’s disease, schizophrenia and ADHD (Kish, Shannak, & Hornykiewicz, 1988; Peran et al., 2010; Seeman, 2011).

Dopamine (DA) also plays an important role for procedural learning and memory functions. First, DA modulates the efficacy of corticostriatal synapses by influencing long-term depression (LTD) and long-term potentiation (LTP), which ultimately weakens and strengthens the synapse, respectively. In addition, sensitivity to phasic (“burst”) release of DA in response to specific stimuli appears to be critical for certain forms of learning. For example, medication that increases the baseline level of DA in Parkinson’s disease patients may impair learning under certain conditions, presumably because the increased baseline DA level masks the effects of the stimulus-specific phasic DA release (Cools, Lewis, Clark, Barker, & Robbins, 2007; Frank, 2005).

Increased baseline levels of DA may also have a differential effect on the ability to learn from positive versus negative feedback. Whereas learning from positive feedback has been shown to be intact in Parkinson’s disease patients on medication, it is impaired in patients off medication. The opposite pattern is observed for learning from negative feedback; whereas pa-
tients on medication show impaired learning, patients off medication actually show enhanced learning (Frank, 2005).

Another, probably equally important, structure for procedural memory functions is the cerebellum, including the corticocerebellar circuits which are formed by projections from the cerebellum, via the dentate nucleus and the thalamus, to contra-lateral regions in cerebral cortex (including motor, premotor, prefrontal and posterior parietal cortices), and back-projections from these cortical regions, via the pons, to the dentate nucleus and the cerebellum. Analogous to the organization of the corticostriatal circuits, the corticocerebellar connections appear to form closed loops in which distinct regions of the cerebellum receive input from, and project to, specific regions of the cortex (Strick, Dum, & Fiez, 2009). Although the corticostriatal and corticocerebellar circuits were originally described as being anatomically distinct, more recent evidence suggests that they are linked to each other at the cortical level as well as by direct links between the striatum and the cerebellum (Bostan, Dum, & Strick, 2010; Bostan & Strick, 2010; Pandya & Yeterian, 1996).

Since long time, the cerebellum and the corticocerebellar circuits are considered important for a range of motor-related functions such as motor adaptation, balance, automatization of motor skills, procedural skill learning, and speech articulation (Doyon et al., 2009; O’Halloran, Kinsella, & Storey, 2012). More recently, however, several cognitive and linguistic functions have also been associated with the cerebellum and the corticocerebellar circuits, including executive control (Koziol, Budding, & Chidekel, 2011; O’Halloran et al., 2012), working memory (Ferrucci et al., 2008), retrieval from declarative memory (including lexical retrieval) and syntactic processing (see O’Halloran and colleagues, 2012, for a review).

Accordingly, it has been suggested that the corticocerebellar circuits may be broadly divided into one “motor” and one “non-motor” circuit with specific portions of the dentate nucleus being associated with each circuit (Dum & Strick, 2003). The motor circuit consists of projections and back-projections between motor and premotor cortices and the dorsal part of the dentate nucleus whereas the nonmotor loop connects regions in the prefrontal and posterior parietal cortices with the ventral part of the dentate nucleus (Strick et al., 2009).

It has been suggested that the corticostriatal circuits and corticocerebellar circuits contribute to different aspects of procedural motor skill learning, with corticostriatal circuits being particularly important for motor sequence learning and corticocerebellar circuits being involved in motor adaptation (Doyon et al., 2009). On a similar note, it has been proposed that different behavioural manifestations of ADHD might be related to which of these circuits is/are affected (Durston, van Belle, & de Zeeuw, 2011).

An extensively used task for the study of non-language procedural memory, specifically implicit sequence learning, is the serial reaction time (SRT)
task (Nissen & Bullemer, 1987). Because a version of the SRT task was used to test procedural learning and memory in Study I and Study II, a brief review of the behavioral and brain imaging literature on this task will be given here.

In this task, participants are typically shown four boxes or circles arranged horizontally across a computer screen. Whenever a stimulus appears in one of the four positions, participants are to press one of four corresponding response keys as quickly and accurately as possible. In the implicit version of this task, participants are not told that the stimuli are presented according to a fixed sequence (as opposed to the explicit version, in which the sequential pattern is verbalized and memorized prior to practice). Sequences can be either deterministic (Nissen & Bullemer, 1987) such that the location of the stimulus can be fully predicted based on its preceding location; or probabilistic (Howard & Howard, 1997; Schvaneveldt & Gomez, 1998) in which case the statistical structure of the sequence contains some irregularities. Sequence learning is seen as improvements in the accuracy and/or reaction times (RTs) of responses, as compared to a randomly ordered sequence introduced as a control condition at the end of practice. When administered as an implicit task, learning in the SRT task appears to be largely, though not completely, incidental and non-conscious (Howard & Howard, 1992; Willingham, Nissen, & Bullemer, 1989). Evidence suggests that probabilistic sequences are more likely not to yield explicit knowledge compared to deterministic sequences (Stefaniak, Willems, Adam, & Meulemans, 2008).

A fundamental aspect of sequence learning in the SRT task, and of procedural learning more generally, is that it takes place over an extended time-period that may be divided into distinct phases based on both behavioral characteristics and neural correlates of performance (Debas et al., 2010; Hauptmann, Reinhart, Brandt, & Karni, 2005; Korman, Raz, Flash, & Karni, 2003; Orban et al., 2010; Robertson, Pascual-Leone, & Miall, 2004). Typically, an initial fast acquisition stage, characterized by a rapid improvement in performance (as evidenced by a decrease in both response speed and errors), is followed by a gradual decrease in the learning rate and a trend towards an asymptote (Hauptmann et al., 2005; Korman et al., 2003). This asymptotic shape of the learning curve is suggested to reflect a saturation of learning that appears to be necessary for consolidation processes to occur normally (Hauptmann & Karni, 2002; Hauptmann et al., 2005; Karni et al., 1998). Consolidation refers to the process by which an initially labile memory trace becomes more robust and resistant to interference (Doyon et al., 2009; Robertson et al., 2004). Sometimes this process involves an actual increase in performance, without further practice, a phenomenon referred to as off-line learning (Hauptmann et al., 2005; Nemeth et al., 2010; Song, 2009; Song, Howard, & Howard, 2007). The end point of procedural learning is automaticity of the learned behavior. When a skill is automatized it
can be performed effortlessly even when attention is directed elsewhere (as in dual task situations; Seger & Spiering, 2011).

Brain imaging studies suggest that implicit sequence learning in the SRT task depends largely on the cortico-striato-cerebellar procedural memory brain network described above (for a review, see Doyon and colleagues, 2009). In addition, recent studies have highlighted a role for the medial temporal lobe (MTL) in sequence learning (Albouy et al., 2008; Gheysen, Van Opstal, Roggeman, Van Waerbeke, & Fias, 2011; Schendan, Searl, Melrose, & Stern, 2003; Simon, Vaidya, Howard, & Howard, 2012) under both explicit and implicit conditions. Importantly, the neural correlates of sequence learning have been shown to be modulated by the amount of practice with the task; whereas early learning is characterized by a rather widespread activation pattern that includes the MTL, prefrontal cortex, striatum and cerebellum, studies including extended practice, and later learning stages, suggest an increasingly important role for the striatum in learning stages beyond the fast acquisition stage (Doyon et al., 2009; Rieckmann & Backman, 2009; Rieckmann, Fischer, & Backman, 2010; Simon et al., 2012).

Behavioral and brain imaging data contrasting children and adults on the SRT task (Thomas et al., 2004) suggest somewhat less efficient learning in the child group compared to the adult group, as well as slight differences in brain activation patterns. Specifically, children recruited subcortical areas (putamen) relatively more than adults who instead showed greater activation in the premotor cortex.

The declarative memory system

In contrast to procedural learning, which is slow and gradual, learning in declarative memory is typically rapid and can occur after a single exposure to the stimulus (Squire, 2004). Declarative memory is traditionally described as encompassing two different forms of explicit (but see Henke, 2010, for an alternative definition) memory; episodic memory (memory for personal experiences) and semantic memory (memory for facts, concepts or “world-knowledge”; Tulving, 1972, 2002). In addition to the difference in the type of information being processed, the experience associated with each type of memory is suggested to be a key distinction.

Episodic memory involves “mental time-travel” in the sense that the memory takes us back to a situation/episode that happened in the past. We revisit, or re-live, the experience in our minds. Tulving (2002) defined the quality of episodic memory as self-knowing or remembering and suggested that remembering always involves mental time-travel. In contrast, semantic memory is defined as knowledge that is independent of a specific context or situation, for example the meaning of a word or general fact knowledge (e.g. Paris is the capital of France). Tulving described the experience associated with semantic memory as knowing. The qualitative differences between epi-
sodic and semantic memory is reflected in studies showing that the brain activation patterns associated with both encoding and retrieval of episodic and semantic memory are at least partly distinct (Cabeza & Nyberg, 2000; Nyberg, Forkstam, Petersson, Cabeza, & Ingvar, 2002; Wiggs, Weisberg, & Martin, 1999).

There is ample evidence that encoding of new episodic and semantic memories is dependent on the integrity of the MTL system (Cohen & Squire, 1980; Howard Eichenbaum, 2000; Eichenbaum, 2000; Mishkin, 1978; Scoville & Milner, 1957; Squire & Zola-Morgan, 1991). Evidence from patient studies (Scoville & Milner, 1957) and neuroimaging studies (Gilboa, Winocur, Grady, Hevenor, & Moscovitch, 2004; Ryan et al., 2001) suggest that the MTL is necessary also for retrieval of declarative memories for some time after encoding (months to years) but that at least semantic memories can eventually be retrieved without the engagement of the MTL. The increasing independence of the MTL for semantic memory retrieval appears to be gradual in nature such that MTL activation decreases linearly as a function of the age of the memories (Smith & Squire, 2009).

The role of the MTL in episodic memory retrieval is a matter of debate. The standard model of systems consolidation (Squire, Cohen, & Nadel, 1984) proposes that once an episodic memory is consolidated (a process that might take months to years), the MTL is no longer necessary for its retrieval. This position is supported by patient studies such as that of HM (Scoville & Milner, 1957) in which remote episodic memories were reported to be spared. However, based on a review of a number of more recent patient studies, Nadel and Moscovitch (1997) have challenged the standard model of systems consolidation, and instead suggested that when damage to the MTL is complete, retrieval of remote episodic memory is also impaired. Further support for this position comes from brain imaging studies reporting hippocampal activation for remote as well as recent episodic memories (Rekkas & Constable, 2005).

In addition to the MTL, the frontal cortex has been shown to play an important role in both encoding and retrieval of declarative memory (Nyberg et al., 1996; Tulving, Kapur, Craik, Moscovitch, & Houle, 1994). Depending on the specific paradigm used to assess declarative memory, the relative demand on frontal lobe dependent executive functions underlying encoding strategies and recall of information may be increased or decreased. For example, increased demands on working memory and executive functions have been associated with intentional as compared to incidental encoding, and with free recall as compared to recognition (Stuss & Knight, 2002). Other structures of importance for declarative memory include the lateral temporal cortex, the amygdala, and the parietal lobe (Nyberg, 2008).

One commonly used paradigm for the assessment of aspects of declarative memory, which was also used in Study III, is the old/new recognition memory paradigm. In human studies, participants are typically presented
with a list of items in an initial encoding session and, after a given time interval, asked to indicate whether or not this item was encountered in the previous session. Impaired recognition memory has consistently been reported in patients with MTL lesions (Kopelman et al., 2007; Manns, Hopkins, Reed, Kitchener, & Squire, 2003), and brain imaging studies indicate that they engage an episodic memory brain network for both visual and verbal stimuli (Henson, 2005; Kim & Cabeza, 2009). For example, encoding of items that are successfully remembered in a subsequent test has been reported to be associated with increased MTL activation compared to items that are forgotten (Brewer, Zhao, Desmond, Glover, & Gabrieli, 1998; Weis, Klaver, Reul, Elger, & Fernandez, 2004). In contrast, successful recognition of previously presented items (hits) appears to be associated with a deactivation of the MTL compared to correctly rejected foils (Rombouts, Barkhof, Witter, Machielsen, & Scheltens, 2001). (However, such findings should be interpreted with caution since a relative difference in MTL activity between these two categories of items could just as well reflect increased activation for the foils, which are new to the subject—i.e. the novelty effect; Tulving & Kroll, 1995; Nyberg, 2005.)

Performance in recognition memory tasks is widely held to rely on two cognitive subcomponents; familiarity and recollection (Jacoby, 1991; Mandler, 1980; Yonelinas, 1994). Familiarity is defined as the feeling (with varying degrees of certainty) of having experienced an item before but without any knowledge of the context in which it appeared (Yonelinas, 2002). Recollection is defined as the recognition of an item as having been experienced before, coupled with knowledge about the context in which this item was experienced (Yonelinas, 2002). Familiarity and recollection are sometimes referred to as item memory and source memory, respectively (Henson, 2005). A widely used example to illustrate this distinction is the common experience of recognizing a person as familiar (vaguely or strongly) but being unable to retrieve contextual information about how, where and when you have met this person.

According to single-process views of recognition memory, familiarity and recollection are points on a continuum of subjective confidence that reflect quantitative differences in memory strength (Heathcote, Raymond, & Dunn, 2006; Squire & Wixted, 2011). Thus, familiarity can be described as “sub-recollective” memory. Conversely, dual-process theories view familiarity and recollection as two qualitatively different processes (Brown & Aggleton, 2001; Howard Eichenbaum & Lipton, 2008; Yonelinas, 2002) often assumed to have at least partly different neural underpinnings (Howard Eichenbaum & Lipton, 2008).

Researchers arguing for a dual-process view of recognition memory call upon converging evidence from behavioral, neuroimaging, lesion and single-cell recording studies of both humans (Rugg & Curran, 2007; Woodruff, Hayama, & Rugg, 2006; Yonelinas, Otten, Shaw, & Rugg, 2005) and ani-
mals (particularly monkeys and rodents) showing distinct functional and anatomical correlates of familiarity and recollection (Diana, Reder, Arndt, & Park, 2006; Howard Eichenbaum & Lipton, 2008; Yonelinas, 2002). Based on such evidence it has been suggested that the hippocampus proper is necessary for recollection but not for familiarity-based judgments, which instead are thought to depend on the perirhinal cortex. The parahippocampal gyrus has been suggested to contribute aspects of contextual (in particular spatial) information to the recollective experience (for reviews, see Yonelinas, 2002, and Eichenbaum and colleagues, 2007). Importantly, correct endorsement or rejection of items in the old/new recognition memory paradigm can be accomplished based on familiarity without recollection.

Interactions between the two memory systems

As reviewed above, converging evidence from human and animal studies suggest that the procedural and declarative memory systems rely on at least partly dissociable neural substrates and support different cognitive functions (Poldrack & Rodriguez, 2004; Squire & Stuart M. Zola, 1996). However, the two systems do not work in isolation. Rather, the relative involvement of the procedural and declarative systems during cognitive task performance appears to be modulated by the to-be-learned material on the one hand (Foerde, Knowlton, & Poldrack, 2006; Poldrack et al., 2001; Shohamy et al., 2004; Ullman, 2004), and by complex “competitive” and “cooperative” interactions between the two systems on the other (for reviews see Foerde & Shohamy, 2011; Poldrack & Packard, 2003; Ullman, 2004).

Of particular relevance, animal lesion studies have revealed that damage to one system may actually enhance learning by the other system (Chang & Gold, 2003; Mitchell & Hall, 1988; Schroeder, Wingard, & Packard, 2002). This effect has been demonstrated in both directions in animals; lesions to the striatum have been shown to enhance learning by the MTL, and lesions to the MTL have been shown to yield enhanced striatal learning (Lee, Duman, & Pittenger, 2008). Such findings have been taken as evidence for a competitive relationship between the two systems that may interfere with learning and processing under normal conditions. On this view, the enhanced performance of the unimpaired system may reflect the removal of competitive interference by the damaged system (Chang & Gold, 2003). Neuroimaging studies suggest that somewhat similar competitive mechanisms may exist in humans. For example, negative correlations between striatal and MTL activity have been observed in healthy participants during learning in the SRT task; as striatal activity increases with practice, MTL activity decreases (Lieberman, Chang, Chiao, Bookheimer, & Knowlton, 2004; Poldrack et al., 2001; Seger & Cincotta, 2005).

Evidence for a cooperative relationship between the two systems comes from studies showing that lesions to one system may induce a shift of func-
tions such that the unimpaired system takes over functions that would normally rely on the impaired system. For example, studies of patients with Parkinson’s disease have shown that the MTL may serve a compensatory function in the case of striatal pathology. Similar compensatory mechanisms have been reported in studies of Huntington’s disease and in studies of aging in which declarative memory has been shown to take over certain cognitive functions that are normally performed by the procedural memory system (Beauchamp, Dagher, Panisset, & Doyon, 2008; Moody, Bookheimer, Vanek, & Knowlton, 2004; Rauch et al., 2007; Rieckmann et al., 2010; Ullman & Pierpont, 2005).

The neurobiological mechanisms that mediate the interactions described above still remain to be elucidated. One alternative may be that such interactions are mediated by direct anatomical links between the two systems. However, although direct links between the MTL and dorsal striatum have been found in rodents (Sorensen & Witter, 1983), to this date there is little evidence for direct connections between the MTL and dorsal striatum in humans and other primates (Poldrack & Rodriguez, 2004). One possibility, therefore, is that such connections are mediated by the well-established links between the MTL and the ventral striatum. Alternatively, it has been proposed that the interactions between the procedural and declarative memory systems are mediated by the prefrontal cortex, to which both the striatum and the MTL are strongly connected (Poldrack & Rodriguez, 2004).

Predictions of the procedural memory deficit hypothesis

Nicolson and Fawcett were the first to suggest a link between impaired procedural memory and DD (Nicolson & Fawcett, 1990; Nicolson et al., 2001). Their “dyslexic automatization deficit”, proposed in 1990, suggested that a domain-general deficit in the automatization of skills (cognitive and motor) could explain the pattern of impairments observed in the disorder. They further suggested that individuals with DD used “conscious compensation” to overcome automatization deficits. Thus, impairments may be revealed only when such compensation is hindered, for example by adding a secondary task that occupies the cognitive resources otherwise recruited for compensation.

In 2001, Nicolson and Fawcett proposed the “cerebellar deficit hypothesis” according to which abnormalities in the cerebellum can account for the full range of impairments observed in the disorder (see Figure 3). More recently, influenced by the work of Ullman and colleagues (see below), Nicolson and Fawcett have proposed a “neural systems view” of developmental learning disorders, including DD and SLI, in which an impaired procedural memory system is contrasted with an intact declarative memory system (Nicolson & Fawcett, 2007).
In 2005, Ullman and Pierpont proposed the “procedural deficit hypothesis” (PDH) as an explanatory account of SLI (Ullman & Pierpont, 2005). The PDH is based on a similar domain-general approach to that of Nicolson and Fawcett, and attempts to account for a range of linguistic, cognitive and motor deficits in the form of an underlying dysfunction of the procedural memory brain system.

The PDH is generated from Ullman’s declarative/procedural (DP) model of language (Ullman, 2001a, 2001b, 2004). The DP-model is a dual-systems account of language and as such it assumes that idiosyncratic and rule-governed aspects of language are supported by distinct cognitive/linguistic systems (e.g. Chomsky, 1995; Pinker, 1999). Idiosyncratic knowledge, which includes, for example, arbitrary sound-meaning associations and irregular word forms (e.g. teach – taught), is thought to be memorized in a mental lexicon. Rule-governed knowledge, which is the knowledge of how to combine words and parts of words into phrases, sentences and complex words, is subserved by a distinct mental grammar. The DP-model proposes that the linguistic distinction between the mental lexicon and mental grammar can be largely mapped onto the distinction between the declarative and procedural memory systems in the brain (Squire, 2004). Specifically, the DP-model posits that the mental lexicon mainly depends on the network of brain structures constituting the declarative memory system, whereas the
mental grammar relies on the procedural memory brain network (Ullman, 2004).

The views of Nicolson and Fawcett and Ullman and Pierpont are not identical, but the PDH and the “neural systems view” make very similar testable predictions. For the sake of simplicity, I will therefore combine the predictions of the two theories and refer simply to the “PDH” in the subsequent discussion. Note that the most recent version of the magnocellular theory of DD (Stein, 2001) also includes the prediction that cerebellar functions, and thus aspects of procedural memory, are impaired in the disorder. The present thesis was not designed to differentiate between the PDH and the magnocellular theory, and the predictions below may be at least partly consistent also with the magnocellular theory.

The PDH specifically predicts that SLI and DD should be associated with abnormalities of procedural memory brain structures and/or of the white matter tracts connecting these areas. The heterogeneity both within and between the two disorders is hypothesized to be a consequence of the exact locus of aberrance in the procedural memory brain system (it is proposed that DD might be associated primarily with impairments of the corticocerebellar circuits, whereas for SLI, the corticostriatial circuits are affected (Nicolson & Fawcett, 2007). Moreover, the PDH predicts impairments of both language and non-language functions that depend on these brain structures, including (but not limited to) implicit sequence learning tasks (e.g. SRT tasks).

Based on the assumptions of the DP-model, the PDH predicts an association between procedural memory and grammar, but not between procedural memory and vocabulary, which instead is expected to be associated with declarative memory. Thus, with respect to SLI, procedural memory deficits are predicted to be found in children with grammatical impairments but not in children who have primarily vocabulary deficits.

In DD, a procedural memory dysfunction is thought to underlie reading problems both directly, through impaired skill automatization, and indirectly, via phonological processing problems. That is, a procedural memory deficit is predicted to have a detrimental effect on phonological processing skills (through articulation and/or sequencing problems) which in turn hinders reading development. On this view, the effect of procedural memory on reading is partly mediated by phonological processing skills (also see Figure 3).

Functions that are independent of the procedural memory system are predicted to function normally in the majority of cases. As previously noted, specific predictions are made regarding the declarative memory system, which, according to the DP-model, underlies the mental lexicon. Analogous to the reasoning above, the PDH predicts that the brain structures that constitute the declarative memory system (in particular the MTL), and the white
matter tracts connecting them, are intact, together with the language and non-language functions that depend on this system.

The PDH recognizes that the cortico-striato-cerebellar network is not exclusively dedicated to procedural memory but is also involved in many other cognitive functions, including recall of declarative memory. Accordingly, across language and non-language domains, recognition is predicted to be spared while a gradually increasing impairment may be seen for cued and free recall (with free recall relying more on frontal lobe structures compared to recognition and cued recall).

An innovative and important aspect of the PDH framework is the prediction that the declarative memory system can compensate for (take over) certain functions that normally relies on the procedural memory system. It is argued that such compensation may potentially explain much of the improvement seen in children with SLI and DD over the course of development. For example, it is proposed that children with SLI may store complex linguistic structures, that are normally composed by the procedural system as an automatic application of linguistic rules (e.g. “walk+ -ed”), as chunks (i.e. “walked”) in lexical/declarative memory. In a similar vein, it is hypothesized that individuals with DD may compensate for persisting phonological decoding problems by the memorization of whole words or parts of words as “pictures” or chunks. Based on this prediction one might expect that better declarative memory should be associated with better grammatical ability in SLI and with better reading ability in DD. That is, correlations should be found between measures of declarative memory and grammar in SLI, and reading in DD, but not in typically developing children.

It follows from the prediction of domain-generality that the PDH can be falsified by examining non-language memory functions in SLI and DD. By focusing on non-language learning and memory in these disorders it is possible to avoid the confounding impact that, for example, phonological deficits could have on a language-based task.

**Procedural and declarative memory in SLI**

Tomblin and colleagues (Tomblin, Mainela-Arnold, & Zhang, 2007) were the first to use the SRT task to investigate procedural learning in adolescents with SLI. They found that the SLI group showed slower initial learning rates than the control group, even though at the end of training, performance did not differ between groups. Moreover, a positive correlation was found between performance on grammatical tests and procedural learning whereas no such effect was found for performance on tests of vocabulary. Impaired performance on different versions of the SRT task has since been replicated by Lum and colleagues (Lum, Gelgic, & Conti-Ramsden, 2010; Lum, Conti-Ramsden, Page, & Ullman, 2011). However, null results have also been re-
ported (Gabriel, Maillart, Guillaume, Stefaniak, & Meulemans, 2011; Lum & Bleses, 2012).

In addition, other aspects of procedural memory have been found to be impaired in SLI. Kemeny and Lucaks (Kemény & Lukács, 2009) used the Weather Prediction (WP) task, and reported that school-age children with SLI showed poorer performance at probabilistic categorization learning relative to a control group. In the WP task, participants are presented with one or more cards with different geometric shapes and, on each trial, asked to predict a categorical outcome (i.e., either “sunshine” or “rain”). Responses are followed by probabilistic feedback for each trial. The WP task has been shown to involve procedural memory brain structures (in particular the striatum) in the early stages of learning and impaired performance has been shown in patients with basal ganglia degeneration (Parkinson’s disease; Knowlton, Mangels, & Squire, 1996).

Lee and Tomblin (Lee, 2012, Lee & Tomblin, 2012) studied different aspects of procedural learning within the same adult individuals with and without SLI. The tasks in this study were all chosen to represent different aspects of procedural learning with the common denominator being that all tasks were known to depend on the basal ganglia. Lee and Tomblin reported performance in the SLI group to be impaired at 3 out of 4 tasks (with the SRT-task being the only null result).

Studies using statistical learning paradigms, which appears to depend largely on brain structures supporting procedural memory (Karuza et al., 2013), have also found deficits in language impaired individuals (e.g. Evans, Safran, & Robe-Torres, 2009; Plante, Gomez, & Gerken, 2002; von Koss Torkildsen, Dailey, Aguilar, Gomez, & Plante, 2013; see Arciuli & Torkildsen, 2012, for a review). In addition, processing of sequential structures in music has been shown to be impaired in children with SLI (Jentschke, Koelsch, Sallat, & Friederici, 2008).

Studies of declarative memory in SLI have yielded mixed findings. Several studies of declarative memory for visual stimuli suggest intact performance in SLI (Baird, Dworzynski, Slonims, & Simonoff, 2010; Bavin, Wilson, Maruff, & Sleeman, 2005; Dewey & Wall, 1997; Lum et al., 2010); by contrast, many studies using verbal material have reported impairments (Alt & Plante, 2006; Dewey & Wall, 1997; Lum et al., 2010). It thus appears that some, but certainly not all (e.g. Alt & Plante, 2006; McGregor, Newman, Reilly, & Capone, 2002), of the inconsistency might be explained by whether language or non-language stimuli are used. Lum and colleagues (Lum, Conti-Ramsden, Page, & Ullman, 2012) argued that impaired performance on many declarative memory tasks may be the result of phonological/language problems in SLI rather than declarative memory per se. Accordingly, they claimed to show that verbal declarative memory was not impaired in SLI once verbal working memory and language deficits were controlled for (Lum et al., 2012).
In line with the prediction that declarative memory may play a compensatory role in SLI, Fonteneau and van der Lely reported that syntactic processing in SLI children with grammar deficits evoked neural responses that are normally associated with semantic processing in typically developing individuals (Fonteneau & van der Lely, 2008). This finding was interpreted by the authors as possibly reflecting a compensatory use of the declarative memory system for the processing of grammar in children with SLI.

Structural and functional neuroanatomical studies of SLI have implicated a variety of brain structures to be affected in the disorder. Structural abnormalities include reduced grey matter volumes in frontal cortex (e.g. Broca’s area), the parietal lobes, and the perisylvian region as well as atypical patterns of asymmetry (De Fosse et al., 2004; Gauger, Lombardino, & Leonard, 1997; Herbert et al., 2005; Jernigan, Hesselin, Sowell, & Tallal, 1991; Elena Plante, Swisher, Vance, & Rapcsak, 1991). In addition, there is evidence for reduced volume in the right caudate nucleus (Badcock, Bishop, Hardiman, Barry, & Watkins, 2012).

Functional MRI studies have revealed abnormal patterns of activity during language related tasks in frontal, temporal and parietal areas (Friederici, 2006; Hugdahl et al., 2004; Weismer, Plante, Jones, & Tomblin, 2005). Im et al (2007) found functional abnormalities in the frontal lobes, the thalamus, the basal ganglia, and the cerebellum in participants with SLI, using positron emission tomography (PET). Interestingly, structural imaging revealed no abnormalities in the same SLI participants.

Procedural and declarative memory in DD

Impaired performance at procedural memory tasks has been associated with dyslexia in studies using implicit versions of the SRT-task (Howard, Howard, Japikse, & Eden, 2006; Jimenez-Fernandez, Vaquero, Jimenez, & Defior, 2011; Menghini, Hagberg, Caltagione, Petrosini, & Vicaria, 2006; Menghini et al., 2008; Stoodley, Harrison, & Stein, 2006; Vicari et al., 2005; Stefano Vicari, Marotta, Menghini, Molinari, & Petrosini, 2003), but null-results have also been reported (Kelly, Griffiths, & Frith, 2002; Waber et al., 2003; Russeler, Gerth, & Munte, 2006). In addition, impaired performance of the dyslexic group has been reported in studies using artificial grammar learning paradigms (Pavlidou, Kelly, & Williams, 2009, 2010).

Few studies have directly tested declarative memory functions in DD, and those that have done so have yielded inconsistent findings. Whereas some studies have reported that declarative memory is normal in the disorder, others have found a deficit. For example, three of the sequence learning studies mentioned above have contrasted impaired performance in the dyslexic group in the implicit sequence learning condition with intact performance in an explicit (declarative) version of the same task (Jimenez-Fernandez et al., 2011; Vicari et al., 2003). Intact performance was also reported for an im-
licit learning task ("the contextual cueing task"; Chun & Phelps, 1999), previously shown to depend on the MTL rather than the procedural memory system (Howard et al., 2006; Jimenez-Fernandez et al., 2011).

In addition, learning and retention of non-verbal information has been shown to be intact in the paired-associate learning task (Li, Shu, McBride-Chang, Liu, & Xue, 2009; Messbauer & de Jong, 2003), which is a classic declarative (episodic) memory paradigm. The same studies reported impairments at learning when verbal stimuli were used (Messbauer & de Jong, 2003). However, these group differences disappeared when phonological impairments were controlled for, suggesting that the impairment might not be related to declarative memory per se but to underlying phonological problems. Accordingly, in a third study, paired-associate learning with verbal stimuli was found to be intact in DD when short, high-frequency words (which minimizes the effect of phonological processing problems), were used (Mayringer & Wimmer, 2000).

Evidence supporting the prediction of a compensatory role for declarative memory comes from studies indicating that persistent phonological decoding problems in individuals with DD may be associated with an increased reliance on "chunking" and whole word memorization for reading (Shaywitz & Shaywitz, 2008; van der Leij & van Daal, 1999). In addition, behavioral interventions have been found to lead not only to reading improvements, but also to changes in the hippocampus and other MTL structures, in both functional and structural imaging studies (Eden et al., 2004; Temple et al., 2003).

Studies of structural and functional neuroanatomy in participants with DD have yielded mixed and sometimes contradictory findings. As for SLI, a variety of brain structures have been reported to be abnormal in the disorder. Galaburda and colleagues (1985) described atypical symmetry of the left and right plana temporalia (PT), due to enlarged right PT, in participants with dyslexia. However, this finding has not been replicated by more recent studies (Eckert et al., 2003). Other studies have reported decreases in gray matter in the left temporal lobe, frontal lobe, caudate nucleus, thalamus and cerebellum (Brown et al., 2001; Eckert, 2004; Eckert et al., 2003) and occipital cortex (Eckert et al., 2005) as well as reduced brain activation during word processing at the left occipito-temporal junction (Paulesu et al., 2001).
Summary and study objectives

The procedural memory deficit hypothesis (PDH) posits that an impairment of procedural memory underlies a range of linguistic, cognitive and motor impairments observed in SLI and DD. Importantly, the procedural memory dysfunction is proposed to be domain-general in the sense that both language and non-language learning that depend on the procedural memory brain system are affected. Thus, the predictions of the PDH may be tested using a non-language procedural learning paradigm, such as implicit sequence learning tasks.

Studies designed to test the PDH using implicit sequence learning tasks have yielded inconsistent results. It has been proposed that the type of sequence used, as well as the time interval examined, may account for some of this inconsistency (Du & Kelly, 2012; Orban, Lungu, & Doyon, 2008). A fundamental aspect of procedural learning is that it takes place over an extended time-period that may be divided into distinct stages based on both behavioral characteristics and neural correlates of performance. Yet, no study of implicit sequence learning in children with SLI or DD has included learning stages beyond a single practice session. Thus, group differences in procedural memory consolidation and longer-term learning remain unexplored.

The overall aim of the work described in this thesis was to test the PDH by examining non-language procedural memory, specifically implicit sequence learning, in children with SLI (Study I) and children with DD (Study II), compared to typically developing control children. In addition, the studies were designed to provide new evidence about the nature of a potential procedural memory deficit in SLI and DD by being the first to i) extend the examination of procedural learning to include not only an initial practice session, but also overnight consolidation and longer-term learning, and ii) use a variant of the SRT task that has not previously been used with children with SLI or children with DD: the Alternating Serial Reaction Time (ASRT) task (Howard & Howard, 1997; Howard et al., 2004). In contrast to the tasks used in previous studies, the ASRT task allows for an assessment of sequence specific learning separate from general motor skill learning. Moreover, it is possible to examine sequence learning continuously throughout the task, rather than only at a single point at the end of the task.

The PDH framework includes the prediction that aspects of declarative memory remain intact in SLI and DD, and that this system may serve a com-
pensatory role in learning in the two disorders. Study III aimed at testing this prediction with respect to DD by examining previously unexplored aspects of declarative memory in children with this condition.
Research questions

The specific research questions addressed by the studies in this thesis are:

Study I: Is non-language implicit sequence learning impaired in children with SLI? If so, is this deficit specifically related to performance on grammatical tests?

Study II: Is non-language implicit sequence learning impaired in children with a clinical diagnosis of DD? If so, is this deficit mediated by phonological processing skills (as assessed by a nonword repetition task)?

Study III: Is recognition memory after incidental encoding intact in children with DD? If so, is there evidence that declarative memory may serve a compensatory role for the reading deficits in DD?
Methods

This thesis builds on data from two projects; one project focusing on children with SLI, and one project focusing on children with DD. The SLI project, which generated Study I, was conducted in collaboration with the Brain and Language Lab at Georgetown University and the Child Language Research Center at the University of Iowa.

The DD project (Study II and Study III) was conducted at the Department of Neuroscience, Speech-Language Pathology (SLP) research group, at Uppsala University. The same procedural and declarative research tasks were used in the two projects (translated to Swedish for the DD project). Analyses of the declarative memory data from the SLI study are ongoing and will not be included in this thesis.

Ethical approval for the SLI project was obtained by the University of Iowa Institutional Review Board (IRB). The DD project was approved by the ethical review board in the city of Uppsala (dnr 2007/153). All parents or guardians provided informed written consent; children provided informed written assent. Children in the SLI project received 20 USD, and children in the DD project received a cinema ticket, for participation.

The SLI project (Study I)

Participants

Thirty-one children with SLI and 31 typically developing (TD) children participated in the study. Children were matched for age (mean = 10.0 years), sex and handedness across groups (see Table 1 for participant characteristics of the final set of children included in the statistical analyses).

Inclusion and exclusion criteria:

- All children were monolingual English speakers.
- Apart from language impairment in the SLI group, none had any known sensory or developmental disorders, including autism, mental retardation, and cerebral palsy, and none had had any head trauma requiring medical care.
- All children had normal hearing (American Speech-Language-Hearing Association [ASHA], 1997).
All children had a performance IQ (PIQ) standard score ≥ 75.

In addition, the ADHD Rating Scale-IV, home-version (DuPaul, Power, Anastopoulos, & Reid, 1998) was administered at the time of experimental testing in order to identify children with significant ADHD symptoms. These children (4 TD and 7 SLI) were excluded from the statistical analyses in Study 1 in order to avoid confounding effects of attention deficits.

Table 1. Age and standardized tests: Summary scores and comparisons for the final set of children included in statistical analyses.

<table>
<thead>
<tr>
<th>Variable</th>
<th>SLI (n = 21)</th>
<th>TD (n = 27)</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Age</td>
<td>10.05</td>
<td>1.08</td>
<td>9.92</td>
</tr>
<tr>
<td>Handedness</td>
<td>0.74</td>
<td>0.53</td>
<td>0.67</td>
</tr>
<tr>
<td>LComp</td>
<td>-1.45</td>
<td>0.29</td>
<td>0.18</td>
</tr>
<tr>
<td>PIQ</td>
<td>91</td>
<td>11.23</td>
<td>106</td>
</tr>
</tbody>
</table>

Abbreviations: LComp = Language Composite score; PIQ = Performance IQ.
Note: Handedness scores are based on the Edinburgh Handedness Inventory (Oldfield, 1971). LComp and PIQ have a mean of 100 and standard deviation of 15.

The children were recruited from schools in Iowa by the Child Language Research Center at the University of Iowa. Children were initially categorized as having potentially impaired or normal language development on the basis of their scores on classroom-administered listening and reading tasks. They were then given a set of diagnostic language tests (Table 2).

Table 2. Tests used for categorization of children into SLI and TD groups.

<table>
<thead>
<tr>
<th>Ages 7:0-8:11</th>
<th>Ages ≥ 9:0</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPVT-R</td>
<td>PPVT-R</td>
</tr>
<tr>
<td>CELF-3:</td>
<td>CELF-3:</td>
</tr>
<tr>
<td>Concepts and directions</td>
<td>Concepts and directions</td>
</tr>
<tr>
<td>Listening to paragraphs</td>
<td>Listening to paragraphs</td>
</tr>
<tr>
<td>Recalling sentences</td>
<td>Recalling sentences</td>
</tr>
<tr>
<td>Word structure</td>
<td>Formulated sentences</td>
</tr>
<tr>
<td>Sentence structure</td>
<td></td>
</tr>
</tbody>
</table>

Note:
PPVT-R = Peabody Picture Vocabulary Test – Revised (Dunn, 1997).
CELF – 3 = Clinical Evaluation of Language Fundamentals – 3 (Semel, 1995).

A language composite score (LComp) was computed on the basis of subtests from the Clinical Evaluation of Language Fundamentals - Third Edition.
(CELF-3; Semel, Secord, & Wiig, 1995) and the Peabody Picture Vocabulary Test – Revised (PPVT-R; Dunn & Dunn, 1997). The language composite score was computed by dividing the sum of the (sub)test z-scores by the standard deviation of the combined variances and covariances (Crocker & Algina, 1986). Following the EpiSLI standard (Tomblin et al., 1997; Tomblin, Records, & Zhang, 1996), children who fell at or below -1.14 SD on this composite score were considered language impaired, whereas those above this cutoff were considered to have normal language.

The EpiSLI standard is a system for identification of language impairment in children developed by Tomblin and colleagues (Tomblin et al., 1996). It uses a scheme where 5 composite scores represents different dimensions of language ability according to a two-dimensional matrix composed by modality (expressive and receptive) and domain (vocabulary, grammar and narration) of language. The single composite score of -1.14 SD has been shown to be equivalent to the child performing within the 10th percentile on two or more of these composite measures. In addition, this cut-off has been shown to be consistent with clinical assessment of language impairment in children (Tomblin et al., 1996).

**General procedure**

Testing was performed by an experienced English-speaking experimenter, and took place during daytime in a van equipped especially for this purpose, either at the child’s school or home. Stimuli were presented (on a CRT screen), and responses were captured, with E-prime version 1.2. Participants were seen on two occasions (session 1 and session 2). For a majority of children the between-session-interval was approximately 24 hours. However, due to practical reasons this interval was extended for some children up to as long as 18 days. Importantly, the interval did not differ significantly between groups. Moreover, the between-session-interval was found to be unrelated to task performance in session 2.
The DD project (Study II and Study III)

Participants

Twelve children with DD and 17 TD control children participated in the study. The two groups were matched for sex, age ($mean = 11.0$ years) and handedness across groups (Table 3).

Inclusion and exclusion criteria

- All children in the DD group were diagnosed with dyslexia by a certified speech-language pathologist within one year before the experimental testing.
- All children in the TD group performed at or above a stanine score of 4 out of 9 ($\geq -0.75$ SD) on two reading tests administered at the time of experimental testing.
- All children were mono-lingual Swedish-speaking (however, English as a second language taught in school was accepted).
- None had any apparent or known motor or cognitive impairment except for reading and writing problems in the DD group.
- All had normal (or corrected to normal) vision and normal hearing as reported by parents.
- All TD children had a PIQ standard score $\geq 80$ as assessed with Raven’s Standard Progressive Matrices Plus version (this criterion was not used for the DD group, see Methodological considerations and limitations).

Children with DD were recruited from speech-language pathology clinics in the cities of Stockholm, Uppsala, Gävle and Västerås (all situated in middle Sweden). Letters were sent out to the clinics with a request to forward an invitation to participate in the study to all children who fulfilled the inclusion criteria described above. A letter including information about the study, an anamnestic questionnaire, and a form on which to provide written consent for participation was given by the speech-language pathologist to parents of children who were deemed eligible for the study. Volunteers for the study sent the anamnestic questionnaire and the written consent to the Department of Neuroscience, SLP research group, at Uppsala University.

Parents were contacted by the examiners by phone in order to receive further information about the study and have the opportunity for asking questions. Parents could choose whether they wanted to be contacted by the examiner for further information about the study and for scheduling, or if they preferred that scheduling was arranged with the child’s teacher at school.

Typically developing children were recruited from schools in the Stockholm-Uppsala area. These children ($n = 46$) were recruited for a study on sex differences in procedural and declarative memory and language in TD chil-
children (Moritz & Jerremalm, 2009), as well as for serving as a control group in the two DD studies. Letters were sent out to principals at 15 different schools with a request to forward an invitation to children in 3rd, 4th and 5th grades and their parents. The schools were chosen with the informal aim of having them represent areas with varied socio-economic profiles (however, no analysis of socio-economic status was performed).

Parents who were interested were asked to fill out an anamnestic questionnaire (same as for children with DD) and to send their written consent (and the child’s written assent) to the SLP research group at Uppsala University. Parents were contacted by the examiners by phone in order to receive further information about the study and have the opportunity for asking questions. Scheduling procedures were the same as for the DD group (see above).

Out of the 46 TD children, 3 children were excluded due low PIQ scores (with standard scores of 55, 65 and 75) and 13 children were excluded due to stanine scores below 4 on at least one of the two reading tests. Thus, 30 children fulfilled the reading and PIQ criteria for the TD group. These children were matched to the DD group for age, sex and handedness by excluding the 9 youngest and the one oldest TD participants, as well as 3 left-handed TD children.

Table 3. Participant demographics and cognitive characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>DD (n = 12)</th>
<th>TD (n = 17)</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Age in years</td>
<td>11.0</td>
<td>0.71</td>
<td>11.1</td>
</tr>
<tr>
<td>Sex (f/m)</td>
<td>5/7</td>
<td></td>
<td>5/12</td>
</tr>
<tr>
<td>Handedness</td>
<td>85.1</td>
<td>16.4</td>
<td>92.2</td>
</tr>
<tr>
<td>PIQ</td>
<td>87.9</td>
<td>12.1</td>
<td>97.1</td>
</tr>
<tr>
<td>Phonological decoding</td>
<td>1.75</td>
<td>0.87</td>
<td>5.24</td>
</tr>
<tr>
<td>Orthographic reading</td>
<td>1.92</td>
<td>1.16</td>
<td>5.76</td>
</tr>
<tr>
<td>NWR</td>
<td>106</td>
<td>5.2</td>
<td>111</td>
</tr>
<tr>
<td>TROG</td>
<td>57.9</td>
<td>30.1</td>
<td>75.6</td>
</tr>
<tr>
<td>PPVT</td>
<td>152</td>
<td>16.4</td>
<td>160</td>
</tr>
</tbody>
</table>

Abbreviations: PIQ = Performance IQ (Raven, 1998); NWR = Nonword repetition (Wass et al., 2008); TROG = Test for Reception of Grammar (Bishop, 1982); PPVT = Peabody Picture Vocabulary Scale - Third Edition (Dunn & Dunn; 1997). Note: Handedness scores are based on the Edinburgh Handedness Inventory (Oldfield, 1971).
Tests used for assessment of cognitive, language and reading characteristics

Participants were given a set of behavioural tests in order to characterize their receptive vocabulary (Peabody Picture Vocabulary Test - Third Edition [PPVT-III]; Dunn & Dunn, 1997), grammatical comprehension (Test for Reception of Grammar [TROG]; Bishop, 1982; Holmberg & Lundälv, 2002), verbal working memory (nonword repetition; Wass et al., 2008), orthographic reading and phonological decoding skills (Olofsson, 1994) and PIQ (Standard Progressive Matrices – plus version; Raven, 1998). All tests were administered and scored according to the instructions in the manuals. Population norms were used when available. Because of the lack of Swedish population norms for the vocabulary test (PPVT) and the nonword repetition test, group comparisons were based on raw scores for these tests.

As expected, there were significant group differences for the two reading measures as well as for the nonword repetition test. In addition, grammatical comprehension was poorer in the DD group compared to the TD group (the group difference was significant when the comparison was based on raw scores but not when it was based on population norms). The two groups did not differ significantly in vocabulary or PIQ, although the difference in PIQ approached significance. The PIQ range in the DD group was 70-115 and the TD range was 80-140.

The two reading tests were paper and pencil Swedish adaptations (Olofsson, 2003) of the computerized phonological decoding and orthographic reading tasks developed by Olson, Forsberg, Wise and Rack (1994). In the phonological decoding test, the task was to decide, and underline with a pencil, which one of three or four pseudo-words was a pseudo-homophone of a real word. (i.e. “sounds” like a real word). The score corresponds to the number of correctly identified pseudohomophones within two minutes, with a maximum score of 80. In the orthographic reading test, participants were asked to underline the true word in true word-pseudohomophone pairs. Because the phonological codes for the pairs were identical, the word and its pseudo-homophone would be pronounced the same in Swedish. Thus, in order to make a correct response, participants had to use word-specific orthographic knowledge. The score was the number of correctly chosen words in two minutes, with a maximum score of 120.

As seen in the inclusion criteria, all TD children had stanine scores ≥ 4 out of 9 on both reading tests (corresponding to performance at or above – 0.75 SD). All children in the DD group had stanine scores of ≤ 3 on both tests, except for one child who had a stanine score of 5 on the orthographic reading test. The performance of this child is consistent with previous evidence suggesting that the phonological decoding problems characteristic of DD can sometimes occur together with intact or even superior orthographic skills (Siegel, Share, & Geva, 1995).
When using a clinically identified (rather than research identified) DD sample, it is expected that some children with DD will present with broader language problems in addition to reading deficits (Pennington & Bishop, 2009; Ramus et al., 2013). In the present DD sample, one child scored within the 5th percentile on TROG, based on population norms in the manual (-2.52 SD from the mean of all children in the present study). Vocabulary (PPVT) scores were in the normal range for this child (-0.23 SD from the mean of all children in the present study). In addition, one child had low PPVT scores (-2.5 SD from the mean of all children in the present study) coupled with TROG scores within the 25th percentile.

General procedure

Experimental testing took place in a quiet room in the child’s school or home over two consecutive days. The research tasks (ASRT and DecLearn) stimuli were presented on the screen of a portable PC computer running Windows, using E-Prime version 1.2.

The between-test sessions interval was approximately 24 hours (+/- 1 hour) for all children. Each test session took about 70-90 minutes, including breaks. The order of the two research tasks – ASRT and DecLearn – was counterbalanced between groups based on odd and even subject numbers.
Research tasks

Procedural memory: the Alternating Serial Reaction Time Task

Procedural memory, specifically implicit sequence learning, was tested with the Alternating Serial Reaction Time (ASRT) task, originally developed by James and Darlene Howard (Howard & Howard, 1997). Learning in this task has been shown to rely largely on the procedural memory cortico-striato-cerebellar brain network, although more recently a role for the MTL has also been emphasized, in particular early in learning (Bennett, Madden, Vaidya, Howard, & Howard, 2011).

As described in the Introduction, classic SRT tasks (e.g. Nissen & Bullemer, 1987) typically consist of a series of blocks in which events are structured according to a deterministic or probabilistic sequence. Sequence learning is operationalized as the difference in RTs and number of errors between the final sequence block and a subsequent block in which events are random.

In contrast to classic SRT tasks, the sequential structure in the ASRT task is made up of continuously alternating pattern and random events. That is, throughout the task, every second event/location on the screen is randomly distributed. This structure has a couple of important advantages over the classic SRT task. First, it allows for a separation of general motor skill learning (i.e. the improvement in speed and accuracy that is the result of perceptual-motor practice) and sequence specific learning (i.e. the improvement in speed and accuracy that is the result of an increasing sensitivity to the sequential structure). These two measures are often confounded in the classic SRT tasks (Remillard, 2008).

Second, the alternating structure allows for both general skill learning and sequence specific learning to be assessed continuously throughout the task, in contrast to the classic SRT task, in which learning is typically assessed at a single point in time at the end of the task. Finally, the probabilistic nature of the sequence has been shown not to yield explicit knowledge, even after extended practice (Howard et al., 2004; Howard & Howard, 1997; Song et al., 2007).

In the ASRT task, sequence specific learning is typically expressed as a continuously increasing difference between trials that follow the sequential pattern and trials that are random. For reaction times, sequence specific learning is seen as increasingly faster responses to pattern compared to random trials. For accuracy, sequence learning is typically expressed as a progressive decrease in the accuracy of responses to random trials whereas accuracy for pattern trials tends to remain quite stable throughout the task (Howard et al., 2004). General skill learning, on the other hand, is seen in the form of the sequence independent (across both pattern and random trials) reduction in response speed as a function of practice with the task.
In this task, four horizontally arranged open circles were displayed on the computer screen (see Figure 4). As in classic SRT tasks, a sequence of visual stimuli (here, a picture of a dog) appeared in one of the four locations. Participants were asked to press one of four horizontally arranged buttons on a serial response (SR)-box whenever the stimulus appeared in the corresponding location on the screen. Specifically, they were asked to “catch the dog” as quickly and accurately as possible by pressing the button corresponding to the circle in which the dog appeared. They were instructed to use the middle and index fingers of both hands. All instructions and feedback were displayed visually on the screen as well as read aloud to the participant. The instructions included practice items to ensure the participant understood the task, as well as correctly mapped the response buttons.

![Image](Image.png)

**Figure 4.** Practice slide in the Alternating Serial Reaction Time task.

Target locations were determined by a repeating eight-element structure in which fixed and random locations alternated. All participants received the same 8-item sequence pattern, 1r2r4r3r (where “r” represents a random event and the numbers represent locations on the screen). That is, the dog appeared in position 1 (the left-most circle), then randomly in any of the four circles, then in position 2, and so on. Each stimulus presentation and response constituted one trial. Trials were organized into blocks of 85 trials: 5 warm-up random trials (not included in the analyses) followed by 10 repetitions of the 8-item sequence (Howard et al., 2004; Song et al., 2007). Participants were encouraged not to stop during a block, but to take a break for 20 seconds or more after each block. On the first day of testing (session 1) participants completed 20 blocks (i.e. 1700 trials and 200 repetitions of the 8-item se-
sequence) and in session 2 they completed 5 blocks (425 trials and 50 repetitions of the sequence).

Participants were guided to about 92% overall accuracy by automatically generated feedback at the end of each block. If accuracy was below 91%, the feedback displayed on the screen was “Great job! Can you try even harder to press the right buttons?” If accuracy was above 93% the feedback was “Great job! Can you go even faster?” At accuracy levels between 91% and 93% the feedback was simply “Fantastic!” together with a picture of the dog on leash. The task was self-paced, such that the correct button had to be pressed before a new stimulus would appear on the screen. However, the experimenter controlled the beginning of each new block by clicking the mouse.

**Post practice interview**

Even though previous studies using the ASRT task have consistently shown that participants (including adults) do not develop explicit knowledge of the pattern (e.g., Howard, Howard, Japikse et al., 2004; Howard et al., 2006; Howard & Howard, 1997), we interviewed each participant after the completion of both test sessions to probe for any signs of explicit awareness of the sequence. The interview was designed not to inform the participant about the pattern but to elicit spontaneous comments that might reveal explicit awareness of the sequential structure. The question “Did you notice anything in particular when you were playing the game?” was followed-up by the question “Was there anything else you noticed or thought about?” until the participants had nothing more to add. The interviews were recorded and analyzed after the experimental sessions.

As expected based on previous studies (Howard, Howard, Japikse et al., 2004; Howard et al., 2006; Howard & Howard, 1997), no participant was able to describe any aspect of the sequential pattern. Common comments in these interviews included statements such as “it was fun/boring”.

**Data reduction and statistical analysis.**

There are two commonly used procedures for statistical analysis of the ASRT task. One approach is to compare RTs and accuracy levels for pattern trials to those of the interspersed random trials. Another option is to use a “triplet” approach, in which runs of three events that occur with higher frequency are compared to those that occur with lower frequency.

Howard and colleagues (Howard et al., 2004; Howard & Howard, 1997) have previously shown that rather than learning the higher-order four-element structure of the sequence (which is interspersed with random events) most people appear to learn the lowest-level regularity that can be detected in this task, namely that certain triplets (i.e. runs of three events) occur more frequently than others. Because of the alternating structure of the ASRT task, triplets that start and end on pattern events will occur more often than triplets...
that start and end on random events (e.g. “1 r 2” compared to “r 2 r” in our 1r2r4r3r sequence). With the specific sequence used in this project (1r2r4r3r), there will be 16 possible high frequency (HF), triplets (“1 r 2”, “2 r 4”, “4 r 3”, and “3 r 1” – all with four possible random event variations, that is 4 × 4). All other runs of three events will be low frequency (LF) triplets. On average, the HF triplets occur about 5 times more often than the LF triplets (Song, Howard, & Howard, 2008).

Importantly, some of the triplets that start and end on random events will by chance form a structure-consistent triplet. That is, in the “r 2 r” triplet, the two random events may by chance be, for example, 1 and 2 (creating the structure consistent triplet “1 2 2”). The response pattern for such a random structure consistent (HF) triplet may be similar to a true structure consistent triplet (which starts and ends on pattern events). Thus, if the task is analyzed on the basis of (the more intuitive) pattern versus random trials contrast, statistical power to detect learning may be decreased due to increased error variance.

The triplet approach was used in Study I whereas the trial type approach was used in Study II. The rationale for using the trial type approach as the main analysis in Study II was to allow for a comparison with the one previous study that used the ASRT task with dyslexic participants (Howard et al., 2006).

Another difference between Study I and Study II relates to the organization of blocks into “epochs” (Study I) versus “learning stages” (Study II). In addition, statistical analyses in Study I were based on a “final RT” learning measure that combines the effects of RT and accuracy into one single learning measure (see below for details). By contrast, Study II followed the approach used in previous ASRT studies (including the one previous ASRT study with dyslexic participants) and included separate RT and accuracy based learning measures. Because of these methodological differences, a detailed description of the specific procedures for data reduction and statistical analysis used in each study is given below.

Study I

Data reduction and processing was performed in Excel. For each participant, each trial was categorized into HF or LF based on whether or not it was the final trial in any of the 16 possible HF triplets. The first 7 trials in each block were excluded; the first 5 trials in each block were random practice items and thus the first triplet in the sequence ended on the 8th trial. Following previous ASRT studies, trials that constituted the final trial in “trills” (e.g. 121) and “repetitions” (e.g. 111) were excluded, as they have been shown to be associated with pre-existing response tendencies (for details, see Howard et al., 2004).

The median RTs for HF triplets and LF triplets were calculated separately for each block and for each participant. Next, the mean of these block medi-
ans was computed for each participant for each epoch (5 blocks), that is, for epochs 1 through 5 (epochs 1-4 in session 1, and epoch 5 in session 2), again separately for HF and LF triplets. In contrast to previous ASRT studies (Howard et al., 2004; Howard & Howard, 1997; Song et al., 2007), RTs for all correct responses, not just for first responses that were correct, were included in these computations. Since each trial proceeds to the next one only when a correct response is made (whether or not it is the first response), RTs for all trials were included in this approach.

This “final RT” measure has the advantage of being sensitive to the combined learning dependent changes in RT and accuracy. If sequence specific learning occurs, the difference in RT between HF and LF trials will be enhanced with this measure because it will add the relatively more errors on structure inconsistent trials to the RT of LF trials. Thus, if indeed there is sequence learning, LF trials will display yet longer reaction times. Without sequence specific learning, however, errors will be evenly distributed across pattern consistent (HF) and pattern inconsistent (LF) trials, and thus not affect HF and LF mean reaction times in any systematic way.

Finally, since using the absolute RT difference between LF and HF triplets may result in participants (and groups) with overall longer response times falsely displaying more learning, the difference between LF and HF RTs was normalized (Dye, Green, & Bavelier, 2009; Faust, Balota, Speiler, & Ferraro, 1999; Madden, Pierce, & Allen, 1996). This was done by dividing, for each participant, the RT difference between LF and HF triplets for each epoch by the average RT (that is, over both LF and HF triplets) for this same epoch: \( \frac{\text{LF mean RT for epoch } X - \text{HF mean RT for epoch } X}{((\text{LF mean RT for epoch } X + \text{HF mean RT for epoch } X) / 2) \). 

General perceptual-motor skill learning was operationalized as a decrease in average RT (independent of triplet frequency) over epochs. Sequence specific learning was operationalized as an increase over epochs in the normalized RT difference between LF and HF triplets.

**Study II**

Data reduction and processing was performed in Excel. Following previous ASRT studies, trials that constituted the final trial in “trills” (e.g. 121) and “repetitions” (e.g. 111) were excluded, as they have been shown to be associated with pre-existing response tendencies (for details, see Howard et al., 2004). For RTs, median values were calculated separately for pattern and random trials for each block and each subject. Next, following Bennett and colleagues (Bennett et al., 2011), these median values were averaged across 10 consecutive blocks in session 1, and across the 5 blocks in session 2, in order to obtain mean values for pattern and random trials, again for each subject, for an early learning stage (stage 1: blocks 1-10), an intermediate learning stage (stage 2: blocks 11-20) and a late learning stage, which in-
cluded an overnight interval (stage 3: blocks 21-25). A similar data reduction procedure was performed on accuracy.

Group differences in general skill learning and/or sequence specific learning were examined with 2 (group: DD vs TD) × 2 (trial type: pattern vs random) × 3 (learning stage: 1-3) mixed design ANOVAs, for RT and accuracy, with group as a between-subject variable and trial type and learning stage as within-subject (repeated measures) variables.
Declarative memory: the DecLearn task

Declarative memory was tested with an object recognition memory task developed by the Brain and Language Lab at Georgetown University. Similar tasks have previously been shown to engage the network of brain structures underlying declarative memory, including the MTL, for both non-verbal and verbal stimuli (Henson, 2005; Kim & Cabeza, 2009).

The object recognition task consists of three phases; i) incidental encoding, ii) recognition 10 minutes after encoding and iii) recognition 24 hours after encoding. The stimuli were black-and-white line drawings of real objects and made-up objects (Figure 5).

![Real object](image1.png) ![Made-up object](image2.png)

**Figure 5.** Examples of the real and made-up objects used as stimulus materials.

The images used for the real and made-up objects were taken from a variety of sources. For the real objects, items were drawn from, and modified as necessary, various clipart galleries (including free websites and purchased collections), and from a previous study by Snodgrass and Vanderwart (1980). For the made-up objects, items were selected and modified from previous studies by Eals and Silverman (Eals & Silverman, 1994), Laine et al. (Laine et al., 2003) and Williams and Tarr (Williams & Tarr, 1997). The images of made-up objects were selected based on their nameability (that is, low nameability) determined through previous pilot work. All images were resized, touched up, rotated, and/or converted to black-and-white to create
the final set of stimuli. The items were presented in a pseudo-randomized order, with no more than 3 consecutive real or made-up objects.

There were three different sets of objects used in this task: i) those presented in the encoding phase (as well as in subsequent phases), ii) those used as foils in the 10 minute recognition phase and iii) those used as foils in the 24 hour recognition phase. Each of these three sets of objects consisted of 32 real objects and 32 made-up objects. The physical size of the images was 13.7 × 10.3 centimeters, and the viewing distance was approximately 50 centimeters.

Participants were instructed to place their left and right index fingers on the designated buttons on a serial response box (E-prime SRBox) that was placed in front of them, and to make a response by pressing one of these buttons. Preceding each stimulus, a crosshair appeared in the center of the screen for 1000 milliseconds (ms), followed by the item for 500 ms, also in the center of the screen. In cases where the participant responded before 500 ms, the item remained onscreen until the 500 ms finished, to equalize presentation duration across stimuli and participants. After the item presentation, the crosshair reappeared on the screen until the subject responded, or up to 4500 ms. As soon as the subject made a response through the SRBox, a 200 ms advance tone sounded, followed by 800 ms of fixation. If instead the subject made no response within the 4500 ms response period, a 400 ms time-out tone sounded, followed by 600 ms of fixation. After this the 200 ms advance tone sounded followed by 800 ms of fixation. The next item then began with 1000 ms of fixation.

In the incidental encoding phase, participants were told they were going to be presented with pictures of “real” and “made-up” objects on the screen. They were asked to indicate, through a button press, whether the object was real (existed in reality) or made-up (did not exist in reality). Similar categorization tasks have previously been used to promote incidental word encoding (Wagner et al., 1998). The instructions included 2 sample items to ensure that all participants understood the task and correctly mapped the response buttons. The instructions and sample items were followed by 3 practice items with the same timing parameters as the test items. All instructions were visible on the screen and were simultaneously read aloud to the participants. A reminder appeared at the bottom of the screen throughout the task indicating the mapping of the SRBox buttons (i.e. “real”/”made-up”).

The incidental encoding phase was followed by a 10 minute break during which participants were encouraged to stretch their legs or have a snack. Just before the subsequent 10 minute recognition phase, participants were told they were going to see pictures of real and made-up objects again, some of which they saw previously and some of which they did not. They were asked to indicate, through a button press, whether or not they had seen the object earlier. As in the encoding phase, the instructions included sample items, which were followed by practice items. Presentation and timing was the
same as in the encoding phase, but the reminder “real”/”made-up” was changed to “yes”/”no”. Additionally, the question “seen before?” was always displayed on the screen, above the “yes” and “no” options. Finally, after a 24 hour interval participants were given the 24 hour recognition phase of the task. Instructions, presentation and timing were the same as in the 10 minute recognition phase.

Responses were captured using E-prime version 1.2. Two versions (A and B) of the task, for which the response buttons for “real”/”made-up” and “yes”/”no” were reversed, were assigned to consecutive participants in each group.

**Data reduction and statistical analysis.**

Reaction times were calculated for correct responses only, and filtered by excluding responses faster than 300 milliseconds (ms) or greater than 4500 ms. Median RTs were used in order to avoid undue influence from outlier RTs.

Analyses were based on d-prime (d’), which is a measure of accuracy that takes response bias (i.e. preference for either “yes” or “no” responses) into account. This measure is calculated by subtracting the relative rate of false alarms (responding “yes” to a foil item) from the relative rate of hits (correctly responding “yes” to items that were presented in the encoding phase): 

\[ d' = z(\text{hits}) - z(\text{false alarms}) \]

A d’ score of (close to) zero indicates chance performance. Higher d’ scores indicate greater accuracy in correctly endorsing old items as well as correctly rejecting foil items.
Results

Study I: Procedural memory in children with SLI

Procedural learning and memory, specifically implicit sequence learning, was examined in 21 children with SLI and 27 TD control children (see Paper I for details). Children were given the ASRT task in an initial learning session (session 1) and an average of three days later to test for consolidation and longer-term learning (session 2).

No significant group differences were observed when children with SLI were compared to those with typical development. However, re-categorizing children based on grammar, instead of the original broader language score, revealed significant differences between those with poor grammar scores ($n = 19$) and those with normal performance ($n = 29$). Specifically, the grammar impaired group performed poorer in the second test session, in which overnight consolidation and longer-term learning was assessed (Figure 6). When grammar was examined as a continuous variable across all children, a significant association between grammar and the amount of sequence learning in the second test session was observed.

Although no significant group differences were observed in initial procedural learning, visual inspection of figure 6a hints at the possibility of a lack of saturation of learning in the grammar impaired group, as indicated by the non-asymptotic shape of their learning curve.
Figure 6. Sequence learning and consolidation for the grammar impaired (GI) and normal grammar (NG) groups of children. For both groups, the figure displays the means and standard errors, for each epoch, of the normalized reaction time (RT) difference between low frequency and high frequency triplets, which indicates sequence specific knowledge. These are shown, with performance IQ (PIQ) covaried out, for (A) initial sequence learning (epochs 1–4); (B) consolidation and retention (epoch 4 vs. epoch 5); and (C) longer-term learning (epoch 1 vs. epoch 5).

Key findings in Study I

- Grammar, rather than broader language measures, is associated with procedural memory deficits in SLI.
- The procedural memory deficit in children with poor grammatical ability may be associated with impaired consolidation mechanisms rather than with impaired initial learning.
- However, visual inspection of Figure 6a suggests that impaired consolidation could in fact be the result of inefficient initial learning mechanisms, resulting in a lack of saturation of learning (non-asymptotic learning curve).
Study II: Procedural memory in children with DD

Procedural learning and memory, specifically implicit sequence learning, was examined in 12 children with DD and 17 TD control children (see Paper II for details). Children were given the ASRT task in an initial practice session (session 1) and in a second practice session occurring after a 24 hour interval (session 2). Statistical analyses were based on “learning stages” with the 20 practice blocks in session 1 constituting stage 1 (10 blocks) and stage 2 (10 blocks) and the 5 blocks in session 2 constituting learning stage 3.

The children with DD showed a profile of learning that was similar to that of the children with SLI in Study I, with a significant impairment emerging only in session 2/stage 3, after a 24 hour interval (Figure 7). A correlation analysis revealed that the association between sequence learning in session 2 and reading skill held also when reading was examined as a continuous as opposed to categorical variable (Figure 8).

In contrast to Study I, the analyses in Study II included a contrast between the effects of overnight consolidation versus the effects of further practice in session 2/stage 3. These analyses suggest that the DD impairment may not be related to overnight consolidation of the learned sequence but to the effects of further practice beyond the initial practice session on day 1.

![Figure 7. Pattern-random accuracy difference (i.e. sequence learning) as a function of learning stage for the DD and TD groups.](image-url)
Additional results not presented in the submitted manuscript

In order to test if the relationship between sequence learning and reading was mediated by phonological processing skills, or by any of the other language and cognitive measures in the protocol, a set of correlation analyses were performed. These analyses showed that the amount of sequence learning in session 2 was unrelated to phonological processing skills as assessed with a nonword repetition task \( (r = .158, p = .415) \) as well as to vocabulary (PPVT; \( r = -.014, p = .943 \)) and PIQ (\( r = -.189, p = .326 \)). The correlation between sequence learning and grammar (TROG) was stronger \( (r = .312) \) but statistically non-significant \( (p = .10) \). Accordingly, the effect of sequence learning on reading skill remained significant \( (F(1, 23) = 5.67, p = .026, \eta_p^2 = .198) \) when the effects of these language and cognitive tests were controlled for in a multiple regression analysis. None of the other factors had a significant effect in this analysis.

Because the three language measures (PPVT, TROG and nonword repetition) were moderately correlated, the multiple regression analysis was also performed with the three language tests combined (by adding the standardized raw scores and dividing by 3) into a single composite language score (CombLang). The effect of sequence learning on reading skill remained significant when controlling for CombLang in addition to PIQ \( (F(1, 25) = 6.66, p = .016, \eta_p^2 = .210) \). CombLang had an independent effect in this analysis.
that was similar in size to that of sequence learning \((F(1, 25) = 7.15, p = .013, \eta^2_p = .222)\).

Control analyses in which the pattern-random accuracy difference (i.e. sequence learning) was normalized to adjust for the (non-significant) group difference in overall (across both pattern and random trials) accuracy produced an identical significance pattern to the analyses reported above (stage 3 main effect of group \(p < .05\)).

**Key findings in Study II**

- Children with DD showed impaired sequence learning in session 2, after a 24 hour interval.
- The impairment may not be related to overnight/off-line consolidation but rather to the effects of further practice in session 2.
- Sequence learning in session 2 accounted for unique variance in reading skill independent from the effects of the other language and cognitive tests included in the protocol.
- The effect of sequence learning on reading skill was not mediated by phonological processing skills as assessed with a nonword repetition task.
Study III: Declarative memory in children with DD

In this study, an old/new recognition memory paradigm with incidental encoding was used to examine previously untested aspects of declarative memory in 12 children with DD and 17 TD control children (see Paper III for details). The recognition memory paradigm was chosen in order to minimize the effects of potential group differences related to encoding strategies and free recall.

The DD group was not only not impaired at the task, but actually showed superior recognition memory, as compared to the TD children (Figure 9). These results were not driven by group differences in PIQ, sex or speed-accuracy trade-off effects. The prediction about a compensatory role of declarative memory in the DD group was tested by performing correlation analyses, separately within DD and TD groups, between recognition memory accuracy and the combined reading score. These analyses produced a marginally significant correlation \(r = .64, p = .06\) in the DD group whereas no such relationship was found in the TD group.

![Figure 9. Recognition memory accuracy in the 10 minute and 24 hour recognition sessions displayed for the DD and TD groups.](image)
Key findings in Study III

- Children with DD showed enhanced recognition memory after incidental encoding.
- Future studies with larger samples are needed in order to examine whether declarative memory may serve a compensatory role for reading problems in DD.
Discussion

Summary of findings

This thesis examines non-language procedural memory in children with SLI and children with DD. In addition, the status of declarative memory in children with DD is investigated.

Study I compared implicit sequence learning in children with SLI and typically developing control children. This study revealed an association between grammatical ability and consolidation and/or longer-term learning of the non-language sequential pattern. The association between grammar and non-language sequence learning was found with grammar performance as a categorical variable (i.e. as a group difference when children were categorized into impaired and normal grammar groups) as well as with grammar as a continuous variable in a regression analysis.

In Study II, the same implicit sequence learning paradigm was used to test procedural memory in children with DD compared to typically developing peers. In this study, there was an association between implicit sequence learning and reading skill. Analogous to the findings in Study I, the association was found with reading as a categorical as well as a continuous variable. The results were similar to those found in Study I also in that a significant group difference emerged only in the second test session after a 24 hour between-sessions interval.

In contrast to Study I, the analyses in Study II included a contrast between the effects of overnight consolidation versus the effects of further practice on day 2. These analyses suggested that the DD impairment may not be related to overnight consolidation of the learned sequence but to the effects of further practice beyond the initial practice session. In contrast to the predictions of the PDH, the sequence learning deficit was unrelated to phonological processing skills as assessed with a nonword repetition task. Notably, sequence learning had an effect on reading skill that was independent from that of PIQ, vocabulary, grammar and nonword repetition test scores.

Study III examined the hypothesis that aspects of declarative memory remain spared in DD by comparing recognition memory after incidental encoding in children with DD and typically developing children. The findings suggest that recognition memory may not only be spared, but even enhanced, in the disorder. A marginally significant correlation between recognition memory and reading in the DD, but not the TD, group hints at the possibility
that declarative memory may serve a compensatory role for reading problems in DD. However, future studies using larger samples are required in order to further investigate this issue.

Do the findings support the procedural memory deficit hypothesis?

Study I provided evidence for an association between poor performance on tests of grammatical processing and non-language sequence learning deficits. The findings in Study I are thus consistent with the PDH prediction that a domain-general procedural learning mechanism underlie the extraction of language as well as non-language structural regularities, and that a dysfunction of this learning mechanism is associated with grammar impairments in children with SLI. In addition, the lack of an association between sequence learning and vocabulary test scores may be in line with Ullman’s view that vocabulary acquisition does not depend on the procedural memory system but on the declarative memory system (but note that a potential association between vocabulary and non-language declarative memory was not tested here).

The fact that no significant group differences were found when children were categorized based on a broader language composite scores (including vocabulary knowledge) suggest that the PDH might not serve well as an explanatory account for SLI in general but only for the grammatical problems that are prevalent in the disorder. Notably, SLI is a heterogeneous disorder and although grammatical impairments seem to be a core characteristic of the majority of cases, vocabulary deficits are also commonly found (Bishop, 2006; Leonard, 1998). This could potentially help explain some of the inconsistent results of previous studies of implicit sequence learning in children with SLI (see Introduction).

The findings in Study II are less straightforward. Although the association between sequence learning and reading skill as a categorical and continuous variable is in line with the PDH, the fact that sequence learning was not associated with phonological processing ability (as assessed with a nonword repetition task) may not be. Ullman’s version of the PDH predicts that a procedural memory deficit underlies the grammatical as well as the phonological problems, at least in SLI (Ullman & Pierpont, 2005). In the Nicolson and Fawcett model, phonological problems partly mediate the procedural memory effect on reading skill (Nicolson & Fawcett, 2011; Nicolson et al., 2001). In both models, one would expect to find a significant association not only between sequence learning and reading but also between sequence learning and phonological processing. It is possible, however, that the nonword repetition test used in the present study did not tap the phonological
processes most relevant to reading, and that other measures of phonological processing, such as phonological awareness and rapid naming, would have yielded different results (see Methodological considerations and limitations for further discussion).

The results in Study III provided support for the prediction that recognition memory after incidental encoding, which is known to rely on the declarative MTL system, remain intact, and may even be enhanced, in DD. The prediction about a compensatory role for declarative memory was tested with correlation analyses of recognition memory accuracy and reading scores. These analyses revealed a marginally significant association between reading and recognition memory in the DD group but not in the TD group. The lack of significance is difficult to interpret given the small sample size, and future studies are needed in order to confirm or reject this prediction.

Alternative interpretations

Impairments on a non-language task, such as the one used in Study I and Study II, challenges any account that posits a deficit specific to language and/or phonological processing as the underlying cause of SLI (Clahsen, 1989; Joanisse, 2004; Rice, Kenneth Wexler, & Cleave, 1995; van der Lely, 2005) and DD (Snowling, 2000; Stanovich, 1988; Vellutino et al., 2004). Per definition, any such account would predict intact non-language learning in the two disorders, or at least, would not predict any correlations between non-language learning and individual grammar test performance (Study I) and reading skill (Study II), as was found here. The present findings are thus in line with data suggesting that the neurocognitive deficits in children with SLI and DD may go beyond a selective language and/or phonological impairment.

In addition, the findings in Study I are not explained by a phonological working memory deficit (Archibald & Gathercole, 2006; Gathercole & Baddeley, 1990). Two aspects of the results seem to suggest that they may also not be accounted for by previously proposed processing difficulties, either related to general processing capacity (Kail, 1994; Leonard et al., 1992; Miller et al., 2001; Norbury et al., 2001) or to briefly presented stimuli (Tallal & Piercy, 1973a, 1973b; Tallal, 1990; Tallal, Miller & Fitch, 1993). First, the ASRT task was self-paced, and thus allowed participants to proceed at their own comfortable speed, and second, early learning (in epoch 1) in children with SLI appeared to be at least as efficient as that of the TD children.

Similarly, the self-paced task together with the fact that overall reaction times and general skill learning were comparable in the DD and TD groups in Study II, suggests that the impaired sequence learning in the DD group
was not due to group differences in general processing speed (Wolf & Bowers, 1999) or attentional mechanisms (Hari & Renvall, 2001).

However, though the two studies have demonstrated an association between sequence learning impairments and poor grammatical ability (Study I) and poor reading (Study II), the nature of these associations remains to be elucidated. Although it is possible that the observed relationships reflects an underlying procedural memory impairment that manifests itself in a domain-general deficit in extracting sequential regularities from both visual and auditory input and/or in the consolidation or automatization of skills with a sequential component, this is not the only possible interpretation of the data.

In particular, the results from Study II, which indicate that the observed sequence learning impairment may be independent of phonological processing problems in DD encourage consideration of alternative explanations. Indeed, if replicated with a broader set of phonological tasks, this finding challenges the PDH, and may be more consistent with alternative views.

One such alternative explanation may be that reading problems and procedural memory deficits tend to co-occur in DD but are causally unrelated. That is, for reasons yet unknown, a procedural memory deficit may be more common in children with DD compared to their typically developing peers, but this impairment does not cause the reading problems, or affect them in any substantial way. Such a view is supported by evidence suggesting that sensori-motor impairments, such as those predicted by both the PDH and magnocellular (Stein, 2001) views, may be neither necessary nor sufficient to cause the reading problems observed in DD, and may be present only in a limited subset of cases (Ramus et al., 2003; White et al., 2006). However, while this view is compatible with the observed group difference in sequence learning, it seems inconsistent with the linear relationship between reading and implicit sequence learning, independent of diagnostic category, observed in Study II, as well as in two previous studies (Bennett et al., 2008; Howard et al., 2006).

In addition, this view may be difficult to reconcile with the fact that implicit sequence learning accounted for unique variance in reading skill also when phonological and broader language measures were controlled. Crucially, previous studies designed to evaluate the relative contributions of phonological deficits and sensori-motor impairments to reading have not included implicit sequence learning tasks of the type employed in Study I and Study II. Rather, the sensori-motor tasks used in those studies were designed specifically to tap “cerebellar” motor functions, such as bead threading and balance tasks (Ramus et al., 2003; White et al., 2006). Consequently, these tasks may have been less sensitive to cognitive aspects of procedural memory as well as to potential striatal deficits.

Another possible alternative explanation is that the phonological deficit and the procedural memory deficit are causally unrelated but that the co-occurrence of these deficits leads to reading problems that are severe enough
to draw pedagogical and clinical attention. On this view, procedural learning problems may not cause the phonological impairment in DD but may contribute independent variance to individual reading ability by affecting, for example, the ability to extract orthographic sequential regularities and the automatization of reading skills. Such a “double deficit” view has previously been proposed for phonological processing problems and rapid naming ability (Wolf & Bowers, 1999).

This view would be in line with studies of children at risk for DD, in which it has been shown that phonological problems alone are not sufficient to cause severe reading problems (Gallagher, Frith, & Snowling, 2000; Snowling et al., 2003; Wimmer & Schurz, 2010). This view would also be in line with the data from Study II, as it would be able to explain the effect of implicit sequence learning on reading skill as a categorical as well as a continuous variable, and the fact that this effect was independent from that of phonological processing skills tapped by the nonword repetition test.

Potential brain mechanisms underlying such a hypothetical double deficit may be contemplated in the light of genetic and neuroanatomical evidence suggesting that the phonological deficit commonly associated with DD may stem from abnormalities in neuronal migration and axon growth affecting the left perisylvian cortex involved in phonological processing (Darki et al., 2012; Fisher & Francks, 2006; Galaburda et al., 2006; Galaburda et al., 1985; Giraud & Ramus, 2013). Experimental animal studies have suggested that these primary cortical abnormalities may in turn induce secondary anomalies in the thalamus. These secondary thalamic anomalies appear to not always accompany the primary cortical anomalies but seem to depend on foetal hormonal conditions (Galaburda et al., 2006).

It has been suggested that co-occurring thalamic anomalies may account for a range of lower-level visual, auditory and motor impairments sometimes associated with DD. As discussed above, however, such sensori-motor deficits have been suggested to play a very limited, if any, role in reading development. Although admittedly speculative, I would like to suggest the possibility that such secondary thalamic anomalies may extend to affect the function of the cortico-striato-thalamo-cortical circuit assumed to underlie the type of implicit sequence learning probed by the ASRT task. I further suggest the possibility that this dysfunction may have a direct effect on reading that is not mediated by phonological or broader languages skills. As previously discussed, these effects may relate to the extraction of probabilistic orthographic regularities and to the automatization of reading skills, which would have a detrimental effect on reading fluency, in particular. On this view, the inconsistent results of previous studies of implicit sequence learning in DD seem natural, since an additional procedural memory deficit may not always be present in DD. Thus, some studies are bound to find a group difference in implicit sequence learning while others are not.
Animal studies investigating the effects of the cortical anomalies implicated in DD have shown that their effects may not only be detrimental. Consistent with the idea of competing memory systems (see Introduction), lesions that led to impaired performance of rats on certain working memory tasks were also associated with enhanced learning in MTL dependent spatial water maze task. Intriguingly, such findings fit well the observed DD advantage at the MTL dependent recognition memory task in Study III.

An alternative explanation to the DD advantage at recognition memory observed in Study III is that it was not the result of an enhancement in this group, but rather the result of relatively “impaired” performance in the TD group. According to the neuronal recycling hypothesis (Dehaene & Cohen, 2007), learning to read entails a tradeoff in which the building up of a sight-word lexicon takes place at the cost of certain other visual skills. Support for this hypothesis comes from the tradeoff between reading and other aspects of visual cognition that has been observed in illiterate adults who learn to read (Dehaene et al., 2010) and in dyslexic participants following remediation (Lorusso, Facoetti, Toraldo, & Molteni, 2005). This hypothesis would predict that the DD advantage at recognition memory observed in the present study would diminish as the dyslexic children improve their reading ability. A future follow-up study may be warranted to specifically test this prediction.

Methodological considerations and limitations

The three studies included in the present thesis have various methodological limitations that may be addressed by future studies. One of the most obvious methodological limitations of the present work may be the small sample sizes employed. It is well-known that small sample sizes lead to low statistical power to detect “real” effects (i.e. effects that are present in the populations we wish to generalize to). In addition, when a statistically significant effect is found in a study with small samples, it is less likely, compared to a significant effect in a study with larger samples, to reflect a true effect in the population (Button et al., 2013). This problem is particularly large in Study II and Study III in which sample sizes were very small. Therefore, the findings in these studies need to be interpreted with caution until they have been replicated in studies with larger samples.

Another limitation of all three studies is that a single task was used for the assessment of procedural and declarative memory, respectively. By necessity, this restricts any conclusions that can be drawn about procedural and declarative memory functions in SLI and DD to implicit sequence learning and recognition memory after incidental encoding. Future studies including tasks designed to tap different aspects of procedural and declarative memory
may help increase our understanding of memory-related strength and weaknesses in the two disorders.

A limitation with particular relevance to the procedural memory studies (Studies I and II) is that visuo-spatial working memory was not controlled for. Given that a visuo-spatial working memory capacity of at least \( n - 2 \) is required in order to extract the sequential regularity of the ASRT task, it cannot be excluded that impairments of visuo-spatial working memory acted as a confounding variable in these studies. Thus, it remains possible that the observed implicit sequence learning deficit is not related to the extraction of sequential regularities per se but to an underlying visuo-spatial working memory impairment. Although the seemingly efficient early learning in the SLI group appears to argue against an underlying working memory deficit, the data from the DD group (with a marginally significant early learning impairment) may be more consistent with such an interpretation. Future studies should take this possibility into account and include an appropriate measure of visuo-spatial working memory in the protocol.

In addition, the nature of the procedural memory deficit observed in session 2, in both Study I and Study II, could have been examined more convincingly. The epoch-based analysis approach in Study I, did not address the question of consolidation versus further practice effects in session 2, at all. Although the by-block analyses with the aim of addressing these effects in Study II entailed some improvement over Study I, it is desirable that future studies extend the paradigm for a more careful examination of consolidation versus further practice effects. Specifically, group differences in consolidation could be examined much more convincingly by the inclusion of an interference task in session 2. Such a design would allow for a direct examination of one of the core aspects of consolidation, namely the resilience of the learned sequential representations to interference by the introduction of a novel sequence (or randomly structured items). If the sequence learned in session 1 has been well consolidated, interference from the novel sequence will be small and recovery will be fast; by contrast, consolidation problems will yield a larger interference effect. Moreover, the pattern of potential group differences in the effect of further practice in session 2 may emerge more clearly if more trials are included.

In Study II, the inclusion of a wider range of “phonological” tasks would greatly have strengthened the conclusions that may be drawn regarding the relationship between sequence learning, phonological processing and reading. In particular, the study suffers from a lack of data from phonological awareness and rapid naming tests. Although nonword repetition tasks appear to tap at least some aspects of the phonological processing problems associated with DD (Ramus & Szenkovits, 2008), they do not capture the range of phonological problems typically presented by affected children. The inclusion of phonological awareness and rapid naming tasks (which may be more strongly associated with reading skill compared to nonword repetition;
Bishop et al., 2009; Melby-Lervag, Lyster, & Hulme, 2012) will allow for a more thorough investigation of this issue and may be highly theoretically informative.

Two different principles were used for participant recruitment in the SLI and DD projects; whereas children in the SLI project were research identified, the DD project consisted of children that were clinically identified as having dyslexia. This is an important distinction because the two recruitment procedures will yield samples that serve slightly different research purposes. Whereas the research identified sample in the SLI project may be used to address the question about the relationship between procedural memory and language learning in the general population of school-aged children (independent of a clinical diagnosis), the clinically identified DD sample will only generalize to the clinical population of children with dyslexia.

As noted in the Introduction, clinically identified samples typically show a higher rate of co-morbidity with other developmental disorders, and children that are clinically identified as being dyslexic may be expected to show a higher rate of co-occurrent language problems compared to research identified samples for which broader language problems are often used as an exclusionary criterion (Ramus et al., 2013). Therefore, Study II and Study III were not primarily designed to examine the relationship between memory functions and reading skill per se, but between memory functions and clinically identified DD compared to a group of children with typical development.

In the present DD sample, two children showed indications of broader language problems encompassing grammatical understanding and/or vocabulary. The inclusion of these children in the DD group may have been a confounding variable in the analyses of the relationship between DD (defined as a deficit specific to reading) and procedural and declarative memory functions. However, the fact that the association between sequence learning and reading skill remained significant when the effects of vocabulary and grammar test scores were controlled for, seem to argue against this possibility.

On the other hand, the research based recruitment procedure used in the SLI project may give rise to doubts about the clinical relevance of the results (i.e. do the results extend to children that are clinically identified with SLI?). The lack of data for whether or not children had also received a clinical diagnosis of SLI hinders generalizations to the clinical population. However, because previous studies have shown that the language categorization procedure employed by Tomblin and colleagues corresponds well with clinical assessments of SLI (Tomblin et al., 1996), the findings from Study I may still have some clinical relevance.

In sum, there are advantages and disadvantages associated with each of the two recruitment procedures employed, and ultimately the choice concerns which population one wishes to study and which specific research
questions are being addressed. As long as one is clear on the fact that research identified and clinically identified samples differ in some respects, either approach may be appropriate.

In Study I, there was a significant group difference not only in language but also in PIQ. Although the same PIQ criterion of $\geq 75$ was applied to both the SLI and TD groups, the correlation between language ability and PIQ entailed that the categorization based on language ability led to substantial differences also in PIQ. The range in the SLI group was 78-116 and the TD range was 81-146. In order to exclude the possibility that a group difference in procedural learning was due to generally lower intellectual ability in the SLI group, the effects of PIQ on sequence learning was controlled for in the statistical analyses.

In the DD project (Study II and Study III), a slightly different approach was used. Here, it was decided that the TD group should perform within broadly normal limits on all cognitive and linguistic measures for which population norms were available, and the PIQ criterion for the TD group was set to $\geq 80$ (which also matched the performance of the SLI project TD group). The reason for this was to ensure that the TD children could be considered typically developing in all areas. The initial ambition was to have the same PIQ criterion for the DD group but this criterion was later abandoned for the following reason: The proportion of children with DD who scored below 80 on the PIQ test was 25% compared to 5% in the TD group. Two different possibilities were considered as explanations for this finding. First, it is possible that a large proportion of children who are clinically identified with DD also have below normal intellectual ability. If so, excluding DD children due to low PIQ seems inconsistent with the aim of having the DD sample reflect the clinical population.

Alternatively, the design and administration of the PIQ test may have entailed a disadvantage for the DD group. Indeed, the PIQ test was self-administered and was given at the end of the second test session after a series of cognitive, language and reading tests had already been completed. It seems plausible that the reading tests, and possibly also the language tests, may have been more tiring for the DD group, compared to the TD group, which in turn may have had a negative impact on their motivation and ability to sustain enough concentration on the PIQ test at the end of the test session. If this is the case, the PIQ scores do not reflect the same underlying cognitive processes in the two groups, and thus the application of a single cutoff criterion for both groups would have biased the DD sample towards representing “top performers”.

Future studies may benefit from giving the PIQ test at a time when children in both groups are likely to be well-rested such as in the beginning of the session before any reading tests have been administered. It is also possible that choosing a different type of test or administration procedure (e.g. experimenter administered) would yield a different pattern of results.
Finally, with the present, cross-sectional, design any causal directions of the observed effects remain elusive. Future studies with the aim of testing predictions about possible underlying impairments in developmental disorders need to employ a longitudinal design, starting at birth, and including a wide range of motor, cognitive and language tasks.

Clinical significance

Children with language and/or reading impairments constitute a large proportion of the patients encountered by speech-language pathologists. An increased understanding of learning and memory functions in affected children is therefore of great clinical interest.

Clinical and pedagogical assessment and intervention for SLI and DD typically focuses largely, if not exclusively, on language and reading skills. The findings presented in this thesis suggest that non-language learning and memory functions may constitute an important factor for the understanding, and potentially also for the remediation, of SLI and DD. Taken together with previous research, the present work emphasizes the importance of going beyond a narrow focus on language and reading related skills in clinical and pedagogical assessment of SLI and DD. The inclusion of tasks tapping non-language learning and memory functions (such as the ones employed in the present studies), in the routine test protocol of speech-language pathologists, may be a great step towards gaining a more complete clinical understanding of the two disorders. With increased knowledge about learning and memory related strength and weaknesses in the two disorders it may be possible to develop innovative remediation programs designed to optimize the effects of clinical and pedagogical intervention.

For example, if, as suggested by Study I, the grammatical impairments associated with SLI are consequences of a domain-general impairment of procedural memory consolidation, then the intervention for promoting grammatical development need to be designed with the aim of optimizing the consolidation process. And, if as indicated by Study II, an important aspect of the reading problems in DD is an inability to benefit from further practice beyond a certain level, and to achieve fluency, this too has implications for how to design intervention programs. Similarly, the results from Study III suggest that a potentially compensatory role of declarative memory merits further clinical interest.

Admittedly, much more research is required before direct clinical benefits may be obtained. First, more research is needed in order to reject or confirm and refine the results presented in this thesis. In addition, the understanding of procedural memory processes remains poorly understood and knowledge of how specific aspects of procedural learning and memory may be enhanced even more so. Similarly, more research is required in order to understand
how a shift of functions to a potentially intact declarative memory may be supported. Nevertheless, the work presented here emphasizes the clinical relevance of advances within the field of neuroscience of learning and memory for the clinical speech-language pathologist.

Conclusions and avenues for future research

The present thesis includes three studies that examined aspects of non-language procedural and declarative memory functions in children with SLI and children with DD compared to typically developing (TD) control children. Study I extended previous work on implicit sequence learning in children with SLI by including a second test session for the examination of consolidation and longer-term procedural learning. In line with the predictions of the PDH, the results indicated an association between poor performance on grammatical tests and poor consolidation of the learned sequential structure.

In Study II, the same paradigm was used to examine implicit sequence learning in children with DD. The results from this study were similar to those in Study I in that the DD group showed impaired performance in the second test session. However, follow-up analyses suggested the impairment may actually not be related to the consolidation process but to the effects of further practice in session 2. Notably, the relationship between sequence learning and reading skill was not mediated by phonological processing skills as assessed by a nonword repetition task.

Study III explored aspects of declarative memory in DD that are predicted by the PDH to be intact in the disorder, and that had not previously been investigated. It was shown that recognition memory after incidental encoding may not only be intact in DD but may even be enhanced. A marginally significant correlation between recognition memory accuracy and reading scores was found for the DD group, suggesting that a potential compensatory role of declarative memory merits further investigation with larger samples.

There are many exciting possibilities for how to improve and extend the work presented here. First, as previously discussed, there are methodological improvements to be made in future studies, including making sure that sample sizes are sufficiently large to produce more reliable findings. Future studies would also benefit from including a wider range of motor, cognitive and language tasks in the protocol.

With respect to SLI, the results from Study I suggest that poor grammatical ability may be related to a deficit in procedural memory consolidation. However, the relationship between implicit sequence learning and deficits in phonological processing in SLI remains unexplored. Future studies should include analyses of the relationship between phonological processing, grammar and implicit sequence learning in SLI in order to test the PDH pre-
diction that phonological processing deficits (such as impaired nonword repetition) also stem from a deficit in procedural memory. Such data would be of great theoretical interest, and may inform theoretical accounts of the disorder. Notably, the results from Study II suggest that phonological processing skills may be unrelated to procedural memory, at least in DD. If this finding is replicated in children with SLI, it would fit well with previous research showing that although grammar and phonological processing deficits often co-occur in SLI, they appear to have distinct genetic origins (Newbury, Bishop, & Monaco, 2005).

Another potentially fruitful avenue for future research is to extend the examination of procedural learning in SLI and DD to encompass even later learning stages compared to what was investigated here. Preferably, such an investigation should include a larger number of practice trials on the second day as well as additional practice sessions given on subsequent days.

If DD, as indicated by Study II, is associated with an impairment related to the effects of extended practice, and to skill automatization, the group difference in sequence learning may be expected to increase even further as practice continues. Such findings would be of great theoretical interest, but may also have implications for clinical and pedagogical intervention programs. Importantly, previous studies have shown that even though clinical and pedagogical intervention may ameliorate reading accuracy in individuals with DD, reading fluency often remains notoriously difficult to achieve (Shaywitz & Shaywitz, 2008). The possibility that the persisting lack of reading fluency is related to an underlying cortico-striato-cerebellar dysfunction should be a worthwhile subject for further exploration. Intriguingly, studies examining the effects of dopaminergic medication in children with co-occurrent ADHD and DD, suggest that pharmacological intervention affecting the function of corticostriatial circuits may have a beneficial effect on reading performance in affected children (Keulers et al., 2007). Future studies are needed to further examine a possible link between cortico-striato-cerebellar dysfunction and a domain-general skill automatization deficit in DD, as well as potential pharmacological and behavioral interventions to promote reading fluency.

The inclusion of brain imaging technology would be a great step towards a better characterization of procedural and declarative memory functions in the two disorders. Such techniques may allow for an investigation of learning and memory processes at the level of brain function, and would thus help test some of the predictions of the PDH more directly compared to the behavioural paradigms used in the present studies. First, brain imaging could be used to confirm (or reject) the assumption that the procedural and declarative memory tasks employed in the present studies elicit activation in cortico-striato-cerebellar and MTL brain structures, respectively, at least in TD children.
Second, brain imaging would allow for a direct examination of the prediction that declarative memory may serve a compensatory role in the face of procedural memory deficits in SLI and DD. For example, direct evidence for this prediction would be obtained if cognitive and/or linguistic tasks that elicit cortico-striato-cerebellar activation in TD children would be found to elicit MTL activation in SLI and DD children. Intriguingly, such a phenomenon has previously been observed in populations afflicted with cortico-striatal impairments, including in studies of aging and of Parkinson’s disease (Beauchamp et al., 2008; Moody et al., 2004; Rieckmann et al., 2010). In general, an increased understanding of compensatory mechanisms that may occur during development in the two disorders, and to what extent such mechanisms may be enhanced and exploited for therapeutical purposes, should be a high priority goal for future research.

Collectively, the three studies have shown that non-language learning and memory functions may be a highly relevant aspect of the cognitive profile in two disorders often characterized as being specific to language and reading. The results lend partial support for the PDH and suggest further refinements to the theory. Taken together with previous research, the studies emphasize the importance of going beyond a narrow focus on language and reading functions in the characterization of the two disorders. Such a broader cognitive, motor and linguistic approach may inform the development of future clinical and pedagogical assessment and intervention practices for SLI and DD.
Bakgrund

Specifik språkstörning och dyslexi innebär en påtaglig försening av språkrespektive läsutvecklingen som inte har någon uppenbar orsak. Överlappende mellan de båda diagnoserna är stort, både i form av symptom och samförkomst.

Syftet med denna avhandling var att testa en ny hypotes, the procedural deficit hypothesis (PDH), om att många av symptomen hos barn med språkstörning och barn med dyslexi har sin grund i en nedsatt funktion i det så kallade ”procedurella” minnessystemet. Detta minnessystem utgörs av ett nätverk av hjärnstrukturer där cortico-striatala och cortico-cerebellära bansystem är särskilt viktiga.

Minnessystemet är viktigt för inlärning och processande av motoriska och kognitiva ”färdigheter”, så som att cykla och spela piano. Det ligger också till grund för omedveten inlärning och processande av regelbundna mönstre och sekvenser i omgivningen. Det procedurella systemet är även engagerat i vissa typer av språkligt processande, såsom vid förståelse och produktion av grammatiska konstruktioner (som ju har en sekventiell karaktär), framplacering av ord och möjligen även vid automatisk avkodning vid läsning. Procedurella inlärning sker gradvis över tid och ”färdigheterna” utmärks av att de efter tillräckligt träning kan utföras automatiskt även när vår uppmärksamhet är riktad åt annat håll.

En viktig och innovativ aspekt av PDH är att hypotesen förutsätter att det ”deklarativa” minnessystemet ska fungera normalt och att det utgör en möjlig källa till kompensation för nedsatta procedurella minnesfunktioner. Det deklarativa minnessystemet har sin neurala bas i ett nätverk av hjärnstrukturer där mediala temporalloben (inkusive hippocampus) är en central komponent. Detta system engageras bland annat vid inlärning av ”faktakunskap” (semanstiskt minne) samt vid minne för personliga upplevelser (episodiskt minne), som till exempel vid igenkänning av personer, bilder eller föremål som vi sett tidigare. Sådan inlärning är som regel mycket snabb och kan ske efter att vi exponerats för ett stimulus vid ett enda tillfälle.

Nedsättningen i det procedurella minnet är enligt PDH generell så tillvida att den drabbar både språkliga och icke-språkliga funktioner som beror på de aktuella hjärnstrukturerna på ett likartat sätt. Detsamma gäller för den intakta deklarativa minnesförmågan. Denna prediktion innebär att hypotesen kan
testas med hjälp av icke-språkliga testuppgifter och att man därmed kan undvika att resultaten påverkas av språkliga faktorer, såsom fonologiska svårigheter, som man egentligen inte är intresserad av att mäta.

Översikt över avhandlingens delstudier

Studie I

Frågeställning: Har barn med specifik språkstörning en nedsatt icke-språklig procedurell inlärnings- och minnesförmåga? Är denna svårighet i så fall specifikt kopplat till grammatiska svårigheter?

Metod: Studien genomfördes i samarbete med Brain and Language Lab vid Georgetown University och Child Language Research Center vid University of Iowa. Deltagare var 21 barn i gruppen med specifik språkstörning och 27 barn i den normalutvecklade kontrollgruppen.

Testuppgiften var en så kallad ”serial reaction time” (SRT) uppgift, som ofta används för att pröva procedurell sekvensinlärning och som visat engagera det cortico-striato-cerebellära hjärnätverket.


Testet gavs vid två tillfällen. Under dag 1 genomförde barnen 200 repetitioner av sekvensen. Dag 2 gavs en kortare version (50 repetitioner) för att pröva hur mycket barnen kom ihåg av den inlärda sekvensen efter ett interval på ca 3 dagar.

Resultat: Inga signifikanta gruppsskillnader observerades när barn med språkstörning och barn med normal språkutveckling jämfördes med varandra. När kategoriseringen av barnen istället baserades enbart på tester avsedda att pröva grammatisk förmåga visade det sig att gruppen barn med grammatiska svårigheter även hade signifikant sämre procedurell minnesförmåga. Trots att inlärningen under dag 1 inte skilde sig åt, så presterade gruppen med grammatiska svårigheter signifikant sämre på dag 2.

Studie II

Frågeställning: Har barn med kliniskt diagnosticerad dyslexi en nedsatt icke-språklig procedurell inlärnings- och minnesförmåga? Är denna svårighet i så fall kopplad till fonologiska problem?


Resultat: Barnen med dyslexi uppvisade en sekvensinlärningskurva som påminde om den hos barn med grammatiska svårigheter i Studie I, medsignificant lägre resultat under dag 2. Uppföljningsanalyser visade dock att nedsättningen inte tycktes vara kopplat till problem med minneskonsolidering under testintervallet utan till effekterna av fortsatt ”träning” under dag 2. Sambandet mellan sekvensinlärning under dag 2 och läsförmåga var obe- roende av såväl fonologisk förmåga (nonordsrepetition), ordförråd och icke-verbal IQ.

Kommentar: Fynden tyder på att det finns ett samband mellan procedurell sekvensinlärning och läsförmåga som är oberoende av (åtminstone vissa aspekter av) de fonologiska svårigheter som är så vanligt förekommande vid dyslexi. Resultaten ger visst stöd för PDH, men är mer i linje med en ”double-deficit”-syn på dyslexi där just samförekomsten av fonologiska svårigheter och procedurella svårigheter skulle kunna leda till särskilt grava lässvårigheter. Utifrån detta synsätt skulle de procedurella aspekterna kunna vara kopplade till en svårighet att automatisera läsfärdigheterna, vilket gör läsningen mödosam och långsamt.
Studie III

Frågeställning: Har barn med kliniskt diagnosticerad dyslexi intakt deklarativt igenkänningsminne? Finns det i så fall tecken på att deklarativt minne används för att kompensera vid läsning?


Kommentar: Resultaten tyder på att dyslexi inte bara är förknippat med specifika svagheter utan även kan innebära en tidigare inte uppmärksammad styrka i form av ett förstärkt deklarativt igenkänningsminne. Möjligheten att en sådan styrka kan användas för att kompensera för svårigheter inom andra områden behöver utforskas med större grupper.
Sammanfattning och slutsatser

Studie I och Studie II har tillsammans visat på ett samband mellan icke-språklig procedurell sekvensinlärningsförmåga och grammatiska svårigheter, respektive lässvårigheter, hos barn. I Studie III visades att dyslexi kan vara förknippat med en förstärkt förmåga till deklarativt igenkänningsminne.

De tre delstudierna tyder på att det kan vara fruktbart att vidga det kliniska och pedagogiska perspektivet vid dessa diagnoser till att även omfatta aspekter av icke-språkliga inlärnings- och minnesfunktioner. En ökad förståelse för minnesfunktioner, och deras betydelse för symptomen vid språkstörning och dyslexi, skulle kunna leda till nya och effektivare interventionsprogram för drabbade barn.
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References


Seeman, P. (2011). All roads to schizophrenia lead to dopamine supersensitivity and elevated dopamine D2(high) receptors. *CNS Neuroscience & Therapeutics, 17*(2), 118-132. doi: 10.1111/j.1755-5949.2010.00162.x


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