Neuroscience 333 (2016) 27–34

SACCADE ADAPTATION IN YOUNG PEOPLE DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER COMBINED TYPE

AMANDA J. CONNOLLY, [a*] **NICOLE J. RINEHART** [b] **AND JOANNE FIELDING** [a,c]

[a] *School of Psychological Sciences, Faculty of Medicine Nursing and Health Sciences, Monash University, Clayton, Victoria, Australia*

[b] *Deakin Child Study Centre, School of Psychology, Deakin University, Burwood, Victoria, Australia*

[c] *Department of Medicine, University of Melbourne, Parkville, Victoria, Australia*

Abstract—Growing evidence suggests Attention Deficit Hyperactivity Disorder (ADHD) often co-occurs with Autism Spectrum Disorder (ASD), and a better understanding of the nature of their overlap, including at a neurobiological level, is needed. Research has implicated cerebellar-networks as part of the neural-circuitry disrupted in ASD, but little research has been carried out to investigate this in ADHD. We investigated cerebellar integrity using a double-step saccade adaptation paradigm in a group of male children age 8–15 (n = 12) diagnosed with ADHD-Combined Type (-CT). Their performance was compared to a group of age and IQ-matched typically developing (TD) controls (n = 12). Parent reported symptoms of ADHD-CT and ASD were measured, along with motor proficiency (Movement ABC-2). We found, on average, the adaptation of saccade gain was reduced for the ADHD-CT group compared to the TD group. Greater saccadic gain change (adaptation) was also positively correlated with higher Movement ABC-2 total and balance scores among the ADHD-CT participants. These differences suggest cerebellar networks underlying saccade adaptation may be disrupted in young people with ADHD-CT. Though our findings require further replication with larger samples, they suggest further research into cerebellar dysfunction in ADHD-CT, and as a point of neurobiological overlap with ASD, may be warranted.

Key words: Attention Deficit Hyperactivity Disorder, Motor, Autism Spectrum Disorder, saccade, adaptation, cerebellum.

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorders (ASD) are two highly prevalent neurodevelopmental disorders, reportedly diagnosed in approximately 5.3% (Polanczyk et al., 2014) and 0.6% (Elsabbagh et al., 2012) of young people worldwide. The core diagnostic features of ADHD, combined type (ADHD-CT) are clinically significant levels of inattentiveness and/or hyperactivity/impulsivity, and for ASD social-communication impairments and restricted/stereotyped behavior and interests (American Psychiatric Association, 2013). Increasingly, these separate diagnoses are being recognized as co-occurring often, with a high rate of overlap in symptoms, which may suggest that they are part of the same overarching disorder (van der Meer et al., 2012). However, this is far from conclusive and there are still many gaps in our understanding of how these two disorders overlap.

Motor symptoms offer an opportunity to further understand this overlap. Though not part of the core diagnostic criteria, motor impairment is a neurodevelopmental symptom that is commonly observed in both children with ADHD-CT and ASD. Young people with ADHD-CT display a wide range of gross and fine motor coordination difficulties (Kaiser et al., 2015), significant enough to meet criteria for Developmental Coordination Disorder (DCD) in up to 55% of young people with ADHD-CT (Brossard-Racine et al., 2012). Higher rates of clinically significant motor impairment are found among children with ASD – up to 80% (Green et al., 2009) – such that it has been considered a ‘‘cardinal feature” of ASD (Fournier et al., 2010). In a clinical research context, motor symptoms are more easily measured and quantified, and less affected by rater subjectivity or contextual effects compared to symptoms of inattention, hyperactivity/impulsivity, social-communicative and restricted/repetitive behaviors (Minshew et al., 2004; Dowd et al., 2010).

Specifically, cerebellar-related motor impairment is of interest, for several reasons: (1) clear patterns of motor impairment, including gait and balance problems, reflective of cerebellum dysfunction have also been found in groups with ASD (Rinehart et al., 2006); (2) increasing research suggests the cerebellum has a key role in other non-motor functions, such as integrating information from different sensory modalities (Ronconi et al., 2016), that are also found to be impaired in neurodevelopmental disorders including ASD (Fatemi et al., 2012); (3) differences in cerebellum structure and function

*Corresponding author. Address: School of Psychological Sciences, Level 4, 18 Innovation Walk, Monash University, Clayton, Victoria 3168, Australia.
E-mail address: Amanda.Connolly@monash.edu (A. J. Connolly).

Abbreviations: ADHD-CT, Attention Deficit Hyperactivity Disorder-Combined Type; ASD, Autism Spectrum Disorder; CRS-R, Conners Rating Scale-Revised; FSIQ, full scale IQ; MABC-2, Movement Assessment Battery for Children – 2nd edition; PRI, perceptual reasoning index; SRS, Social Responsiveness Scale; TD, typically developing; VCI, verbal comprehension index.

http://dx.doi.org/10.1016/j.neuroscience.2016.06.053
0306-4522/

have been reported by imaging studies, for ADHD-CT and ASD groups alike, compared to Typically Developing (TD) groups, and; (4) differentiation of performance between ADHD-CT and ASD groups on tasks involving the fronto-striatal network, another key motor network, have been more thoroughly researched and identified, but far fewer studies have investigated cerebellar-networks (Dowd et al., 2010).

Ocular motor paradigms, or the study of saccades, offer a fine-grained approach to study networks involved in motor function, and in particular, the double-step saccade adaptation paradigm is one method by which the functional integrity of the cerebellar-motor network can be examined. The cerebellum, vermis lobules VI–VII, plays an important role in motor learning and correction of saccade amplitude:velocity (main sequence) relationship over time to accurately meet target stimuli, the process called adaptation. Lesions to the cerebellar vermis lobules VI–VII region in monkeys and humans consequently slows saccade initiation, produces greater inaccuracy, and impaired adaptation of saccade metrics (Barash et al., 1999; Desmurget et al., 1998). Cerebellar vermal lesion patients are found to achieve saccade adaptation, however, the timescale over which it is achieved is varied and saccade metrics are significantly altered compared to healthy controls (Xu-Wilson et al., 2009). Impairment of saccade adaptation is also evident with disruption to the pathway from the cerebellum to cortical motor areas via the thalamus, as have been shown in studies of patients with thalamic lesions (Gaymard et al., 2001; Zimmermann et al., 2015).

The saccade adaptation process is induced experimentally using a saccade adaptation paradigm, in which the location of a visual target is moved as a saccade is made, creating a perceived visual error. Over multiple trials, saccade amplitude is progressively reduced to correct for the error. The processes involved in this paradigm are also automatic and subconscious, and avoid higher-level, cognitive learning strategies, making it advantageous in investigating cerebellar motor impairment.

The aim of the current study was therefore to investigate cerebellar-related motor impairment in children with ADHD-CT using a saccade adaptation paradigm, as compared to TD children. An inward adaptation (i.e. shortening saccade amplitude) paradigm, as opposed to an outward saccade adaptation (i.e. lengthening saccade amplitude) paradigm, was chosen because this type has been used in studies with children with ASD, and because inward adaptation is found to be more stable, efficient, and to involve different underlying processes, compared to outward adaptation (Straube et al., 1997; Catz et al., 2008).

Based on previous ADHD-CT and ASD motor research, we hypothesized that children with ADHD-CT would display cerebellar-related impairments, including poorer adaptation and increased variability of saccades compared to TD participants. We also predicted that greater impairment on the saccade adaptation task would be correlated with poorer performance on a standardized measure of motor coordination i.e. the Movement ABC-2 (Henderson et al., 2007).

EXPERIMENTAL PROCEDURES

Participants

This study was approved by Monash University and Southern Health Human Research Ethics Committees. Parents of participants provided informed consent prior to the commencement of the study, and written assent was provided by the participants in accordance with the Declaration of Helsinki.

There were 24 participants who took part in the study: 12 with a diagnosis of ADHD-CT and 12 without a diagnosis of ADHD-CT or any other disorder i.e. TD children. Participants were males, aged between 8 and 15 years. Participants diagnosed with ADHD-CT were recruited from private pediatricians in Melbourne, Victoria. Diagnosis of ADHD-CT was confirmed by review of a diagnostic report or letter and consultation with pediatricians. No participant had a co-occurring diagnosis of ASD from their pediatrician.

Participants without a diagnosis of ADHD-CT, or any other DSM-5 diagnoses, (henceforth referred to as TD participants) were recruited from the community. Other exclusion criteria included the presence of visual impairments, genetic, or neurological conditions. Exclusion criteria were confirmed through interview with participant's parents, in which participants' developmental, medical and psychiatric history was also obtained. Current medications were also recorded, with 10 (83%) participants with ADHD-CT taking stimulant medication such as methylphenidate (Ritalin) on a regular basis.

Parent interview and all other measures were administered by trained Provisional Psychologists and/or doctoral psychology students under the supervision of a registered Clinical Psychologist (NR).

All participants had average or above average intellectual functioning. This was assessed by administration of the Wechsler Intelligence Scale for Children – 4th edition, with Full Scale (FSIQ), Verbal Comprehension (VCI) and Perceptual Reasoning (PRI) scores calculated.

ADHD-CT and ASD symptoms

We characterized the ADHD-CT (inattention, hyperactivity/impulsivity) and ASD (social responsiveness) symptoms of our sample using gold standard, clinically-used measures. Namely, the DSM inattention and hyperactivity/impulsivity subscales from the Conners Rating Scale-Revised (CRS-R), parent version (Conners, 1997). The CRS-R consists 80 items, that form 14 subscales, and has good reliability and validity for use in young people aged 6–18 (Conners et al., 1998). Parents were asked to provide responses to items on the CRS-R that reflected their child's behavior while off their ADHD-CT medication.

Social responsiveness symptoms were measured using the Social Responsiveness Scale (SRS), parent