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Simple and complex motor skills in children with dyslexia and/or attention deficit/hyperactivity disorder

Towards a unifying framework of sequential motor impairments in neurodevelopmental disorders

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Résumé

Les difficultés motrices sont de plus en plus rapportées à travers différentes maladies neurologiques incluant les troubles neurodéveloppementaux et les troubles neurodégénératifs. À partir de ces observations, des théories ont émergé et suggèrent que la co-occurrence de symptômes moteurs à travers les maladies neurologiques pourrait être un indicateur de mécanismes neurologiques aberrants communs aux différents troubles, ainsi qu'un indice de vulnérabilité cérébrale. La dyslexie et le trouble déficitaire de l'attention avec ou sans hyperactivité (TDA/H) sont deux troubles neurodéveloppementaux avec une prévalence élevée, qui sont associés à une multitude de difficultés cognitives et motrices, lesquelles se chevauchent fréquemment. L'existence simultanée de symptômes cognitifs est généralement bien reconnue et plusieurs auteurs ont développé des théories qui unifient les troubles neurodéveloppementaux afin d'expliquer cette co-occurrence. Cependant, moins d'accent a été mis sur la présence concomitante de difficultés motrices, possiblement en raison des résultats contradictoires dans la littérature en ce qui a trait à la présence des déficits moteurs. Ces divergences sont à leur tour probablement liées aux multiples outils utilisés pour l'évaluation des troubles moteurs. De plus, peu d'études ont exploré quelles composantes des habiletés motrices sont affectées de manière similaire chez les populations atteintes de dyslexie ou du TDA/H. L'objectif de cette thèse est de clarifier la co-occurrence de difficultés motrices chez des enfants et adolescents atteints d'une dyslexie ou d'un TDA/H en évaluant plusieurs composantes du fonctionnement moteur. De plus, la présence d'une association entre les symptômes cognitifs communs et les difficultés motrices est examinée afin d'appuyer l'hypothèse selon laquelle les mécanismes neurologiques atypiques qui sous-tendent les problèmes moteurs sont similaires dans les deux conditions (dyslexie et TDA/H).

Cette thèse est composée de deux études empiriques. Le premier article évalue les habiletés motrices fines et globales avec des tâches qui varient entre la coordination simple et la coordination séquentielle plus complexe, et ce chez des enfants et adolescents qui ont reçu un diagnostic de dyslexie seulement, de TDA/H seulement ou un diagnostic comorbide. Les résultats suggèrent que les enfants avec une dyslexie et/ou un TDA/H présentent des difficultés motrices co-occurrentes en coordination unimanuelle et bimanuelle séquentielle en comparaison

à des enfants qui ont un développement typique. Par ailleurs, la vitesse motrice simple est préservée chez ces premiers. De plus, les enfants avec un TDA/H seulement ont des difficultés plus prononcées sur une tâche de coordination bimanuelle asynchronisée et ils obtiennent des résultats déficitaires sur une tâche de dextérité manuelle. Ces résultats suggèrent que les enfants avec un TDA/H ont des difficultés motrices plus sévères et plus étendues.

Le deuxième article explore la relation entre les habiletés cognitives et les difficultés en motricité séquentielle chez les enfants avec une dyslexie et/ou un TDA/H. Les résultats indiquent que les habiletés communes en mémoire de travail visuelle et en fluence mathématique sont des prédicteurs des difficultés motrices, sans différentiation entre les groupes. Toutefois, une exception a été observée chez le groupe TDA/H pour lequel les habiletés en fluence mathématique ne contribuent pas significativement aux habiletés bimanuelles synchronisées. De plus, les symptômes diagnostiques de chaque syndrome, soit la lecture en dyslexie et l'inattention dans le TDAH, ne contribuent pas significativement à prédire la performance motrice. Les résultats appuient la notion de la présence de mécanismes neurologiques communs qui sous-tendent ces difficultés motrices analogues.

Cette thèse suggère que les enfants avec une dyslexie et/ou un TDA/H présentent fréquemment des difficultés communes en motricité séquentielle. À notre connaissance, ces résultats sont parmi les premiers à suggérer que la dyslexie et le TDA/H présentent une relation similaire entre leurs symptômes cognitifs et moteurs. Ces conclusions appuient l'hypothèse selon laquelle la dyslexie et le TDA/H sont différentes facettes d'une atypie développementale commune et que des difficultés en motricité séquentielle pourraient être un indicateur d'une vulnérabilité cérébrale. Ces résultats fournissent des informations importantes qui permettraient de guider l'évaluation et le dépistage des troubles neurodéveloppementaux. Ils encouragent également le développement et la mise en place d'interventions motrices qui intègrent la planification motrice séquentielle.

Mots-clés : Troubles neurodéveloppementaux, Dyslexie, Trouble déficitaire de l'attention avec ou sans hyperactivité, Comorbidité, Motricité séquentielle, Coordination unimanuelle et bimanuelle, Habiletés cognitives, Développement cérébral atypique.

Abstract

There is growing evidence that motor abnormalities are present in many neurological illnesses, ranging from neurodevelopmental disorders to neurodegenerative dementia. Theories have emerged suggesting that co-occurring motor impairments across disorders can be indicators of a vulnerable brain state and common aberrant underlying mechanisms. Dyslexia and Attention Deficit disorder with or without hyperactivity (AD) are two prevalent neurodevelopmental disorders and are associated with a collection of cognitive and motor symptoms that often co-occur. The co-occurrence of cognitive symptoms across dyslexia and AD is generally accepted and authors have developed unifying frameworks to better understand accumulating evidence of overlapping symptoms. However, less emphasis has been placed on co-occurring motor impairments, in part due to the inconsistency of findings associated with the many different assessment tools used across studies. In addition, few studies have explored what components of motor abilities are similarly impaired in both disorders. The objective of the current thesis is to clarify the presence of co-occurring motor difficulties in dyslexia and AD by assessing a variety of abilities associated with motor functioning. In addition, the relationship between co-occurring cognitive symptoms and motor difficulties is examined across both disorders to support the putative presence of a common aberrant mechanism that may underlie co-occurring motor weaknesses in dyslexia and AD.

The thesis is comprised of two empirical articles. The first paper assesses fine and gross motor abilities that range from simple to complex sequential coordination, in children with dyslexia only, AD only, and both disorders (Combo). Results suggest that children with dyslexia and/or AD have co-occurring difficulties compared to their typically developing peers on unimanual and bimanual sequential coordination in the presence of preserved simple motor speed. In addition, children with AD have more severe problems in complex bimanual out-of-phase coordination and are impaired on measures of dexterity. These results suggest that children with AD may have weaknesses on a wider range of motor abilities and have more profound bimanual coordination difficulties.

The second paper examines the relationship between cognitive abilities and co-occurring sequential motor difficulties in dyslexia and AD. Capabilities in visual working memory and math fluency were found to be significant predictors of motor abilities without differentiation

between disorders, with one exception by which math fluency did not contribute to performance on bimanual in-phase coordination in the AD group. Moreover, the distinctive symptoms of reading in dyslexia and inattention in AD did not contribute significantly to sequential motor performance. The results suggest that the pattern of motor difficulties is similar in dyslexia and AD, and support the presence of common mechanisms that underlie co-occurring motor weaknesses.

We suggest that dyslexia and AD often have co-occurring sequential motor difficulties, and to our knowledge these findings are among the first to show a shared relationship between cognitive abilities and sequential motor weaknesses. The findings support the idea that dyslexia and AD are different facets of a common atypical development and that shared sequential motor difficulties are indicators of a vulnerable brain state. The findings provide important information to help guide assessment and early screening of neurodevelopmental disorders, as well as encourage the development and application of motor intervention programs that integrate sequential motor planning.

Keywords: Neurodevelopmental disorders, Dyslexia, Attention Deficit/Hyperactivity Disorder, Comorbidity, Sequential motor skills, Unimanual and bimanual coordination, Cognitive abilities, Atypical Brain Development.

Table of contents

List of tables

Article 1

Article 2

List of figures

Introduction

Article 1

Article 2

Appendix I

Liste of acronyms

TDA/H: Trouble déficitaire de l'attention avec ou sans hyperactivité

AD or ADHD: Attention deficit disorder with or without hyperactivity

DCD: Developmental coordination disorder

Dys: Dyslexia

Combo/Comb: Comorbid dyslexia and AD

ALL: All groups combined

C1/C2/C3: Controls

LTT: The Leonard Tapping Task

UniSeq: Unimanual Sequential Tapping

BiBal: Bimanual balanced/In Phase Tapping

BiUnbal: Bimanual unbalanced/Out of Phase Tapping

RT/RapidT: Rapid (repetitive) Tapping

T1: Trial 1

T2: Trial 2

DH: Dominant Hand

NDH: Non-Dominant Hand

Seq: Sequential

Om: Omission

Pers: Perseverative

Uni: Unimanual

Bal: Balanced

GPB: Grooved Pegboard

SRTT: Serial reaction time Task

TONI-4: Test of Non-verbal Intelligence 4th edition

WIAT-II: Wechsler Individual Achievement Test, 2nd edition

CDTD: Cerebellar Deficit Theory of Dyslexia

ABD: Atypical Brain Development theory

MDM: Multiple Deficit Model

NSS: Neurological soft signs

DSM-V: Diagnostic and statistical manual of mental disorders, 5th edition

M1: Primary motor area

PMC: Premotor cortex

SMA: Supplementary motor area

ACC: Anterior cingulate cortex

VWFA: Visual Word Form Area

DTI: Neuroanatomical and diffusion tensor imaging

List of abbreviations

e.g.: For example

i.e.: That is

Etc.: Etcetera

To perseverance.

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Introduction

Motor System

Movement planning

The motor system represents a significant portion of both the brain and spinal cord, and movement depends on complex connectivity between the brain, the spinal cord, the muscles, and the implicated body part (R. Carter, Aldridge, Page, & Parker, 2009). The control of movement has therefore been described as a hierarchical system (Gazzaniga, Ivry, & Mangun, 2009) where a lower level action is a simple involuntary muscle reflex stemming from nerve activation in a spinal cord loop. A higher-level action can be voluntary, for example, consciously deciding to flex a finger. Higher level voluntary control requires more complex goal directed actions, such as executing commands. For example, to grasp a bottle of water you must move your arm in the right direction and at the right speed, your fingers must open in anticipation of the shape of the bottle, and the correct force needs to be applied to lift it (Gazzaniga et al., 2009). These higher-level voluntary movements include an abstract representation of the goal and the selection of the appropriate commands for executing the action. The abstract representation relates to a motor plan that is hierarchical and depends on the complexity of the goal (Gazzaniga et al., 2009; Hanakawa, Dimyan, & Hallett, 2008). Therefore, pointing to a location in space requires only planning the direction and speed of the movement, i.e. the kinematic, which is defined as the motion and pattern of movement without consideration of force or mass, such as velocity, position and acceleration of body parts (Gazzaniga et al., 2009). However, most actions require more complex planning and include a sequence of movements (Desrochers, Burk, Badre, & Sheinberg, 2015; Gazzaniga et al., 2009). In the latter case movements must be linked in the proper sequence (e.g., in a tennis-serve throwing the ball in the air, twisting the wrist, and rotating the arm to hit the ball with the racquet) and precise timing (i.e. appropriate speed and direction of the hand holding the racquet to hit the ball) to successfully execute the movement. Furthermore, the execution of a voluntary action demands sensory information that includes proprioception (e.g. the position of your body), visual feedback (e.g. position of the target you want to reach), as well as kinematic abilities (e.g. the ability to apply the appropriate direction and speed; Orban et al., 2011; Sober & Sabes, 2003). Everyday sequential actions such as reaching for a doorknob and turning and pulling it to open a door seem trivial when the motor

system is functional, yet such actions require planning of a sequence of movements accompanied by appropriate kinematic abilities, as described above. In sum, a goal directed movement is associated with different levels of motor planning and with the selection of appropriate components of a motor command, such as speed and direction. Executing a sequence of movements is a crucial aspect of higher-level complex planning and is included in most motor behavior.

Unimanual and bimanual coordination

Everyday actions usually require the coordination of both hands and this actuality adds to the complexity of motor planning underlying a bimanual movement *versus* a unimanual movement (Debaere, Wenderoth, Sunaert, Van Hecke, & Swinnen, 2004; Rueda-Delgado et al., 2014). Studies suggest that bimanual movements are by their nature less accurate and generally require longer reaction times (Garry & Franks, 2000; Toyokura, Muro, Komiya, & Obara, 2002). For bimanual movements, the motor system must prepare multiple movements concurrently and integrate separate motor plans, and consequently bimanual movements are more challenging to execute (Gazzaniga et al., 2009; Oostwoud Wijdenes, Ivry, & Bays, 2016). Although some studies suggest that bimanual in-phase or synchronized coordination does not require more complex planning than unimanual movements (Pollok, Butz, Gross, & Schnitzler, 2007; Urbano et al., 1998), it has been suggested that bimanual in-phase movements are more demanding only when they require complex movements, such as a sequence (Toyokura et al., 2002). In addition, reports suggest that in-phase bimanual movements are produced more accurately than out-of-phase or asynchronous movements (Rueda-Delgado et al., 2014; Serrien & Brown, 2002). In-phase bimanual coordination is generally faster than out-of-phase, however, both require more complex motor planning than unimanual coordination probably because both require multiple motor plans to be integrated.

Fine and gross motor abilities

Fine and gross motor skills differ in that the former requires subtle finger movements and the latter arm or leg coordination (R. Carter et al., 2009; Piek, Baynam, & Barrett, 2006). Operationally we define fine motor skills as those finger movements that require subtle movements of the tips, and gross motor abilities as those requiring upper or lower limb

movements (e.g., hand/arm coordination). The tasks used to measure fine and gross motor abilities differ greatly from study to study.

Motor adaptation and sequential motor learning

Motor planning abilities are titrated in tandem with the novelty of a situation and adapt rapidly when learning a sport, or when increasing efficiency by practice when honing keyboard skills. During the former, the motor system plans and monitors specific movements in order to stabilize performance and this planning relies on visual feedback, as well as on-going monitoring of obstacles or errors during action performance (Gazzaniga et al., 2009; Luft & Buitrago, 2005; Russeler, Kuhlicke, & Munte, 2003) Practice is required to consolidate the movement and results in rapid behavioral gains over a short period of time, also known as the « early learning phase » or « motor adaptation » (Penhune & Steele, 2012). Repeated practice over extended periods of time typically leads to motor skill automatization where the motor program does not need to be consciously planned to be executed (Doyon, Penhune, & Ungerleider, 2003; Orban et al., 2011). In this regard, complex motor sequential planning is paramount for the novice player to produce the relevant command based on external cues, whereas for a professional, motor output relies primarily on internalized routines. These different abilities are defined as stages in sequential learning and have been frequently examined with serial reaction time tasks (SRTT) that require subjects to adapt to a new motor sequence and learn to execute it efficiently and rapidly without making errors (Doyon et al., 2003).

Neuroanatomy: motor areas

The hierarchical planning of voluntary action (i.e. directional pointing *versus* complex sequencing) that was previously described on a behavioral level is also relevant to the anatomical correlates of motor output. The lowest level is the spinal cord reflex, followed by subcortical, and cortical higher-level command centers. For example, basic muscle reflexes are subserved by neurons that connect the spinal cord to the muscles whereas cortical and subcortical regions are recruited when a voluntary movement is required (Boecker et al., 1994; Gazzaniga et al., 2009). The primary motor area (M1) is defined as the core « green light » of movement and simple voluntary finger flexion is primarily associated with activation in this area. M1 is the primary brain area for voluntary movement having a very low threshold to

initiate motor responses compared to other motor areas. M1 is required for the initiation of voluntary movement and is associated with an organized map (homunculus) that is related to muscles in associated body parts. M1 neurons are prime movers and most directly control kinematics, such as velocity and direction (Sanes & Donoghue, 2000; Squire et al., 2008). The premotor cortex (PMC) is associated with preparation and guidance of movement, such as visual orientation to reach a target through its connections to visuomotor areas (Squire et al., 2008). The supplementary motor area (SMA) and the parietal cortex are also engaged depending on motor planning complexity (Boecker et al., 1994; Sadato, Campbell, Ibanez, Deiber, & Hallett, 1996). The parietal lobe is connected to several brain areas that process relevant visual and somatosensory information in order to select and plan spatially coordinated movements (Debaere, Wenderoth, Sunaert, Van Hecke, & Swinnen, 2003; Debaere et al., 2004). The SMA has been linked to the initiation and control of more complex movements that are less automatic, such as sequencing and bimanual movements, and is included in loops involving subcortical regions, such as the basal ganglia (Toyokura et al., 2002). In addition, subcortical regions such as the cerebellum and basal ganglia contribute to movement production and monitoring, in conjunction with the thalamus which plays an important role in the relay of information, including motor information, between the cortex and subcortical regions (Bosch-Bouju, Hyland, & Parr-Brownlie, 2013; Doyon et al., 2003; Orban et al., 2011; Squire et al., 2008). The cerebellum, which is divided into three lobes, receives information from multiple sources such as visual regions and projects to motor and frontal lobe areas (Squire et al., 2008). It plays a role in rapid coordinated movements and is paramount in error detection in ongoing movements, and is therefore primarily involved in motor adaptation (Penhune & Steele, 2012). The basal ganglia which include the striatum, the subthalamic nucleus and the globus pallidus receive an extensive array of cortical inputs and contribute to the smooth control and selection of movement, as well as efficient automatization during sequential learning (Doyon et al., 2003; Penhune & Steele, 2012). Motor planning is therefore defined as a multifocal process involving multiple brain regions, including parallel and consecutive activations of cortico-striatal and cortico-cerebellar loops, the relative contributions of which vary according to task demands (Doyon et al., 2003).

Neuroanatomy: bimanual coordination

Bimanual coordination is associated with augmented neural activity due to the necessity for inter hemispheric communication (Rueda-Delgado et al., 2014), which leads to complex excitatory and inhibitory processes between the hemispheres that is also associated with increased activation in the cerebellum and the SMA, bilaterally (Debaere et al., 2004; Habas & Cabanis, 2006; Toyokura et al., 2002). For instance, the SMA has been shown to actively connect to M1 cortices, in both hemisphere, during bimanual movements (Grefkes, Eickhoff, Nowak, Dafotakis, & Fink, 2008). There is evidence that this functional coupling is particularly important in the early phases of acquisition of a novel bimanual task, as shown through higher activation between the premotor, sensorimotor and posterior parietal regions (Gerloff & Andres, 2002). Interestingly the anterior cingulate cortex (ACC), a structure associated with higher-order processes such as attention (Carson & Kelso, 2004), has been shown to be activated only in out-of-phase movements (Bélanger et al., 2015; Habas & Cabanis, 2006; Pollok et al., 2007). The ACC is divided in regions, which includes the dorsal regions associated with the frontoparietal attention network, known to be required for complex movements (C. S. Carter et al., 1998; Squire et al., 2008) .

Motor-cognition link: behavior and anatomy

Motor planning is associated with different levels of complexity both on the behavioral and on the anatomical level. A significant aspect of this complexity is cognitive control through moment-to-moment monitoring of motor execution (Desrochers et al., 2015; Diamond, 2000). For instance, executing a sequence of movements requires mental manipulation and rehearsal of the different steps of the motor sequence (i.e. working memory), staying on task (i.e. attention), as well as avoiding and detecting errors, which further relies on the ability to restrain inappropriate movements (i.e. inhibition). These cognitive abilities are essential for the skillful execution of a motor plan (Diamond, 2000). To support the link between cognitive and motor abilities, studies have established the role of higher-order brain regions, such as the frontal cortex, in efficiently executing complex cognitive and motor behaviors (G Leonard, Milner, & Jones, 1988; Rushworth, Walton, Kennerley, & Bannerman, 2004). For instance, activity of the prefrontal cortex and the ACC are correlated with complex bimanual coordination and attentional control (C. S. Carter et al., 1998; Desrochers et al., 2015; Pollok et al., 2007; Serrien

& Brown, 2003) and coactivation of the prefrontal cortex and the cerebellum has been demonstrated on working memory tasks (Schumacher et al., 1996; Stern et al., 2000). The basal ganglia, which plays a role in sequential learning, has also been linked to reward-based learning through its neuroanatomical connection with the prefrontal cortex (Koziol, Barker, Joyce, & Hrin, 2014). The parietal lobe is also relevant for cognitive processes, such as reading, logical and mathematical thinking (Biotteau et al., 2016; Gazzaniga et al., 2009). The motor system then is multifaceted and is associated with complex networks that include both motor and non-motor output. Essentially, the entire brain is implicated in the execution of movements and therefore it is not surprising that cerebral abnormalities can lead to diverse motor problems.

Primary and secondary motor deficits in neurological disorders

Motor problems vary in accordance with the hierarchical planning of movement and the brain regions affected. Dense hemiplegia can be seen in stroke patients (Langhorne, Coupar, & Pollock, 2009) and in such cases the motor output of the muscles is compromised. Neurodegenerative disorders can be characterized by multiple motor impairments (Levit-Binnun, Davidovitch, & Golland, 2013; Peralta & Cuesta, 2017) and in this regard Parkinson's disease is associated with motor deficits emanating from compromised basal ganglia that include resting state tremors and rigidity, balance problems, slowness in initiating movement and lack of force control (Dickson, 2017; Gazzaniga et al., 2009). Both elementary muscle control and planning of movement kinematics are lost. Other primary motor disabilities, such as developmental coordination disorder (DCD), can be linked to difficulties with more complex motor planning, such as planning a sequence but in the presence of preserved muscle kinematics (Adams, Lust, Wilson, & Steenbergen, 2017; Gheysen, Van Waelvelde, & Fias, 2011). Hence, disorders with primary motor deficits can often be identified according to the level of motor planning or component (e.g. kinematics) that is affected, as well as to specific aberrant brain regions. Importantly, atypical motor planning can also be observed in disorders where motor problems are not the primary diagnostic feature, but are identified as subtler secondary symptoms (Hadders-Algra, 2002; Levit-Binnun et al., 2013; Peralta & Cuesta, 2017). Secondary motor problems are more challenging to identify as they are often expressed in a less severe manner (clumsiness, irregular movements, discoordination) rendering the identification of the affected motor components more difficult (Chan et al., 2010; Levit-Binnun et al., 2013). These

problems are rarely associated with a primary structural or functional deficit ascribed to a particular motor brain area (e.g. the basal ganglia in Parkinson's disease; Dickson, 2017). Rather, multifocal and widespread network anomaly is often identified in the disorders that includes aberrant activation of motor brain regions (Brown et al., 2001; Seidman, Valera, & Makris, 2005). This is particularly the case for neurodevelopmental disabilities, which are often associated with large-scale atypical development of the brain and for which motor weaknesses are frequently reported as a secondary symptom (Gilger & Kaplan, 2001; Levit-Binnun et al., 2013). Amongst these, Dyslexia and Attention Deficit/Hyperactivity Disorder (AD) are the two most prevalent neurodevelopmental disorders and have both been associated with secondary motor problems (Brookes, Tinkler, Nicolson, & Fawcett, 2010; Kaiser, Schoemaker, Albaret, & Geuze, 2014). The impact of these secondary motor symptoms on everyday activities are not insignificant. Poor motor abilities have been linked to indecipherable handwriting (Brossard-Racine, Majnemer, Shevell, Snider, & Belanger, 2011; Noda et al., 2013) and impaired motor coordination has been associated with poor adaptive functioning in disorders such as AD (Wang, Huang, & Lo, 2011). These subtle motor impairments are also associated more globally with poor academic success, lack of interest in recreational activities and low self-esteem, and thus can affect overall quality of life (Fernandes et al., 2016; Piek et al., 2006; Vuijk, Hartman, Mombarg, Scherder, & Visscher, 2011).

Co-occurring secondary motor impairments across disorders: an indicator of brain vulnerability

As outlined above, there is growing evidence that subtle motor irregularities are present across several neurological disorders, ranging from neurodevelopmental disorders to degenerative psychopathologies (Levit-Binnun et al., 2013; Peralta & Cuesta, 2017). For instance, the presence of motor anomalies is well established in developmental disorders such as autism and schizophrenia, and is associated with poor outcomes in neurodegenerative disorders such as Alzheimer's disease (Jahn et al., 2006; Mostofsky et al., 2006; Scarmeas et al., 2005). Motor weakness has also been identified as an early indicator of brain vulnerability, as its presence in childhood is associated with higher odds of developing psychopathology later in life (Bryson et al., 2007; Sigurdsson, Van Os, & Fombonne, 2002). Therefore motor impairment manifests a reliable co-occurring secondary symptom across neurological disorders and is a significant

indicator of atypical neurological functioning (Levit-Binnun & Golland, 2011). Authors have suggested that subtle co-occurring motor manifestations in neurological disorders might reveal commonalities in aberrant brain connections across disorders and support a systems neuroscience perspective that claims that invariant secondary symptoms present across disorders may reflect common abnormalities in global or large-scale brain networks through abnormal subcortical and cortical connections (Levit-Binnun et al., 2013; Menon, 2011). Hence, as Levit-Binnun et al. (2013) suggest, a global network failure reflected by subtle motor impairments could be a marker of brain vulnerability, leading to diverse neurological irregularities (Levit-Binnun et al., 2013). This unifying framework proposes that a vulnerable brain that has been exposed to abnormalities in brain organisation during early development could be expressed through motor problems. In sum, co-occurring secondary motor impairments could be a common marker of brain vulnerability across developmental disorders, such as dyslexia and AD (Pitzianti et al., 2017).

Dyslexia

Dyslexia is a neurobiological disorder with a prevalence rate of about 4 % and ranging from 5% to 17. 5 % when co-morbid with other developmental disorders (Germano, Gagliano, & Curatolo, 2010; Willcutt & Pennington, 2000). It is defined as a persistent deficit in literacy achievement, and more specifically, as an inability to acquire normal reading skills, which is not attributable to other disabilities, such as intellectual functioning, or to insufficient instruction (American Psychiatric Association, 2013). The disorder is a written language processing problem and does not interfere with the basic ability to think or to understand complex ideas. At the behavioral level, it is a heterogeneous syndrome characterized by a primary phonological decoding deficit, which often affects reading, spelling and reading comprehension, and is associated with other secondary cognitive symptoms, such as deficits in verbal fluency, working memory, information processing, executive function and motor skill (Menghini et al., 2010; Willcutt et al., 2010).

Several theories have emerged to explain the mechanisms underlying the primary reading impairment in dyslexia, including the “Phonological Deficit Hypothesis” that suggests

that reading problems are due to inefficient processing of phonemic language (Snowling, 2001). According to this theory, dyslexic individuals are unable to parcellate words into sounds and match these to letters or groups of letters. As such, dyslexia is described as a core disability in the formation of phonological representations and linked to a deficient phoneme-grapheme association, the immediate consequence of which is poor reading and writing (McCandliss & Noble, 2003). In keeping with this conceptualization, children with dyslexia generally show a core phonological problem (Ramus, 2003; Stoodley & Stein, 2011). The theory does not account for the plethora of cognitive problems that often coexist in dyslexia, including the presence of executive dysfunction and motor impairments (Fawcett, Nicolson, & Dean, 1996; Menghini et al., 2010; Reiter, Tucha, & Lange, 2005). Accordingly, others posit that a primary neurocognitive deficit is not sufficient to explain all of the observed symptoms and that individuals with dyslexia may have more general brain disruptions that impact several cognitive domains (McGrath et al., 2011; Moura et al., 2016; Willcutt et al., 2010). Dyslexia is thus viewed as a multifactorial entity and associated cognitive problems are not restricted to language brain areas, nor solely to a dysfunctional phonological system, but rather to multifocal cortical systems including the motor system (Gilger & Kaplan, 2001; Menghini et al., 2010).

Motor problems in individuals with dyslexia

Though there is evidence of motor impairments at different levels of motor planning and in various motor components in dyslexia (Fawcett et al., 1996; Lum, Ullman, & Conti-Ramsden, 2013; Stoodley, Fawcett, Nicolson, & Stein, 2006; P.H. Wolff, George, Marsha, & Drake, 1990), findings across studies are inconsistent (Irannejad & Savage, 2012; White et al., 2006) in part due to the wide variety of methods used and the lack of explicit hierarchical measures of movement. Studies have used test batteries that include several components of motor skills, such as fine, gross or sensorimotor abilities (Fawcett, Nicolson, & Maclagan, 2001; Getchell, Pabreja, Neeld, & Carrio, 2007; Ramus, Pidgeon, & Frith, 2003; Thomson & Goswami, 2008), however, to our knowledge, few studies have explicitly focused on differentiating simple kinematic planning, complex sequencing, unimanual and bimanual coordination in children with dyslexia (P.H. Wolff et al., 1990).

Differentiating gross, fine and bimanual motor impairments in dyslexia

Though there is evidence of gross motor impairments in dyslexia (Getchell et al., 2007; R. I. Nicolson & Fawcett, 1994; Rochelle & Talcott, 2006; Westendorp, Hartman, Houwen, Smith, & Visscher, 2011) studies have demonstrated this using ability measures that range from rapid and accurate pointing (Stoodley et al., 2006) to complex ball skills (Westendorp et al., 2011), as well as from simple postural stability (R. I. Nicolson & Fawcett, 1994) to more complex dual-task balance abilities (Brookes et al., 2010; Moe-Nilssen, Helbostad, Talcott, & Toennessen, 2003). Notwithstanding the importance of understanding the impact of such impairments, it is difficult to identify what components of gross motor planning are affected. Studies rarely conceptualize motor proficiency using a hierarchical approach to directly compare motor planning stages in one sample or by using tools that measure equivalent levels of motor planning and the same body parts between studies. For example, rapid pointing requires kinematic control of both speed and direction, while ball skills rely on bimanual and sequential movements, and can be examined with leg or arm movements. As previously mentioned, kinematic control, sequential movements and bimanual coordination are distinct features of motor planning and are associated with distinct anatomical correlates (Doyon et al., 2003; Rueda-Delgado et al., 2014). Wolff and colleagues (1984,1990) were among the first to differentiate motor speed, unimanual and bimanual coordination in a population with dyslexia (P. H. Wolff, Cohen, & Drake, 1984; P.H. Wolff et al., 1990). The studies measured unimanual finger movements and different components of bimanual coordination, and showed that subjects with dyslexia tapped with greater variability than age-matched controls when required to execute rapid and continuous asymmetric finger movements to a metronome beat. Participants with dyslexia, though error prone, were able to make unimanual finger movements and did not show a general slowness in responding. The authors concluded that the primary source of difficulty was the inability to coordinate rapid inter-limb asymmetric timed movements of the two fingers (P.H. Wolff et al., 1990). To our knowledge this latter finding has not been replicated using a method that differentiates levels of complexity of motor planning, and that includes simple motor speed, unimanual, and bimanual coordination in populations with dyslexia. Other studies have assessed fine motor skills using a potpourri of methods and employing different levels of complexity (Ramus et al., 2003; Vuijk et al., 2011) and not surprisingly inconsistent findings have emerged

(Getchell et al., 2007; Irannejad & Savage, 2012) that are likely due to the large range of tasks used. These tasks include speeded writing, drawing a continuous line, finger tapping, peg moving and bimanual coordination (Brookman, McDonald, McDonald, & Bishop, 2013; Iversen, Berg, Ellertsen, & Tonnessen, 2005; Lam, Au, Leung, & Li-Tsang, 2011). It is clear that writing requires a sequence of finely coordinated movements whereas peg placing relies primarily on precision grip. In addition, to our knowledge, no systematic review on motor difficulties in dyslexia has been published. In sum, it is difficult to conclude what aspects of fine or gross motor skills are impaired in dyslexia when the components and level of planning required by the tasks vary so greatly across studies.

Sequential learning in dyslexia

Among the most consistent deficits reported in dyslexia are those associated with sequential learning (Howard, Howard, Japikse, & Eden, 2006; Lum et al., 2013). Serial reaction time (SRT) paradigms are well recognized measures of sequencing abilities and automatization skills, and are often used to detect motor sequence learning impairments in dyslexia (Menghini, Hagberg, Caltagirone, Petrosini, & Vicari, 2006; Stoodley, Ray, Jack, & Stein, 2008). Notably, tasks that require sequences, such as finger to thumb apposition, typically reveal impairment in dyslexic subjects (Ramus et al., 2003), though they have been rarely explicitly linked to sequencing abilities. Some authors (Fawcett et al., 2001; R. I. Nicolson, Fawcett, & Dean, 2001) suggest that difficulties with sequential learning stem from a defective automatization process of motor sequences, which is associated with atypical functioning of the cerebellum. These observations have led to the development of the Cerebellar Deficit Theory of Dyslexia (CDTD; R. I. Nicolson et al., 2001) that includes four key elements. First, the deficits observed in dyslexia can be attributed to failure of skill automatization. Second, the cognitive, information processing and motor skill impairments can be linked to cerebellar dysfunction. Third, neuroanatomical correlates of structural deficits in the cerebellum can explain the functional impairments described above. Fourth, it would be possible to create an ontogenetic model that predicts the plethora of deficits in dyslexia explained by cerebellar dysfunction, with emphasis on sequential learning impairments (R. I. Nicolson & Fawcett, 2007). Although the Cerebellar Deficit Hypothesis is still debated (Irannejad & Savage, 2012), this theory highlights the importance of assessing motor abilities, as well as motor sequencing more specifically, in individuals with

dyslexia. Further investigation that readily distinguishes the integrity of fine and gross motor abilities, as well as different levels of complexity of motor planning, including sequencing abilities and bimanual coordination, could prove useful to clarify the discrepancies reported across motor studies of dyslexia.

Neuroanatomy of dyslexia

Neuroanatomical correlates of dyslexia are associated with multifocal brain regions and networks, including motor brain areas (Brown et al., 2001; M. A. Eckert et al., 2003). Studies have demonstrated functional and structural differences in the occipitotemporal cortex of individuals with dyslexia, particularly in the Visual Word Form Area (VWFA) that is associated with skilled reading tasks (Skeide et al., 2016). Several studies have shown abnormal activation of left temporoparietal and occipitotemporal junction areas during phonological tasks in populations with dyslexia (Price & Mechelli, 2005). This neuroanatomical network supports the core phonological decoding impairment in dyslexia, as the dorsal temporoparietal region is linked to the processing of the letters of a visual word into phonological segments, whereas the ventral occipitotemporal area is associated with the fast processing of familiar visual words (Price & Mechelli, 2005; Richlan, Kronbichler, & Wimmer, 2009). Although many studies have interpreted these atypical activations as a core phonological deficit, others have taken a broader approach by examining anatomical correlates in relation to other co-occurring symptoms in dyslexia, such as motor impairments. For instance, the inferior parietal lobule, which includes the angular and supramarginal gyri, both involved in phonological and semantic processing, is also linked to motor abilities and has been shown to be affected in dyslexia (Lacourse, Orr, Cramer, & Cohen, 2005; Mattingley, Husain, Rorden, Kennard, & Driver, 1998; van der Mark et al., 2011). Structural differences have also been identified in the cerebellum, the basal ganglia and the frontal cortex (Brown et al., 2001; M. Eckert, 2004; M. A. Eckert et al., 2003; Rae et al., 2002; Waldie & Hausmann, 2010). A study by Eckert et al. (2003) found significantly reduced brain volume in the right anterior lobes of the cerebellum and in the pars triangularis bilaterally (inferior frontal gyrus) in children with dyslexia, and anomalies in cerebellar-frontal circuits (M. A. Eckert et al., 2003). These structural alterations are in keeping with the idea of a multifactorial causality underlying the primary (i.e. reading) and secondary impairments (i.e motor skills) in dyslexia.

Figure 1. Dyslexia: neural correlates

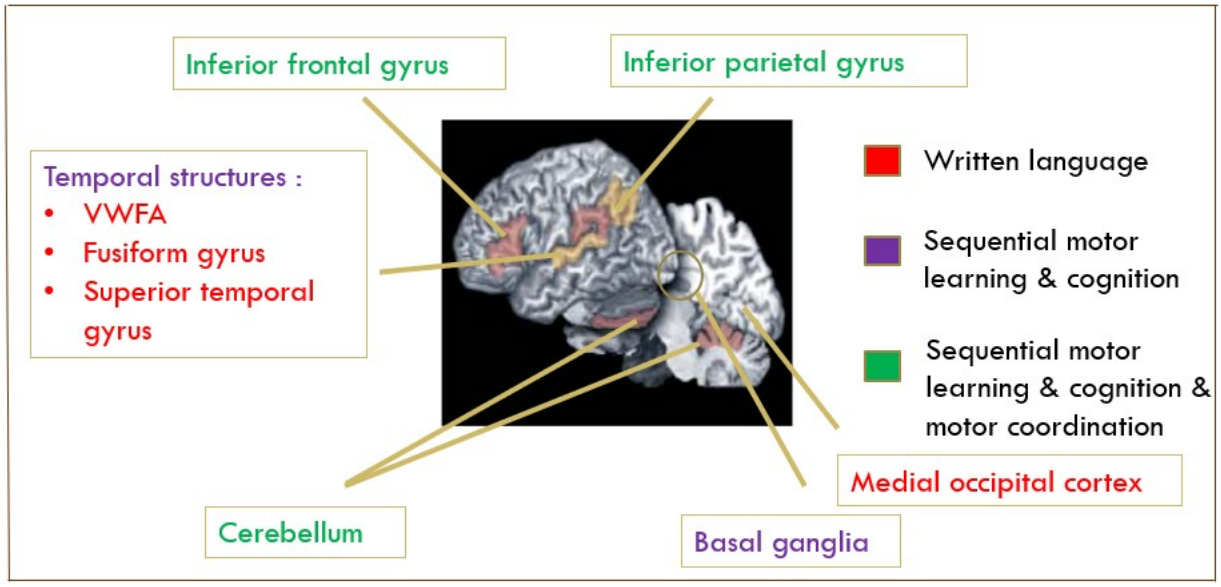


Figure 1. (Brown et al., 2001; M. A. Eckert et al., 2003; Waldie & Hausmann, 2010)

Attention Deficit/Hyperactivity Disorder (AD)

Attention Deficit/Hyperactivity Disorder (AD) is a neurodevelopmental disorder characterized by inattentiveness, impulsivity and hyperactivity, that impacts academic achievement and is linked to reduced abilities in every-day life, such as organization skills or athletic abilities (Willcutt, 2012). The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V; 2013) states that children with AD present a consistent pattern of inattention and/or hyperactivity-impulsivity that affects negatively social and academic or occupational activities. Children can have a combined presentation (inattention and hyperactivity-impulsivity), a predominantly inattentive presentation or a predominantly hyperactive/impulsive presentation, all of which interfere with development and functioning (American Psychiatric Association, 2013). More broadly, children with AD show characteristic deficits across neuropsychological measures, including attentional control, working memory, response inhibition, set shifting, planning and motor control (Barkley, 1997; Nikolas & Nigg, 2013). Consensus as to the primary deficit in AD has not been reached due in part to the highly heterogenous symptomatology of the disorder and its high comorbidity rates, up to 87%, with other psychiatric and neurological conditions, such as anxiety, conduct disorder, learning disabilities and motor disorders, the latter

being comorbid in 30% to 50% of AD cases. (Cubillo, Halari, Smith, Taylor, & Rubia, 2012; Roberts, Martel, & Nigg, 2013; Zablotsky, Bramlett, Visser, Danielson, & Blumberg, 2017). Nonetheless, several authors support the notion of a primary executive functioning impairment, as poor executive control of behavior can lead to the surfeit of cognitive difficulties mentioned above, such as reduced attentional control and poor motor planning abilities (Barkley, 2003; Dickstein, Bannon, Castellanos, & Milham, 2006; Roberts et al., 2013).

Motor planning problems in individuals with AD

Motor impairments are a well-established feature of AD (Kaiser et al., 2014) and a range of methods has been used to measure motor skills in AD. Gross motor development has been shown to be altered using tasks of locomotive abilities (e.g. run, hop, skip) and object control skills (e.g. two-hand strike, catch, kick; Harvey et al., 2007). Fine motor skills such as manual dexterity are affected as well, and these include bead threading, peg moving, hand writing and drawing tasks (Adi-Japha et al., 2007; Brossard-Racine, Majnemer, Shevell, et al., 2011; Scharoun, Bryden, Otipkova, Musalek, & Lejcarova, 2013). While it is generally accepted that both fine and gross motor skills are affected in AD (Kaiser et al., 2014), certain authors have emphasized an association between AD and more complex motor planning difficulties, such as sequencing or bimanual coordination, in counter distinction to simple lower level motor planning and kinematics, such as finger tapping (Duda, Casey, & McNevin, 2015; Klimkeit, Sheppard, Lee, & Bradshaw, 2004; Rubia et al., 1999; Scharoun et al., 2013; Yan & Thomas, 2002). To our knowledge, few studies have parcellated movement complexity in AD in order to distinguish the preserved and affected components of motor planning.

Bimanual coordination in AD

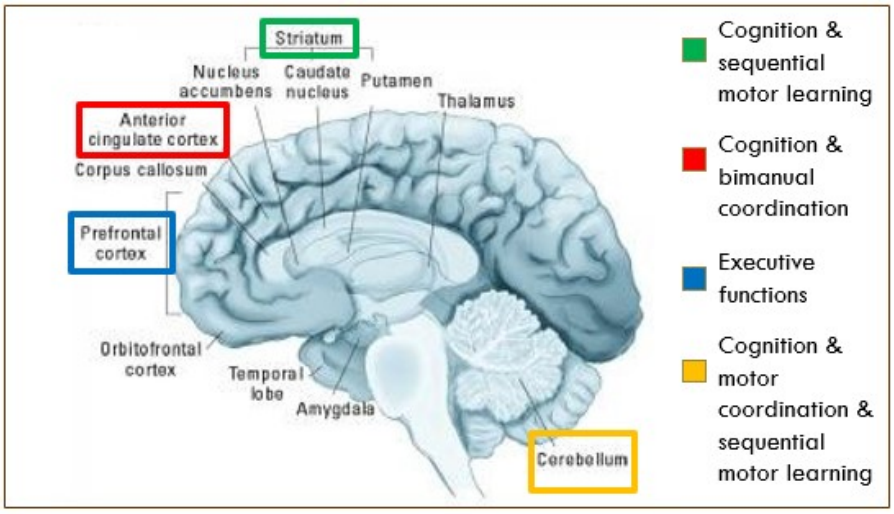
Performance on complex tasks, such as bimanual coordination, is impaired in AD populations, and this is an idea that supports the ‘‘executive functioning deficit hypothesis’’ (Kaiser et al., 2014; Klimkeit et al., 2004; Rubia et al., 1999) an idea that suggests that executing complex motor behaviors, such as bimanual coordination, relies primarily on executive functions (Bangert, Reuter-Lorenz, Walsh, Schachter, & Seidler, 2010; Hernandez et al., 2002). Indeed, children with AD show significantly less stable and less accurate bimanual movements than their typically developing peers when more complex in-phase and out-of-phase coordination is

evaluated (Klimkeit et al., 2004). However, impairments have also been observed on tasks that require only unimanual movements (Kaiser et al., 2014). Hence, discriminating between proficiencies in complex unimanual and bimanual motor skills may be essential to comprehend the nature of motor difficulties in AD.

Neuroanatomy of AD

The heterogeneity of AD corresponds to the widespread reports of aberrant brain regions and neural networks (Dickstein et al., 2006; Makris, Biederman, Monuteaux, & Seidman, 2009). Although some studies promote the idea of a primary frontal lobe focus because of the region's fundamental link to executive functioning (Rubia et al., 1999), more recent convergent neuroimaging data suggest that the brains of individuals with AD are affected in a more extensive manner, implicating dysfunction of fronto-striatal-cerebellar structures and networks that better explain the plethora of motor and cognitive manifestations (Brossard-Racine, Majnemer, & Shevell, 2011; Giedd, Blumenthal, Molloy, & Castellanos, 2001; Seidman et al., 2005). For example, findings reveal that children with AD have reduced brain volumes in key frontal (particularly the prefrontal cortex) and subcortical structures (basal ganglia and the cerebellum). Bush and colleagues (2005) reviewed several neuroimaging studies in AD and observed frontal lobe dysfunction that includes altered neural activity in the anterior cingulate, dorsolateral, and ventrolateral prefrontal cortex, but also in associated striatal, parietal and cerebellar regions (Bush, Valera, & Seidman, 2005). Studies also report atypical development of multiple pathways in AD, such as fronto-striatal, fronto-parietal, fronto-cerebellar and fronto-temporo-limbic networks (Cubillo et al., 2012). These studies support models that suggest that multiple aberrant pathways could explain the diverse phenotypes of AD, which translate not only into cognitive and motor difficulties, but also into atypical emotional regulation and motivational processes (Nigg, Goldsmith, & Sachek, 2004; Sonuga-Barke, 2005). In line with the multifaceted nature of AD, these findings suggest the importance of widely distributed neural insufficiencies leading to abnormal cognitive, motivation regulation and motor functioning.

Figure 2. AD: neural correlates



(Bush et al., 2005; Seidman et al., 2005)

Dyslexia and AD: co-occurring secondary cognitive and motor symptoms

Dyslexia and AD are often comorbid, with 25 to 40% of children with either dyslexia or AD meeting the criteria for the other disorder (Willcutt & Pennington, 2000). This is not surprising as both dyslexia and AD have been defined as heterogenous disorders at the behavioral and anatomical level (Brown et al., 2001; Menghini et al., 2010; Moura et al., 2016; Seidman et al., 2005). These reports are in line with evidence of common atypical brain development (e.g. impaired cerebellar functioning), and shared genetic and etiological components (Pennington, 2006; Stoodley, 2016; Willcutt et al., 2010). For example, a study by Loo (2004) reported the existence of genetic factors that have multiple phenotypic expressions resulting in AD or dyslexia symptomatology through shared linkage on a specific gene (Loo et al., 2004). Notwithstanding the importance of distinguishing one disorder from the other with primary characteristic symptoms for diagnostic and treatment purposes, the overlap of secondary symptoms has garnered attention from researchers (McGrath et al., 2011; Moura et al., 2016). As Gilger & Kaplan (2001) suggest, the overlap of symptoms has become the rule rather than the exception (Gilger & Kaplan, 2001). For example, studies that have jointly assessed dyslexia and AD report shared processing speed deficits (McGrath et al., 2011; Shanahan et al., 2006). Moreover, impairments in working memory and academic skills such as mathematical abilities,

have also been described in both dyslexia and AD (Alloway, Rajendran, & Archibald, 2009; Kaufmann & Nuerk, 2008; Mati-Zissi & Zafiropoulou, 2003; Menghini, Finzi, Carlesimo, & Vicari, 2011; Pastura, Mattos, & Araujo, 2009; Simmons & Singleton, 2008). Notably, difficulties with motor skills are frequently reported in both dyslexia and AD (Fawcett et al., 1996; Kaiser et al., 2014; Rochelle & Talcott, 2006). As a result, unifying frameworks have been developed that speculate that dyslexia and AD share risk factors that lead to nonspecific and various impaired underlying mechanisms that translate into overlapping cognitive deficits (Gilger & Kaplan, 2001; Kaplan, Dewey, Crawford, & Wilson, 2001; Pennington, 2006). For example, the **Multiple Deficit Model** (MDM; Pennington, 2006) suggests that neurodevelopmental disorders are heterogenous and originate from complex interactive effects of genetics and environmental factors leading to multiple cognitive risk factors, which engender co-occurring symptoms and syndromes (Moura et al., 2016). Comorbidity is not necessarily expressed through increased severity, but rather through the interaction of a constellation of factors resulting in the overlap of deficits. This framework is in keeping with models of multiple aberrant pathways, examined primarily in AD (Sonuga-Barke, 2005), which could also be hypothesized in neurodevelopmental disorders in general, as well as explain the high prevalence of comorbidity with other neurological and psychiatric disorders. Gilger and colleagues (2001) further propose an **Atypical Brain Development (ABD)** framework that suggests a unifying concept of the etiology of neurodevelopmental disorders that are viewed as different facets of nonspecific atypical development that affect diverse neurological circuits (Gilger & Kaplan, 2001). These unifying frameworks of developmental disorders such as dyslexia and AD are in line with previously described theories in systems neuroscience stating that persistent co-occurring secondary disabilities, such as in motor skills, can be important nonspecific indicators of the various forms of expression (i.e. neurological disorders) of brain vulnerability and support the idea of large scale network aberrations common across neurological disorders (Levit-Binnun et al., 2013; Levit-Binnun & Golland, 2011).

Although co-occurring *cognitive* symptoms have been the topic of growing interest in the scientific literature (Katz, Brown, Roth, & Beers, 2011; Kibby & Cohen, 2008; McGrath et al., 2011; Tiffin-Richards, Hasselhorn, Woerner, Rothenberger, & Banaschewski, 2008), little attention has been given to the manifestation of co-occurring *motor* difficulties across dyslexia and AD (Tiffin-Richards, Hasselhorn, Richards, Banaschewski, & Rothenberger, 2004). Yet,

motor irregularities are thought to be an important marker of brain vulnerability (Peralta & Cuesta, 2017; Pitzianti et al., 2017). This gap in the literature might be due, at least in part, to the wide variety of motor skills that have been assessed in each disorder. Skills requiring fine and/or gross abilities have been examined, as well as a range of simple to complex motor planning tasks, rendering interpretation difficult. Hence, jointly investigating different levels of motor planning abilities in both dyslexia and AD could clarify the presence of co-occurring difficulties.

To understand the purported role of co-occurring motor weaknesses in dyslexia and AD, it is pertinent to investigate their association with other overlapping cognitive symptoms. Foremost, as previously stated and supported by neuroimaging studies, motor planning is linked to non-motor abilities, particularly in more complex motor planning that requires cognitive control (Diamond, 2000; Rigoli, Piek, Kane, & Oosterlaan, 2012). In addition, early motor development may also play an important role in cognitive abilities, particularly executive functions (Oberer, Gashaj, & Roebers, 2017; Rigoli et al., 2013; Roebers & Kauer, 2009). For instance, Piek and collegues (2008) state that gross motor abilities in typically developing children at 4 years of age predict performance on subtests of working memory and processing speed at school age (Piek, Dawson, Smith, & Gasson, 2008). A systematic review by Van der Fels and colleagues (2015) found that the strongest correlation was between cognitive abilities and complex motor skills, such as bilateral body coordination (van der Fels et al., 2015). The authors hypothesized that these results could be due to the higher demand on cognitive skills required in complex motor output. In light of the recurring reports of motor and cognitive symptoms in each disorder, the relation between motor and cognitive skills has been applied to children with dyslexia and AD, although to a lesser extent (Davis, Pass, Finch, Dean, & Woodcock, 2009; Westendorp et al., 2011). However, perhaps due to the inconsistent findings on the nature of the motor impairments present in dyslexia and AD, as well as the lack of studies directly comparing motor impairments in dyslexia and AD, the relation between cognitive and motor skills has been studied in silos for each disorder. Poor motor skills have been linked to weakened academic abilities in children with learning disabilities such as dyslexia (Rae et al., 2002; Viholainen et al., 2006; Westendorp et al., 2011), as well as in children with AD (Davis et al., 2009; Rubio-Grillo, Salazar-Torres, & Rojas-Fajardo, 2014). For example, Davis and colleagues (2009) showed that sensorimotor abilities could explain a moderate portion of the

variance in academic achievement and cognitive process in children with AD, suggesting that motor development plays a role in non-motor abilities (Davis et al., 2009). Studies have also suggested a connexion between motor abilities and executive functions, namely working memory, in dyslexia (Reynolds & Nicolson, 2007) and AD (Tseng, Henderson, Chow, & Yao, 2004; Ziereis & Jansen, 2016). As stated previously, both academic and working memory abilities are co-occurring cognitive impairments in both disorders. To our knowledge, no studies have jointly examined the relationship between co-occurring motor and cognitive impairments in dyslexia and AD. Our approach could help clarify the presence of shared mechanisms that underlie aberrant motor functioning in both disorders.

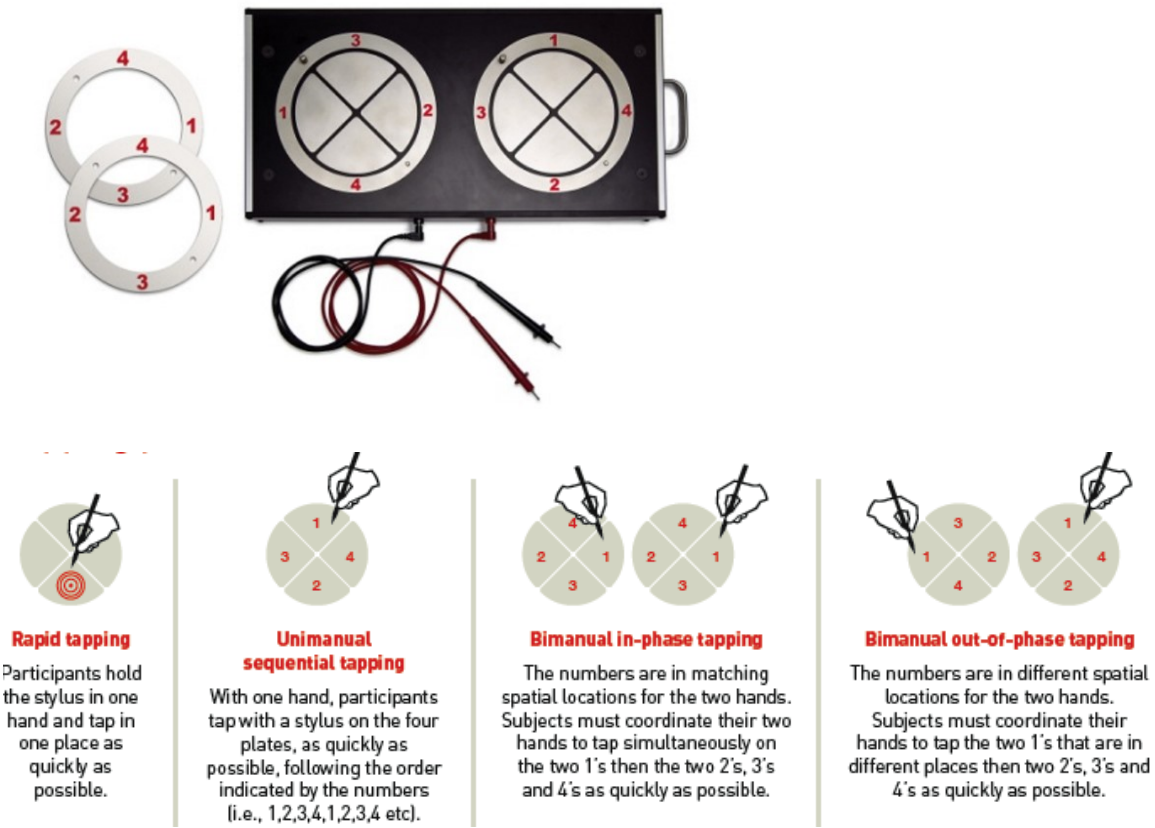
Methodological approach for studying different components of motor planning: the Leonard Tapping Task

Figure 3. The Leonard Tapping Task (LTT) is a computerized adaptation of the Thurston's tapping task (Thurston, 1944). The latter was designed to rapidly measure different levels of complexity of motor planning and has been used in research and clinical settings (Hernandez et al., 2002; G Leonard et al., 1988). The LTT is part of an ongoing validation study with 1800 participants aged 6 to 95 years (Bélanger, 2017; Bélanger et al., 2015; G. Leonard et al., 2010). Its application in neurodevelopmental disorders is of particular interest as it assesses different levels of motor planning and could help clarify the inconsistent findings in the literature on motor difficulties in dyslexia and AD. The LTT includes four conditions of varying complexity. The lower level condition is measured with repetitive tapping, which relies primarily on the kinematic of speed. A higher level of complexity in motor planning is required in the condition during which the subject must tap unimanually in a sequence, which necessitates both speed and monitoring of a sequence. The subsequent two conditions involve bimanual coordination, both in-phase and out-of-phase, which recruits competing motor plans as well as greater cognitive control. Finally, learning is required as the LTT is a novel task where on-going monitoring is essential as well as error detection, and rapid adaptation is expected over the repetition of two trials.

In conclusion, as motor abnormalities are a fundamental and consistent indicator of brain irregularities, their presence across dyslexia and AD could support a common general

connectivity disturbance and provide early indications of atypical development in childhood (Levit-Binnun et al., 2013). First, assessing abilities ranging from simple motor planning to complex sequencing and bimanual coordination, as well as both fine and gross skills, could prove useful to elucidate the reported inconsistencies in motor manifestations in dyslexia and AD. Second, examining co-occurring motor and cognitive symptoms in dyslexia and AD could help clarify the role of the putative underlying motor difficulties and support the notion of a common network aberration. This could provide important information to help guide assessment and early screening of neurodevelopmental disorders.

Figure 3. The Leonard Tapping Task (LTT)



(Bélanger et al., 2015)

Objectives and hypotheses

The aim of this thesis was to further our knowledge on the nature of motor difficulties in the two most common neurodevelopmental disorders, dyslexia and AD. To do so, two studies were planned with the following specific aims.

Article 1 aimed to assess various levels of motor abilities in children with dyslexia, AD or the comorbid diagnoses in order to clarify which aspects of motor planning are potentially impaired in both disorders. The objective was to examine simple to complex motor planning abilities, using fine and gross motor tasks. It was hypothesized that complex sequential planning would be a co-occurring motor weakness in dyslexia and AD.

Article 2 aimed to further the investigation of the co-occurring motor weaknesses to support a common mechanism underlying the atypical brain development in dyslexia and AD. The relationship between motor difficulties and cognitive abilities was assessed in both disorders. It was hypothesized that the relation between cognitive and motor abilities would be similar in dyslexia and AD, and that shared secondary cognitive abilities would be significant predictors of the co-occurring sequential motor difficulties.

Article 1

Shared and differentiated motor skill impairments in children with dyslexia and/or attention deficit disorder: from simple to complex sequential coordination

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Abstract

Dyslexia and Attention deficit disorder (AD) are prevalent neurodevelopmental conditions in children and adolescents. They have high comorbidity rates and have both been associated with motor difficulties. Little is known, however, about what is shared or differentiated in dyslexia and AD in terms of motor abilities. Even when motor skill problems are identified, few studies have used the same measurement tools, resulting in inconstant findings. The present study assessed increasingly complex gross motor skills in children and adolescents with dyslexia, AD, and with both Dyslexia and AD. Our results suggest normal performance on simple motor-speed tests, whereas all three groups share a common impairment on unimanual and bimanual sequential motor tasks. Children in these groups generally improve with practice to the same level as normal subjects, though they make more errors. In addition, children with AD are the most impaired on complex bimanual out-of-phase movements and with manual dexterity. These latter findings are examined in light of the Multiple Deficit Model.

Keywords: Dyslexia, attention deficit disorder, sequential coordination, manual dexterity, motor adaptation, unifying framework.

Introduction

Dyslexia and Attention Deficit, with or without Hyperactivity Disorder (ADHD), are common neurodevelopmental conditions in childhood and adolescence. Prevalence in school age children ranges from 5% to 15% and 5.9% to 7.1% in the United States, respectively (Handler, Fierson, & Section on, 2011; Willcutt, 2012). In addition, 60% to 80% of children with ADHD or Dyslexia have a comorbid diagnosis, with 25% to 40% of children meeting the criteria for both conditions (Germano, Gagliano, & Curatolo, 2010; Willcutt & Pennington, 2000).

Dyslexia and motor functioning

Dyslexia is characterized by a failure to attain efficient reading skills despite adequate intellectual abilities and sufficient instruction (Stoodley & Stein, 2011). Its phenotypic expression varies according to the severity of the reading impairment, the type of errors made (phonological and/or visual memory), and the presence of other impairments in writing and reading comprehension (Roderick I. Nicolson & Fawcett, 2011; Stoodley, Harrison, & Stein, 2006). Several theories have been proffered to explain the mechanisms underlying dyslexia. Primary amongst these is the "Phonological Deficit Hypothesis", which posits inefficient phonological representations linked to deficient phoneme-grapheme associations (Stoodley & Stein, 2011). Other cognitive problems often coexist, for instance with working memory (Menghini, Finzi, Carlesimo, & Vicari, 2011; Reiter, Tucha, & Lange, 2005), prompting recent studies to articulate new theories that attempts to account for the plethora of observed symptoms by invoking impairments in the auditory, visual, and motor domains (Chaix et al., 2007; Moura et al., 2016; Ramus, 2003). In keeping with this conceptualization, dyslexia can be viewed as a multifactorial entity where associated cognitive problems are thought not to be limited to language brain areas, nor solely to a dysfunctional phonological system, but rather to multifocal cortical systems (Habib, 2000; Menghini et al., 2010). Neuroanatomical and diffusion tensor imaging (DTI) findings support this perspective by identifying widespread structural and functional discordances in dyslexic brains compared to healthy control subjects, including in the occipitotemporal cortex, in the cerebellum and in the bilateral pars triangularis (Eckert et al., 2003; McCandliss & Noble, 2003; Rae et al., 2002; Shaywitz et al., 2002). The Cerebellar

Deficit Theory of Dyslexia (CDTD) was derived from these observations in an attempt to unify the multiple functional impairments observed in Dyslexia (R. I. Nicolson, Fawcett, & Dean, 2001). This theory suggests that impairments can be attributed to a failure of skill automatization leading to information processing and motor skill impairments that can be linked to cerebellar dysfunction. Thus, the CDTD predicts inefficient implicit motor sequential learning and procedural skills in subjects with dyslexia. These findings are further substantiated by Serial Reaction Time Task (SRTT) studies that show procedural learning deficits in dyslexic populations (Howard, Howard, Japikse, & Eden, 2006; Menghini, Hagberg, Caltagirone, Petrosini, & Vicari, 2006; Stoodley, Ray, Jack, & Stein, 2008). Although support for the CDTD has been inconsistent, the theory underscores the importance of cerebellar-cortical interactions in explaining functional symptoms of dyslexia by taking into account motor impairments (Kibby, Fancher, Markanen, & Hynd, 2008; Stoodley & Stein, 2013).

Dyslexic children were shown to be motorically less adept than their typically developing peers, however results across studies have been inconsistent, in part due to methodological differences. Deficits that are more consistently reported in children with dyslexia are with gross motor skills, more specifically balance and postural tasks (Getchell, Pabreja, Neeld, & Carrio, 2007; Iversen, Berg, Ellertsen, & Tonnessen, 2005; Moe-Nilssen, Helbostad, Talcott, & Toennessen, 2003; R. I. Nicolson & Fawcett, 1994; Ramus, Pidgeon, & Frith, 2003; Rochelle & Talcott, 2006; Westendorp, Hartman, Houwen, Smith, & Visscher, 2011). These studies often support the CDTD hypothesis because of the cerebellum's known implication in balance skills (Morton & Bastian, 2004). Studies also suggest fine motor skill impairments, for instance with peg moving or bead threading (Iversen et al., 2005; R. I. Nicolson & Fawcett, 1994; Ramus et al., 2003), though results are more variable in the literature. The inconsistencies found are often associated with the presence of comorbidities in the dyslexia groups, including attention deficit disorder, developmental coordination disorder (DCD) or language disorders (Irannejad & Savage, 2012; Moe-Nilssen et al., 2003; Ramus et al., 2003; Rochelle & Talcott, 2006). For instance, a study found that motor speed (finger tapping) and peg moving impairments are associated to language impairments rather than dyslexia per se (Brookman, McDonald, McDonald, & Bishop, 2013). Further, dyslexic populations' performances have been shown to be influenced by task complexity. For example, dyslexics

were impaired on tasks combining speed and accuracy performances but not when speed was measured alone, or on a task demanding complex out-of-phase coordination of fingers in comparison to less complex synchronized movements (Brookes, Tinkler, Nicolson, & Fawcett, 2010; R. I. Nicolson & Fawcett, 1990; Stoodley, Fawcett, Nicolson, & Stein, 2006; Wolff, George, Marsha, & Drake, 1990). However, to our knowledge, a limited number of findings address the impact of task complexity on motor performances among dyslexic populations. Finally, studies on procedural learning of sequences with a Serial Reaction Time (SRT) paradigm have supported the presence of automatization and procedural memory impairments in dyslexic populations (Lum, Ullman, & Conti-Ramsden, 2013). Interestingly, some of the impairments reported in children with dyslexia included sequential movements, for example finger to thumb, though few studies outside of the SRT paradigm have specifically measured sequencing skills. Employing assessment techniques that sample fine and gross motor abilities, ranging from simple motor speed, to sequential motor skills and to complex coordination would contribute to resolving these discrepancies.

ADHD and motor functioning

Attention Deficit/Hyperactivity Disorder (ADHD) is characterized by developmentally inappropriate inattentiveness, impulsivity and hyperactivity with consequent impairment in academic achievement and reduced success in every-day life (Barkley, 2003). The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (2013) lists the following ADHD specifications: a) primarily inattentive; b) primarily hyperactive/impulsive; and c) combined type, however, controversy remains on the cataloguing of differences in the phenotype definition of ADHD (Association, 2013; Sheikhi, Martin, Hay, & Piek, 2013; Swanson et al., 2012; Vitola et al., 2016). For the purpose of the present study, the term AD will be used to avoid characterizing differences in phenotype definition across studies, the main purpose being to evaluate motor skills in relation to a general Attention deficit disorder with or without a hyperactivity diagnosis.

Children with AD show deficits on different neuropsychological measures, including vigilance, working memory, response inhibition, set shifting, planning and motor control

(Dahan, Ryder, & Reiner, 2016; Nikolas & Nigg, 2013; Roberts, Martel, & Nigg, 2013). Barkley's model of Attention Deficit Disorder suggests that AD is linked to inefficiencies in internalizing sensory input (internally represented information) that then lead to deficient motor control as well as a lack of efficacy in different cognitive capacities that include motor inhibition and the execution of complex motor sequences requiring flexibility (i.e. fluency such as writing and drawing) (Barkley, 1997; Makris, Biederman, Monuteaux, & Seidman, 2009). Identification of a core deficit remains elusive, which has encouraged studies on neuroanatomical differences in AD populations. Various studies have focused on frontal lobe involvement, which might account for the surfeit of cognitive difficulties mentioned above (Dickstein, Bannon, Castellanos, & Milham, 2006). Frontal lobe dysfunction in AD is associated with smaller brain volumes in this region and altered activity in the anterior cingulate, dorsolateral, and ventrolateral prefrontal cortex, as well as in associated striatal, parietal and cerebellar regions; these later findings may suggest abnormal functioning of fronto-striatal and fronto-parietal neural circuitry (Bush, Valera, & Seidman, 2005; Giedd, Blumenthal, Molloy, & Castellanos, 2001; Seidman, Valera, & Makris, 2005). Interestingly, the frontal lobe has been associated to «higher order» motor skills, namely bimanual coordination (G Leonard, Milner, & Jones, 1988; Rueda-Delgado et al., 2014).

The presence of motor impairment in AD populations is widely reported. Several studies have readily distinguished fine and gross motor skills and suggested impairments in both domains (Kaiser, Schoemaker, Albaret, & Geuze, 2014; Pitcher, Piek, & Hay, 2003; Scharoun, Bryden, Otipkova, Musalek, & Lejcarova, 2013; Tseng, Henderson, Chow, & Yao, 2004; Yan & Thomas, 2002). Some of these authors have also suggested that the complexity of the task influences the degree of impairment, for instance by showing that more complex upper limb tasks accentuate differences between children with AD and their typically developing peers (Kaiser et al., 2014; Yan & Thomas, 2002). In addition, a study reported that children with AD make significantly less accurate movements than control groups with in-phase and out-of-phase bimanual coordination, further substantiating the link between frontal-lobe dysfunction and bimanual coordination impairments (Klimkeit, Sheppard, Lee, & Bradshaw, 2004; G Leonard et al., 1988). Procedural learning difficulties and sequential movement deficits in AD populations have also been reported (Barnes, Howard, Howard, Kenealy, & Vaidya, 2010;

Duda, Casey, & McNevin, 2015; Prehn-Kristensen et al., 2011). However, debate is still present on the etiology of these impairments, for example whether they emerge from attentional problems, inhibition impairments or the presence of comorbid diagnosis, such as DCD.

Comorbid AD and dyslexia

AD and dyslexia share high comorbidity rates and are both characterized by cognitive and motor skill impairments (Moura et al., 2016; Pennington, 2006; Shanahan et al., 2006). Some authors suggest that it is the presence of co-morbid disabilities that account for shared symptoms, for instance subjects with dyslexia who have motor skill deficits have comorbid high attention deficit ratings which explains shared symptoms rather than dyslexia per se (Chaix et al., 2007; Rochelle & Talcott, 2006). However, the overlap of impairments between disorders such as dyslexia and AD have led others to postulate a unifying framework for complex disorders. Theories such as the Atypical Brain Development theory (ABD) (Gilger & Kaplan, 2001) or the Multiple Deficit Model (Pennington, 2006; Willcutt et al., 2010) acknowledge the underlying nonspecificity of the mechanisms responsible for the various and shared symptoms in neurodevelopmental disorders. Rather than hypothesizing that a single neurocognitive deficit could provide a sufficient explanation for the plethora of symptoms, they suggest that neurodevelopmental disorders are heterogenous and that their etiology is multifactorial and originates from the interactive effects of genes and environmental risk factors (Kaplan, Dewey, Crawford, & Wilson, 2001; Moura et al., 2016; Pennington, 2006). Not surprisingly, motor functioning is frequently impaired in heterogeneous neurodevelopmental disorders like dyslexia and AD, conceivably because of its associated elaborate neural networks that are often included in the widely distributed neural correlates of each disorder (Debaere, Wenderoth, Sunaert, Van Hecke, & Swinnen, 2003, 2004). However, comparing these disorders on motor performance has received less attention and this is particularly so for those children who have a comorbid diagnosis. It could help shed light on individual motor performances, as wells as the hypothesis of an interactive effect when both disorders are present.

Objectives and hypothesis

The primary goal of this study is to assess and compare a range of motor skills in children with Dyslexia alone, AD alone, AD/Dyslexia, and their typically developing peers (control groups). More specifically, we assessed fine and gross motor skills ranging from simple speed, through unimanual sequential movements, to complex bimanual coordination. We predict that given the lack of reported simple motor speed deficits, subjects with dyslexia and AD or both, will not be impaired on motor tasks that require a simple speeded repetitive movement. However, given the reported sequencing and gross motor deficits in both populations, we predict that impairment will be apparent on the gross unimanual sequential conditions in the three clinical groups. In addition, given the added complexity of bimanual coordination, our clinical groups will be impaired on these conditions. However, given the findings on bimanual coordination and its link to frontal-based mechanisms, we expect that subjects who have AD and AD/Dyslexia will demonstrate significantly greater impairment than Dyslexia participants. A second goal is to identify differences in sequential motor skill acquisition as determined by examining practice effects from Trial 1 to Trial 2 because of the reported deficits in sequential skill learning in both populations. We hypothesize that our three clinical groups will show less efficient sequential skill acquisition as evidenced by lower improvement scores from Trial 1 to Trial 2 than the control groups. A third goal is to measure fine motor skills. Given the inconsistent results with manual dexterity in dyslexic populations, we predict that the dyslexia group will not be impaired because of the relative simplicity of the chosen task. Contrariwise, impairments will be present in the AD and Combined groups because of the more consistently reported fine motor skill impairments in populations with attention deficit disorders. Finally, we measure accuracy by comparing performance errors made on the different conditions. We predict that the experimental groups will make more errors than the control groups, though it is an open question as to what type of errors will characterize performances.

Materials and methods

Participants in the experimental groups

Twenty-seven children with dyslexia (DYS, 16 males; Mage = 13.8; SD = 2.4 years), 27 children with Attention Deficit with or without Hyperactivity Disorder (AD; 20 males; Mage = 12.7; SD = 2.4 years) and 27 children with combined AD and dyslexia (COMB; 19 males; Mage = 12.7; SD = 2.6 years) were recruited in the context of a larger study on learning disabilities at a special education school for French and English speaking children with learning disabilities in Montreal, Quebec. See Table 1 for participants' demographic and characteristics. Children are admitted to this school if they are two years behind in specific classes (French/English and arithmetic classes) and if they have diagnosed learning impairments (reading, writing, executive functions, etc.) with normal or superior intellectual abilities. All participants and their legal guardian gave written informed consent to participate in this study approved by the Montreal Neurological Institute (McGill University) and compliant with the 1964 Declaration of Helsinki.

Children were included in the AD group if they had a previous clinical diagnosis of AD as reported in the medical questionnaire completed by parents. They were excluded if they had a history of dyslexia. Children were included in the dyslexia group if they had a previous clinical diagnosis of dyslexia, in the absence of AD (See Clinical measures section below). Children were included in the combined AD/dyslexia group if they had previous diagnoses of AD and dyslexia.

Exclusion criteria for all groups were: 1) Documented medical history of learning disabilities other than AD or Dyslexia (dysphasia, dyspraxia and dyscalculia), traumatic brain injury, neurological or psychiatric conditions, or an IQ rating below 80.

Control participants

Each clinical group was compared to 27 typically developing children (DYS/C1, AD/C2, COMB/C3) matched for age (within a year), gender, handedness, and IQ (M=100; IQ +/- 20 points) (Dyslexia (C1): 16 males; Mage = 13,8; SD = 2,4; AD (C2): 20 males; Mage = 12,7; SD = 2,4; Combined (C3): 19 males; Mage = 12,7; SD = 2,6). 81 Control participants were

selected from a bank of 1800 participants aged 6 to 95 years old recruited and tested in the context of a larger study on motor skills in children and adolescents (G. Leonard et al., 2010). The exclusion criteria for this group were: 1) presence of learning disabilities 2) premature birth (less than 37 weeks' gestation) 3) traumatic brain injury or 4) neurological/psychiatric conditions.

A limited number of participants was included in our experimental groups for matching purposes; the groups also include participants with other birth complications or co-morbidities (See Table 1). We believe however that our sample remains representative of the population considering the high prevalence of other complications or disabilities in children with dyslexia or AD.

Clinical measures

The following tasks were included in the protocol for descriptive purposes and to verify inclusion and exclusion criteria in the clinical groups.

TONI 4 (Test of non-verbal intelligence, Fourth Edition): This test was designed to assess non-verbal general intelligence while avoiding the confounding effects of a person's linguistic or motor skills on global performance in individuals aged 6 to 90 years old. The TONI 4 taps into the capacity to reason abstractly while minimizing cognitive abilities such as reading, writing speaking or listening. The examinee must focus on differences and similarities among abstract/figural content, identifying the rule or rules to find the correct response (Brown, Sherbenou, & Johnsen, 2010).

Medical- Educational-Social Questionnaire: A custom medical questionnaire from the Montreal Neurological Institute was used to collect information on participants' medical and developmental history including information on previous diagnoses of AD, language and learning disabilities, medical and psychiatric disorders, and history of traumatic brain injury. Other information included socio-economic status, parental education, treatment or remediation received and medication.

Wechsler Individual Achievement Test, Second Edition (Wechsler, 2002): This standardized assessment battery measures academically linked skills as well as functions typically affected

by learning disabilities. Pseudo-Word Decoding and Spelling subtests were used to support the diagnosis of dyslexia. In the Spelling subtest, the examinee must write dictated letters, letter blends and words. The Pseudo-Word Decoding subtest evaluates the ability to apply phonetic decoding skills. The examinee must read aloud a list of nonsense words designed to imitate the phonetic structure of words in the English or French language. Reading and writing disability were defined as a standard score below 80 on these subtests.

Conners 3- Parent forms (Conners, 2008): This behavioral questionnaire measures the presence of attention deficit/hyperactivity disorder and associated problems and disorders. It features multiple content scales that assess ADHD related problems such as inattention, hyperactivity, executive functioning, learning, aggression, and peer/family relations. These are summed into an ADHD and ADD Index score as well as a Global Index score. The ADHD and ADD Index scores (Mean= 50, SD=10) were used to support the diagnosis of AD, as defined by a standard score over 60 (borderline range or higher).

Measures of motor performance

Handedness questionnaire: We used a modified version of the Edinburgh Handedness Inventory (Oldfield, 1971) that includes eighteen questions about stated hand preference for eighteen actions (e.g. throw a ball) to which individuals can answer «right hand always», «right hand most of the time», « both hands equally often», «left hand most of the time» or «left hand always». The total possible score is 90. An individual with a score of 18 to 29 is considered right-handed, 30 to 54 ambidextrous, and 55 to 90 left-handed. For the purpose of this study, we used the terms Dominant Hand (DH) and Non-Dominant Hand (NDH).

Grooved Pegboard (GPB) (Trites, 1977): This well validated dexterity test was used to measure fine motor skills. There are 25 key shaped holes in which the subject must insert one peg at a time. All the pegs have a round side and a square side and must be rotated to match each hole on the pegboard before they can be inserted. There are five rows of five holes each that need to be filled twice (In condition) with each hand, as quickly as possible, starting with the dominant hand (i.e., dominant--non-dominant--non-dominant--dominant). Pegs are inserted from left to right with the right hand, and vice versa for the left. In addition, the subject is timed for taking

the pegs out (Out condition) after each trial from the bottom (Right hand: right to left and left hand: left to right). A time score is computed for each hand on each trial.

Leonard Tapping Task (LTT; Fig 1): This task was designed to rapidly assess simple (i.e. unimanual rapid tapping) and complex motor (i.e. bimanual out of phase movements) coordination and motor sequencing. It is being validated on 1800 participants aged 6 to 95 years (G. Leonard et al., 2010). The task is a modified computerized version of the Thurstone apparatus (Thurston, 1944), designed to measure both unimanual and bimanual coordination. The Thurstone apparatus and its adaptation (LTT) have been used extensively in a clinical setting (Montreal Neurological Institute), as well as in studies on motor coordination (Hernandez et al., 2002; G Leonard et al., 1988). The LTT is composed of two symmetrical round metal plates with 4 equally sized quadrants numbered from 1 to 4 on which the subject must tap with a stylus following a sequential order with either one hand at a time or both hands together. Four conditions are administered and conditions 1, 2 and 3 are repeated twice after the first three trials are completed, without any time interval in between. Condition 4 is performed after both trials of conditions 1 to 3 are achieved.

1. Unimanual Sequential Tapping (UniSeq): The subject holds a stylus in his right hand or left hand and taps on the metal plates sequentially in a numerical order (1, 2, 3, 4) and continues the sequence for 30 seconds as fast as possible. The participants begin the first trial using their dominant hand, and the second using the non-dominant hand.

2. Bimanual In-Phase (or balanced) Tapping (BiBal): Rings are positioned around each plate in order to change the numbers on the quadrants (hence they are in corresponding positions for both hands). The subject holds a stylus in each hand and must tap simultaneously both 1s, 2s, 3s an 4s, and continue sequentially as fast as possible for 30 seconds.

3. Bimanual Out-of-Phase (or unbalanced) Tapping (BiUnbal): The rings previously set for the BiBal condition are removed (hence the numbers of each plate are not in corresponding positions). The subject holds a stylus in each hand and must simultaneously tap both 1s, 2s, 3s and 4s, and continue sequentially as fast as possible for 30 seconds.

4. Rapid Repetitive Tapping (RT): The subject holds a stylus in the right hand or left hand and taps on a metal plate (quadrant 4 with the left hand and quadrant 2 with the right hand) as fast as possible for 15 seconds with each hand, starting with the dominant hand. The measure consists in the total number of taps by each hand.

Five error types were documented: Sequential, Omission, Perseverative, Unimanual and Balance errors:

1. Unimanual Sequential Tapping: Omission, sequential and perseverative errors are recorded. An Omission is recorded if the subject taps with the stylus on any quadrant on the non-designated side. A sequential error is recorded if the subject taps with the stylus on a quadrant on the designated plate that does not follow the numerical order of the sequence (1, 2, 3, 4). A perseverative error is recorded if the subject taps with the stylus on the same quadrant a second consecutive time.
2. Bimanual Tapping: For both In-Phase and Out-of-Phase tasks, all error types are possible. An omission error occurs when the subject taps on only one of the two metal quadrants or if the subject taps with both hands on the same quadrant. A perseverative error is recorded if the subject taps again on the same quadrant with one or both hands. A sequential error is recorded if the subject taps with both hands on any other quadrant that does not follow the sequence. If the subject taps on two quadrants that do not correspond and neither one corresponds to the right sequence, a sequential error is recorded. A balance error is recorded when one hands taps on the correct quadrant (sequentially ordered) but the other hand taps on a non-corresponding quadrant. A unimanual error is recorded when one of the hands fails to tap.
3. Rapid Repetitive Tapping: Only Omission errors are recorded. They are counted when a subject does not touch the designated metal quadrant, but rather contact is made outside of the rings or with another quadrant.

Data Analyses

Age, gender, IQ and Handedness scores were compared between the three experimental groups (DYS; AD; COMB) and their matched control group (C1; C2; C3) using a one-way ANOVA for each variable.

In order to assess differences in motor performance, the number of correct taps performed on each condition (unimanual or bimanual) of the LTT was measured (see Fig 2). Each experimental group was compared to its matched control group on the four LTT conditions. Table 2 indicates the mean performances of the six groups on each condition.

For the RT condition, a repeated measures 2-way ANOVA was computed with Hand (Dominant Hand (DH); Non-Dominant Hand (NDH)) as the within-subject factor and Group (DYS/ C1; AD/ C2; COMB/ C3) as the between subject factor. For the UniSeq, a repeated-measures ANOVA was used with Hand (DH; NDH) and Trial (T1; T2) as the within-subject factors and Group (DYS/ C1; AD/ C2; COMB/ C3) as the between-subject factor. For the BiBal and BiUnbal conditions, repeated measures ANOVA with Trial (T1; T2) as the within-subject factor and Group (DYS/ C1; AD/ C2; COMB/ C3) as the between subject factor were computed.

Performance on each condition (RT; UniSeq; BiBal; BiUnbal) were compared with separate repeated-measures ANCOVA with either/or Hand (DH; NDH) and Trial (T1; T2) as the within-subject factor, Group (DYS; AD; COMB) as the between-subject factor and Age or Handedness scores as covariates.

Error analyses was conducted using the average number of errors for both hands for the Rapid Tapping (RT). The average number of errors for both hands and both trials was used for the UniSeq condition, whereas the average of both trials for the bimanual conditions was measured. Further, in order to control for motor speed, the number of errors of each type (Om; Pers; Uni; Bal; Seq) was divided by the total number of taps on each condition (RT; UniSeq; BiBal; BiUnbal). As a result, the mean ratio of errors (see Fig 3) was compared for each condition between the experimental groups and their respective controls (DYS/ C1; AD/ C2; COMB/ C3) using independent two-tailed T-Tests on all error types across the four conditions. For the comparisons between the experimental groups, the mean ratio of errors of each type (Omission, perseverative, sequential, unimanual and balanced) were compared on each condition (RT,

UniSeq, BiBal, BiUnbal) using one-way ANCOVA with Group (DYS, AD, COMB) as the between-subject factor and Age or Handedness scores as covariates. Only the significant effects are reported at a p level of 0.05.

Finally, the performances on the GPB (See Table 3) were computed as the time taken to complete 5 rows for the In and Out conditions separately using repeated measures ANOVA with Hand (DH; NDH) and Trial (T1; T2) as the within-subject factors and Group (DYS/ C1; AD/ C2; COMB/ C3) as the between-subject factor. Furthermore, two separate repeated-measures ANCOVA were computed with Hand (DH; NDH) and Trial (T1; T2) as the within-subject factors and Group (DYS; AD; COMB) as the between-subject factor in order to compare performances on both conditions while controlling for Age or Handedness scores.

Post-hoc analyses were conducted accordingly using repeated measures ANOVA for triple interactions, one-way ANOVA and independent T-Tests for group comparisons on single dependent variables and paired T-Tests to measure differences in performances within each group. Bonferroni corrections were used with multiple comparisons. Statistical significance was set at $p < 0.05$.

Results

Group analysis

Table 1 contains the demographic details for the experimental groups and their matched control groups derived from four one-way ANOVA. Results showed that the groups did not differ significantly on age ($F_{(5,156)} = 1.717$; $p = 0.134$), gender ($F_{(5,156)} = 0.488$; $p = 0.765$), IQ ($F_{(5,156)} = 0.538$; $p = 0.747$) and handedness scores ($F_{(5,156)} = 1.645$, $p = 0.151$). More specifically, Post-Hoc Tukey HSD tests indicated that DYS children and their matched control group (C1) did not differ in terms of age ($p = 1.00$), gender ($p = 1.00$), IQ ($p = 1.00$) and handedness score ($p = 1.00$) and that AD children and COMB children also did not differ from their respective control groups (C2; C3) on all of the variables mentioned above ($0.963 \leq p \leq 1.000$). Parent ratings of Inattention and hyperactivity on the Conners short and long questionnaire for the three experimental groups were analyzed. A simple one-way ANOVA indicated that the groups

differed on the Inattention ($F_{(2,77)}$ = 20.890; $p < 0.001$) and Hyperactivity/Impulsivity scales ($F_{(2,77)}$ = 12.182; $p < 0.001$). Post-Hoc Tuckey HSD test indicated that the AD and COMB groups did not differ on the Inattention ($p = 0.503$) and hyperactivity ($p = 0.412$) scales and were significantly higher than the DYS group on both scales ($p < 0.001$; $p = 0.002$). Hence, Parent ratings of AD were in the expected direction on the Inattention and Hyperactivity Scales. Scores on the WIAT-II reading and writing subtests were in the expected direction as well. A simple one way ANOVA indicated that the groups differed on the Spelling test ($F_{(2,78)}$ = 5.360; $p = 0.007$) and Reading test ($F_{(2,78)}$ = 11.699; $p < 0.001$). Post-hoc Tuckey HSD test indicated that the DYS children scored significantly lower on the Spelling ($p = 0.006$) and Reading ($p < 0.001$) subtests than the AD children, while the COMB group scored significantly lower on the Reading ($p < 0.001$) subtest and was marginally significantly lower than the AD group on the Spelling subtest ($p = 0.074$). DYS and COMBO children did not differ significantly on either subtest ($p \geq 0.606$).

As shown in table 1, the three experimental groups include participants with birth complications, such as emergency c-sections or premature birth, as well as other disabilities such as auditory processing disorders. Other health problems were controlled for as much as possible; however, the reality of "other complications" is an expected finding in these three types of clinical populations.

Dyslexia group (DYS) vs. control group (C1)

Table 2, Figs 2A and 3A. The number of taps with each hand was compared on the RT condition. Results showed no difference between groups ($F_{(1,52)}$ = 0.272; $p = 0.604$). Not surprisingly, a significantly higher number of taps (see Figs 1 and 4) was performed with the dominant hand compared to the non-dominant hand ($F_{(1,52)}$ = 82,176; $p < 0.001$). On the UniSeq condition, results showed a significant Hand x Trial x Group interaction ($F_{(1,52)}$ = 5.286; $p = 0.026$). Post-hoc analysis included two repeated-measures ANOVA with Trial as the within-subject factor and Group as the between-subject factor for the DH and the NDH. Results revealed a main effect of Trial ($F_{(1,52)}$ = 4.867; $p = 0.032$) and Group ($F_{(1,52)}$ = 11.917; $p = 0.001$) for the DH, and a significant Trial x Group interaction ($F_{(1,52)}$ = 4.231; $p = 0.045$) for the NDH. Thus, for the

DH, both DYS and C1 showed an increase in the number of taps from trial 1 to trial 2, with the DYS group performing more poorly overall. For the NDH condition, post-hoc analyses using paired T-tests with Bonferroni corrections showed a higher increase in performance observed in the DYS group from T1 to T2 ($T= -4.08$; $p < 0.01$) with their NDH compared to the C1 group ($T= -2.615$; $p = 0.06$), with the DYS group generally completing a lower number of taps on trial 1 ($T= -3.243$; $p = 0.008$), but not on trial 2 ($T = -2.502$; $p = 0.064$). Comparison of the number of taps on the BiBal condition revealed that both groups increased number of taps on trial 2 compared to trial 1 ($F_{(1,52)} = 57.326$; $p < 0.001$) and that the DYS participants make overall significantly less taps than the C1 group ($F_{(1,52)} = 7.849$; $p = 0.007$). On a more complex bimanual condition, the BiUnbal, results showed a significant Trial x Group interaction ($F_{(1,52)} = 5.716$; $p = 0.02$). Post-hoc analysis with Bonferroni corrections revealed that C1 performed an increased number of taps on trial 2 compared to trial 1 ($T = -6.407$; $p < 0.01$), while the DYS group's performance did not improve significantly ($T= -2.046$; $p = 0.204$). In addition, the C1 group made overall significantly more taps than de DYS group ($T_{Trial1}=-2.787$; $p = 0.028$; $T_{Trial2} = -3.461$; $p = 0.004$). Mean error ratios analysis showed that the DYS performed more sequential errors compared to their controls on the UniSeq condition ($T_{(52)} = 2.89$; $p = 0.006$).

Table 3 and Fig 4A. Results on the GPB showed that performance on the In condition were greater with the DH compared to the NDH ($F_{(1,52)} = 21.501$; $p < 0.001$) and increased from T1 to T2 ($F_{(1,52)} = 38.811$; $p < 0.001$) with no groups differences ($F_{(1,52)} = 1.696$; $p = 0.199$). Results on the Out condition revealed a significant Hand x Time interaction ($F(1,52) = 5.426$; $p = 0.024$). Bonferroni corrected post-hoc analysis showed that while the performances increased with both hands from T1 to T2 ($T_{DH} = 8.563$; $p < 0.01$; $T_{NDH} = 6.837$; $p < 0.01$), performances with the DH did not differ from the NDH at T1 ($T = -0.820$; $p = 0.416$) but did so at T2 ($T = 3.258$; $p = 0.008$)

Attention deficit disorder group (AD) vs. control group (C2)

Table 2, Figs 2B and 3B. On the RT condition, results showed a significantly higher number of taps with the dominant hand compared to the non-dominant hand ($F_{(1,52)} = 70.802$; $p < 0.001$)

without distinction between groups ($F_{(1,52)} = 1.044$; $p = 0.312$). On the UniSeq condition, results revealed that both groups performed more taps with their DH than with their NDH ($F_{(1,52)} = 37.634$; $p < 0.001$), and on trial 2 compared to trial 1 ($F_{(1,52)} = 24.767$; $p < 0.001$). Furthermore, AD participants made overall significantly less taps than their matched C2 group ($F_{(1,52)} = 15.292$; $p < 0.001$). On the BiBal condition, results indicated that both groups made more taps on trial 2 than on trial 1 ($F_{(1,52)} = 83.962$; $p < 0.001$), and that AD participants made overall significantly less taps than their controls ($F_{(1,52)} = 14.277$; $p < 0.001$). On the BiUnbal condition, results revealed that both groups performed more taps on trial 2 than on trial 1 ($F_{(1,52)} = 24.850$; $p < 0.001$), and that AD participants made overall significantly less taps than the C2 group ($F_{(1,52)} = 22.183$; $p < 0.001$). Mean error ratios analysis showed that the AD performed more sequential ($T_{(52)} = 2.304$; $p = 0.025$) and perseverative ($T_{(52)} = 4.775$; $p < 0.001$) errors compared to their controls on the UniSeq condition, and more unimanual errors in the BiUnbal condition ($T_{(52)} = 2.502$; $p = 0.016$).

Table 3 and Fig 4B. On the GPB, the participants showed increased performances in the In condition with their DH compared to their NDH ($F_{(1,52)} = 25.14$; $p < 0.001$), and in T2 compared to T1 ($F_{(1,52)} = 109.066$; $p < 0.001$). However, the AD participants were slower overall compared to their matched controls ($F_{(1,52)} = 10.041$; $p = 0.003$). On the Out condition, results revealed a significant Hand x Trial interaction ($F_{(1,52)} = 4.463$; $p = 0.039$) but no Group effect ($F_{(1,52)} = 3.895$; $p = 0.054$). Post-hoc analysis using Bonferroni corrections indicated that the performances with both hands increased from T1 to T2 ($T_{DH} = 9.816$; $p < 0.01$; $T_{NDH} = 8.678$; $p < 0.01$), and did not differ at T1 ($T = -1.189$; $p = 0.96$) but did so at T2 ($T = 4.665$; $p < 0.01$).

Combined group (COMB) vs. control group (C3)

Table 2, Figs 2C and 3C. Results on the RT condition showed that the COMB group did not differ from their controls ($F_{(1,52)} = 0.541$; $p = 0.465$). However, there was a significantly higher number of taps with the DH compared to the NDH ($F_{(1,52)} = 51.204$; $p < 0.001$). On the UniSeq condition, results revealed that both groups made more taps with their DH than with their NDH ($F_{(1,52)} = 34.585$; $p < 0.001$) and there was a significant improvement from trial 1 to trial 2 ($F_{(1,52)}$

= 33.053; $p < 0.001$). COMB participants made significantly less taps than their matched C3 group ($F_{(1,52)} = 8.659$; $p = 0.005$). On the BiBal condition, the results revealed that both groups improved from T1 to T2 ($F_{(1,52)} = 109.181$; $p < 0.001$). The COMB group performed significantly less taps overall compared to C3 ($F_{(1,52)} = 5.058$; $p = 0.029$). On the more complex condition (BiUnbal), the results indicated that both groups made more taps on trial 2 than on trial 1 ($F_{(1,52)} = 32.490$; $p < 0.001$) and that COMB participants made overall significantly less taps than the C3 group ($F_{(1,52)} = 5.976$; $p = 0.018$). Mean error ratios analysis showed that the COMB group performed fewer omission errors compared to their controls on the BiBal condition ($T_{(52)} = 2.021$; $p = 0.048$).

Table 3 and Fig 4C. On the GPB, performance analysis on the In condition showed a significant Hand x Time interaction ($F_{(1,52)} = 5.36$; $p = 0.025$) without distinction between groups ($F_{(1,52)} = 2.491$; $p = 0.121$). Bonferroni corrected post-hoc analysis indicated that the performances with both hands increased from T1 to T2 ($T_{DH} = 9.218$; $p < 0.01$; $T_{NDH} = 3.416$; $p = 0.004$), and differed at T1 ($T = -4.039$; $p < 0.01$) and T2 ($T = 6.567$; $p < 0.01$). On the Out condition, a significant Hand x Time interaction ($F_{(1,52)} = 15.953$; $p < 0.001$) was observed. Post-hoc analysis with Bonferroni corrections revealed that the performances with both hands increased from T1 to T2 ($T_{DH} = 9.947$; $p < 0.01$; $T_{NDH} = 3.995$; $p < 0.01$), and did not differ at T1 ($T = -0.126$; $p = 0.901$) but did so at T2 ($T = 5.391$; $p < 0.004$). In addition, the results showed a significant Hand x Group interaction ($F_{(1,52)} = 10.092$; $p = 0.003$). However, post-hoc analysis using Bonferroni corrections revealed similar performances between both groups with their DH ($T = -0.045$; $p = 0.964$) and their NDH ($T = -2.085$; $p = 0.084$).

Experimental groups (DYS vs. AD vs. COMB)

Table 2, Figs 2D and 3D. On the RT condition, the results reveal no significant effects of Hand ($F_{(1,77)} = 3.409$; $p = 0.069$) or Group ($F_{(2,77)} = 2.853$; $p = 0.064$) after controlling for the Age variable. On the UniSeq condition, the participants from the three experimental groups improved on their number of taps from trial 1 to trial 2 ($F_{(1,77)} = 13.68$; $p < 0.001$) without differences between groups ($F_{(2,77)} = 0.134$; $p = 0.875$) or Hand ($F_{(1,77)} = 1.455$; $p = 0.231$) when

controlling for the Age factor. On the BiBal condition, the results revealed no differences of Trial ($F_{(1,77)} = 0.008$; $p = 0.931$) or Group ($F_{(2,77)} = 1.413$; $p = 0.25$) on the number of correct taps when controlling for Age. On the BiUnbal condition, results showed no significant improvement on the number of taps from trial 1 to trial 2 ($F_{(1,77)} = 1.582$; $p = 0.212$). However, a significant Group difference was observed when controlling for Age ($F_{(2,77)} = 3.444$; $p= 0.037$). Post-hoc Bonferroni comparisons showed that the AD group ($M = 19.695 \pm 1.171$) performed overall less taps compared to the DYS ($M = 23.841 \pm 1.186$; $p = 0.048$) group and that the COMB group's performance ($M = 22.983 \pm 1.17$) did not differ from AD ($p = 0.148$) or DYS ($p = 1.000$) groups. Mean error ratio analysis showed significant Group effects of perseverative errors in the UniSeq condition ($F_{(2,78)} = 5.486$; $p = 0.006$) and balanced errors on the BiUnbal condition ($F_{(2,78)} = 3.503$; $p= 0.035$). Post-hoc Bonferroni comparisons show that the AD group performed more perserverative errors compared to the DYS ($p = 0.009$) and COMB ($p = 0.024$) groups in the UniSeq condition, while the COMB performed fewer balanced errors than the DYS group in the BiUnbal condition ($p = 0.038$).

Table 3 and Fig 4D. On the GPB, results on the In condition revealed significant Time x Hand ($F_{(1,77)} = 5.366$; $p = 0.023$) and Time x Group ($F_{(2,77)} = 4.864$; $p = 0.01$) interactions when controlling for the Handedness score. Post-hoc comparisons of the mean performances estimated with fixed covariates in 95% confidence intervals revealed greater increases in performances with the dominant hand across trials ($M_{t1} = 65.826 \pm 1.23$; $M_{t2} = 59.071 \pm 1.13$) compared to the non-dominant hand ($M_{t1} = 71.947 \pm 1.663$; $M_{t2} = 67.02 \pm 1.44$). Further, the AD group showed overall slower performances but improved significantly more from trial 1 to trial 2 ($M_{t1} = 75.625 \pm 2.304$; $M_{t2} = 67.46 \pm 2.041$) compared to the DYS ($M_{t1} = 63.212 \pm 2.278$; $M_{t2} = 59.617 \pm 2.018$) and COMB groups ($M_{t1} = 67.823 \pm 2.27$; $M_{t2} = 62.059 \pm 2.011$). On the Out condition, results indicated that the participant's speed performances improved from trial 1 to trial 2 ($M_{t1} = 21.272 \pm 0.305$; $M_{t2} = 19.034 \pm 0.266$; $F_{(1,77)} = 7.815$; $p = 0.007$) without distinction for the Hand ($F_{(1,77)} = 1.93$; $p = 0.169$), or Group factors ($F_{(2,77)} = 2.442$; $p = 0.094$) when controlling for the Age variable.

Discussion

Our study sought to characterize and differentiate motor skill impairments in dyslexia and Attention Deficit Disorder (AD), two prevalent neurodevelopmental disorders that share high comorbidity rates. We confirm that there is a common gross unimanual and bimanual sequential coordination impairment in both disorders. However, neither is compromised on motor speed or motor adaptation, with the exception of the dyslexia group that did not improve significantly on the bimanual out-of-phase condition. Our findings of additional impairments in our AD group on the most complex bimanual coordination task and on manual dexterity are consistent with Pennington's Multiple Deficit Model (Pennington, 2006). Hence, our data support a unifying framework for the understanding of neurodevelopmental disorders.

Our data make clear that documented motor deficits in dyslexic and AD subjects are not attributable to motor slowness in responding. In keeping with this suggestion, we note that neither group was impaired on rapid unimanual repetitive movements nor in the rapidity with which they could remove pegs from the Grooved Pegboard. We therefore suggest that kinematics and sensorimotor integration are not functionally impaired in these neurodevelopmental disorders. Kinematics include velocity, force, and movement frequencies, and constitute basic components of motor outputs that rely on sensorimotor networks, for instance the primary motor cortex and the supplementary motor areas (Boecker et al., 1994; Penhune & Steele, 2012; Rueda-Delgado et al., 2014; Sanes & Donoghue, 2000).

The addition of complexity that places increased demands on the integration of sequential motor skills and gross coordination, differentiates AD, Dyslexic and Comorbid subjects from their normally developing peers. The motor difficulty expressed by these groups is already apparent when the task is novel and requires spatial-sequential control even in the unimanual paradigm. In addition to performing fewer taps than their respective control peers, the dyslexic group and AD group, were differentiated by their greater propensity to commit sequential errors, suggesting that they had difficulty implementing the appropriate sequence when speed and accuracy were needed. This observation is in keeping with the deficits in sequencing skills reported in both disorders, although they have been reported to a lesser extend in children with AD (Lum et al., 2013; Shiels Rosch, Dirlikov, & Mostofsky, 2013). Given that these difficulties exist in the unimanual sequential conditions it is not surprising that both in-

phase and out-of-phase bimanual coordinated movements are also impaired. Bimanual coordination is considered a « higher order » task because of the added complexity of coordinating both hands (Rueda-Delgado et al., 2014). Hence, our findings shed light on shared atypical motor development in all three groups when a task requires gross sequential movements. Our findings also provide insight into the presence of common brain development abnormalities associated with this type of motor output. They have relevance for every-day activities that require elaborate planned sequential movements and require optimal cognitive functioning. Indeed, the fundamental motor impairments expressed by the AD, dyslexic and combined children may have its greatest impact when approaching novel motor tasks; learning situations where cognitive functions, such as attention and working memory are important prerequisites to master a complex motor output (Desrochers, Burk, Badre, & Sheinberg, 2015; Jueptner et al., 1997). In this regard, widely distributed neural networks are necessary for accurate cognitive-motor output. For example, the cerebellum has been associated with procedural motor abilities as well as with working memory and executive functions (E, Chen, Ho, & Desmond, 2014; Molinari et al., 2008; Stoodley & Schmahmann, 2009); and the cingulate cortex and parasagittal frontal regions have been associated with complex motor coordination as well as inhibition and attention (Desrochers et al., 2015; G Leonard et al., 1988; Rueda-Delgado et al., 2014). Interestingly, many of these cognitive-motor neural networks have been shown to be functionally depressed in both disorders, namely the prefrontal cortex in AD and the cerebellum in dyslexic populations (Dickstein et al., 2006; Eckert et al., 2003). Future studies investigating the link between gross sequential motor skills and cognitive functions could provide added insight into atypical neurodevelopment in both disorders. Such studies would contribute to our understanding of the mechanisms underlying the relationship between motor and cognitive impairments. This would be of particular interest in the context of the ongoing debate regarding the links between motor and academic skills, such as reading acquisition (Loras, Sigmundsson, Stensdotter, & Talcott, 2014; Piek, Dawson, Smith, & Gasson, 2008; Roebers et al., 2014).

Despite the shared motor impairments in all three groups compared to typically developing children, performance on the more complex bimanual out-of-phase coordination task differentiated AD from dyslexic and comorbid children, suggesting they had added

difficulty with complex co-ordination. These findings are in line with studies that suggest motor deficits on more complex motor coordination in AD populations, which includes bimanual coordination (Klimkeit et al., 2004). They were slower than their controls and dyslexic children, and motor perseveration was more often seen compared to control, dyslexic and comorbid children. The latter type of error (tapping on the same plate twice) might be representative of difficulty inhibiting automatic responses which is a widely reported primary symptom associated with AD children (Pennington, 2006; Polner, Aichert, Macare, Costa, & Ettinger, 2015; Willcutt et al., 2010). This disinhibition is in line with Barkley's hypothesis suggesting fragile inhibition control in AD populations. The added difficulty with asynchronized bimanual coordination is also in line with theories associating atypical frontal-based mechanisms with bimanual coordination (Barkley, 1997; Dahan et al., 2016; Gilbert, Isaacs, Augusta, Macneil, & Mostofsky, 2011; Hernandez et al., 2002; G Leonard et al., 1988; Rubia et al., 1999; Rueda-Delgado et al., 2014). Interestingly, a preliminary PET study on adults using the Leonard Tapping Task suggests that out-of-phase bimanual movements rely on the prefrontal cortex and the cingulate cortex, more so than for any other condition on the task (Bélanger et al., 2015). However, our in-phase coordination task, which requires symmetrical bimanual coordination, did not differentiate between groups with neurodevelopmental disabilities. Our findings suggest that bimanual in-phase movements perhaps do not demand heavy reliance on frontal-based mechanism, concurring with reports that in-phase movements are less demanding because of our natural tendency to use both our limbs simultaneously (Rueda-Delgado et al., 2014). Although impairments in inhibitory/frontal-based mechanisms may account for added difficulties in complex motor skills, an unexpected finding was that the COMB children were not also additionally impaired on the most complex coordination task, nor did they make more errors. Thus, deficits typically associated to an AD diagnosis, including behavioral inattention and hyperactivity, cannot be the sole factors in explaining the impairment observed in the complex out-of-phase coordination among our AD group. In addition, the AD children were the only ones with deficits on a manual dexterity task, which is in line with a study that suggested that fine motor skill deficits in AD are not associated to inattention, but rather to comorbid DCD (Pitcher et al., 2003). We could hypothesize that the more severe motor problems in our AD group is associated with development coordination problems that were not identified by medical diagnosis. Interestingly, our AD group did comprise a higher number of children with co-morbid

factors that are linked to atypical brain development (Moreira, Magalhaes, & Alves, 2014). These findings could indicate that while there is an overlap of motor deficits in both disorders, children with more widespread symptoms (reading and attentional) are not additionally impaired; rather the more severe and widespread impairments in our AD group could originate from the additive and interactive effects of the supplementary factors that hindered brain development. This is in line with studies with similar findings where the presence of comorbidity did not have an additional impact on task performances (Biotteau, Chaix, & Albaret, 2015; Moura et al., 2016). In addition, many children with AD remain in regular schools and classes, as their symptoms are not severe enough to jeopardize successful learning. Our AD group might be representative of the more severe cases of AD, presumably because of other factors that hindered neurodevelopment and more specifically frontal-based mechanisms. Hence, our findings support a unifying framework, such as the Multiple Deficit Model (Pennington, 2006), which posits that the overlap of neurocognitive symptoms in neurodevelopmental disorders can originate from interactive effects of genes and environmental risk factors, rather than from a single etiology. Our findings evidence the presence of a primary unifying impairment in gross sequential motor development in dyslexia and AD. Further studies that investigate the additive and interactive effects of multiple factors that hinder neurodevelopment as well as their association to more severe symptoms would be useful. We could better comprehend the overlap in these disorders and how to intervene optimally on functional impairments rather than on a specific diagnosis.

Although we predicted that participants with combined or separate disorders would generally show less improvement with repeated practice, we showed that they in fact improved similarly on most sequential conditions of the LTT over two short periods of 30 seconds. Hence, impairment in motor learning could not differentiate these children with typically developing peers. Motor sequence learning is characterized by rapid behavioral gains in the initial stages of motor practice, within a single session, whereas the later stages (slow, consolidation, automatization, retention) occur with practice over multiple sessions and offline mechanisms (Doyon, Penhune, & Ungerleider, 2003; Luft & Buitrago, 2005). Since our experiment was based on two conditions of 30 seconds within a single session, it is likely that the improvements observed here reflect changes in rapid motor adaptation rather than differences in skill

consolidation or automatization. Further substantiating our findings is the evidence of the role of kinematics and dynamics in performance improvement in the SRTT paradigms (Orban et al., 2011). Considering that our three experimental groups did not differ from their respective controls on measures of simple motor speed, it is possible that the improvements observed on the sequential conditions from Trial 1 to Trial 2 reflect adaptations in motor kinematics and dynamics rather than procedural learning per se. Nevertheless, our results show that AD and dyslexia do not generally impeach fast motor adaptations in the early stages of motor learning with the exception of the dyslexic participants that did not improve on the most complex coordination task. This could be the result of a compound effect of the complexity of the task and the well-documented impairments in procedural motor skill on motor adaptation. Further experiments that compare AD and dyslexia performances that readily differentiates motor adaptation and procedural learning over longer periods of time would be necessary to better understand how motor coordination learning is impacted by both neurodevelopmental disorders.

In conclusion, both disorders remain motorically challenged with gross sequential motor skills that rely on joint cognitive-motor control processes. Our study supports the hypothesis that motor skill impairment is a co-occuring symptom among both populations. The differences in motor skills with typically developing children is neither related to general motor slowness in responding or inability to adapt in the fast learning phase. Our findings support the Multiple Deficit hypothesis. The later theory unifies the considerable overlap of neurocognitive deficits between these developmental disorders and accentuates the importance of the additive and interactive effects of multiple factors to the understanding of the complex and dimensional symptomatology of developmental disorders. Our findings shed light on the importance of measuring motor skills at a young age for they can be useful indicators, among others, in identifying children who are at risk of neurodevelopmental disorders. Finally, early intervention with physical training to stimulate brain development is a field that offers an interesting approach, especially that a few recent studies have shown positive outcomes (Lucas et al., 2016; Memarmoghaddam et al. 2016), though it remains an area to be extensively explored. Further studies linking motor development and cognitive functions that target neurodevelopment as a complex multidimensional concept could help increase positive outcomes in terms of motor and cognitive interventions.

Limitations

As mentioned in our Clinical Measures section, reading and spelling disabilities were defined as a performance of -1.3 SD on these two subtests. However, for the DYS group, the mean performance is 83.22 (11.69) on the reading subtest, which is equivalent to -1.1 SD (See Table 1). This suggests that our DYS group performed slightly better than expected in terms of reading performances. We believe that this variability could be associated with children who have improved due to receiving special education, particularly because the WIAT-II subtest does not include a time limit. Our group could also include children with surface dyslexia rather than phonological dyslexia, which is assessed with irregular words rather than pseudo-word reading. As for the COMB group, results on the reading subtest is also higher than expected (See Table 1). Again, this could be due to improvements in the performances associated with receiving special education or with the presence of children with subclinical reading and spelling difficulties, which warranted a comorbid medical diagnosis.

We obtained the confirmation of a medical diagnosis of AD, but no cognitive testing was done to confirm its presence and no differentiation was made between attention deficit disorder and attention deficit disorder with hyperactivity. As mentioned in our Clinical Measures section, the ADHD and ADD Index scores from the Conners-3 questionnaire were defined by a standard score over 60 (borderline range or higher). As shown in Table 1, the AD group's mean performances are higher than the 60 T score cut off, though the large standard deviations indicate high variability in our group. We believe this could be due to factors such as medication, which was not controlled for, as well as improvement due to interventions offered in the specialized school. The same patterns of high variability on the Conners-3 scales were observed in our DYS and COMB group, though the mean group performances correspond to our cut-off criteria. The general variability in our groups suggests that they are comprised of children who are partially compensated or who have subclinical symptoms of either one of the disorders. However, this possible explanation is based on a limited number of tests, whereas the medical diagnosis is typically based on a complete cognitive evaluation which is required to attend the specialised school. Finally, participants with the dual diagnosis unexpectedly made fewer errors than their controls on certain conditions, which could suggest an artefact in our group. Gender was not controlled for when comparing between experimental groups.

In conclusion, our participant groups conceivably include children that are partially compensated in terms of academic or attentional symptoms. We believe, however, that the direction of the differences between group means on the reading and Conners-3 indexes, combined to the reported medical diagnosis, support our groups' validity and represent the general population of children that attend specialised schools.

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Table 1. Descriptives

Groups	Age*	TONI-4*	Handedness*	WIAT-II*		Conners (Parent)*		Other problems
				Reading	*Spelling*	*Inattention*	*Hyperactivity*	
DYS (n=27)	13.78	97.85	24.81	83.22	71.7	54.96	50.73	BC *(n=2); APD (n= 3);*
(16 males)	*2.38*	*8.05*	*12.43*	*11.69*	*7.7*	*10.21*	*9.33*	*LT(n=1); P (n=1)*
C1 (n=27)	13.78	97.74	24.33	-	-	-	-	BC *(n=2)*
(16 males)	*2.37*	*7.16*	*14.5*					
AD (n=27)	12.59	97.9	33.15	98.11	80.59	73.82	68.33	BC *(n=4); APD (n= 4);*
(20 males)	*2.21*	*9.7*	*22.33*	*11.28*	*12.1*	*11.61*	*15.21*	*LT (n=5); P (n=3)*
C2 (n=27)	12.59	100.11	30.44	-	-	-	-	LT *(n=1);* Hypo. *(n=1)*
(20 males)	*2.21*	*9.62*	*20*					
COMB (n=27)	12.63	99.59	25.78	82.89	74.37	70.37	63.67	LT*(n=3);* P *(n=2)*
(19 males)	*2.57*	*11.24*	*11.95*	*16.11*	*10.43*	*11.89*	*14.77*	
C3 (n=27)	12.63	100.9	23.37	-	-	-	-	-
(19 males)	*2.57*	*10.94*	*9.73*					

BC, Birth complications; APD, Auditory Processing Disorder; LT, Late talking; P, Premature; Hypo., Hypothyroidism. *Means and standard deviations (SD).

Table 2. Leonard Tapping Task performances by group and condition (Trials 1 & 2).

Groups	RT*		UniSeq- DH*		UniSeq- NDH*		BiBal*		BiUnbal*	
	DH	NDH	Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2
DYS	96.73	86.38	100.93	102.44	91.74	99.07	47.26	59.11	23.74	26.59
(n=27)	*7.47*	*10.28*	*21.43*	*21*	*19.4*	*19.66*	*18.81*	*23.27*	*8.47*	*9.67*
C1	95.56	85.3	119.63	125.07	109.33	112.3	63.37	75.04	32.56	39.67
(n=27)	*8.58*	*9.43*	*25.9*	*22.33*	*20.45*	*19.17*	*22.17*	*22.57*	*12.09*	*17.08*
AD	91.85	79.37	91.44	96.19	83.85	89.3	35.96	46.19	17.67	20.33
(n=27)	*12.12*	*12.82*	*19.68*	*17.08*	*19.29*	*19.49*	*14.43*	*16.13*	*5.39*	*6.82*
C2	93.81	82.67	112.82	116.15	101.93	106.67	55.57	65.59	27.52	32.85
(n=27)	*8.65*	*8.76*	*21.51*	*20.86*	*18.45*	*18.13*	*24.18*	*21.23*	*9.35*	*13.28*
COMB	89.96	78.37	92.78	97.7	82.96	90.07	37.89	47	20.56	24.15
(n=27)	*9.11*	*11.25*	*25.21*	*21.97*	*22.05*	*17.88*	*19.38*	*20.05*	*6.94*	*8.82*
C3	91.59	80.7	110.04	115.48	101.33	107.59	49.78	61.82	26.3	32.85
(n=27)	*9.78*	*14.82*	*24.66*	*25.81*	*24.14*	*23.62*	*23.63*	*24.95*	*11.74*	*15.82*

DH, Dominant Hand; NDH, Non-Dominant Hand. * Mean number of taps and standard deviations (SD) of a given Leonard Tapping Task condition are listed

Table 3. Performances by group and Grooved Pegboard (GPB)

Groups	GPB - 1st Trial*				GPB - 2nd Trial*			
	DH		NDH		DH		NDH	
	IN	OUT	IN	OUT	IN	OUT	IN	OUT
DYS (n=27)	60.92 *8.65*	20.39 *2.15*	65.69 *10.87*	20.73 *2.67*	56.77 *7.9*	18.31 *1.88*	62.62 *9.72*	19.23 *2.28*
C1 (n=27)	58.7 *12.59*	20.26 *2.77*	62.74 *11.24*	20.44 *3.27*	54.07 *9.88*	18 *2.37*	58 *8.27*	19.11 *3.11*
AD (n=27)	71.78 *13.78*	22.26 *3.58*	79.15 *18.19*	22.56 *3.24*	62.67 *13.79*	20.73 *2.67*	72 *15.07*	20.3 *3.04*
C2 (n=27)	63.22 *9.01*	20.63 *2.37*	66.70 *10.43*	21.19 *2.25*	55.96 *7.26*	18.22 *1.85*	61.89 *8.89*	19.44 *1.85*
COMB (n=27)	64.78 *9.91*	21.41 *3.91*	71 *14.72*	20.3 *3.5*	57.78 *7.58*	18 *2.70*	66.44 *13.66*	19 *3.46*
C3 (n=27)	60.48 *10.92*	21 *3.15*	64.96 *11.39*	22.22 *4.26*	54.7 *9.97*	20.73 *2.67*	62.41 *11.94*	20.96 *3.66*

*Mean completion time and standard deviations (SD) for each hand on the IN and Out conditions of the Grooved Pegboard

Fig 1. The Leonard Tapping Task (LTT)

Fig 2. Motor performances on the Leonard Tapping Task (LTT) between experimental groups and control groups.

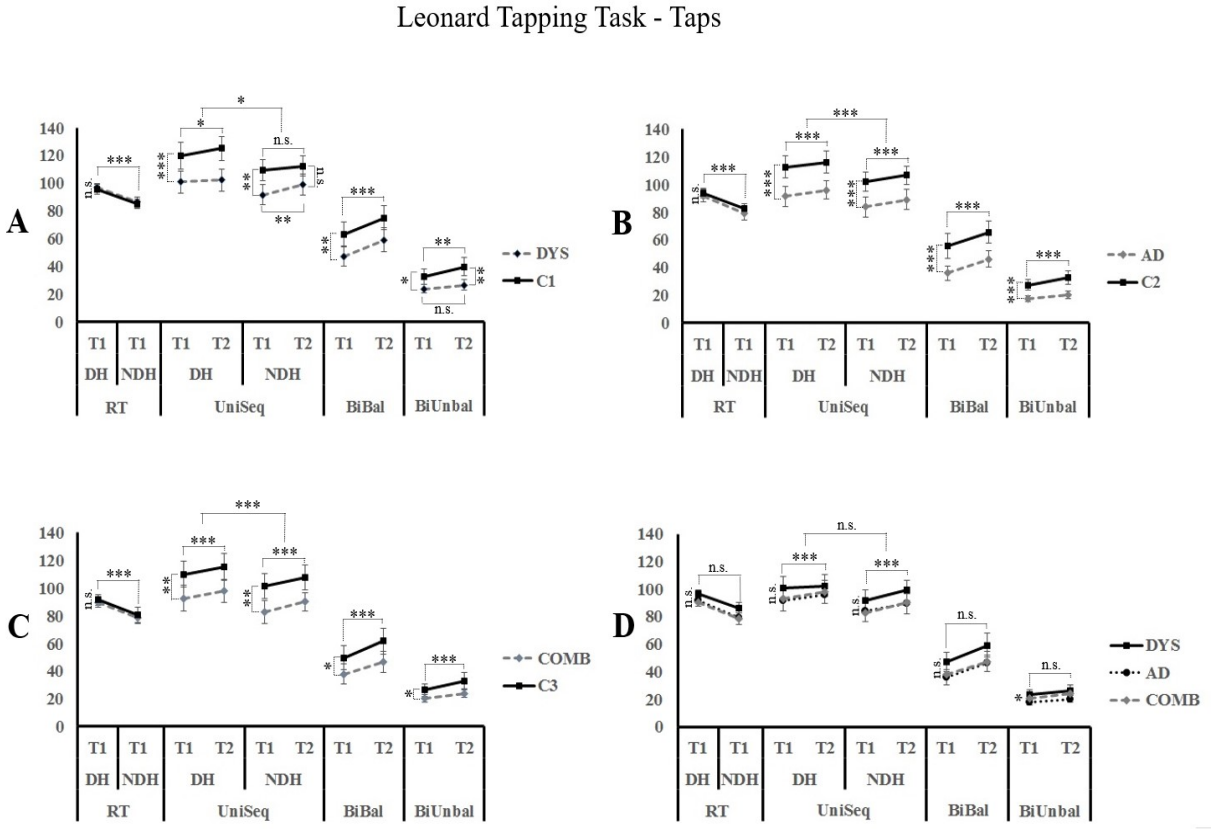

Fig 2. Performances are expressed as the number of correct taps per condition on the LTT between A) dyslexia (DYS) versus controls (C1); B) Attention Deficit Disorder (AD) versus controls (C2); C) Combined Dyslexia and Attention Deficit Disorder (COMB) versus controls (C3); D) Dyslexia (DYS) versus Attention Deficit Disorder (AD) versus Combined dyslexia and Attention Deficit Disorder (COMB). *p < 0.05; **p < 0.01; ***p < 0.001; n.s. = non- significant. Only the simple effects are reported when post-hoc analysis are not required. T1 = Trial 1; T2 = Trial 2; DH = Dominant Hand; NDH = Non-Dominant Hand; RT = Rapid Tapping; UniSeq = Unimanual Sequential; BiBal = Bimanual Balanced; BiUnbal = Bimanual Unbalanced.

Fig 3. Error ratios on the Leonard Tapping Task (LTT) between experimental groups and control groups.

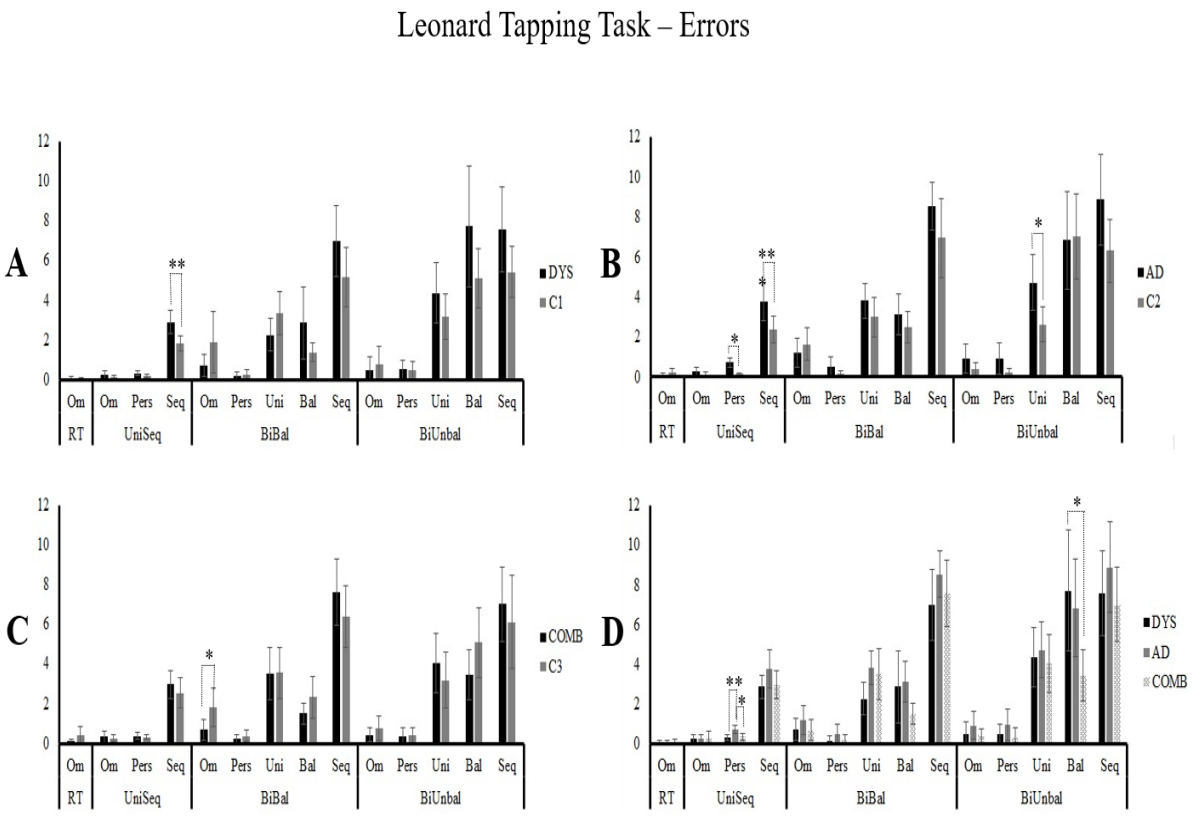

Fig 3. Performances are expressed with the mean ratio of errors per condition, computed with the number of errors of each category (omissions (Om), perseverative (Pers), sequential (Seq), unimanual (Uni), and balanced (Bal)) divided by the number of taps on any given condition of the LTT. Ratios were averaged between the dominant hand (DH) and the non-dominant hand (NDH) for the rapid tapping condition (RT), between the DH and NDH on trial 1 and 2 for the unimanual sequential condition (UniSeq), and between trial 1 and 2 for the bimanual balanced (BiBal) and unbalanced (BiUnbal) conditions. A) dyslexia (DYS) versus controls (C1); B) Attention Deficit Disorder (AD) versus controls (C2); C) Combined Dyslexia and Attention Deficit Disorder (COMB) versus controls (C3); D) Dyslexia (DYS) versus Attention Deficit Disorder (AD) versus Combined dyslexia and Attention Deficit Disorder (COMB). *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$; unreported comparisons are non-significant. Only the simple effects are reported when post-hoc analysis are not required.

Fig 4. Motor performances on the Grooved Pegboard (GPB) between experimental groups and control groups.

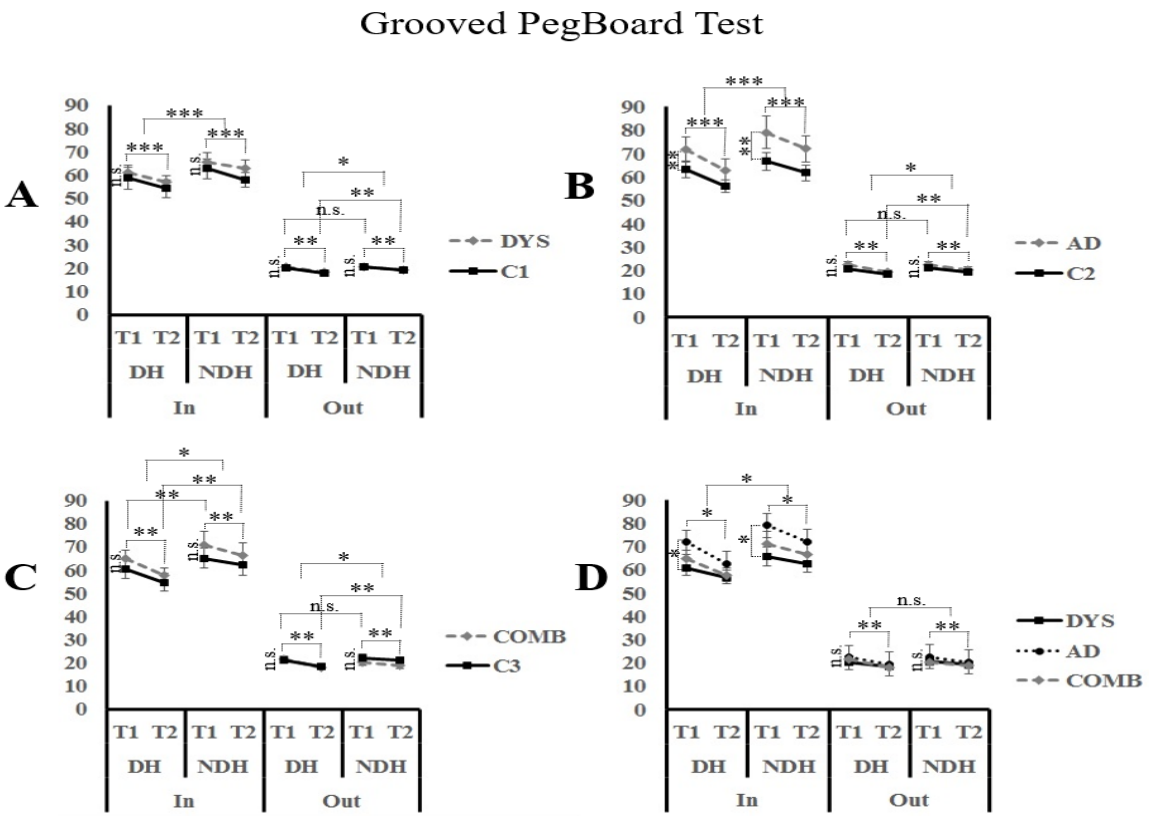

Fig 4. Performances are expressed with the completion times on the GPB between A) dyslexia (DYS) versus controls (C1); B) Attention Deficit Disorder (AD) versus controls (C2); C) Combined Dyslexia and Attention Deficit Disorder (COMB) versus controls (C3); D) Dyslexia (DYS) versus Attention Deficit Disorder (AD) versus Combined dyslexia and Attention Deficit Disorder (COMB)*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$; n.s. = non-significant. Only the simple effects are reported when post-hoc analysis are not required.

Article 2

Cognitive predictors of sequential motor abilities in children wit Dyslexia and/or Attention Deficit/Hyperactivity Disorder

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Abstract

This study examined cognitive predictors of sequential motor skills in 215 children with dyslexia and/or attention deficit/hyperactivity disorder (AD). Visual working memory and math fluency abilities contributed significantly to performance of sequential motor abilities in children with dyslexia (N= 67), AD (N=66) and those with a comorbid diagnosis (N=82), generally without differentiation between groups. In addition, primary diagnostic features of each disorder, such as reading and inattention, did not contribute to the variance in motor skill performance of these children. The results support a unifying framework of motor difficulties in children with neurodevelopmental disorders such as dyslexia and AD.

Keywords: Dyslexia, Attention Deficit/Hyperactivity Disorder, sequential motor skills, cognitive abilities, Atypical Brain Development.

Introduction

Dyslexia and Attention Deficit/Hyperactivity Disorder (AD) are prevalent neurodevelopmental disorders that are characterized by primary diagnostic symptoms, as well as various secondary cognitive dysfunctions (Pennington, 2006; Willcutt et al., 2010; Willcutt & Pennington, 2000). Research efforts to date have focused on explaining the mechanisms underlying both the primary symptoms associated with each disorder as well as the secondary impairments. For instance, the phonological deficit hypothesis suggests that the primary deficit in dyslexia is a lack of phonological awareness, which has been shown to be a reliable diagnostic marker of the disorder (Snowling, 2001; Vellutino, Fletcher, Snowling, & Scanlon, 2004). It has further been posited that this primary phonological decoding deficit can also explain the presence of secondary impairments, such as working memory problems, through an aberrant phonological loop and diminished verbal span (Ramus, 2001; Wilson & Lesaux, 2001). The mechanisms underlying AD may be harder to identify because of the heterogeneous nature of the disorder (Roberts, Martel, & Nigg, 2013), however, a core frontal lobe dysfunction has been proposed to explain the surfeit of accompanying cognitive difficulties (Dickstein, Bannon, Castellanos, & Milham, 2006; Shue & Douglas, 1992). This latter proposal submits that executive functions, such as attentional control and inhibition which are known to depend on the frontal lobes (Hernandez et al., 2002), are consistently associated with primary deficits in AD and can in turn impact other functions such as the ability to maintain and manipulate information in working memory (Barkley, 1997, 2003). While these theories address a number of questions regarding the mechanisms underlying diagnostic features of each disorder, they fall short in adequately explaining the multitude of secondary symptoms and their significant overlap across dyslexia and AD (Gilger & Kaplan, 2001; Kaplan, Dewey, Crawford, & Wilson, 2001; Pennington, 2006)

Notwithstanding the significance of the primary diagnostic symptoms of dyslexia and AD, several studies have highlighted commonalities between dyslexia and AD, such as the high comorbidity rates between the two entities (Germano, Gagliano, & Curatolo, 2010), their similar atypical brain development (Stoodley, 2016), shared genetic risk factors and etiology (Loo et al., 2004; Willcutt et al., 2010), and the presence of common secondary cognitive symptoms (Moura et al., 2016; Shanahan et al., 2006). These latter encompass slowed information processing

(Shanahan et al., 2006), working memory deficits (Alloway, Rajendran, & Archibald, 2009; Menghini, Finzi, Carlesimo, & Vicari, 2011; Tiffin-Richards, Hasselhorn, Woerner, Rothenberger, & Banaschewski, 2008), academic difficulties including mathematical abilities (Czamara et al., 2013; De Clercq-Quaegebeur, Casalis, Vilette, Lemaitre, & Vallee, 2017; Kaufmann & Nuerk, 2008; Morken & Helland, 2013; Pastura, Mattos, & Araujo, 2009) and motor skills problems (Fawcett, Nicolson, & Dean, 1996; Kaiser, Schoemaker, Albaret, & Geuze, 2014; Marchand-Krynski, Morin-Moncet, Belanger, Beauchamp, & Leonard, 2017). While overlapping cognitive difficulties, such as slowed information processing, have been the subject of a growing number of studies (Katz, Brown, Roth, & Beers, 2011; Kibby & Cohen, 2008; McGrath et al., 2011; Willcutt, Pennington, Olson, Chhabildas, & Hulslander, 2005), the observation that both dyslexia and AD typically occur in combination with compromised motor abilities has received relatively little attention (Raberger & Wimmer, 2003; Tiffin-Richards, Hasselhorn, Richards, Banaschewski, & Rothenberger, 2004). Though motor skills are seldom compared across the two disorders, fine and gross motor difficulties have been reported in AD and in dyslexia separately (Iversen, Berg, Ellertsen, & Tonnessen, 2005; Kaiser et al., 2014; Lum, Ullman, & Conti-Ramsden, 2013; Rochelle & Talcott, 2006). In a previous study examining gross sequential motor abilities in children with dyslexia and/or AD, authors reported co-occurring difficulties on unimanual and bimanual sequential coordination, while basic motor speed was preserved (Marchand-Krynski et al., 2017). These findings are supportive of previous reports of impairments in complex sequential motor abilities in both AD and dyslexia (K. A. Barnes, Howard, Howard, Kenealy, & Vaidya, 2010; Lum et al., 2013; Stoodley & Stein, 2013; Yan & Thomas, 2002). The findings are of functional importance because sequential motor skills and coordination are integral to everyday activities and can be associated with diverse difficulties, ranging from academic problems (e.g., writing) to difficulties in athletic performance (e.g., coordination problems during sporting activities; Brossard-Racine, Majnemer, Shevell, Snider, & Belanger, 2011; Lucas et al., 2016; Piek, Baynam, & Barrett, 2006; Wang, Huang, & Lo, 2011). In addition, motor impairments are consistently reported in neurological disorders across the lifespan (Levit-Binnun, Davidovitch, & Golland, 2013; Peralta & Cuesta, 2017), for example, in developmental and degenerative conditions such as Autism Spectrum Disorders and Alzheimer's disease (Scarmeas et al., 2005; Stevenson, Lindley, & Murlo, 2017). Given that motor skill impairments can be an important metric of a fragile brain state, we suggest that poor sequential

motor skills may reflect a common underlying brain vulnerability and be a marker for shared atypical neurodevelopment across dyslexia and AD (Levit-Binnun et al., 2013). Additional studies on shared secondary motor weaknesses could further our understanding of these proposed common underlying mechanisms.

Motor development has been shown to parallel cognitive maturation in typically developing children (E. E. Davis, Pitchford, & Limback, 2011; van der Fels et al., 2015) and therefore to understand the putative role of co-occurring motor difficulties in dyslexia and AD, it is germane to examine links with overlapping cognitive symptoms within the two disorders. Other studies suggest that motor proficiency at a young age predicts cognitive skills such as working memory or academic abilities (Cameron et al., 2012; Murray et al., 2006; Piek, Dawson, Smith, & Gasson, 2008; Roebers et al., 2014), implying developmental association between the two. This putative motor-cognition link has been demonstrated in dyslexia and AD, although separately for each disorder. In this regard poor motor skills have been associated with reduced academic achievement in children with dyslexia or at family risk of dyslexia (Thomson & Goswami, 2008; Viholainen et al., 2006; Westendorp, Hartman, Houwen, Smith, & Visscher, 2011) and in children with AD (A. S. Davis, Pass, Finch, Dean, & Woodcock, 2009; Rubio-Grillo, Salazar-Torres, & Rojas-Fajardo, 2014). Motor abilities have also been linked to executive function, such as working memory in children with AD (Tseng, Henderson, Chow, & Yao, 2004; Ziereis & Jansen, 2016) and in children with dyslexia (Reynolds & Nicolson, 2007).

There are broad unifying frameworks that are applicable to the study of dyslexia and AD, and that may explain the presence of common underlying mechanisms. The Atypical Brain Development theory (Gilger & Kaplan, 2001) and the Multiple Deficit Model (Pennington, 2006) have emerged from studies of the overlapping symptoms within developmental disorders, and describe dyslexia and AD as heterogeneous and multifactorial entities. The Multiple Deficit Model suggests that the plethora of cognitive problems in a single disorder is attributable to the additive and interactive effects of gene and environmental factors that lead to weaknesses in multiple cognitive domains (Pennington, 2006; Willcutt et al., 2010). The Atypical Brain Development theory further suggests a unifying concept of the etiology of neurodevelopmental disorders, where dyslexia and AD could be viewed as different facets of a nonspecific atypical

brain development that affect diverse neurological circuits (Gilger & Kaplan, 2001). These theoretical frameworks are in line with recent systems neuroscience work that attempts to unify a wide range of psychopathologies by describing their common characteristics (Levit-Binnun et al., 2013; Levit-Binnun & Golland, 2011). System neuroscientists posit that invariant secondary symptoms (e.g., motor problems) that are present across neurological disorders could be indicators of disturbances in general networks characteristic of brains that are vulnerable to psychopathologies (Levit-Binnun et al., 2013; Peralta & Cuesta, 2017). These types of common nonspecific vulnerabilities would indicate more large-scale network deficits that affect basic input/output and regulation processing (Menon, 2011). The current study attempts to provide support for possible common aberrant underlying mechanisms that affect secondary, nonspecific abilities in AD and dyslexia.

The principal purpose of the present study was to investigate the relationship between motor difficulties and secondary cognitive impairments in AD and dyslexia. The first objective was to assess primary and secondary cognitive abilities in dyslexia, AD and in the comorbid manifestation of these disorders (Combo). We hypothesized that scores on measures of primary symptoms, namely reading and spelling in dyslexia, and inattention/hyperactivity in AD, would be significantly different according to diagnosis, while scores on secondary cognitive measures, i.e working memory and mathematical abilities, would not differ according to Group (Dyslexia, AD and Combo). The second objective was to explore the potential of a moderating effect of Group membership on the association between cognitive and motor abilities. We hypothesized that Group would not significantly affect the nature of the relationship between cognitive abilities and sequential motor weaknesses, as measured with the Leonard Tapping Task (LTT; Marchand-Krynski et al., 2017). The third objective was to explore the putative role of co-occurring motor difficulties by examining their relationship with cognitive abilities. We hypothesized that shared working memory and academic skills would be significant predictors of performance on the LTT. More specifically, we predicted that secondary cognitive abilities would contribute to gross sequential motor abilities that have been previously shown to be impaired using the LTT. We additionally hypothesized that the effect of cognitive abilities on simple motor speed, which is preserved in dyslexia and AD (Marchand-Krynski et al., 2017) would be low and not clinically significant. Conversely, we predicted that the disorders' primary symptoms (e.g., reading abilities

in dyslexia and inattention in AD) would not predict the common motor difficulties. To our knowledge, few have studied the two disorders in tandem and the relationship between shared secondary motor and cognitive abilities in an attempt to explain their common underlying manifestations.

Methods

Participants

We recruited 240 children with learning impairments, aged 8 to 19 years old, from a special education school for French and English-speaking children in Montreal, Quebec. Children are admitted to this school if they are two years behind in specific classes (French/English and arithmetic classes) and if they have diagnosed learning impairments (reading, spelling, executive functions, etc.). All participants and their legal guardians provided written informed assent/consent and the study was approved by the Montreal Neurological Institute (McGill University) research ethics board and the study is compliant with the 1964 Declaration of Helsinki.

A medical and developmental questionnaire was used to collect information on the participants' history that included information on previous diagnoses of learning disabilities (Attention deficit/hyperactivity disorder, dyslexia, language disorders), medical, and psychiatric disorders. Twenty-five participants were subsequently excluded because their learning disability did not include a diagnosis of dyslexia or AD as reported in the medical questionnaire completed by the parents.

The final study sample was comprised of 215 participants, 67 with dyslexia (Dys), 66 with Attention Deficit Disorder with or without Hyperactivity (AD) and 82 with a combined diagnosis (Combo). Outliers were identified following a 3.5 standard deviation criterion. Four participants had outlier data on the bimanual conditions of the LTT which was replaced with the mean performance of their respective group.

Children who were diagnosed with dyslexia and/or AD in addition to a comorbid diagnosis (e.g., language disorders, birth complications, premature birth and auditory processing disorders)

were included in the experimental groups. We believe that our sample is representative of the high prevalence of other complications or disabilities in the general population of children with dyslexia or AD (Kaplan et al., 2001). Hence, no exclusion criteria were applied, other than the absence of a diagnosis of dyslexia or AD.

Materials

Academic skill measures

The TONI 4 (Test of Non-Verbal Intelligence, Fourth Edition; L. Brown, Sherbenou, & Johnsen, 2010) was used to measure fluid intelligence (IQ) and employs non-verbal abstract reasoning. The examinee must focus on differences and similarities among abstract/figural content and identify the rules leading to the correct response. This non-verbal instrument avoids the possible confounding effects of a person's linguistic or motor skills.

The Wechsler Individual Achievement Test, Second Edition (WIAT-II; Wechsler, 2002) was used to measure academic skills. This standardized assessment battery measures functions typically affected in learning disabilities. Reading skills were measured using Pseudo-Word Decoding for which the examinee must read aloud a list of nonsense words. This subtest evaluates phonetic decoding abilities. Spelling skills were measured with a Spelling subtest during which the participant must write dictated letters, letter blends and words. This subtest evaluates spelling abilities, such as phoneme-grapheme decoding, by assessing errors in written language.

The Math Fluency subtest of the Woodcock-Johnson Test of Achievement-III (Woodcock, Mather, & McGrew, 2001) was chosen to evaluate basic mathematical skills. The examinee must resolve as many mathematical problems (additions, subtractions, multiplications and divisions) as possible in three minutes. This test measures numerical facility through speeded (automatic) retrieval of arithmetic procedures.

Raw scores (number of correct responses) were compared for all three academic tasks (Reading, Spelling and Math Fluency) in order to have comparable data between subtests.

Cognitive and behavioral measures

Attention/Hyperactivity

Conners 3- Parent forms (Conners, 2008) is a behavioral questionnaire that can establish the presence or absence of attention deficit/hyperactivity disorder (ADHD) and other associated problems. The questionnaire features multiple content scales that assess ADHD related problems such as inattention, hyperactivity/impulsivity, executive functioning, learning problems, aggression, and peer/family relations. For the purpose of this study, only the Inattention and Hyperactivity/Impulsivity scales were included.

Visual Working memory

Figure 1. An adapted version of the Petrides Visual Working Memory Task (VWM; Petrides, Frey, & Chen, 2001) is an externally-ordered visual working memory task validated with functional neuroimaging work (Keightley et al., 2014; Stern et al., 2000). The subject is familiarized with a set of five pattern stimuli (abstract paintings). First, a red dot appears, followed by a sequence of four pattern stimuli, randomly selected from the original set. Then, a green dot appears followed by one of the five pattern stimuli. The participant must identify if the last image was present in the previous familiar set of four stimuli. The subject responds by activating the appropriate mouse key (YES or NO). Three practice items are done before beginning the task. The number of correct responses are recorded. This task requires the subject to keep track or monitor the stimuli.

Motor skill measures

The Leonard Tapping Task (LTT; Marchand-Krynski et al., 2017) was used to assess a range of sequential motor skills, more specifically hand/arm movements, from simple (e.g., rapid tapping) to complex motor coordination (e.g., bimanual out of phase/unbalanced movements; see Marchand-Krynski et al., 2017 for an extensive description of the task). The LTT is composed of two symmetrical round metal plates with 4 equally sized quadrants numbered from 1 to 4 on which the subject must tap with a stylus following a sequential order with either one hand at a time or both hands together. Four conditions are administered: condition 1 (unimanual sequential

tapping: UniSeq) is executed with each hand separately, condition 2 (bimanual in-phase/balanced tapping: BiBal) and 3 (bimanual out-of-phase/unbalanced tapping: BiUnbal) are executed with both hands together. All three conditions are repeated twice after the first three trials are completed, without any time interval in between. Condition 4 (rapid tapping: RapidT) is performed which each hand separately over 1 trial, after both trials of conditions 1 to 3 are achieved. The total number of correct taps performed is recorded. For the purpose of this study, the average of both hands (Dominant Hand and Non-Dominant Hand) was analyzed for the unimanual and rapid tapping conditions, and the average performance of Trial 1 and Trial 2 was analyzed for conditions 1 to 3 as well.

Data analyses

Age, gender, and IQ were compared between the three experimental groups (Dys, AD, Combo) using one-way ANOVAs. Preliminary analyses comparing motor performance between clinical groups were rerun to verify the results observed in a previous study of a subset of subjects using the LTT (Marchand-Krynski et al., 2017). Hence, between group differences on the LTT (RapidT; UniSeq; BiBal; BiUnbal) were analysed using one-way ANCOVAs with Group (Dys; AD; Combo) as the between-subject factor and Gender as the covariate. The main analyses were subsequently conducted. Between group differences on academic (Reading; Spelling; Math Fluency) and cognitive ability measures (Inattention, Hyperactivity/Impulsivity, Visual Working Memory) were also analysed using one-way ANCOVAs with Group (Dys; AD; Combo) as the between-subject factor and Gender as the covariate. Post-hoc analyses were conducted accordingly, with Tukey HSD for the simple ANOVAs and with Bonferroni corrected comparisons for the ANCOVAs. Statistical significance was set at $p < 0.05$.

Pearson's partial correlations were computed to examine the relationship between Reading, Spelling, Math Fluency, Inattention, Hyperactivity/Impulsivity, Visual Working Memory, and motor performance on the four conditions of the LTT (RapidT; Uniseq; Bibal; BiUnbal). Age, gender and IQ were used as control variables as there is a linkage with the development of motor abilities (Largo, Fischer, & Rousson, 2003; Smits-Engelsman & Hill, 2012). An effect size correlation of r=.10 was defined as small, r=.30 as moderate and r=.50 as large (Cohen, 1977).

PROCESS macro for SPSS (Hayes & Montoya, 2017) was used to produce a moderation regression analysis. The objective was to measure whether the nature of the relationship between cognitive and motor skills changes according to Group membership. For the purpose of this study, we used a multicategorical moderator: Group (Dys, AD, Combo). Interaction effects were measured with Group (Dys; AD; Combo) as the Moderator variable (M), the motor condition as the dependent variable (Y) and the cognitive task as the independent variable (X). For each test of moderation, Age, Gender, and IQ were entered as covariates. The Johnson-Newman Technique was used to compute for which group (Dys; AD; Combo), as operationalized by M, the independent variable (Reading; Spelling; Math fluency; Inattention; Hyperactivity/Impulsivity; Visual working memory) exerts an effect on the dependent variable (RapidT; UniSeq; BiBal; BiUnbal) with a level of significance at 0.05. The omnibus R2 change (R-square increase due to interaction) inference for the effect of the independent variable at values of M results in a conclusion that there is or is not a difference between the pairs of slopes when M is a specific value.

A hierarchical multiple regression analysis was used to identify the contribution of the cognitive variables to gross sequential motor skills (RapidT, UniSeq, BiBal, BiUnbal), after controlling for the influence of demographic characteristics (Age, Gender, IQ), for all children combined (ALL). Age, Gender and IQ were entered in the first block, and the remaining cognitive variables (i.e. Reading, Spelling, Math Fluency, Attention, Hyperactivity/Impulsivity and Visual Working Memory) were entered in the second block. If a significant moderation interaction was reported, it was estimated separately in the multivariate hierarchical regression where the interaction term was integrated to produce the regression coefficient for each group.

Results

Table 1 displays the descriptive statistics and the results of between group analyses using a simple one-way ANOVA on the demographic variables. No significant differences were found between the groups on age ($F_{(2,214)} = 2.191$; $p = 0.114$) and non-verbal IQ ($F_{(2,214)} = 0.312$; $p = 0.732$). A significant difference was found on gender ($F_{(2,214)} = 5.982$; $p = 0.003$) and Post-hoc Tukey HSD indicated that the Dys group had significantly fewer boys than the AD ($p=0.007$) and Combo

(p=0.009) groups. Hence, in the subsequent between group analyses on the dependant and independent variables, ANCOVAs were produced with Gender as a covariate.

On the tests of academic achievement, when controlling for Gender, the scores on the WIAT-II Reading and Spelling subtests were generally in the expected direction. Groups differed on the Reading test raw scores ($F_{(2,211)} = 13.469$; $p < 0.001$) and the Spelling test raw scores ($F_{(2,211)} = 10.367$; $p < 0.001$). Post-hoc with Bonferroni corrected comparisons indicated that both the Dys and Combo groups scored significantly lower on the Reading subtest ($p< 0.001$) than the AD group, while they did not differ significantly from each other ($p = 1.00$). On the Spelling subtest, both the Dys and Combo groups also scored significantly lower than the AD group ($p= 0.004$), without differing significantly from each other ($p = 1.00$). No group differences were observed on the Math Fluency raw score when controlling for Gender ($F_{(2,211)} = 0.661$; $p = 0.517$).

Parent ratings of Inattention, Hyperactivity/ Impulsivity on the Conners-3 questionnaire for the three groups were analyzed using an ANCOVA with Gender as a covariate. Groups differed on the Inattention ($F_{(2,211)} = 30.523$; $p <0.001$) and Hyperactivity/Impulsivity scales ($F_{(2,211)} = 19.873$; $p<0.001$). Post-hoc with Bonferroni corrected comparisons revealed that the Dys group had significantly lower scores than the AD and Combo groups ($p<0.001$), while the AD and the Combo groups did not differ significantly ($p=0.068$). On the Hyperactivity scale, the same pattern was observed whereby the Dys group was significantly lower than the AD and Combo groups ($p<0.001$), and AD and Combo groups did not differ ($p=1.00$). Hence, parent ratings of Attention deficit/Hyperactivity disorder were in the expected direction on the Inattention and Hyperactivity scales.

On the Visual Working Memory measure (VWM), no differences were observed between groups on the number of correct responses when controlling for Gender ($F_{(2,211)} = 1.633$; $p = 0.198$).

When controlling for Gender, results were generally consistent with a previous study on the motor performance measures (LTT). No group differences between experimental groups were observed on the RapitT ($F_{(2,211)} = 1.430$; $p = 0.242$) and the UniSeq condition ($F_{(2,211)} = 1.181$; $p = 0.309$), but contrary to the previous study (Marchand-Krynski et al., 2017), a main effect of group was observed on the BiBal coordination conditions ($F_{(2,211)} = 3.129$; $p = 0.046$). However, Post-hoc

with Bonferroni corrected comparisons indicated that the Dys group did not perform significantly more taps than the AD group, though a trend was present (p=0.050), while the Combo group did not differ from the Dys or AD groups ($p \geq 0.190$). Finally, consistent with previous reports, a main effect of group was observed on the BiUnbal condition ($F_{(2,211)} = 3.593$; $p = 0.029$). Post-hoc with Bonferroni corrected comparisons revealed that the AD group performed significantly fewer taps then the Dys group (p=0.026) and the Combo group did not differ from the AD or the Dys groups ($p \geq 0.264$).

Partial Correlations and Moderation effect

Tables 2-5 show the partial correlations found between the scores on each condition of the Leonard Tapping Task (RapidT, UniSeq, BiBal, BiUnbal), and the scores obtained on the academic (Reading, Spelling, Math Fluency) and cognitive ability measures (Inattention, Hyperactivity/Impulsivity, Visual Working Memory). The correlations were computed for each clinical group separately (Dys, AD, Combo) and for all groups combined (ALL). The omnibus R2 change (R-square increase due to interaction) from the moderation regression are reported for each variable on each motor condition.

As shown in Table 2, the Rapid Tapping (RapidT) condition was not significantly correlated with Reading for either the Dys, the AD, the Combo or ALL combined groups ($0.096 \leq r \leq 0.226$; $0.075 \leq p \leq 0.452$). RapidT was not significantly correlated with Spelling for either the Dys, Combo or ALL combined groups ($0.043 \leq r \leq 0.113$, $0.102 \leq p \leq 0.733$), though a significant correlation was observed in the AD group ($r_{(61)} = 0.328$, $p=0.009$). RapidT was correlated with Math Fluency in most groups (AD, Combo, ALL) ($0.201 \leq r \leq 0.313$, $0.003 \leq p \leq 0.035$), with the exception of the Dys group ($r_{(62)} = 0.011$, $p=0.928$). Neither Visual Working Memory, Inattention or Hyperactivity/Impulsivity were significantly correlated with RapidT for either group ($0.007 \leq r \leq 0.168$, $0.139 \leq p \leq 0.914$). The R-square increase due to interaction (Table 2) was not significant for either variables. The absence of a significant moderation effect indicates that the association between the performance on the Rapid Tapping and Reading ($R2 = 0.021$, $F_{(2,206)} = 0.250$, $p = 0.779$), Spelling ($R2 = 0.0015$, $F_{(2,206)} = 0.195$, $p = 0.823$), Math Fluency ($R2 = 0.0055$, $F_{(2,206)} = 0.690$, $p = 0.503$), Visual Working Memory ($R2 = 0.0097$, $F_{(2,206)} = 1.447$, p =

0.2376), Inattention (R2 =0.0039, $F_{(2,206)} = 0.569$, p = 0.567) or Hyperactivity/Impulsivity (R2 =0.0098, $F_{(2,206)} = 1.631$, p = 0.198) does not differ significantly according to group membership.

As shown in Table 3, the Unimanual Sequential Tapping condition (UniSeq) was significantly correlated with Reading for the AD ($r_{(61)} = 0.375$, p= 0.002) and ALL ($r_{(219)} = 0.152$, p= 0.027) groups, but not with the Dys ($r_{(62)} = 0.72$, p= 0.570) or Combo ($r_{(77)} = 0.186$, p= 0.101) groups. In the Dys, AD and ALL groups, Spelling was also correlated with UniSeq ($0.174 \leq r \leq 0.303$, $0.011 \leq p \leq 0.029$), while it was not for the Combo group ($r_{(77)} =0.181$, p= 0.110). Math Fluency was significantly correlated with UniSeq for each group ($0.349 \leq r \leq 0.451$, $0.000 \leq p \leq 0.002$). UniSeq was correlated with Visual Working Memory for the Combo ($r_{(77)} =0.349$, p=0.002) and ALL ($r_{(210)} =0.230$, p=0.001) groups, but not for the Dys ($r_{(62)} =0.196$, p=0.120) and AD groups ($r_{(61)} =0.222$, p=0.081). Neither Inattention or Hyperactivity/Impulsivity scales were correlated with UniSeq in either group ($0.004 \leq |r| \leq -0.196$, $p \geq 0.126 \leq 0.975$). The R-square increase due to interaction (Table 3) was not significant for either variables. The absence of a significant moderation effect indicates that the association between the performance on the Unimanual Sequential Tapping and Reading (R2 =0.0057, $F_{(2,206)} = 1.02$, p = 0.363), Spelling (R2 =0.0027, $F_{(2,206)} = 0.482$, p = 0.618), Math Fluency (R2 =0.0015, $F_{(2,206)} = 0.268$, p = 0.765), Visual Working Memory (R2 =0.0014, $F_{(2,206)} = 0.290$, p = 0.749), Inattention (R2 =0.0055, $F_{(2,206)} = 0.813$, p = 0.445) or Hyperactivity/Impulsivity (R2 =0.0008, $F_{(2,206)} = 0.099$, p = 0.906) does not differ significantly according to group membership.

As shown in Table 4, Bimanual Balanced (BiBal) was significantly correlated with Reading in the AD group ($r_{(61)} = 0.280$ p=0.026), but not in the other groups ($0.005 \leq |r| \leq -0.101$, $0.428 \leq p \leq 0.946$). Spelling was not correlated with either groups ($-0.0034 \leq |r| \leq 0.111$, $0.321 \leq p \leq 0.765$). Math Fluency was significantly correlated with BiBal for the Dys, Combo and ALL groups ($0.204 \leq r \leq 0.286$, $0.003 \leq p \leq 0.022$), but not for the AD group ($r_{(61)} = 0.099$, p=0.441). BiBal was significantly correlated with Visual Working Memory, but only for the Combo ($r_{(77)} =0.298$, p=0.008) and ALL groups ($r_{(210)} =0.217$, p=0.001), while it was not the case in the Dys ($r_{(62)} =0.162$, p=0.202) and AD groups ($r_{(61)} =0.202$, p=0.112). The Inattention scale was significantly correlated with BiBal in the ALL combined group ($r_{(210)} = - 0.142$, p=0.039), but not for each individual group ($-0.070 \leq |r| \leq - 0.130$, $0.311 \leq p \leq 0.542$). Finally, the Hyperactivity/Impulsivity

scale was correlated with BiBal for the AD ($r_{(61)}$ =- 0.314, p=0.012) and ALL groups ($r_{(210)}$ = -0.172, p=0.012), but not for the Dys ($r_{(62)}$ =0.003, p=0.984 or Combo groups ($r_{(77)}$ =-0.133, p=0.244). The R-square increase due to interaction (Table 4) was not significant for either variables, apart from the Math Fluency variable. The absence of a significant moderation effect indicates that the association between the performance on the Bimanual Balanced and Reading (R2 =0.022, $F_{(2,206)}$ = 0.717, p = 0.49), Spelling(R2 =0.0016, $F_{(2,206)}$ = 0.233, p = 0.792), Visual Working Memory (R2 =0.0025, $F_{(2,206)}$ = 0.628, p = 0.535), Inattention (R2 =0.0022, $F_{(2,206)}$ = 0.506, p = 0.604) or Hyperactivity/Impulsivity (R2 =0.0013, $F_{(2,206)}$ = 0.381, p = 0.685) does not differ significantly according to group membership. However, the R-square increase due to interaction is significant for the Math Fluency variable (R2 =0.162, $F_{(2,206)}$ = 3.844, p = 0.023). Following the significant interaction term of Math Fluency (X) on Bimanual Balanced coordination (Y), we observed a significantly different effect in the Dys group compared to the AD group (β = -0.302, [-0.478, -0.069], t = -2.643 p =0.009), whereas it was not significantly different between the Dys and Combo groups (β = -0.721, [-0.303, 0.173], t = -0.541 p =0.589) or between the AD and Combo groups (β = 0.230, [-0.018, 0.4352], t = 1.812 p =0.071). Exploration of the conditional effects shows that there is a significantly stronger correlation in the Dys group (β = 0.323, [0.115, 0.470], t = 3. 255 p =0.001) compared to the AD group (β = 0.021, [-0.130, 0.168], t = 0. 248 p =0.804).

As shown in Table 5, Bimanual Unbalanced (BiUnbal) was not significantly correlated with Reading ($0.007 \leq |r| \leq - 0.137$, $0.114 \leq p \leq 0.953$) or Spelling ($0.018 \leq r \leq 0.098$, $0.391 \leq p \leq 0.888$) for either groups. Math Fluency was significantly correlated with BiUnbal for the Combo ($r_{(77)}$ =0.456, p<0.001) and ALL combined ($r_{(210)}$ =0.242, p<0.001) groups, but not for the Dys ($r_{(62)}$ =0.212, p=0.093) or AD groups ($r_{(61)}$ =0.159, p=0.213). BiUnbal was correlated with Visual Working Memory for the ALL group ($r_{(210)}$ = 0.189, p=0.006), but not for either individual group ($0.185 \leq r \leq 0.230$, $0.067 \leq p \leq 0.103$). The Inattention scale was correlated with BiUnbal for the ALL combined group ($r_{(210)}$ = -0.163, p=0.017), but not for each individual group ($- 0.059 \leq |r| \leq -0.235$, $0.062 \leq p \leq 0.605$). Finally, the Hyperactivity/Impulsivity scale was not significantly correlated with BiUnbal for either groups ($-0.095 \leq |r| \leq - 0.115$, $0.095 \leq p \leq 0.458$). The R-square increase due to interaction (Table 5) was not significant for either variables. The absence of a significant moderation effect indicates that the association between the performance on the

Bimanual Unbalanced Tapping and Reading (R2 =0.0005, $F_{(2,206)} = 0.111$, $p = 0.895$), Spelling(R2 =0.0012, $F_{(2,206)} = 0.260$, $p = 0.771$), Math Fluency (R2 =0.0088, $F_{(2,206)} = 2.234$, $p = 0.11$), Visual Working Memory(R2 =0.0063, $F_{(2,206)} = 0.795$, $p = 0.453$), Inattention(R2 =0.0099, $F_{(2,206)} = 2.183$, $p = 0.115$) or Hyperactivity/Impulsivity (R2 =0.0019, $F_{(2,206)} = 0.292$, $p = 0.747$) does not differ significantly according to group membership.

Hierarchical Multiple Regression Analysis

Table 6-9 presents the hierarchical multiple regression analysis for each Leonard Tapping condition. Multicollinearity was tested by examining variance inflation factors (VIFs), and all values were less than 10 (range from 1.102-2.428). Demographic characteristics and IQ were entered in the first block and cognitive abilities were entered in the second block to assess their unique contribution to the variance of motor performances after controlling for Age, Gender and IQ.

As show in Table 6, for the Rapid Tapping condition (RapidT), demographic characteristics entered in block 1 explained 33.1% of the variance for the rapid repetitive tapping performance ($F_{(3,211)} = 34.849$, $p < 0.001$). Age ($\beta = 0.536$, $t = 9.495$, $p < 0.001$), I.Q. ($\beta = 0.206$, $t = 3.631$, $p < 0.001$) and Gender ($\beta = 0.136$, $t = 2.406$, $p = 0.017$) were statistically significant. After entry of the cognitive abilities in block 2, the total variance explained by the model as a whole was 36.4% of the variance of rapid tapping. The cognitive control measures explained an additional 3.3% of the variance of rapid tapping, after controlling for Age, Gender and IQ, and was not statistically significant (R2 =0.33, $F_{(6,205)} = 1.772$, $p = 0.106$).

As shown in Table 7, for the Unimanual Sequential condition (UniSeq), demographic characteristics entered in block 1 explained 36.9% of the variance for the unimanual sequential tapping performance ($F_{(3,211)} = 41.163$, $p < 0.001$). Age ($\beta = 0.596$, $t = 10.861$, $p < 0.001$) and I.Q. ($\beta = 0.120$, $t = 2.179$, $p = 0.030$) were statistically significant, while Gender was not ($\beta = -0.105$, $t = -1.908$, $p = 0.058$). After entry of the cognitive abilities in block 2, the total variance explained by the model as a whole was 48.5%. The cognitive control measures explained an additional 11.6% of the variance of unimanual sequential tapping, after controlling for Age, Gender and IQ (R2 =0.116, $F_{(6,205)} = 7.663$, $p < 0.001$). In the final model, only four measures

were statistically significant, with Age recording the higher beta value ($\beta = 0.368$, $t = 5.479$, $p < 0.001$), followed by Math Fluency ($\beta = 0.332$ $t = 4.828$, $p < 0.001$), Visual Working Memory ($\beta = 0.157$, $t = 2.955$, $p = 0.003$) and Gender ($\beta = -0.113$, $t = -2.528$, $p = 0.012$). IQ, Reading, Spelling, Inattention or Hyperactivity/Impulsivity did not contribute significantly to predicting motor performance on the UniSeq condition ($-0.22 \leq \beta \leq 0.79$, $0.448 \leq t \leq 1.263$, $0.208 \leq p \leq 0.783$).

As shown in Table 8, for the Bimanual Balanced (BiBal), when taking into account the Math Fluency*Group interaction, demographic characteristics entered in block 1 explained 53% of the variance for the bimanual balanced tapping performance ($F_{(8,206)} = 30.698$, $p < 0.001$). Age ($\beta = 0.517$, $t = 7.609$, $p < 0.001$), IQ ($\beta = 0.273$, $t = 5.083$, $p < 0.001$) and Gender ($\beta = -0.129$, $t = -2.401$, $p = 0.017$) were statistically significant. After entry of the cognitive abilities in block 2, and when taking into account the Math Fluency*Group interaction, the model as a whole explained 56.3% of the variance of bimanual balanced tapping. The six cognitive control measures explained an additional 3.3% of the variance of bimanual balanced tapping and was significant ($R2 = 0.033$, $F_{(5,201)} = 7.66$, $p < 0.001$). In the final model, three variables were statistically significant, with Age ($\beta = 0.542$, $t = 7.831$, $p < 0.001$) recording the higher beta value, followed by IQ ($\beta = 0.246$, $t = 4.889$, $p < 0.001$), Visual Working Memory ($\beta = 0.141$, $t = 2.555$, $p = 0.011$) and Gender ($\beta = -0.137$, $t = -2.571$, $p = 0.011$). Reading, Spelling, Inattention and Hyperactivity/Impulsivity did not contribute significantly to the motor output on the BiBal condition ($-0.362 \leq \beta \leq -0.023$, $-1.451 \leq t \leq -0.262$, $0.15 \leq p \leq 0.79$). The interaction term (Math Fluency) was integrated in the multiple regression analysis to take account of the different relationship for each group. For the Dys ($\beta = 0.341$, $t = 3.456$, $p < 0.001$) and Combo ($\beta = 0.251$, $t = 2.555$, $p = 0.041$) group, Math Fluency contributed significantly to the Bimanual Balanced performance, though it did not for the AD group ($\beta = 0.051$, $t = 0.654$, $p = 0.63$).

As shown in Table 9, for the Bimanual Unbalanced condition (BiUnbal), demographic characteristics entered in block 1 explained 46.4% of the variance for the bimanual unbalanced tapping performance ($F_{(3,211)} = 60.822$, $p < 0.001$). Age ($\beta = 0.587$, $t = 11.603$, $p < 0.001$), I.Q. ($\beta = 0.365$, $t = 7.194$, $p < 0.001$) and Gender ($\beta = -0.163$, $t = -3.230$, $p = 0.001$) were statistically significant. After entry of the cognitive abilities in Bloc 2, the total variance explained by the

model as a whole was 53.5%. The six cognitive control measures explained an additional 7.1% of the variance of bimanual unbalanced tapping, after controlling for Age, Gender and IQ ($R2 = 0.535$, $F_{(6,205)} = 5.198$, $p < 0.001$). In the final model, five measures were statistically significant, with Age recording the higher beta value ($\beta = 0.478$ $t = 7.498$, $p < 0.001$), followed by IQ ($\beta = 0.321$, $t = 6.382$, $p < 0.001$), Math Fluency ($\beta = 0.253$, $t = 3.877$, $p < 0.001$), Gender ($\beta = -0.167$, $t = -3.344$, $p = 0.001$) and Visual Working Memory ($\beta = 0.131$ $t = 2.598$, $p = 0.010$). Reading, Spelling, Inattention or Hyperactivity/Impulsivity did not contribute significantly to the prediction of motor performance on the BiUnbal condition ($-0.104 \leq \beta \leq -0.012$, $-1.404 \leq t \leq -0.199$, $0.16 \leq p \leq 0.84$).

In sum, shared secondary cognitive symptoms (Math Fluency and Visual Working Memory), as well as general characteristics (Age, Gender, IQ) best explain the variance in the understanding of sequential motor weaknesses in both neurodevelopmental disorders. Other primary symptoms specific to each disorder, such as Reading and Inattention, do not contribute significantly to motor performances on the Leonard Tapping Task.

Discussion

The main objective of this study was to examine common cognitive predictors of motor performance in dyslexia and AD to further our understanding of the co-occurrence of motor sequential difficulties. Our results suggest that visual working memory and math fluency are shared predictors of sequential motor abilities in both disorders. We note that math fluency did not significantly predict bimanual balanced coordination in the AD group and primary distinct cognitive symptoms, such as reading and inattention, did not significantly contribute to sequential motor abilities in either disorder. These results support the presence of common mechanisms that underlie sequential motor difficulties in dyslexia and AD. Impaired sequential-motor coordination is viewed as a common indicator of brain vulnerability in these neurodevelopmental disorders.

Shared cognitive predictors of sequential motor skills

Our results support a unifying framework of atypical motor development in dyslexia and AD by suggesting that sequential motor difficulties are dependent on similar cognitive mechanisms. These results add to the growing body of evidence that cognitive abilities play a significant role in the normal development of motor skills as well as in neurodevelopmental disorders (Diamond, 2000; Fernandes et al., 2016; Oberer, Gashaj, & Roebers, 2017; Vuijk, Hartman, Mombarg, Scherder, & Visscher, 2011). Specifically, we support findings that link abilities that require more complex processing, such as working memory, to motor proficiency (Rigoli, Piek, Kane, & Oosterlaan, 2012; Rigoli et al., 2013; van der Fels et al., 2015; Wassenberg et al., 2005). Working memory is required to monitor error correction when creating a motor trace (mental representation of the actions) to control subsequent actions (Behmer & Fournier, 2014; Liao, Kronemer, Yau, Desmond, & Marvel, 2014; Russeler, Kuhlicke & Munte, 2003; Seidler, Bo, & Anguera, 2012). It comes as no surprise that this type of ability is required when monitoring a sequence of movements in a novel situation that is rule driven and guided by visual information (Desrochers, Burk, Badre, & Sheinberg, 2015). We suggest that higher-order visual working memory abilities contribute to sequential motor skills in an undifferentiated manner in dyslexia and AD in that the ability to program a motor sequence relies on the ability to maintain and manipulate visually guided information (Desrochers et al., 2015; Jueptner et al., 1997; Sadato, Campbell, Ibanez, Deiber, & Hallett, 1996). Interestingly, impairments in visual working memory have been evidenced in children with a core developmental coordination disorder (DCD; Leonard, Bernardi, Hill, & Henry, 2015), and DCD's neural correlates include the cerebellum and the prefrontal cortex (Biotteau et al., 2016). Imaging studies suggest that motor sequencing is linked to activation of the prefrontal cortex and cerebellum (Jueptner et al., 1997; Molinari et al., 2008), regions that also contribute to higher-order cognitive abilities such as visual working memory (E, Chen, Ho, & Desmond, 2014; Schumacher et al., 1996; Stern et al., 2000). The cerebellum, the prefrontal cortex and their connections have been shown to be implicated in dyslexia and AD (Bush, Valera, & Seidman, 2005; Christodoulou et al., 2014; M. Eckert, 2004; M. A. Eckert et al., 2003; Ortiz et al., 2015) and a possible explanation is that aberrant motor development in dyslexia and AD relies on these networks and thus motor weaknesses are not simply co-occurring, but are part of common nonspecific atypical brain development. This is in line with the

heterogenous nature of the disorders and could be indicative that dyslexia and AD are different facets of common aberrant large-scale neurological networks, as measured through invariant motor symptoms across disorders (Levit-Binnun et al., 2013)

We have shown that math fluency abilities are related to sequential motor skills in a similar manner in dyslexia and AD, in line with reports of a link between math skills and motor abilities (Gomez et al., 2015; Pieters, Roeyers, Rosseel, Van Waelvelde, & Desoete, 2015). Math fluency, which assesses numerical facility as the subject must rapidly access math facts from memory (Woodcock et al., 2001), has been shown to be impaired in both dyslexia and AD (Ackerman, Anhalt, & Dykman, 1986; Friedman, Rapport, Orban, Eckrich, & Calub, 2017; Simmons & Singleton, 2008). There is a wide range of theorized mechanisms that underlie math fact retrieval facility (M. A. Barnes & Raghubar, 2014). Primary amongst these is the serial-order processing deficit that has been reported in populations with dyslexia (Attout & Majerus, 2015; Szmalec, Loncke, Page, & Duyck, 2011). This theory posits that impaired elementary automatization of serial ordering of any type of information (verbal or visuospatial) can lead to fragile long-term memorization of mathematical facts and procedures (De Visscher, Szmalec, Van Der Linden, & Noel, 2015). Others suggest that difficulties with basic number processing can result from impaired inhibitory processes of semantic memory searches, which has been shown to be affected in children with AD (Kaufmann & Nuerk, 2008). Interestingly, hypersensitivity to interference, which is a more general mechanism that could underlie both serial order processing and semantic memory search, has been theorized to explain poor fact retrieval (De Visscher & Noel, 2014). This deficit is a vulnerability to the similarities across mathematical facts that creates interference and leads to poor automatization of facts and to difficulties with manipulating information adequately and processing it rapidly (De Visscher et al., 2015). Although speculative, the same logic can be applied to efficiently executing a motor sequence, where the ability to adequately maintain and follow a rapid sequential movement relies on mechanisms that are vulnerable to interference of the processing of similar order information, and relies on error and repetition priming (Molinari et al., 2008). Together our results show that the pattern of expression of sequential motor difficulties in dyslexia and AD rely on shared cognitive abilities in an undifferentiated manner. Future neuroimaging studies could jointly examine the presence of

common aberrant mechanisms that underlie visual working memory, math fluency and sequential motor skills in dyslexia and AD.

The shared cognitive abilities as measured in the current study did not contribute significantly to the rapid tapping condition, which is known to rely on basic motor speed kinematics (Boecker et al., 1994). Notably, simple motor speed was shown to be unimpaired in children with dyslexia and AD (Marchand-Krynski et al., 2017). Hence, one possible interpretation is that the relation observed between cognition and motor skills is applied specifically to sequencing skills. Although the current results generally support this hypothesis, we cannot distinguish the contribution of cognitive abilities between unimanual and bimanual coordination as sequencing is required in both conditions. However, some indicators of a differentiation are present and could suggest discriminating mechanisms that arise when the complexity of the sequential motor task increases because of a bimanual element (Rueda-Delgado et al., 2014). Indeed, for the bimanual balanced condition, math fluency did not predict the performance in the AD group, while it did in the dyslexia and combo groups. Interestingly, a significant difference was observed between groups on the bimanual balanced condition, but only a trend was observed where children with dyslexia had better performances than the AD group, which further supports a possible differentiation between disorders. One possible explanation is that children with AD rely on different mechanisms during this task. For example, atypical within and between hemispheric communication has been reported in children with AD (McLeod, Langevin, Dewey, & Goodyear, 2016) and could affect bimanual coordination (Rueda-Delgado et al., 2014). However, this differentiation pattern with math fluency did not reappear in the most complex bimanual unbalanced condition, where children with AD were additionally impaired. Hence, it is possible that the low probability value of the moderation effect on the bimanual balanced is due to multiplicity of testing. Future studies could investigate bimanual balance and bimanual unbalanced coordination, while also controlling for sequential movements. Additional cognitive measures are also needed to examine the possible differentiated mechanisms underlying bimanual motor performances in dyslexia and AD.

Primary diagnostic features and sequential motor skills

Our study additionally suggests that primary diagnostic symptoms, namely reading in dyslexia and inattention/hyperactivity in AD, did not significantly contribute to sequential motor abilities nor was this relation differentiated between groups. This further supports the hypothesis that non-specific shared secondary symptoms can better explain sequential motor difficulties in both disorders, and supports the hypothesis of a unitary etiology leading to motor difficulties in dyslexia and AD (Gilger & Kaplan, 2001; Levit-Binnun et al., 2013). Importantly, the absence of a direct link between reading and motor skills is in accordance with studies that have not reported a relation, particularly in dyslexia (Irannejad & Savage, 2012; Ramus, Pidgeon, & Frith, 2003). Contrary to the Cerebellar Deficit Hypothesis that has frequently suggested a link between reading and motor skills (Fawcett et al., 1996; Nicolson, Fawcett, & Dean, 2001), some authors suggest that impaired cerebellar functioning is not the primary cause of dyslexia, but is part of a widespread neurodevelopmental abnormality which leads to the dyslexic phenotype (Stoodley & Stein, 2013). Our current study supports this by showing that even though motor sequencing abilities are impaired, the characteristic impairment in automatizing phonological codes in dyslexia is not primarily linked to motor sequence decoding (Viholainen et al., 2011). Hence, we do not lessen the importance of the motor system or the cerebellum in the general phenotype, but describe motor problems as a secondary symptom that is linked to a more general atypical development measured with non-specific abilities, such as working memory. The same reasoning can be applied to attention and hyperactivity that are key symptoms in AD (Association, 2013; Willcutt, 2012) in that our results suggest that they do not affect motor sequencing performances in either disorder. The current results do not align with studies that have linked attention to motor abilities (Chaix et al., 2007; Tseng et al., 2004). Intuitively, the attention-motor link is not surprising as moment-to-moment attentional control is inherent to motor actions that range from simple sensorimotor feedback to higher order complex movements (Desrochers et al., 2015; Jueptner 1997). The purpose of the current study was not to negate the importance of attention in proficient motor skills, but rather to underscore that the diagnostic symptomatology of AD (validated with performance on the Conners-3; Conners, 2008), cannot of itself justify the presence of sequential motor weaknesses but that the shared cognitive symptoms across dyslexia and AD can better explain motor difficulties. Future studies could define and assess different

behavioral, as well as cognitive components of attention and hyperactivity in order to establish better its role in motor sequential abilities across both disorders. Our results suggest that spelling ability does not contribute to motor sequencing abilities in either dyslexia or AD and the results correspond with studies that find that spelling is not directly associated with motor abilities (Asberg Johnels, Kopp, & Gillberg, 2014; Sumner, Connelly, & Barnett, 2014; Westendorp et al., 2011), but rather with cognitive abilities such as phonological decoding and working memory (Dekker, Ziermans, Spruijt, & Swaab, 2017; Morken & Helland, 2013). Although spelling deficits are reported in both disorders (Alves, Casella, & Ferraro, 2016), the presence of significant differences between groups in the current study does not support this ability as a shared symptom across dyslexia and AD. Indeed, studies have reported that the mechanisms underlying spelling abilities differ in dyslexia and AD (Re & Cornoldi, 2015). For example, spelling errors originate from core phonological decoding difficulties in dyslexia, while in AD errors are associated with inattention to detail and poor processing speed that leads to errors of omission rather than incorrect phoneme-grapheme association (Adi-Japha et al., 2007; Morken & Helland, 2013). Our results support the hypothesis that shared cognitive abilities, which in turn suppose similar underlying mechanism, contribute to common motor difficulties, while differentiated abilities do not. Future studies could analyse the link between spelling and sequential motor abilities through mediation models using cognitive abilities that have been shown to be primarily linked to spelling, as well as to motor abilities, such as inhibition or working memory.

Age, Gender and IQ as predictors of motor skills

It is important to note that age, gender and non-verbal IQ were also significant predictors of motor abilities for most motor conditions and explained a large percentage of the variance, ranging from 33.1 % to 53 %. This is in line with reports of a positive relationship between age, IQ and increased motor proficiency (Largo et al., 2003; Smits-Engelsman & Hill, 2012), as well as gender differences in abilities such as motor speed (Denckla, 1973; Kokstejn, Musalek, & Tufano, 2017; Larson et al., 2007). These results also support a general network vulnerability approach to neurological disorders; age, gender and IQ are characteristics associated with whole brain function, through efficient myelination for example (Deoni, Dean, Remer, Dirks, & O'Muircheartaigh, 2015), and their link to poor motor skills could indicate a more large-scale

network atypicality. Neuroimaging studies have reported that age, gender and IQ can be associated with differences in white and gray matter density in diverse brain regions, including motor areas such as the frontal cortex and the cerebellum (Pangelinan et al., 2011; Ramsden et al., 2011). Notably, studies have reported lower white and gray matter density in subjects with dyslexia and those with AD (W. E. Brown et al., 2001; Makris, Biederman, Monuteaux, & Seidman, 2009). However, the current study does not differentiate the effects of age, gender and IQ from simple motor speed, as all three were primarily linked to motor speed. Future studies could further investigate the reported relation between age, gender, IQ and motor speed versus more complex motor skills in neurodevelopmental disorders, as well as the link between white/gray matter density and motor proficiency.

Theoretical implications

The current study is in line with cumulative observations of overlapping symptoms in dyslexia and AD, and supports emerging theoretical frameworks such as the Multiple Deficit Model (Pennington, 2006). This theory describes neurodevelopmental disorders as syndromes that emerge from complex gene and environment interactions which translates into multiple disorders with consistent overlapping symptoms. The comorbid group results in the current study supports the Multiple Deficit Model by suggesting that the presence of both disorders does not necessarily lead to added severity in difficulties, but rather to a combination of factors that lead to the presence of multiple symptoms. The Atypical Brain Development theory additionally posits a unifying concept of the etiology of neurodevelopmental disorders. The current study supports this view and suggests that motor weaknesses could be an important indicator of an atypical development that affects more general nonspecific brain networks and develops into similar symptoms across the wide range of developmental disorder. Emerging frameworks in systems neuroscience suggest that invariant secondary motor impairments across neurological disorders could be a marker of a brain that is vulnerable to psychopathologies (Levit-Binnun et al., 2013). In the current study, we support the presence of common underlying mechanisms in children with dyslexia and AD that contribute to the patterns of co-occurring sequential motor difficulties and suggest that this could indicate common brain vulnerability across disorders. Hence, we encourage a unifying framework of neurodevelopmental disorders and suggest that the examination of common secondary motor

weaknesses and their link to cognitive abilities could be a key factor in our understanding of neurodevelopmental disorders.

Clinical implications

The current study also supports the use of motor tasks, and more specifically ones that require sequential abilities, as important tools in the assessment of neurodevelopmental disorders. Clinicians could also examine motor sequencing skills as an early screening of young subjects and for subjects with unclear cognitive profiles to support the presence of a neurodevelopmental disorder. In addition, by suggesting a link between cognitive abilities and sequential movements, we provide support for the use of intervention tools that require both motor sequencing skills and cognitive abilities (Schmidt et al., 2017). Although still at an early stage, there is growing evidence supporting the efficacy of interventions that target both motor and cognitive abilities (Beck et al., 2016; Dahan, Ryder, & Reiner, 2016).

Limitations

While our results support a unifying framework of dyslexia and AD, we cannot confirm that it is not due to the presence of other comorbid disorders that can affect abilities such as visual working memory, or to overlapping primary symptoms that were present in individual subjects. Diagnoses were based on parent reports in a medical questionnaire and clinical diagnostic scores on cognitive tests (standard scores) were not analyzed. We believe, however, that the subjects in the study are representative of the heterogenous nature of the disorders and are an important portion of children that require interventions in a specialized school. Future studies could have more varied cognitive tasks in order to differentiate what components are common between disorders, such as in math fluency, as well as explore the possible differentiating mechanisms underlying the added motor difficulties in AD. We did not control for writing speed in the math fluency test, although some authors have suggested that it could explain a small part of mathematical problems (Pieters, Desoete, Van Waelvelde, Vanderswalmen, & Roeyers, 2012). The absence of a significant relation between reading, spelling and motor skills could also be due to the absence of a time limit, as processing speed has been suggested as an important link between motor skills and academic skills (Shanahan et al., 2006). Hence, both motor and cognitive processing speed

should be readily included in future studies that jointly assess the cognitive-motor relation in dyslexia and AD.

Conclusion

In conclusion, sequential motor difficulties have been previously reported in dyslexia and AD and the current study reports that shared visual working memory and math fluency abilities contribute to sequential motor weaknesses in both disorders. To our knowledge, this is the first study to compare the motor-cognition association in two developmental disorders and to support that the co-occurring motor difficulties rely on similar networks. We encourage a unifying framework of neurodevelopmental disorders and the assessment of sequential motor skills to comprehend better the proposed framework.

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Table 1. Descriptives.

		Dyslexia (n=67)	AD (n=66)	COMBO (n=82)	ALL (n=215)
Gender	***Females***	35	18	24	77
	Males	32	48	58	138
Age*		13.61 *(2.51)*	12.82 *(2.60)*	12.80 *(2.67)*	13.06 *(2.61)*
TONI-4*		98.70 *(11.03)*	97.56 *(10.20)*	98.93 *(11.50)*	98.44 *(10.93)*
WIATT-II*	***Reading***	34.54 *(9.73)*	42.41 *(7.77)*	36.01 *(9.46)*	37.52 *(9.61)*
	Spelling	26.55 *(5.90)*	30.05 *(7.37)*	25.43 *(5.81)*	27.20 *(6.62)*
Woodcock-Johnson-III*	***Math Fluency***	60.12 *(21.31)*	61.59 *(21.64)*	57.82 *(19.04)*	59.69 *(20.54)*
Visual Working Memory*		14.66 *(2.34)*	14.09 *(2.82)*	13.94 *(2.88)*	14.21 *(2.71)*
Conners 3 (Parent)*	***Inattention***	58.12 *(12.11)*	73.67 *(11.57)*	69.18 *(12.02)*	67.11 *(13.44)*
	Hyperactivity	51.18 *(10.05)*	65.59 *(14.83)*	64.59 *(15.11)*	60.72 *(15.03)*
LTT scores*	***RapidT***	86.11 *(10.99)*	89.94 *(11.82)*	84.58 *(10.64)*	84.86 *(11.11)*
	UniSeq	94.81 *(19.07)*	88.74 *(17.41)*	91.99 *(20.89)*	91.87 (19.37)
	BiBal	50.11 *(21.50)*	41.58 *(15.11)*	43.71 *(17.92)*	45.05 *(18.60)*
	BiUnbal	24.69 *(10.56)*	20.08 *(7.66)*	22.59 *(7.85)*	22.48 *(8.88)*

RapidT, Rapid Tapping; UniSeq, Unimanual Sequential Tapping; BiBal, Bimanual Balanced Tapping; BiUnbal, Bimanual Unbalanced Tapping. *Means and standard deviations (SD). Raw scores are reported for the WIAT-II, Woodcock Johnson-III, Visual Working Memory and LTT measures. Standard scores for the TONI-4 and T-scores for the Conners 3 are reported.

Table 2. Partial correlations[a] between Rapid Tapping and cognitive test scores.

RAPID TAPPING		Dyslexia (n=67)	AD (n=66)	COMBO (n=82)	ALL (n=215)	$R^{2\,b}$
WIATT-II	***Reading***	0.096	0.226	0.147	0.122	**0.0021**
	Spelling	0.043	0.328**	0.095	0.113	**0.0015**
Woodcock-Johnson-III	***Math Fluency***	0.011	0.313*	0.238*	0.201**	**0.0055**
Visual Working Memory		0.014	- 0.083	0.168	0.038	**0.0091**
Conners 3 (Parent)	***Inattention***	- 0.066	0.121	- 0.042	- 0.009	**0.0039**
	Hyperactivity	- 0.071	0.169	- 0.044	0.007	**0.0098**

a) Control variables: Age - Gender – IQ. b) R^2 interaction term for the moderation effect by group
*Significant at $\alpha < 0.05$. **Significant at $\alpha < 0.01$. ***Significant at $\alpha < 0.001$.

Table 3. Partial correlations[a] between Unimanual Sequential Tapping and cognitive test scores.

UNIMANUAL SEQUENTIAL TAPPING		Dyslexia (n=67)	AD (n=66)	COMBO (n=82)	ALL (n=215)	$R^{2\,b}$
WIATT-II*	***Reading***	0.072	0.375**	0.186	0.152*	**0.0057**
	Spelling	0.273*	0.303*	0.181	0.174*	**0.0027**
Woodcock-Johnson-III*	***Math Fluency***	0.379*	0.451***	0.349**	0.369***	**0.0015**
Visual Working Memory*		0.196	0.222	0.290*	0.230**	**0.0014**
Conners 3 (Parent)*	***Inattention***	- 0.099	- 0.195	0.004	- 0.079	**0.0055**
	Hyperactivity	0.044	- 0.103	- 0.060	- 0.046	**0.0008**

a) Control variables: Age - Gender – IQ. b) R^2 interaction term for the moderation effect by group
*Significant at $\alpha < 0.05$. **Significant at $\alpha < 0.01$. ***Significant at $\alpha < 0.001$.

Table 4. Partial correlations[a] between Bimanual Balanced Tapping and cognitive test scores.

BIMANUAL BALANCED TAPPING		Dyslexia (n=67)	AD (n=66)	COMBO (n=82)	ALL (n=215)	R^2 [b]
WIATT-II*	***Reading***	- 0.101	0.280*	0.049	0.005	**0.0022**
	Spelling	- 0.064	0.111	- 0.034	- 0.069	**0.0016**
Woodcock-Johnson-III*	***Math Fluency***	0.286*	0.099	0.281*	0.204**	**0.0162***
Visual Working Memory*		0.162	0.202	0.298**	0.217**	**0.0025**
Conners 3 (Parent)*	***Inattention***	- 0.107	- 0.130	- 0.070	- 0.142*	**0.0022**
	Hyperactivity	0.003	- 0.314*	- 0.133	- 0.172*	**0.0013**

a) Control variables: Age - Gender – IQ. b) R^2 interaction term for the moderation effect by group
*Significant at $\alpha < 0.05$. **Significant at $\alpha < 0.01$. ***Significant at $\alpha < 0.001$.

Table 5. Partial correlations[a] between Bimanual Unbalanced Tapping and cognitive test scores.

BIMANUAL UNBALANCED TAPPING		Dyslexia (n=67)	AD (n=66)	COMBO (n=82)	ALL (n=215)	R^2 [b]
WIATT-II*	***Reading***	- 0.137	- 0.066*	0.007	- 0.109	**0.0005**
	Spelling	- 0.044	0.018	0.098	- 0.054	**0.0012**
Woodcock-Johnson-III*	***Math Fluency***	0.212	0.159	0.456***	0.242***	**0.0088**
Visual Working Memory*		0.230	0.214	0.185	0.189**	**0.0063**
Conners 3 (Parent)*	***Inattention***	- 0.235	- 0.109	- 0.059	- 0.163*	**0.0099**
	Hyperactivity	- 0.095	- 0.111	- 0.096	- 0.115	**0.0019**

a) Control variables: Age - Gender – IQ. b) R^2 interaction term for the moderation effect by group
*Significant at $\alpha < 0.05$. **Significant at $\alpha < 0.01$. ***Significant at $\alpha < 0.001$.

Table 6: Hierarchical Multiple Regressions on Rapid Tapping scores for all participants (N=215)

Model	Predictor variables	β	*T*	*p*	R^2	ΔR^2
1	***(constant)***		4.229	<0.001***	0.331***	
	Age	0.536	9.465	<0.001***		
	Gender	0.136	2.406	0.017*		
	IQ	0.206	3.631	<0.001***		
2	***(constant)***		3.554	<0.001***	0.364***	0.033
	Age	0.420	5.629	<0.001***		
	Gender	0.115	1.967	0.051		
	IQ	0.321	6.382	<0.001***		
	Spelling	-0.019	-0.221	0.825		
	Math Fluency	0.191	2.499	0.013*		
	Reading	0.086	1.239	0.217		
	Visual Working Memory	0.012	0.197	0.844		
	Inattention	-0.017	-0.246	0.806		
	Hyperactivity	0.024	0.335	0.738		

β, standardized regression coefficient; R^2, combined explained variance of predictor variables included in the model; ΔR^2, change in explained variance from Model 1 to Model 2;
*Significant at $\alpha < 0.05$. **Significant at $\alpha < 0.01$. ***Significant at $\alpha < 0.001$.

Table 7: Hierarchical Multiple Regressions on Unimanual Sequential Tapping scores for all participants (N=215)

Model	Predictor variables	β	*T*	*P*	R^2	ΔR^2
1	***(constant)***		1.717	0.87	0.369***	
	Age	0.596	10.861	<0.001***		
	Gender	-0.105	-1.908	0.058		
	IQ	0.120	2.179	0.030*		
2	***(constant)***		1.650	0.100	0.485***	0.116***
	Age	0.368	5.479	<0.001***		
	Gender	-0.133	-2.528	0.012*		
	IQ	0.038	0.717	0.474		
	Spelling	-0.022	-0.276	0.783		
	Math Fluency	0.332	4.828	<0.001***		
	Reading	0.079	1.263	0.208		
	Visual Working Memory	0.157	2.955	0.003**		
	Inattention	-0.050	-0.788	0.431		
	Hyperactivity	0.028	0.448	0.654		

β, standardized regression coefficient; R^2, combined explained variance of predictor variables included in the model; ΔR^2, change in explained variance from Model 1 to Model 2;
*Significant at $\alpha < 0.05$. **Significant at $\alpha < 0.01$. ***Significant at $\alpha < 0.001$.

Table 8: Hierarchical Multiple Regressions on Bimanual Balanced Tapping scores for all participants (N=215) taking into account the Math Fluency*Group interaction term

Model	Predictor variables		β	*T*	*P*	R^2	ΔR^2
1	***(constant)***			-3.233	0.001**	0.53***	
	Age		0.517	7.609	<0.001***		
	Gender		-0.129	-2.401	0.017*		
	IQ		0.273	5.083	<0.001***		
2	***(constant)***			-2.821	0.005**	0.563***	0.033***
	Age		0.542	7.831	<0.001***		
	Gender		-0.137	-2.571	0.011*		
	IQ		0.246	4.889	<0.001***		
	Spelling		-0.129	-1.451	0.148		
	Reading		0.036	0.654	0.514		
	Visual Working Memory		0.141	2.555	0.011*		
	Inattention		-0.017	-0.262	0.794		
	Hyperactivity		-0.071	-1.243	0.215		
	Math Fluency	***Dyslexia***	0.341	3.456	<0.001***		
		AD	0.051	0.654	0.631		
		Combo	0.251	2.555	0.041*		

AD, Attention Deficit/Hyperactivity Disorder; Combo, Comorbid Dyslexia and AD

β, standardized regression coefficient; R^2, combined explained variance of predictor variables included in the model;ΔR^2, change in explained variance from Model 1 to Model 2;

*Significant at α < 0.05. **Significant at α <0.01. ***Significant at α <0.001.

Table 9: Hierarchical Multiple Regressions on Bimanual Unbalanced Tapping scores for all participants (N=215)

Model	Predictor variables	β	*T*	*P*	R^2	ΔR^2
1	***(constant)***		-5.588	<0.001***	0.464***	
	Age	0.587	11.603	<0.001***		
	Gender	-0.163	-3.230	0.001**		
	IQ	0.365	7.194	<0.001***		
2	***(constant)***		-3.854	<0.001***	0.535***	0.071***
	Age	0.478	7.498	<0.001***		
	Gender	-0.167	-3.344	0.001**		
	IQ	0.321	6.382	<0.001***		
	Spelling	-0.104	-1.404	0.162		
	Math Fluency	0.253	3.877	<0.001***		
	Reading	-0.074	-1.243	0.215		
	Visual Working Memory	0.131	2.598	0.010*		
	Inattention	-0.058	-0.955	0.341		
	Hyperactivity	-0.012	-0.199	0.843		

β, standardized regression coefficient; R^2, combined explained variance of predictor variables included in the model; ΔR^2, change in explained variance from Model 1 to Model 2;
*Significant at $\alpha < 0.05$. **Significant at $\alpha < 0.01$. ***Significant at $\alpha < 0.001$.

Figure 1. Adapted version of the Petrides Visual Working Memory Task (VWM)

a. Five abstract paintings of the VWM task

b. Examples of trials

Figure 1. Adapted version of the Petrides Visual Working Memory Task (Petrides et al., 2001). (a) The subject is familiarized with five abstract paintings (b) A red dot appears, followed by four of the five paintings presented one at a time. A green dot appears, followed by one painting, and the subject must identify by pressing on a key board (YES or NO) if the fifth painting was among the four previously shown images. Total correct score is computed (number of correct answers).

Discussion

Children with dyslexia and/or attention deficit/hyperactivity disorder (AD) encounter significant motor challenges. Although motor impairments in children with dyslexia or AD have been explored in the past, few have focused on what components of motor skill planning are affected. Results have also been inconsistent, in part due to the wide array of tools used across studies, which then renders their interpretation difficult. Moreover, few studies have explored the range of aspects related to motor impairments in dyslexia and AD in order to understand their co-occurrence. The present thesis aimed to assess simple to complex motor skills in both disorders, as well as their association with cognitive abilities. The primary goal was to investigate what components of motor complexity are similarly impaired in dyslexia and AD. The second goal was to examine the association between co-occurring motor and cognitive difficulties. The obtained results are discussed in the light of unifying theoretical frameworks of neurodevelopmental disorders. Future research avenues and clinical implications are addressed, as well as the limitations of this thesis.

In summary, the first article reports on co-occurring difficulties in gross sequential motor skills as well as preserved motor speed in dyslexia and AD. Motor adaptation is also generally preserved in both disorders, although children with either disorder make more errors than their typically developing peers. In addition, the presence of dexterity weaknesses and added difficulties with bimanual out-of-phase coordination in the group of children with AD suggests that the motor functioning profiles of the two disorders are not identical notwithstanding the commonalities. The second article suggests that shared cognitive abilities, namely visual working memory and math fluency, contribute significantly to the co-occurring motor difficulties in unimanual and bimanual sequential motor planning, generally without distinction between disorders. Moreover, diagnostic features of each disorder, such as reading and inattention, are not associated with sequential motor skills, further supporting the presence of similar mechanisms underlying motor difficulties in both dyslexia and AD.

Dyslexia and AD: A common large-scale vulnerable brain state

The results support an integrative approach to the empirical investigation of neurodevelopmental disorders and highlight the importance of including an assessment of co-occurring secondary

motor difficulties. Current conceptions, drawn from the field of systems neuroscience, suggest that the brain operates within large-scale neural networks organized nonlinearly into coherent networks that work together to support cognition and underlie behavior (Levit-Binnun et al., 2013; Levit-Binnun & Golland, 2011; Menon, 2011). Menon and colleagues (2011) suggest that abnormal signaling can arise from damage of nodes (brain regions) and/or edges (the connections) that spreads to the whole brain network or, at least, to large subnetworks across the brain (Menon, 2011). More specifically, if smaller brain architecture metrics develop abnormally and affect general network functioning, this can result in inefficient or slower large-scale information transfer between subcortical-cortical and cortical-cortical regions (Levit-Binnun et al., 2013). The consequence of the latter is a failure of basic input, output, and regulation processes (Chan et al., 2009). The network perspective is also in line with the view that large-scale brain vulnerability can be explored by focussing on invariant non-specific/secondary impairments present across neurological disorders and that represent a common failure of basic processing, such as motor irregularities (Levit-Binnun et al., 2013). Studies examining non-specific motor symptoms have often used ‘‘neurological soft signs’’ (NSS) assessment batteries, which are defined as subtle non-localizable neurological abnormalities (Chan et al., 2010; Chan et al., 2009; Jahn et al., 2006; Pitzianti et al., 2017). NSS include motor coordination and sequencing abilities, such as finger to thumb apposition, mirror movements and heel to toe opposition (Pitzianti et al., 2017). However, the abilities measured vary from one study to the next and have mostly been examined in adult populations with schizophrenia (Peralta & Cuesta, 2017). Hence, in the current thesis, a tool that rapidly assessed different components of motor skill planning was used to help define what aspects of motor skills were similarly affected in children with both dyslexia and AD. Furthermore, the ability to plan a sequence was examined to determine similarities in their atypical neurodevelopment, and rule driven motor sequencing emerged as an invariant secondary motor weakness across dyslexia and AD. Notably, the presence of a group with comorbid dyslexia and AD whose cognitive and motor performances did not differ from the Dyslexia and AD groups also supported the presence of a more generalized network failure, rather than the addition of more severe specific brain anomalies (Gilger & Kaplan, 2001). Thus, the presence of co-occurring sequential motor difficulties across dyslexia and AD, in addition to comparable associations between cognition and their motor difficulties, was viewed as an indicator that motor symptoms rely on similar large-scale brain networks and could indicate a common vulnerable brain state.

Commonalities in dyslexia and AD: from preserved motor speed to difficulties in sequence planning

We reported that basic motor speed is preserved comparably in dyslexia and AD, and this supports the idea that this particular kinematic ability is unaffected when measured over a very short time-lapse. Hence, the initial quick output of repetitive tapping is not slow compared to typically developing peers in either disorder. However, when basic speed was coupled with a rule driven movement, in this case a sequence, atypical performances emerged in children with dyslexia and/or AD. As previously mentioned, producing movements in a certain order relies on more complex planning at a behavioral and anatomical level (Gazzaniga et al., 2009; Hanakawa et al., 2008), especially in a novel setting where cognitive monitoring is needed to process visual information and to control a predetermined pattern (Desrochers et al., 2015; Sadato et al., 1996). Therefore, despite the relative simplicity of the sequence, in the sense that repeating a simple 1-2-3-4 pattern of hand/arm movements is intuitively less complex than playing a sport, the addition of a motor sequential rule was detrimental in both dyslexia and AD. Nevertheless, children with dyslexia, AD or both were generally able to adapt to this novel task and showed fast behavioral gains, which suggests that the mechanisms underlying motor adaptation are not affected. Motor adaptation has been shown to rely on several mechanisms, such as cognitive abilities and kinematics (Penhune & Steele, 2012). One could posit that children with dyslexia or AD have typical adaptation potential in the speed kinematic, which enables them to improve their performance over a short time span (Doyon et al., 2003). Nonetheless, they made more sequencing errors than their typically developing peers, and baseline as well as post adaptation sequential performances remained poor, supporting the hypothesis that other factors in the rapid monitoring of a novel movement is malfunctioning, such as the cognitive load associated with sequence planning (Desrochers et al., 2015; Jueptner et al., 1997). It is important to note that the motor difficulties were observed during the unimanual sequential condition and that the cognitive abilities predicted the larger portion of the variance in this condition above and beyond demographic variables. This suggests that the presence of a sequencing rule using one hand is already more demanding for these children. Hence, the current study does not address the add on effect of increased complexity when using bimanual sequential coordination, although it has been repeatedly shown to be more demanding and to rely on more complex inter-hemisphere activation (Rueda-Delgado et al., 2014).

The cognition-motor link: support for common network aberrations

The observation that both visual working memory and math fluency predicted the co-occurring secondary motor deficits across dyslexia and AD suggests that similar mechanisms are at play, presumably because analogous larger networks are atypical in both disorders. Both visual working memory and math fluency are generally linked to rapid processing of visual and mental information and both rely on the capacity to temporarily maintain information to keep track of different steps for quick and accurate responding (Boulet-Craig et al., 2017; Menghini et al., 2011; Schumacher et al., 1996). Although various mechanisms could underlie the rapid retrieval of math facts (De Visscher, Szmalec, Van Der Linden, & Noel, 2015), both general math fluency and working memory abilities have been shown to rely on the prefrontal cortex and cerebellum (E, Chen, Ho, & Desmond, 2014; Kazui, Kitagaki, & Mori, 2000; Lebel, Rasmussen, Wyper, Andrew, & Beaulieu, 2010; Petrides, Frey, & Chen, 2001; Schumacher et al., 1996). Both brain regions are associated with motor sequencing (Desrochers et al., 2015; Doyon et al., 2003) and have been suggested to be atypical in both dyslexia and AD (M. A. Eckert et al., 2003; Giedd et al., 2001). Hence, it could be speculated that the similar nature of the cognition-motor relation in dyslexia and AD indicates a failure of common large-scale networks, through aberrant grouping of brain regions, such as the frontal cortex and the cerebellum (Menon, 2011). Notably, studies have reported associations between aberrant cerebello-thalamo-prefrontal networks in neurological disorders and NSS, including motor coordination (Mouchet-Mages et al., 2011). There are several possible explanations for the co-occurrence of abnormal networks associated with both motor sequencing and visual working memory and math fluency, one of which could be altered gray/white matter in the network brain regions that span several lobes or altered dynamics in the interactions between the edges that link them (Menon, 2011; Radua, Via, Catani, & Mataix-Cols, 2011). Studies have reported that dyslexia and AD are associated with atypical white and gray matter density (Brown et al., 2001; Kessler, Angstadt, Welsh, & Sripada, 2014; Rae et al., 2002). Although in the current studies only behavioral measures were available, some authors posit that general disruption of information processing across brain networks can be observed by assessing lower level behavior such as minor motor irregularities (Levit-Binnun et al., 2013). In addition, the important contributions of age, gender and IQ to motor skills can also be interpreted as an indication that motor ability is associated with large-scale networking efficacy as these variables are linked to whole brain maturation (Deoni, Dean, Remer, Dirks, &

O'Muircheartaigh, 2015; Malpas et al., 2016), which in turn is associated with increased white/gray matter through myelination and efficient neural networking (Deoni et al., 2015; Menon, 2011). Neuroimaging studies have found that age and gender are associated with differences in white and gray matter volume in brain regions including motor areas, such as frontal and parietal cortex and the cerebellum (Pangelinan et al., 2011). Others have shown a link between IQ and white matter and cortical thickness, as well as gray matter density in the anterior cerebellum (Ramsden et al., 2011). White and gray matter density are also associated with a plethora of cognitive abilities, including processing speed (Lebel et al., 2010; Moore, D'Mello, McGrath, & Stoodley, 2017; Pangelinan et al., 2011). Notably, authors have suggested that dyslexia and AD are linked through a common risk factor for poor processing speed (McGrath et al., 2011; Shanahan et al., 2006), which could possibly be due to lower white and gray matter density in general brain networks. Thus, the observed associations between common cognitive skills, demographic factor and motor performance could translate to the motor network's reliance on general brain maturation. In sum, one could hypothesize that common network aberrations have emerged because of a more generalized atypical neurodevelopment, without regard for the primary diagnostic symptoms of either AD or dyslexia. Of note, in some cases, primary symptoms were correlated with motor skills while controlling for age, gender and IQ. However, the absence of a predictive relationship between primary symptoms of each disorder and motor performance suggests that the relationship between primary cognitive features and motor abilities is indirect (Rochelle & Talcott, 2006; Viholainen et al., 2011). In other words, the results further support the premise that the hypothesized network failure does not need to rely on primary features of a disorder to be an indicator of brain vulnerability (Levit-Binnun et al., 2013). For example, the specific mechanisms of reading were not predictive of motor skills, which suggests that specific phonological decoding abilities are not directly associated with motor sequence abilities. However, the presence of significant correlations between reading and motor skills could still indicate that more general and nonspecific networks underlie difficulties in both domains, but without a direct link (Stoodley & Stein, 2013). In keeping with the systems neuroscience theory, both domains could be supported by larger network deficits. Further empirical investigations remain to be conducted, especially as this study is among the first to compare neurodevelopmental disorders on their motor-cognition relation, and it did not include neuroimaging methodology to directly support data interpretation of common large-scale brain network failure

The differential results: what can they tell us?

Differences between groups were observed, specifically between the dyslexic and the AD groups, which could indicate the presence of distinctive aberrant mechanisms in motor difficulties. Importantly, the dyslexia group was the only one to lack fast behavioral gains compared to their control group on the complex task of bimanual out-of-phase coordination. This result could indicate that the well-established difficulties in sequential learning among children with dyslexia (Lum et al., 2013) were not compensated for by efficient motor adaptation in the most complex motor task. The processing and manipulation of two distinct serial order rules could be too demanding for children with dyslexia, hence it is possible that they are not able to rely on speed kinematics to improve (Orban et al., 2011; Szmalec, Loncke, Page, & Duyck, 2011). Although math fluency predicted bimanual coordination skills in the groups with dyslexia (Dys and Combo), future studies could specifically examine its relationship with motor adaptation skills. This would help support an association between motor skills and poor automatization of procedural skills, the latter having been previously associated with both motor sequencing and math fluency (Ackerman, Anhalt, & Dykman, 1986; Roderick I. Nicolson & Fawcett, 2011). Furthermore, the AD group's motor performance was significantly different from the other groups on two tasks, which supports dissimilar mechanisms in this group as well. First, children with AD had difficulties with dexterity skills compared to controls, to the dyslexia, and to the combo groups, suggesting that the AD group had problems with motor skills that do not necessarily require a sequence and rely primarily on fingertip dexterity. This result was not surprising as fine motor skill impairments have been more consistently reported in AD (Kaiser et al., 2014; Pitcher, Piek, & Hay, 2003). Moreover, the AD group had additional difficulties with bimanual coordination compared to the dyslexia group. These added weaknesses were found exclusively in children with AD only. The combo group did not have dexterity weaknesses or added difficulty with bimanual coordination. In addition, behavioral attention/hyperactivity were not significant predictors of bimanual coordination difficulties. Hence, these results are not in line with the interpretation that the added motor difficulties are associated with the primary inattention/hyperactivity symptoms of AD (Chaix et al., 2007). A possible interpretation is that the added motor problems in the AD group are associated with other symptoms linked to aberrant frontal based mechanisms in AD (Dickstein et al., 2006; Roberts et al., 2013). For example, inhibition is an impaired prefrontal mechanism in AD, and the AD group had a greater propensity

for perseverative errors, which could indicate poor inhibition (Barkley, 1997). Dexterity abilities have also been shown to rely on prefrontal mechanisms (Ware et al., 2016). Notably, atypical activation of the PFC is among the most consistently reported across neurological disorders and is linked to bimanual coordination (Bélanger et al., 2015; Diamond, 2000; Rueda-Delgado et al., 2014). The results could suggest a more severe interference with prefrontal brain mechanisms in our AD group that lead to added difficulties with complex bimanual coordination and dexterity. This interpretation does not reject the presence of poorer frontal based mechanisms in dyslexia through aberrant networking (Christodoulou et al., 2014; M. A. Eckert et al., 2003), as children with dyslexia only or both disorders remained impaired on bimanual coordination compared to controls and shared similar associations between bimanual coordination and cognitive skills.

In conclusion, the current thesis investigations suggest that sequential motor weaknesses, as measured through gross hand/arm movements, are not only co-occurring difficulties in dyslexia and AD, but also share similar underlying mechanisms. Notwithstanding the well-established heterogeneous nature of both disorders, sequential motor difficulties appear to remain and persist across ages and disorders. Hence, we suggest that the presence of sequential motor difficulties across dyslexia and AD could be an important marker of neurodevelopmental disorders, and viewed as an important secondary symptom that possibly reflects a general network brain vulnerability that leads to several facets of cognitive dysfunction.

Future research avenues

The findings of this thesis could lead to new research paradigms in the assessment of neurodevelopmental disorders. Foremost, future research could jointly differentiate sequential motor abilities from bimanual coordination to further our understanding of the possible added complexity of bimanual coordination and how it can differentiate dyslexia and AD. Research paradigms could also expand the hierarchical conceptualization of the motor difficulties, for instance by measuring other components of kinematics, such as direction, as well as by including other body parts, to better comprehend each level of affected or preserved sequential and non-sequential motor abilities. A more comprehensive assessment of primary and secondary cognitive abilities in dyslexia and AD is required, which could include cognitive measures of attention and inhibition to examine the shared and differentiated relations between cognitive and motor

difficulties. Notably, error assessment in a rapid unimanual sequential output would be an interesting parameter to examine, although the task would need to be longer or more complex in order to have interpretable data on error proficiency. Longitudinal research studies could examine putative gross sequential motor difficulties in younger children (under 8 years) at familial risk for dyslexia or AD in order to support the presence of motor difficulties as a secondary nonspecific symptom that could indicate future psychopathology (Hatakenaka et al., 2016). Future studies could also investigate sequential motor skills across several neurodevelopmental disorders to solidify unifying framework for these disorders, as motor deficits have been consistently reported in other disorders such as autism and schizophrenia (Jahn et al., 2006; Stevenson, Lindley, & Murlo, 2017). In addition, future studies could examine the effects of medication and interventions with large samples of children with neurodevelopmental disorders. Establishing different criteria, such as types and dosage of medication, and frequency or length of interventions, would contribute to our understanding of their impact on these children's performances and their role in rehabilitation. Furthermore, neuroimaging studies that jointly investigate large scale aberrant networks such as the cerebello-thalamo-frontal and fronto-striatal-cerebellar connections in dyslexia and AD could support the notion of overlapping cognitive and motor difficulties, as well as further our understanding of theories on multiple atypical pathways in neurodevelopmental disorders and how these pathways may overlap to explain the heterogenous nature of these disorders (Cubillo et al., 2012; Nigg et al., 2004). Finally, future studies including groups with comorbid dyslexia/AD diagnosis are recommended to control for and support the commonalities in widespread general network failure.

Clinical significance

Motor impairments can affect self-esteem, academic success, and general quality of life (Fernandes et al., 2016; Piek et al., 2006). Although standard neuropsychological assessments include evaluation of motor abilities, this is not always performed and usually only targets fine motor skills. This thesis underscores the importance of evaluating motor skills, and particularly hand/arm sequential motor abilities in both AD and dyslexia, to add to the comprehensive assessment of these neurodevelopmental disorders and to our understanding of their functional impact on daily activities. Specialized schools often include physical activity as an important aspect of the children's daily routine. As there is emerging evidence of positive effects of motor

skill training (Lucas et al., 2016), the findings emerging from this thesis supports the use of motor training as an important factor in brain rehabilitation. More specifically, intervention could focus on motor sequential planning and future studies should investigate this specific type of motor training as an intervention tool. Interestingly, a study by Brossard-Racine and colleagues (2012) showed that after stimulant medication was administered to children with AD and motor problems, some children showed typical motor output, suggesting that a portion of the motor difficulties could be associated with improvement of cognitive abilities; however, a large portion of the children remained impaired. Hence, this study supports the relation between cognition and motor skills, and also shows that medication may not be sufficient to help improve motor skills (Brossard-Racine, Shevell, Snider, Belanger, & Majnemer, 2012). Furthermore, motor development has been repeatedly linked to cognitive abilities throughout development (van der Fels et al., 2015) and as shown in this thesis, their relation is similar across dyslexia and AD. Thus, it could prove beneficial to combine both motor and cognitive rehabilitation, such as motor sequence planning and working memory, in order to rehabilitate more general widespread brain functions in both disorders (Beck et al., 2016).

Limitations

The sample of children used in both studies were recruited from a specialized school. Thus, there is a high probability that their cognitive abilities were compensated, which was not systematically controlled for in terms of their clinical scores on the measures of the primary and secondary cognitive symptoms. There was also variability on most measures of cognition and motor abilities, signaling that some children with dyslexia and some children with AD did not have substantial cognitive or motor skills difficulties. In addition, comorbidities (e.g. Conduct disorder, Tourette syndrome, Anxiety disorder) were not controlled for in the second study, although disorders such as these are also associated with various symptoms, including motor difficulties. More specifically, the presence of high variability in the LTT performances could also be due to children with motor difficulties that correspond to a DCD diagnosis, which was only controlled for via parental report of a previous diagnosis, and could affect the interpretation of motor weaknesses in the ‘‘pure’’ dyslexia and AD populations. The possible presence of DCD was considered a limitation, but also a representation of the variability in the atypical neurodevelopmental population, particularly because the etiology and symptoms of DCD have

not reached consensus, to our knowledge (Zwicker, Missiuna, Harris, & Boyd, 2012). The sample of children requiring specialized education might have more large-scale network aberrations because of comorbidities or more severe atypical development. Hence, the important limitations to the conceptualization of the experimental groups (which were quantitatively uneven) indicates that the conclusion that sequential motor weaknesses are a marker of AD and dyslexia must be nuanced. However, it is reasonable to believe that the sample is representative of the variability in the clinical population as the groups were based on psychological or medical diagnosis, and as certain authors suggest, comorbidities have become the norm rather than the exception. In addition, authors suggest that higher rates of NSS in healthy individuals are associated with more negative symptoms (Chan et al., 2009; Levit-Binnun et al., 2013). Hence, even children that do not have clear cut motor or cognitive difficulties could still have a certain level of vulnerability as measured with other motor aspects, as seen when using NSS batteries. These children also represent an important sample of the atypical neurodevelopmental population that needs specific and intensive intervention through special education. Though we report that basic motor speed is preserved and cognitive abilities did not affect motor speed, it was only measured over one 15 second time period, whereas the sequential conditions had two 30 second trials. Hence, the absence of difficulty could be due to the methodology. In addition, processing speed relies on more than simple motor speed (Shanahan et al., 2006). Notably, processing speed has been suggested as the most reliable common deficit in dyslexia and AD (McGrath et al., 2011), and could be an indicator of poor myelination (Chevalier et al., 2015; Moore et al., 2017). Hence, this ability rather than motor skill per se could be an indicator of brain vulnerability. Moreover, we did not control for handedness in the regression analyses, which could be an important factor related to the lateralization of the motor output, although some studies have suggested that handedness does not affect motor coordination in children (Chan et al., 2010). Finally, the statistical differences found between the AD and Dyslexia groups must be interpreted with caution as they could be due to multiplicity of testing and need to be replicated in an independent sample of children.

Conclusion

This thesis is, to our knowledge, the first to jointly assess the association between motor weaknesses and cognitive abilities in dyslexia and AD. We posit that the similarities in this

relation suggests common underlying brain network aberrations. Our results offer an interesting avenue for future research paradigms. However, because of its novelty, future studies also need to replicate these results and conduct a more comprehensive assessment of shared cognitive abilities in order to support unifying frameworks, and help construct efficient motor skill training for pediatric rehabilitation.

References - Introduction & Discussion

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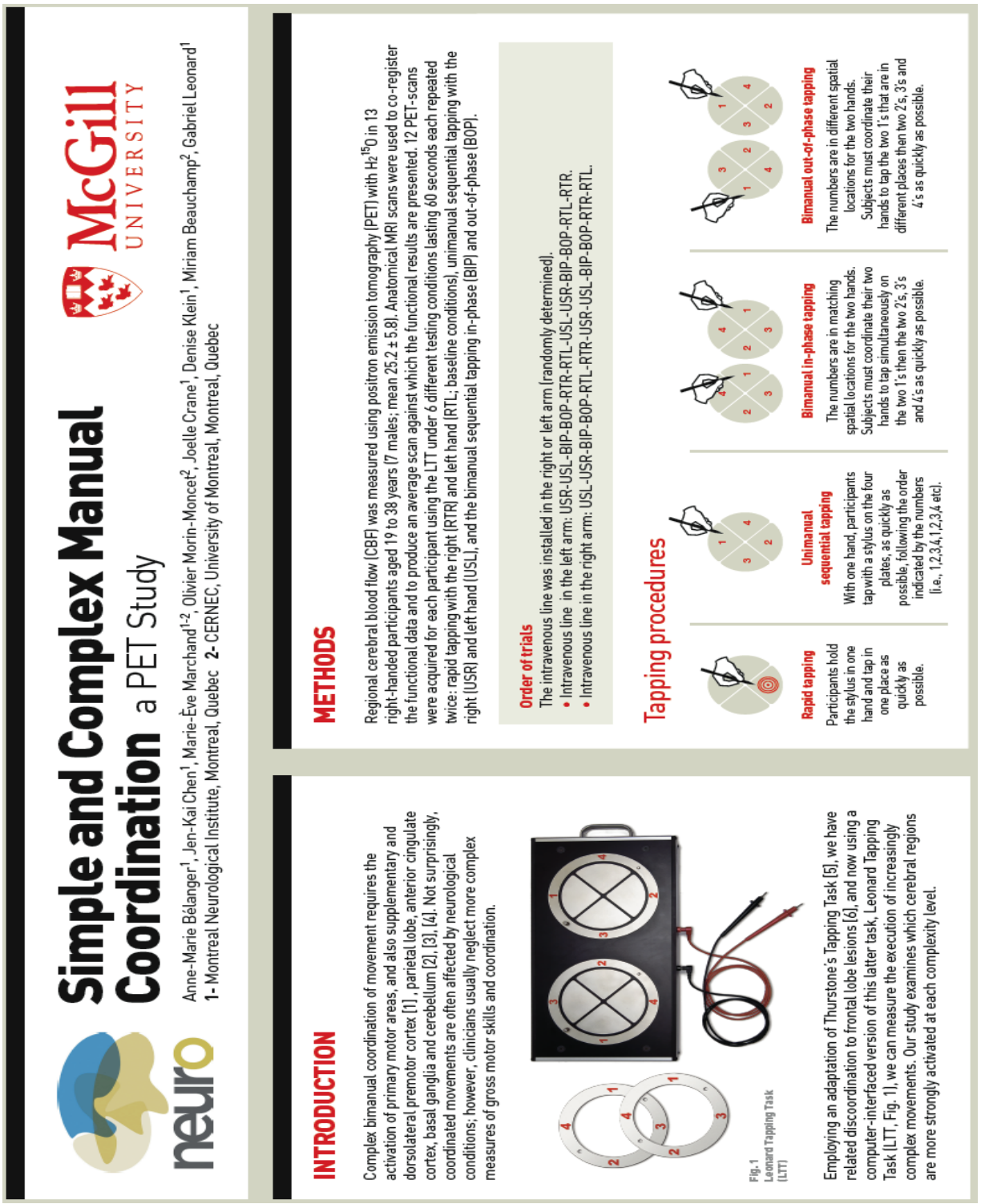
Appendix I

Figure 1. Simple and Complex Manual Coordination: a PET study (Bélanger et al., 2015).

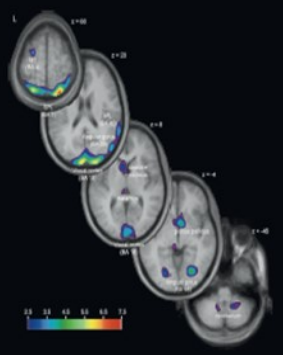


RESULTS Activation peaks found when contrasting tapping conditions

In order to examine brain regions involved with the increase in complexity of the tapping tasks, voxel-wise-t-statistics have been computed to contrast the different conditions.

UNIMANUAL SEQUENTIAL VERSUS RAPID TAPPING

Right Hand



At z=60: left primary motor cortex BA4 (t=4.08, p=.002) and bilateral superior parietal lobule BA7 (right: t=7.69, p<.001; left: t=6.57, p<.001).

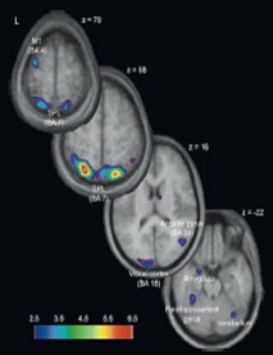
At z=20: right inferior parietal lobule BA40 (t=4.08, p=.01), right angular gyrus BA39 (t=4.67, p<.001) and bimanual visual cortex BA18 (right: t=6.31, p<.001; left: 6.15, p<.001).

At z=8: left caudate nucleus (t=3.61, p=.008), left thalamus (t=3.07, p=.05) and bilateral visual cortex BA18.

At z=-4: right globus pallidus (t=4.72, p<.001) and bilateral lingual gyrus BA18 (right: t=5.25, p<.001; left: t=5.09, p<.001).

At z=-46: bilateral cerebellum (right: t=3.61, p=.008; left: t=3.18, p=.022).

Left Hand



At z=70: left primary motor cortex BA4 (t=4.12, p=.009).

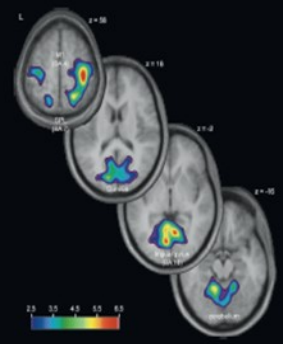
At z=58: bilateral superior parietal lobule BA7 (right: t=5.89, p<.001; left: t=6.92, p<.001).

At z=16: right angular gyrus BA39 (t=3.61, p=.035) and left visual cortex (t=3.75, p=.026).

At z=-22: left amyddala (t=3.47, p=.046), left parahippocampal gyrus (t=3.89, p=.017) and right cerebellum (t=3.70, p=.027).

BIMANUAL VERSUS SUM OF UNIMANUALSEQUENTIAL

In-phase



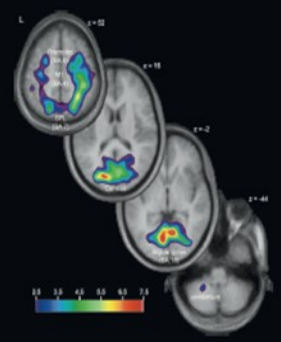
At z=58: bimanual primary motor cortex BA4 (right: t=6.88, p<.001; left: t=4.65, p<.001) and bimanual superior parietal lobule BA7 (right: t=7.31, p<.001; left: t=4.23, p=.001.

At z=16: bilateral cuneus (right: t=5.58, p<.001; left: t=5.16, p<.001).

At z=-2: bilateral lingual gyrus BA18 (t=6.74, p<.001; left: t=6.51, p<.001).

At z=-16: bilateral cerebellum (right: t=4.60, p<.001; left: t=5.76, p<.001)

Out-of-phase



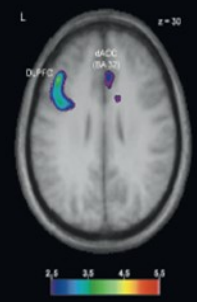
At z=52: bimanual premotor cortex BA6 (right: t=4.83, p<.001; left: t=4.29, p<.001), bimanual primary motor cortex BA4 (right: t=5.36, p<.001; left: t=4.47, p<.001) and bimanual superior parietal lobule BA7 (right: t=7.31, p<.001; left: t=6.42, p<.001).

At z=16: bilateral cuneus (right: t=5.71, p<.001; left: t=7.07, p<.001).

At z=-2: bilateral lingual gyrus BA18 (right: t=7.96, p<.001; left: t=7.84, p<.001.

At z=-44: left cerebellum (t=3.64, p=.003).

BIMANUAL OUT-OF-PHASE VERSUS BIMANUAL IN-PHASE



At z= 30: left dorsolateral prefrontal cortex BA9 (t=4.21, p=.012*) and right dorsal anterior cingulate cortex BA32 (t=3.77, p=.062**).

* Significant using cluster threshold (cluster size = 2344mm3, p = 0.012)

** Trend for significance using cluster threshold (cluster size = 1480mm3, p= 0.062)

For the purpose of this presentation, CBF was averaged between the two trials for each tapping condition. t-values and False Discovery Rate threshold [7] calculated using fMRIstats. Brodmann Areas according to Talairach and Tournoux.

DISCUSSION AND CONCLUSION

The activation patterns in the frontal lobe areas are consistent with our earlier lesion studies showing that patients with frontal lobe lesions were impaired in bimanual out-of-phase tapping compared to patients with temporal lobe lesions. The results of this study support our previous findings suggesting that the LTT is utile in assessing motor skills in patients with brain lesions.

- We show an increased activity in the left primary motor cortex in sequencing tasks for both the right and the left hand, reflecting the hypothesis of a left hemisphere dominance in complex manual tasks.
- We observe increased activity in parietal and occipital lobes across conditions, which suggests heavier reliance on visuospatial processing for the execution of increasingly complex movements.
- Similarly, we show an augmentation in the activity of the cerebellum throughout the tapping tasks, supporting the involvement of this region in feedback processing and error detection.
- For the dominant hand, we show that the basal ganglia and the thalamus are more recruited for the sequencing of movements.
- We demonstrate higher activation of premotor areas for complex bimanual movements compared to unimanual movements.
- Particularly exciting is the recruitment of the anterior cingulate and the lateral prefrontal cortex for the most complex bimanual tasks, perhaps linked to the greater level of attention and monitoring of conflicts required to generate complex movements and the role of working memory in the execution of dissimilar bimanual movements. No other areas are associated with complex bimanual tapping compared to simpler bimanual condition, suggesting that the same areas are involved in both tasks.

FUTURE WORK

- Contrast CBF between first and second trials.
- Contrast CBF between males and females.
- Correlate cortical thickness and tapping scores