DEFICITS IN EYE MOVEMENT CONTROL IN ADULTS WITH FASD

by

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Abstract

Individuals with fetal alcohol spectrum disorder (FASD) are believed to be overrepresented in the criminal justice system (CJS). However, accurate reporting of prevalence rates of FASD in the CJS is a significant clinical challenge. This is a reflection of the fact that the diagnostic process requires collaboration from a multidisciplinary team, and there is a low clinical capacity in Canada for diagnosing FASD. In addition, screening every individual that enters the CJS in this way is prohibitively expensive. However, identifying individuals with FASD in the CJS is essential for two reasons. First, understanding the true prevalence rates of FASD will aid in developing much-needed programming and rehabilitation plans to better address the needs of these individuals. Second, rapid identification of these individuals within the CJS will lead to better outcomes for the individuals, and potentially reduce the high rates of recidivism.

Tracking eye movement behaviours has been shown to differentiate children with FASD from typically developing controls. This may be due to the substantial overlap in the areas of the brain known to control saccades, and the areas known to be sensitive to prenatal alcohol exposure. To the best of our knowledge, studies investigating eye movement control in adults with FASD have never been performed. The objective of this study was to investigate whether eye tracking can differentiate between adults with FASD in the CJS and control groups for each factor (FASD and CJS involvement). In this study, criminal justice involvement did not significantly affect eye movement control. As a result, adults with FASD were compared directly with adults without FASD, regardless of criminal justice involvement. Compared with control adults (n=22), adults with FASD (n=15) exhibited significant differences in eye movement performance, including an overall decreased proportion of correct trials, as well as deficits in accuracy, attention, response inhibition, working memory, and variability. These results support the notion that eye movement tracking identifies differences in brain function between adults with FASD and controls, and could contribute to an inexpensive, rapid, and reliable screening tool for FASD that may one day be used in the CJS.

Co-Authorship

The research described in this thesis was conducted by Cindy Xiao under the supervision of Dr. James Reynolds. The principal investigator of the project was Dr. Kaitlyn McLachlan. Data was collected by Cindy Xiao and Dr. Kaitlyn McLachlan from a northern Canadian community. All statistical analyses were performed by Cindy Xiao. An automated saccade analysis program developed by Donald Brien was used to extract saccade measures used in the analysis of this thesis. Figure 3-2 outlining how saccade metrics are calculated was produced by Donald Brien.

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List of Abbreviations

CJS	Criminal justice system
CN	Caudate nucleus
CV	Coefficient of variation
dlPFC	Dorsolateral prefrontal cortex
FASD	Fetal Alcohol Spectrum Disorder
FEF	Frontal eye fields
IMF	Internal medullary lamina
MLF	Medial longitudinal fasciculus
MRI	Magnetic resonance imaging
PAE	Prenatal alcohol exposure
PPRF	Paramedian pontine reticular formation
SC	Superior colliculus
SD	Standard deviation
SEF	Secondary eye fields
SNpr	Substantia nigra pars reticulata
SRT	Saccadic reaction times

Chapter 1

Introduction

The teratogenic effects of prenatal alcohol exposure (PAE) have been investigated for the past 40 years. Depending on the quantity, frequency, and timing of maternal alcohol consumption during the fetal developmental trajectory, PAE can result in a wide spectrum of impairments in growth, attention, memory, visuo-spatial awareness, executive functioning, and socio-emotional and behavioural functioning. The term Fetal Alcohol Spectrum Disorder (FASD) is used to encompass the range of lifelong clinical diagnoses, which include: Fetal Alcohol Syndrome, partial Fetal Alcohol Syndrome, Alcohol-Related Neurodevelopmental Disorder, and Alcohol-Related Brain Damage. Despite the long-held awareness of the teratogenic effects of PAE, the current prevalence of FASD is estimated to be between 2 – 3% in Canada, which translates to around one million individuals currently affected by FASD (Hrvatin, 2018).

Individuals with FASD are at higher risk for both primary (e.g., cognitive deficits, restricted growth) and secondary (e.g., social deficits, delinquent behaviour) deficits (Kodituwakku, 2009; Paolozza, 2015; Rasmussen, 2005; Rasmussen et al., 2008). This may be due to a combination of cognitive impairments and environmental influence. Individuals with PAE are at higher risk for negative psychosocial influences, such as parental substances abuse, child neglect or maltreatment, disruptions in placement or exposure to familial violence (Kable et al., 2016). Furthermore, individuals with PAE are at risk for adverse life outcomes such as disruption in school, trouble with the law, and alcohol and drug problems (Streissguth et al., 2004).

There has been a recent emphasis on the overrepresentation of individuals with FASD in the criminal justice system (CJS). In one study following 415 individuals with FASD, 14% of children (aged 6 to 11 years), 61% of adolescents (aged 12 to 20 years), and 58% of adults (aged 21 to 51 years) had been reported to experience trouble with the law, with 35% of individuals over the age of 12 having a history of criminal incarceration (Flannigan et al., 2018). In addition to personal hurdles, this also presents a great economic burden. One meta-analysis study focused on all aspects of CJS involvement, including both cost of crimes and criminal cost for victims found the total costs of FASD associated with the CJS in Canada to be about $3.9 billion per year (Thanh & Jonsson, 2015).

Tracking eye movement behaviours in automatic and voluntary tasks has been shown to evaluate sensory-motor integration, visuospatial awareness, memory, attention and executive functioning skills. Eye movement control of children with FASD in these tasks have been previously investigated (Green et al., 2009; Paolozza et al., 2013; 2014a; 2014b; 2015; 2016), with prominent differences found between children with FASD and age-matched controls. Furthermore, these tasks have been shown to mirror psychometric tasks assessing the same skills in children with FASD, suggesting that common brain structures are mobilized for successful inhibitory control (Paolozza et al., 2014a), working memory, and visuospatial processing (Paolozza et al., 2014b).

Currently, there is a lack of reliable tools that may be used in the CJS for rapid screening of individuals suspected of having FASD. The diagnostic process for FASD requires in-depth evaluation lasting 9 – 10 hours and involves a multidisciplinary team of health professionals. However, the clinical capacity for diagnosing individuals with FASD in Canada is low and unable to meet the demands of the general population, let alone special populations such as those involved in the CJS. Identifying individuals with FASD in the CJS earlier will aid with judicial responses and treatments that would best support the needs of these individuals needs goal of decreasing recidivism. However, inconsistent reporting of national prevalence rates of FASD in the Canadian CJS is a barrier for administering available treatments and better addressing current issues facing these individuals. Compounding the problem, there are very few studies which have investigated brain dysfunction in adults with FASD. The objective of this project was to test the hypothesis that adults with FASD would present with deficits in eye movement control similar to those reported for children with FASD. This in turn could lead to the development of new screening tools that may contribute to low-cost, rapid and objective assessment of brain function in adults in the CJS suspected of having FASD.

Chapter 2

Literature Review

2.1 Fetal Alcohol Spectrum Disorder

FASD is an umbrella term for a wide range of outcomes due to PAE. In the majority of cases, a diagnosis requires confirmation of PAE and pervasive brain dysfunction defined by severe impairments in three or more of the neurodevelopmental domains, including motor skills; neuroanatomy/neurophysiology; cognition; language; academic achievement; memory; attention; executive function, including impulse control and hyperactivity; affect regulation; and adaptive behaviour, social skills, or communication (Cook et al., 2016). In some cases, individuals present with three sentinel facial features (a short palpebral fissure length, a smooth philtrum, and a thin upper lip), which has been shown to have high specificity to alcohol exposure and is an accepted biomarker for PAE (Cook et al., 2016). In these cases, maternal confirmation of PAE is not required. However, most cases do not present with all or any of these three facial dysmorphologies, in which case confirmation of PAE is required, and may present a barrier to diagnosis when contact with the mother has been lost, or the mother or family refuses to confirm PAE. In addition, the clinical capacity for FASD diagnosis is around 1,602 cases per year in Canada (Popova et al., 2013), and at prevalence rates recently estimated to be between 2 – 3% in Canada (Hrvatin, 2018), FASD is often underdiagnosed.

In addition to the primary effects of PAE, individuals with FASD are also at a higher risk of being exposed to adverse life outcomes. Some of these circumstances involve adverse environments, such as maternal alcohol abuse, living with an alcoholic parent, child abuse and neglect, removal from the home by authorities, and resulting repetitive periods of foster care or other transient home placements (Streissguth et al., 2004). One study that investigated adverse life outcomes found that 61% of adolescents and adults with FASD had experienced disrupted school experiences, 60% had reported trouble with the law (including assault, shoplifting or theft, assault, burglary, or domestic violence), and 35% had been incarcerated for a crime (Streissguth et al., 2004). In addition, the study found that the odds for these adverse outcomes were increased 2- to 4- times when a diagnosis for FASD was made after age 12, with all or almost all adverse outcomes increasing when there was a low percent of life in a stable or nurturing home, or being a victim of physical abuse, sexual abuse, or domestic violence.

2.1.1 FASD and the Criminal Justice System

Individuals with FASD are believed to be overrepresented in the CJS. One study in` the US suggests that individuals with FASD are at greater risk for being in trouble with the law, which included ever being charged, arrested, convicted, or otherwise being in trouble with the law: of 415 subjects with FASD, 14% of children and 60% of adolescents and adults with FASD had previous trouble with the law, (Streissguth et al., 1996). However, inconsistent reporting is a barrier for determining exact rates of FASD among incarcerated populations. Studies in Western Canada have estimated the prevalence of FASD among youth offenders at 23.3% (Fast et al., 1999), 11.7% (Murphy et al., 2005), and 10.9% (Rojas & Gretton, 2007). One study conducted on adult offenders in Manitoba estimated rates of FASD at 9.9% in the CJS (MacPherson & Chudley, 2007). However, these studies all made estimates based on extrapolations from small samples. Furthermore, the additional complication of FASD being an invisible disorder with very heterogeneous presentations, and the low capacity for diagnosing FASD as well as unclear histories of PAE in many individuals suggests these rates are very likely to be underestimates. A survey conducted in the United States corrections system suggests that less than 1% of cases of FASD have been identified (Burd et al., 2004). Regardless, when compared to the prevalence of FASD in the general population of 2 – 3% (Hrvatin, 2018), these data support the contention that FASD is overrepresented in the CJS (Fast et al., 1999; MacPherson and Chudley, 2007).

Costs attributable to FASD in the CJS are high. One study estimates costs of corrections for youth and adults with FASD at $373.7 million between 2011 and 2012, based on incarceration rates of over 4,000 offenders having FASD on any given day (Popova et al., 2015). Another study including costs attributed to policing, court, correctional services, costs incurred by victims of crimes, and other thirdparties estimated the total annual costs attributable to FASD in the CJS to be closer to $3.9 billion (Thanh and Jonsson, 2015). Identifying individuals with FASD within the CJS may mitigate a portion of these costs by providing insight into the type of programming or rehabilitation plans to mitigate the rate of recidivism, or even ways for better understanding the terms of their parole.

2.2 Saccadic Eye Movements

Saccades are rapid eye movements that center visual targets onto the fovea (Leigh and Zee, 2006). Measuring saccadic behaviours has been shown to be a dependable tool for studying abnormal brain function (Leigh & Kennard 2004; Ramat et al., 2007). This is because tracking eye movement behaviour is easily accessible (all that is required is a system for eye movement tracking), and the neurocircuitry underlying eye movement control has been well studied (Leigh and Zee, 2006). In addition, saccades last less than 100 ms, which is less than the amount of time for the visual system to make a response. This means that each saccade is a ballistic movement where the outcome of the movement is dependent on internal controls and is not influenced by visual system feedback. In other words, sensorimotor integration during a movement does not need to be taken into account during the production of a saccade.

Three structured eye movement tasks were used to probe brain function in the current study: prosaccade, antisaccade and the memory-guided saccade task. The prosaccade task examines a participant's sensorimotor processing and requires an individual to make an automatic saccade towards the appearance of a peripheral visual target. The antisaccade task investigates inhibitory control by testing an individual's ability to inhibit a reflexive saccade towards the appearance of a peripheral target as well as internally producing a voluntary saccade of equal size towards the opposite side of the screen. This also requires visuospatial mapping of an imaginary target. The memory-guided saccade task allows researchers to explore a participant's working memory and visuospatial skills. This task is divided into three sequential blocks of increasing difficulty. The first block requires participants to remember the location of a target that flashes quickly in the visual periphery on a screen while they maintain their gaze on a central fixation point, and then produce a voluntary saccade towards the remembered location after receiving the appropriate “go” signal (disappearance of the central fixation point). The two subsequent blocks increase the number of targets to two, and finally three, targets that flash sequentially around the periphery of the screen. The participants are then required to remember both the location and the order of the two or three targets and indicate this by making a series of saccades towards the remembered locations of the targets and in the same sequence of presentation, again after disappearance of the central fixation point.

These tasks allow for quantification and examination of several different saccade characteristics. Extensive studies have demonstrated a consistent positive relationship between the main sequence features: amplitude, peak velocity, and duration of saccades (Becker, 1989). Amplitude of a saccade is measured as the length of a saccade, expressed in degrees. Accordingly, velocity of a saccade is best described as the speed of the eye movement, expressed as degrees per second (°/s). Other characteristics that can be used to assess the quality of saccades include the trajectory, accuracy, and latency (Leigh and Kennard, 2004). Accuracy is best assessed in the prosaccade task, which requires participants to look towards a visible target. Normally, typically developing participants exhibit small degrees of hypometria, or undershooting the target (Leigh & Kennard, 2004), and inaccuracies are generally adjusted using small corrective saccades (Leigh & Zee, 2006). Latency is defined as the interval between target presentation and onset of saccadic initiation.

2.2.1 Eye Movement Control Tasks

Prosaccade Task

This is a structured task that can be used to measure features of automatic saccades. It requires participants to focus on a central fixation point before making an automatic saccade towards a visual target that suddenly appears on the periphery. (Figure 3-1(A)) The outcome features in this task can more accurately assess a participant’s accuracy in making a saccade towards a target, and the main sequence of their saccades, as this is the only task that requires participants to make a movement towards a visible target on screen.

Antisaccade Task

This is a structured task that can be used to assess higher cognitive functioning. It begins like the prosaccade task by requiring participants to focus on a central fixation point. However, instead of looking towards the target that appears suddenly in the periphery, participants are instructed to inhibit the automatic saccade and initiate a movement away from the visual target in the equal and opposite direction (Figure 3-1 (B)). As a result, in addition to measuring sensory-motor control, this task is also able to assess a participant's higher-level top-down inhibitory control. Error rates between different populations are especially of interest, as they can be used to probe differences in cognitive functioning. Electrophysiological studies in monkeys performing the antisaccade task found that in the superior colliculus (SC), fixation related neurons had increased activity, while saccade-related neurons decreased in activity compared to the prosaccade task (Everling et al., 1999). Due to the recruitment of higher level control, areas such as the frontal cortex and basal ganglia are recruited during performance of this task (Munoz and Everling, 2004).

Memory-guided Saccade Task

This is a structured task that has been shown to assess response inhibition and working memory. Participants were instructed to look at a central fixation point while targets flashed in the periphery. In this study, three conditions of this task were administered in order of increasing difficulty. The first condition involved one target flashing in the periphery, the second condition two targets, and the final condition, three targets. The conditions were called the one-target, two-target, and three-target conditions, respectfully (Figure 3-1 (C, D, E)). The participants were required to wait until the central fixation point had disappeared to make saccades to the remembered locations of the targets in the same order that they had flashed. Different types of errors made in this task are indicative of failures in different areas of top-down control. Timing errors occurred when participants made movements towards the locations of the targets before the fixation point disappeared, and indicated deficits in response inhibition, and possibly attention. Sequence errors occurred when participants looked towards the remembered locations of the targets in the wrong order, and skip errors occurred when participants failed to look at one of the targets in the two- or three-target conditions. These types of errors indicated deficits in working memory and attention.

The dorsolateral prefrontal cortex (dlPFC) has been shown to play an important role in the successful completion of this task. They show fine tuning to spatial locations, and each neuron responds best to a specific area, called the memory field (Funahashi et al., 1989). The dlPFC has also been shown to encode commands to the SC regarding stimulus, delay, and saccade-related activity (Johnston et al., 2007).

2.2.2 Overlap of Neurocircuitry of Saccadic Control and Areas Affected by PAE

Overlapping neurocircuitry between brain regions involved in the production and initiation of saccadic eye movements and areas affected by PAE provides support for the potential of measuring eye movement behaviours as a sensitive tool for differentiating individuals with FASD from control groups. Since many brain regions are involved in receiving and processing information from the environment and producing a saccade, damage to multiple brain regions can produce changes in saccade production and initiation. Furthermore, eye movement control tasks have been shown to relate directly with psychometric tests of response inhibition, working memory and visuospatial skills used for FASD diagnosis (Paolozza et al., 2014a; 2014b).

Many areas of the brain are involved in coding for saccadic main sequence. The localization of a stimulus of interest is represented by the activity of place-coded cells on an internal map within the primary visual cortex. This input is projected to ocular motor neurons, which produce a motor command encoding saccade characteristics (Crawford & Guitton, 1997). In the prosaccade and antisaccade tasks, participants are required to make a saccade either towards or in the opposite direction of a visual target along a horizontal plane in line with the central fixation point. These horizontal saccades are generated by the pons. Excitatory burst neurons found within the paramedian pontine reticular formation (PPRF) are critical in generating the initial force to produce a horizontal saccade, whereas the generation of vertical saccades requires activation of the rostral mesencephalon. The initial velocity of saccades requires activity of excitatory burst neurons within the rostral interstitial nucleus of the medial longitudinal fasciculus (MLF).

Different brain regions and neurons characterize the amplitude and direction of saccades. These structures work together to contribute to differences in saccade metrics and accuracy. Specifically, the nucleus reticularis tegmenti pontis deduces the size and direction of saccades (Van Opstal et al., 1996) before projecting to the dorsal vermis and caudal fastigial nucleus of the cerebellum. The dorsal vermis then further modulates the saccade by regulating the amplitude and trajectory throughout the duration of a saccade (Keller et al., 1983) and works with the fastigial nucleus to control saccade accuracy. The use of an internal feedback model to examine motor commands helps to control saccade accuracy by making rapid adjustments of saccade duration, thereby correcting for projected errors (Robinson & Fuchs, 2001). However, in individuals with FASD, general decreases in cerebellar volume (Archibald et al., 2001; Autti-Rämö et al., 2002; Mattson et al., 1992) and localized changes to the anterior vermis (Autti-Rämö et la., 2002) have been observed.

The SC is another structure involved in saccade production. The layers within the SC are separated by their role in various visual and motor commands. The dorsal layers of the SC are involved in vision commands and contain a map of retinal projections of the visual field, whereas the ventral layers are involved in motor commands and contain a motor map of eye movements (Moschovakis et al., 1988a; Moschovakis et al., 1988b). The direction and size of saccades produced depends on stimulation of specific sites within the ventral layers of the SC. Stimulation to caudal regions within the ventral layers produces larger saccades, while stimulation to the rostral regions produces smaller saccades. Upward and downward saccades are produced through stimulation to the medial and lateral regions of the ventral layers within the SC. These saccades occur in an all-or-none fashion (Leigh & Zee, 2006). Both the frontal and parietal lobes project to the SC.

The frontal and parietal lobes have important roles in the control of eye movements. Regions within the frontal lobe, such as the frontal eye fields (FEF), secondary eye fields (SEF) and dlPFC have specific roles with regards to the control and production of eye movements. The FEF are involved in the production of saccades. Voluntary saccades and learned and complex eye movements are controlled by neurons in the SEF (Petit et al., 1996). The dlPFC also plays a role in voluntary saccades, particularly those that require inhibition and memory (Everling et al., 1998; Sweeney et al., 1996). The posterior parietal and parietal eye fields each have a role in regulating eye movement behaviours. Shifting visual attention to a new relevant object requires the posterior parietal cortex, whereas the parietal eye fields are thought to be predominantly involved in making saccades to specified targets with spatial coordinates (Thier & Anderson, 1998).

Two components of the thalamus contribute to saccade production: the pulvinar and cerebral nuclei of the internal medullary lamina (IML). Neurons within the pulvinar appear to exhibit some responsibility in retinal image motion and shifting visual attention (LaBerge & Buchsbaum 1990; Robinson et al., 1991). The IML appears to be involved in voluntary and visually-guided saccades and may be a source for imitating and redirecting signals from the motor cortex to the cortical eye fields. The IML projects to the frontal lobes and caudate nucleus (CN) of the basal ganglia while receiving inputs from the SC (Schlag-Rey & Schlag, 1984). The CN has many communal connections with other basal ganglia structures such as the substantia nigra pars reticulata (SNpr) and receives inputs from structures in the frontal lobes involved in eye movement control. Additionally, the CN is involved in memory, expectations, attention, and reward, all of which contribute to the regulation of eye movements (Hikosaka et al., 1989; Kato et al., 1995). The SNpr has also been shown to have a role in visually-guided or memory-guided voluntary saccades (Hikosaka & Wurtz, 1983a; Hikosaka & Wurtz, 1983b; Hikosaka &

Wurtz 1983c). In relation to FASD, decreases in volume have been found in the thalamus and basal ganglia, specifically the CN (Lebel et al., 2011).

As mentioned previously, the brain regions important for the production and execution of saccades appear to be regions that are affected by PAE. Specifically, the SC, cerebellum and brainstem are involved in circuits required for the execution of saccades and the correction of the amplitude of saccades (Robinson et al., 2001). The SC produces the signal that encodes a saccade of a particular size (Goossens & van Opstal, 2006) before directly projecting it to the pontine burst generator (Buttner-Ennever, 2008) and indirectly projecting through the cerebellar oculomotor vermis (Scudder et al., 2002). The role of the cerebellum in eye movements is believed to include stopping and steering saccades so that accuracy and consistency are optimized (Quaia et al., 1999). Oculomotor input from the pontine nuclei are sent to the cerebellum, which is then projected to the cerebellar vermis posterior lobe (Scudder et al., 1996). Vermis Purkinje cells further project the signal to the caudal fastigial nucleus which then supplies it to oculomotor circuitry that control saccades, namely, the excitatory and inhibitory burst neurons and omnipause neurons within the brainstem (Robinson & Fuchs, 2001; Scudder et al., 2002). Using an internal feedback model, the cerebellum contributes to saccade accuracy (Quaia et al., 1999), in which feedback from motor execution is compared to the motor command and used to make online corrections to maximize saccade accuracy (Chen-Harris et al., 2008). Previous studies have consistently identified decreased volume of the cerebellum and anterior cerebellar vermis in children with an FASD diagnosis (Archibald et al., 2001; Autti-Rämö et al., 2002; Mattson et al., 1992). Therefore, it seems likely that damage to this brain structure contributes to altered characteristics of saccades (e.g., amplitude, accuracy) in individuals with FASD.

Deficits in working memory can be assessed with the memory-guided saccade task. Successful completion of this task involves the posterior parietal cortex (Wager & Smith, 2003) and the dlPFC (Muri et al., 1996; Pierrot-Deseilligny et al., 1991). Accuracy of memory-guided saccades has been shown to be impaired by lesions and transcranial magnetic stimulation to the dlPFC (Muri et al., 1996). Children with an FASD diagnosis tend to make more mistakes during the memory-guided saccade task (Hemington and Reynolds, 2014; Paolozza et al., 2015). This may be due to deficits in spatial working memory. Magnetic resonance imaging (MRI) has demonstrated that parietal lobes appear to be more severely affected by prenatal alcohol exposure than the temporal and occipital lobes (Archibald et al., 2001). Difficulty with updating the remembered location of multiple targets in the memory-guided saccade task may be another reason for decreased accuracy in children with FASD compared to typically developing children. The parietal cortex may play a part in this process, as it plays an important role in target remapping (Duhamel et al., 1992).

2.2.3 Eye Movement Control in Children with FASD

Measuring eye movement behaviours is one technique that has identified differences between typically developing children and children with an FASD diagnosis (Green et al., 2009; Paolozza, 2015; Paolozza et al., 2013; Tseng et al., 2013). Many studies have shown that the measurement of eye movements can be used to assess sensorimotor control, working memory, and executive function (reviewed in Leigh & Kennard, 2004; Munoz and Everling, 2004). In particular, executive function deficits have been suggested to be a distinctive feature of PAE. This includes problems with impulsivity, planning, and working memory (Rasmussen, 2005). Executive function processes occur in the frontal lobe, and studies have found positive correlations between decreased psychometric verbal memory scores and surface area of the right frontal region of interest (Gross et al., 2017). Thus, given the considerable overlap between the brain structures that produce and regulate saccades (Leigh & Kennard, 2004; Munoz & Everling, 2004) and the areas shown to be susceptible to damage due to PAE, including the frontal lobes, thalamus, basal ganglia, and cerebellum (Rasmussen, 2005), it seems logical to predict that deficits in eye movement control may differentiate individuals with FASD from neurotypical controls. Differences in saccade characteristics have also been demonstrated to show that measuring eye movement behaviours can identify discrepancies in brain function in children and individuals that have been prenatally exposed to alcohol.

In this regard, previous studies looking at eye movement control have found differences between children diagnosed with FASD and age- matched typically developing control children. Children with FASD had longer latencies in both prosaccade and antisaccade tasks, with longer saccadic reaction times (SRT) being seen in antisaccade as compared to prosaccade trials (Green et al., 2009). This may reflect the increased processing required to successfully complete the more difficult antisaccade task. In general, children with FASD also displayed a greater percentage of direction errors than control children in the antisaccade task (Green et al., 2009; Paolozza et al., 2013; 2014a), indicating a weakened inhibitory response, and which appears to reflect deficits in executive function. Additionally, children with FASD displayed an overall decrease in accuracy towards the target. They displayed a greater number of step saccades in order to bring the final endpoint gaze closer towards the target, as well as greater end point errors in both the horizontal and vertical directions (Paolozza et al., 2013, 2014b). Interestingly, one study highlighted that the variability of SRTs in children with FASD were much greater (Green et al., 2009), which supports results finding a high degree of intra-individual variability in children with FASD as compared with typically developing controls (Ali et al., 2018).

Research that involved investigating differences in performances across memory-guided tasks also found that children with FASD tended to make more mistakes, including both sequences errors (looking towards the remembered targets in the wrong order) and timing errors (making a saccade before the go signal), indicating deficits in attention, working memory, and inhibition (Hemington & Reynolds, 2014; Paolozza et al., 2015). Moreover, neurophysiological evidence suggests that children with FASD need to recruit greater cognitive resources to successfully perform the memory-guided saccade task compared with typically developing controls (Hemington & Reynolds, 2015). Taken together, previous studies have demonstrated that deficits in saccadic eye movements provide an objective measure of brain dysfunction in children with FASD. However, to the best of our knowledge deficits in eye movement control have never been assessed in adults with FASD.

2.3 Research Rationale, Objectives, and Hypothesis

Individuals with FASD are at greater risk for adverse outcomes, including criminal justice involvement. In order to pinpoint areas of focus to better serve this population's needs in the CJS, reliable prevalence rates and ways of identifying individuals with FASD need to be established. These methods of identifying individuals with FASD in the CJS must be able to circumvent the lack of resources available to screen every individual upon entry for FASD. Since many areas of the brain that are known to be affected by PAE overlap with areas known to be involved in eye movement control, and tracking eye movements is a more rapid and cost-effective option when compared to the time and specialized training required for diagnostic teams, this method could contribute to a screening tool for rapid identification of individuals at risk for FASD in the CJS.

This research had the goal of investigating whether there is a quantitative difference between eye movement behaviours in adults with FASD in the CJS and corresponding control groups for justice involvement and FASD, as well as a community control group. While this study is the first looking at adults with FASD, previous studies have found differences in eye movement behaviour in children with FASD (Paolozza et al., 2014a; 2014b). As a result, we hypothesize that:

1. Adults with FASD in the CJS will display significant differences in eye movement control compared with adults without FASD in the CJS.
2. Adults without FASD in the CJS will exhibit different patterns of eye movement control compared with community controls.

Chapter 3

Methods and Materials

3.1 Participants

All experimental procedures were reviewed and approved by the Queen’s University Human Research Ethics Board and the University of Guelph Human Research Ethics Board. Four groups of adults between the ages of 18 and 40 including both men and women were recruited from a northern Canadian community. These groups included:

1. Justice-involved FASD Group: Participants with a confirmed FASD diagnosis who are currently involved in the CJS, including both community and correctional settings.
2. Non-justice involved FASD Group: Participants with a confirmed FASD diagnosis who are not currently involved in the CJS.
3. Justice-involved Comparison Group: Participants were screened to confirm no FASD diagnosis and no PAE. Adults who were suspected to have FASD but did not have an official diagnosis were excluded.
4. Typically Functioning Control Group: Participants will include healthy adults from the same northern Canadian community who underwent pre-screening to confirm an absence of PAE or FASD, and/or significant cognitive, neurological, or mental health conditions. Adults who were suspected to have FASD but did not have an official diagnosis were excluded

Exclusion criteria for all participants included visual disturbances other than the need for corrective lenses, which could be worn throughout the duration of the study if required.

In most cases, data collection was completed in one session, but participants were given the opportunity to take a break if needed. Participants were compensated $50 for their time (prorated if experiment was terminated early). All participants completed a consent form. After each section, participants were asked questions to ensure full comprehension. They were also given an opportunity to raise questions or concerns between each section. Demographic information describing all participants is shown in Table 3-1.

Table 3-1 Demographic information from the four participant groups.

	FASD Diagnosis		Controls	
(N = 37)	Justice-involved (n=8)	Justice Control (n=7)	Justice-involved (n=11)	Community Control (n=11)
Age in years (±SD)				
	30.88 (3.14)	28.71 (5.22)	27.73 (4.05)	31.64 (5.50)
Sex N (%)				
Male	8 (100)	2 (28.6)	9 (81.8)	4 (36.4)
Female	0	5 (71.4)	2 (18.2)	7 (63.6)
Socioeconomic status				
Education (< HS/GED)	5 (63%)	1 (14%)	7 (64%)	1 (9%)
Income (<$15,000 per year)	7 (88%)	4 (57%)	4 (36%)	0 (0%)
Estimated Intelligence Quotient (±SD)				
	62.3 (3.2)	62.1 (6.2)	73.2 (10.3)	99.1 (10.1)
Comorbidities Present at Study N (%)				
ADD/ADHD	4 (50%)	2 (29%)	2 (18%)	1 (9%)
Depression	2 (25%)	2 (29%)	5 (46%)	1 (9%)
Anxiety	0 (0%)	2 (29%)	2 (18%)	0 (0%)
Learning Disorder	4 (50%)	4 (57%)	1 (9%)	0 (0%)
Addictions Present at Study N (%)				
Drug Abuse	7 (88%)	4 (57%)	9 (82%)	0 (0%)
Alcohol Abuse	7 (88%)	3 (43%)	9 (82%)	0 (0%)

3.2 Experimental Setup

3.2.1 Eyelink 1000 Portable Eye-tracking System

A portable eye-tracking system, the Eyelink 1000 (SR Research, Kanata, ON) was used to track the saccadic eye movements of participants during the performance of structured and unstructured tasks. Whereas most eye movement studies are normally conducted in a darkened, quiet room, this was not possible in the correctional centre setting. As a result, data from incarcerated participants was collected in an isolated room without windows but with the lights on. Otherwise, the experimental setup was consistent with previous studies, with participants seated in a stable chair approximately 600 mm away from a 17” LED computer screen with an infrared illuminator and infrared camera mounted on the base. For participants that were not currently incarcerated, data was collected in across different sites under conditions as similar as possible to the setup at the correctional centre. A small target sticker was placed on the participants’ forehead to facilitate eye tracking. By default, the right eye was used for all experiments unless difficulties with calibration presented. Before each task, a nine-point calibration routine was completed. If difficulties presented with calibration (calibration process of greater than approximately 15-20 minutes), a five-point calibration was completed. The calibration routine consisted of presenting visual targets at locations that covered the entire visual field of the screen, with participants instructed to fixate on each target. Following calibration, a validation task was completed to ensure that the error between tracked fixation of the participant’s eye and actual location of the calibration targets was < 2°. Once calibration and validation tasks had been successfully completed, participants started performing the eye-tracking tasks. Once initiated, tasks were completed from beginning to end. The tasks were administered in the following order: two blocks of Anti-Prosaccade interleaved, three blocks of different Memory-Guided conditions, and finally one block of Free-Viewing (see below for detailed description of the eye movement tasks).

3.2.2 Muse EEG Headband

A portable EEG headband, the Muse headset with research presets (500 Hz sampling rate, no onboard data processing: InteraXon, Ontario, Canada; see http://developer.choosemuse.com/hardware-firmware/hardware-specifications for full technical specifications) was used to measure brain electrical activity during the performance of all eye-movement tasks. Data was streamed to a laptop running MuseLab (InteraXon, Inc.) Participants were shown how to put on the Muse headset, which places the electrodes at approximately Fpz (reference) and TP9, AF7, AF8, TP10 (channels) by 10-20 International Standards. Before starting calibration with the Eyelink 1000, we started recording with the Muse. To ensure proper recording, we asked participants to blink rapidly at the start of each trial. During the performance of eye movement tasks, the Muse headband was connected to the computer running eye movement tasks in order to produce a time stamp marker at the start of each trial within each of the four eye movement tasks, and one free-viewing task. Due to time constraints, data from this task was not analyzed and results from this task will not be discussed further.

3.2.3 Psychometric Measures

After the completion of the eye-movement tasks, a series of psychometric tests were applied. While these measures were collected in the same session, analysis was conducted separately.

Weschler Adult Intelligence Scale

The Wechsler Adult Intelligence Scale – Fourth Edition (WAIS-IV) is the gold-standard for evaluating overall intellectual functioning. In this study we administered four WAIS-IV subtests: Vocabulary (defining words), Matrix Reasoning (using matrices to solve visual puzzles), Digit Span (listening to verbalized digits and repeating them in the correct order), and Arithmetic (listening to math problems and solving them mentally). These assessed vocabulary, non-verbal spatial reasoning, attention, and working memory.

Weschler Adult Memory Scale

The Wechsler Adult Memory Scale – Fourth Edition (WMS-IV) assesses verbal and non-verbal measures of visual and verbal memory. We administered the Symbol Span subtest, which involves viewing a span of symbols and recalling them, as a measure of visual working memory.

Delay Discounting Task

Two delay discounting tasks measures the preferences between smaller-immediate and larger-delayed monetary rewards. We administered the hypothetical delayed $100 reward and the $1000 reward.

Addictions

Participants were administered the Alcohol Use Disorders Identification Test (AUDIT) and the Drug Use Disorders Identification Test (DUDIT) to assess substance use and misuse. In addition, the Fagerstrom Test for Nicotine Dependence (FTND) was used to assess the level of nicotine dependence.

3.3 Eye Movement Task Paradigms

3.3.1 Anti-Prosaccade Interleaved

The interleaved anti-prosaccade task was a modification of the paradigm used in previous studies (Paolozza et al., 2013, 2014a, b). In the previous studies, the antisaccade and prosaccade tasks were separated by block because the participants were children under the age of 18. Since our participants consisted of participants above the age of 18, modifications involved randomly interleaving trials of both tasks within the same block to increase task difficulty. The colour of the central fixation point was used as an indicator for task (prosaccade versus antisaccade). Participants were instructed that a green central fixation point indicated the prosaccade task, and a red central fixation point indicated the antisaccade task. Each block of the AP task consisted of 60 prosaccade and 60 antisaccade trials. Participants were administered two blocks of the anti-prosaccade interleaved task, for a total of 240 trials (120 antisaccade trials, 120 prosaccade trials).

Similar to the previous papers, trials of both the prosaccade and antisaccade tasks began with illumination of a fixation point (FP) in the middle of the screen for 1,000 ms, after which the FP would disappear for 200 ms (gap period). This was followed by the appearance of a peripheral target at 10°

randomly to the right or left of the location of the central FP. After the appearance of a target, participants were given 1,000 ms to make a saccade in the right direction towards the target (prosaccade) or away from the target (antisaccade) before the start of the next trial. No error feedback was given.

3.3.2 Memory-Guided Saccade Task

This task is a modification of the paradigm used in a previous study (Hemington & Reynolds, 2014). Whereas the previous study included all three conditions in one block of 72 trials, this study separated each condition by block. Each block consisted of 54 delayed memory-guided trials with drift corrections performed every 10 trials. The first block consisted of 54 trials in the one-stimulus condition (1-target memory-guided task), the second block consisted of 54 trials in the two-stimuli condition (2-target memory-guided task), and finally the third block consisted of 54 trials in the three-stimuli condition (3-target memory guided task).

Across all three conditions, trials started with the appearance of a central FP. Participants were told to fixate on the central FP for the entire time it appeared onscreen, and to only make sequential saccades to the one, two, or three remembered locations of the peripheral stimuli in the same order they were presented once the central FP had disappeared. After a randomized period of between 200 – 1,000 ms after appearance of the FP, the first peripheral stimulus flashed onscreen. Depending on the block administered, one, two, or three peripheral stimuli (for 1-target, 2-target, and 3-target, respectively) flashed sequentially onscreen for 100 ms each. After disappearance of the last peripheral stimuli, the FP stayed on-screen for a randomized time period of either 0, 600, or 1,200 ms before disappearing and serving as the go signal. These two randomized time periods were included to deter participants from anticipating stimuli appearance and anticipating the go signal. No error feedback was given.

3.3.3 Free-Viewing Task

This task has been described in a previous study (Tseng et al., 2013). Participants' eye traces were recorded while passively watching video clips. Each clip was one minute long and composed of 2 – 7 seconds of clip snippets. Participants were each administered 10 clips that were unrelated and randomly administered to minimize predictability. Due to time constraints, data from this task was not analyzed and results from this task will not be discussed further.

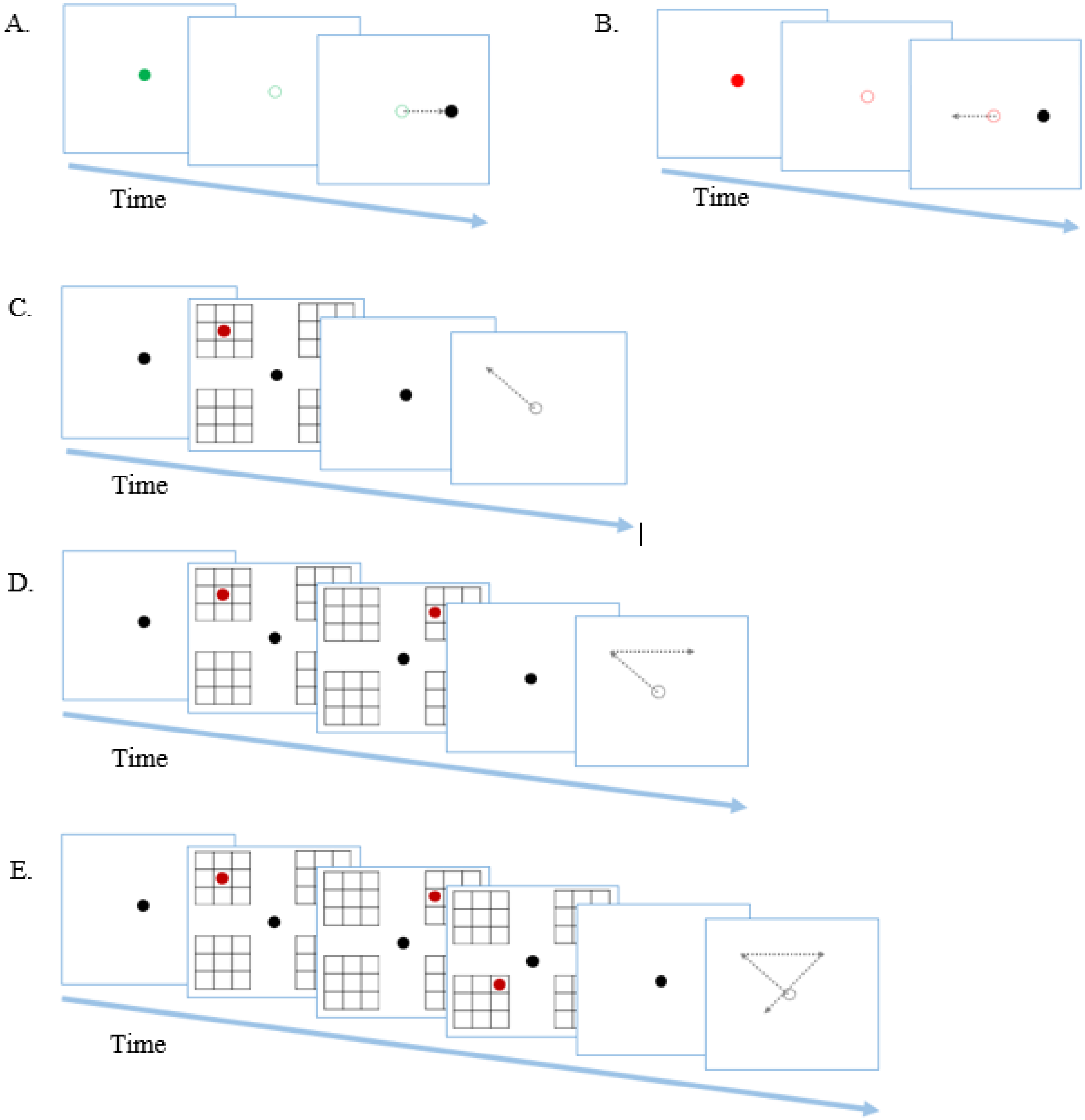

Figure 3-1. Structured saccadic eye movement tasks.

(A) Prosaccade task with green central fixation point and (B) antisaccade task with red central fixation point and peripheral targets (black circles) with the correct saccade (dashed arrows). The delayed memory-guided saccade task paradigms, including (C) 1-target, (D) 2-target, (E) 3-target conditions begin with the participant fixating on the central fixation point (black circles). The participant is asked to remember the location of one (C), two (D), or three (E) peripheral target stimuli that flash sequentially for 100 ms each. Dashed arrows represent correct saccades. Grids are not visible to participants.

3.4 Data Analysis

Eye movement data was collected at a sampling frequency of 500 Hz and processed using custom software developed in Matlab (Version R2017b; Mathworks, Inc., Natick, MA). Saccades were detected based on a speed threshold, calculated by first finding the mode of fixation signal per trial (periods where speed is less than 50 °/s and there are no blinks). The speed threshold was defined as two standard deviations greater than the mode of fixation. Saccades were detected any time the speed of a movement was above the speed threshold for 5 or more consecutive sampling points. Metrics were calculated on these saccades. Saccadic reaction time (SRT) being defined for the prosaccade and antisaccade tasks as the time from appearance of the target to initiation of a saccade. SRT was defined for the memory-guided tasks as the time from disappearance of the central fixation point to initiation of a saccade towards a target. Trials in which eye tracking was lost or eye movements were difficult to detect or track were not considered viable and were discarded.

3.4.1 Automated Analysis

A custom automated analysis program was developed to mark the eye-tracking data. This was done to eliminate experimenter bias that may occur when manually marking the eye-tracking data.

Antisaccade and Prosaccade Automarker

The first step in the analysis program involved cleaning the data before extracting outcome features. This included blink detection and removal, converting the data from pixels displayed on the monitor used for displaying the task to the visual angle relative to the participant and the screen, velocity calculation, and establishing a threshold for saccade detection.

After data cleaning, the automated analysis calculated saccade outcome features by consistently marking the eye traces and calculating quantifiable outcome measures using the following steps:

1. Identify well-behaved saccades (velocity < 1500°/sec, amplitude > 0.75°, and that occur within 600 and 1,250 ms of target onset).
2. Sort well-behaved saccades based on:

    a. Whether they return to fixation (saccades that occur within a 4° square window of the FP)
    b. The number of macrosaccades (defined as discrete saccades of ≥ 2°)
    c. Whether saccades are in the direction of the target
3. Identify the main macrosaccades from the saccades in step 2 (> 3° pre-target, > 2° post-target, and > 0.75 ° steps)
4. Identify whether saccades are correct (towards the target for prosaccade trials and away from the target for antisaccade trials) or a direction error, as well as whether corrective saccades are made after the first saccade (regardless of whether the initial saccade was correct or an error)
5. Identify if a false start occurred in the trial
6. Identify step saccades (saccades that increase the accuracy to the goal after the aim goal-directed saccade, and must occur within 400 ms after the first goal-directed saccade) in the trial
7. Mark the onset of macrosaccades, false starts, and step saccades

Memory-Guided Automarker

Like the anti-prosaccade task automarker, this starts with cleaning the data to ensure consistent marking. The same algorithms are used for blink detection and removal, conversion of data from pixels to a visual angle centered on the screen, velocity calculation, and calculation of a threshold for saccade detection.

The memory-guided automarker consists of the following steps:

1. Identify well-behaved saccades (velocity < 1500°/sec, amplitude > 0.75°, and that occur within 600 and 1,250 ms of target onset).
2. Sort well-behaved saccades based on:
    a. Whether they return to fixation (saccades that occur within an 8° square window of the FP)
    b. The number of macrosaccades (defined as defined as discrete saccades of ≥ 2°)

3. For the remaining saccades from step 1, calculate the first angle offset (Figure 3-2) investigate the direction of each saccade, and calculate the change in direction from one saccade to the next.
4. Identify false starts
5. Mark trials as correct if the number of saccades agree with the trial type (i.e. 1 saccade for Mem1, 2 saccades for Mem2, and 3 saccades for Mem3). When looking at movement from one remembered stimulus to the next, there must be at least 20 ms separating two subsequent saccades.
6. Identify and mark sequence errors.
7. If criteria in steps 5 and 6 are met, identify and mark stop errors
8. If criteria in steps 5, 6, and 7 are met, identify and mark skip errors.
9. Mark step saccades.
10. Mark the onset of all macrosaccades, error types, false starts, step saccades, and the fixation distance of the first saccade.

3.4.2 Calculating Errors

There are a number of different errors measures that were collected from the data. The antisaccade, prosaccade, and memory-guided tasks all measure anticipation errors, false starts, and no saccade trials. Anticipation errors are defined as saccades that are made during the anticipation epoch (< 90 ms) after the go signal (appearance of the target in antisaccade and prosaccade tasks, and disappearance of the FP in the memory-guided tasks). False starts are defined as trials where participants make a saccade during the fixation period but returns their gaze to the FP before initiating the task properly. This can also be considered a correction of an anticipatory error. These two errors can indicate deficiencies or difficulties in attention and inhibitory control. No saccade errors indicated trials where participants made no movement after the go signal.

One error that only occurs in the antisaccade and prosaccade tasks is the direction error. This occurs when participants look in the wrong direction (away from the target for the prosaccade task and towards the target in the antisaccade task).

Errors that occurred exclusively in the two-target and three-target memory-guided tasks include sequence errors, skip errors, and stop errors. Sequence errors occurred in trials where participants looked toward the remembered locations of the peripheral stimuli in the wrong order (for example, looking towards the second target before the first in the Mem2 task). Skip errors occurred when participants looked straight towards a subsequent target, bypassing the previous target (for example, looking towards the third target after the first target without ever making a motion towards the second target in the Mem3 task). The stop errors indicated when a participant stopped making movements after looking towards the remembered location of a target without making any subsequent movements towards following targets (for example, stopping after the first target but ignoring the second target in the Mem2 task.

3.4.3 Outlier Removal

A custom program was developed in Matlab (Version R2017b; Mathworks, Inc., Natick, MA) to automatically remove outliers from the eye-tracking data. Data was separated by group and task. Outliers from each outcome feature were identified as data points greater than two standard deviations away from the group mean and were eliminated.

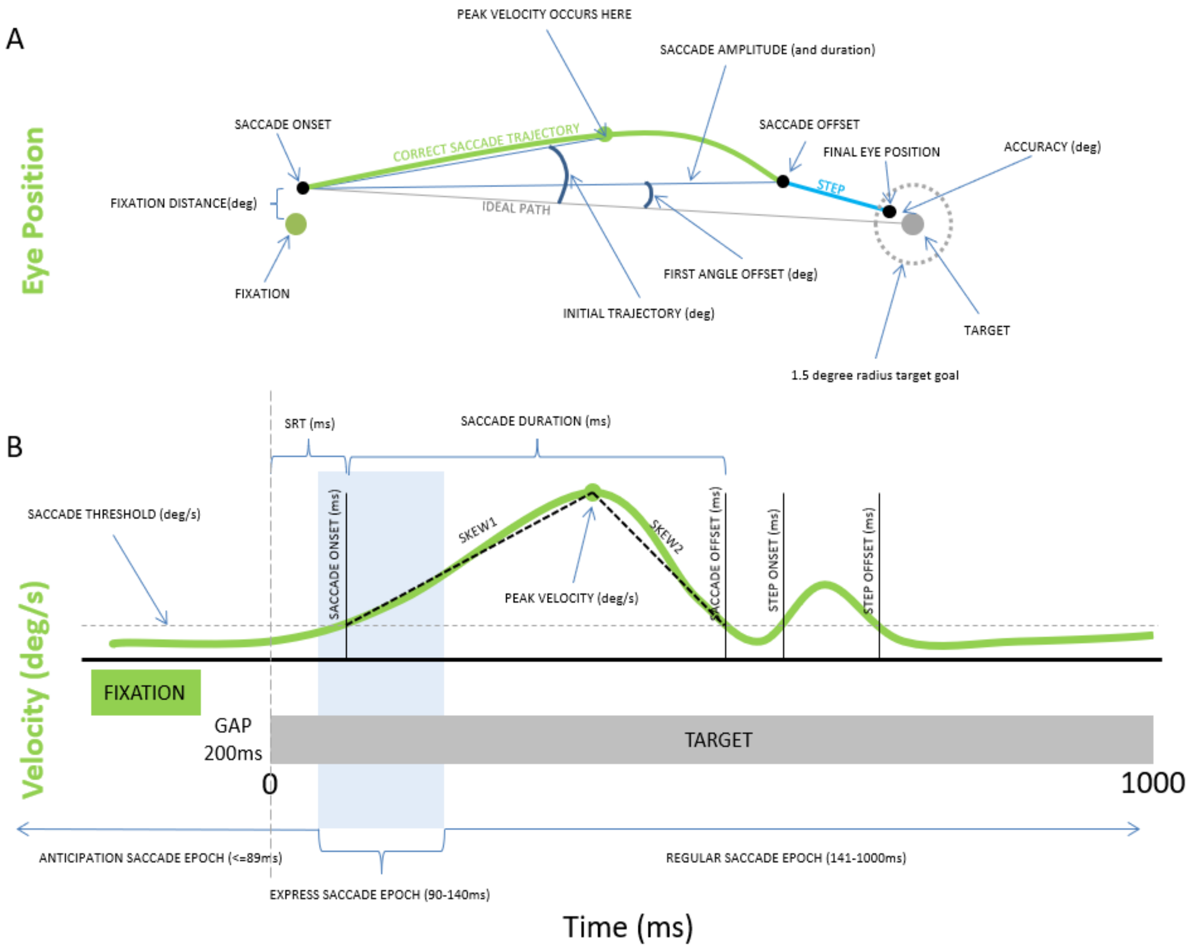

Figure 3-2. Schematic of saccade metric calculation.

Schematic showing how saccade metrics are calculated. (A) Features related to eye position are outlined. (B) Features related to velocity, such as skew are outlined

Chapter 4

Results

4.1 Preliminary Analyses

4.1.1 Demographic Data

The two groups of adults with FASD included the justice-involved group (*n*=8, 8 males) and individuals with FASD living in the community (*n*=7, 2 males), with mean ages (± s.d.) of 31 (3) and 29 (5), respectively. Due to the low number of participants in each group, the two groups were collapsed to create one group of participants with FASD (*n*=15, 10 males) with a mean age (± s.d.) of 30 (4). The group of justice-involved participants without an FASD diagnosis (*n*=11, 9 males) had a mean age (± s.d.) of 28 (4). The group of community control adults (*n*=11, 4 males) had a mean age (± s.d.) of 32 (6). All participant data was collected from a northern Canadian community.

4.1.2 Effect of Repeated Anti-Prosaccade Interleaved Block

First, the two blocks of anti-prosaccade interleaved trials were compared across the three groups (adults with FASD, justice control group, community control group) to determine whether there was an effect of learning on the performance of the anti-prosaccade task. Two-way repeated measures ANOVA with group (FASD, community control, justice control) as the between-subjects factor and block (first anti-prosaccade interleaved block, second anti-prosaccade interleaved block) as the within-subjects factors, did not reveal any significant effect of block for the great majority of outcome measures (data not shown), suggesting that there was no learning effect on the performance of the anti-prosaccade interleaved task. Consequently, the data from the two blocks of anti-prosaccade trials were collapsed together for all subsequent analyses.

4.1.3 Effect of Justice Involvement across the Three Eye Movement Tasks

Next, analyses were performed comparing the three groups across the outcome features of the antisaccade, prosaccade, and memory-guided tasks. One-way ANOVA was conducted to compare the effect of group (FASD, community control, justice control) on outcome features from the three eye movement tasks. None of the major outcome features showed significant differences between the community control group and the justice control group. For example, the frequency of direction errors in the antisaccade task, has been used as a measure for executive function (e.g., response inhibition) in previous studies. One-way ANOVA revealed a significant effect of group on the percent direction errors in the antisaccade task ($F(2,31) = 7.85$, $p = 0.0018$), which was driven by a significant difference between the community control group and the FASD group ($p = 0.0013$). There was no difference between the community control group and the justice control group ($p = 0.28$), while the comparison between the justice control group and the FASD group approached significance ($p = 0.084$) (Figure 4-1). Similar results were obtained for the great majority of outcome measures obtained in all three tasks (i.e., community controls and justice controls did not differ from each other, data not shown). Consequently, the two control groups were collapsed into a single control group for all subsequent analyses.

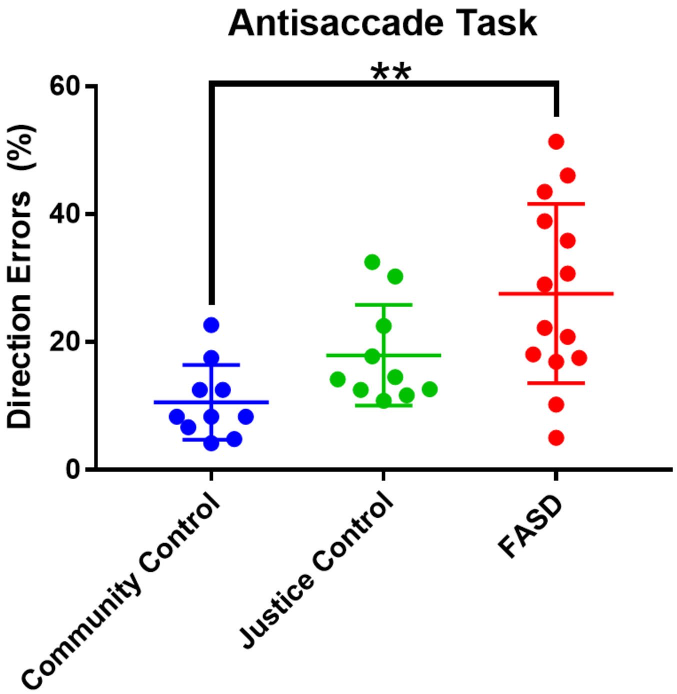

Figure 4-1. Direction errors in the antisaccade task

Participants in the community control group (blue circles) and the justice control group (green circles) did not differ in the frequency of direction errors (*p* = 0.28), whereas the community control group exhibited a lower frequency of direction errors compared with the FASD group (*p* = 0.0013), and the difference between the justice control group and the FASD group approached significance (p = 0.084). Bars represent mean and standard deviation.

4.2 Group Differences: Saccade Performance Outcomes across Adults with FASD and Control

4.2.1 Demographic Data

Once the data had been collapsed based on whether an individual had an FASD diagnosis, the two resulting groups included adults with an FASD diagnosis (*n*=15, 10 males) with a mean age (± s.d.) of 30 (4) and adults without an FASD diagnosis (*n*=22, 13 males) with a mean age of 30 (5).

4.2.2 Outcome Features from the Prosaccade and Antisaccade Tasks

Representative eye traces from a control adult without FASD and an adult with an FASD diagnosis for the prosaccade and antisaccade task are shown in Figures 3.2 and 3.3, respectively. Cumulative distributions of the performance of the prosaccade and antisaccade tasks for all participants are shown in Figure 3.4. Eye movement control outcome features from these two tasks revealed multiple group differences between the adults without FASD and the adults with an FASD diagnosis. Selected outcomes from the two tasks are shown to illustrate some of the major group differences. The outcomes from each task are displayed together to compare the change in performance between the prosaccade task, used mainly for assessing sensorimotor control, and the more difficult antisaccade task, which has been used to assess higher order cognitive processes such as response inhibition. Since the tasks were administered in an interleaved fashion, the tasks also assess attention and working memory in terms of the participants' ability to hold the instruction "green central fixation indicates prosaccade and red central fixation indicates antisaccade" within working memory to perform the tasks successfully. An abbreviated list of the outcome features for these tasks, ranked by effect size, are reported in Table 4-1 for the prosaccade task and Table 4-2 for the antisaccade task. The full lists of all eye-tracking performance outcomes are reported in Appendix A for the prosaccade task and Appendix B for the antisaccade task in Appendix 1.

The selected features include the frequency of direction errors (Figure 4-5), the number of macrosaccades per trial (Figure 4-6) first angle offset (Figure 4-7), saccadic reaction time (Figure 4-8), and the coefficient of variation of saccade amplitude (Figure 4-9). These measures were selected because they represent features of saccade performance (attention, higher order cognitive processing and saccade accuracy) that were consistently found to differentiate adults with FASD from adults without FASD.

The frequency of direction errors (Figure 4-5) was significantly greater in the prosaccade task for adults without FASD (M = 2.51, SD = 0.40) than adults with FASD (M= 0.73, SD = 0.23), (t(32) = 3.45, *p* = 0.0016, *d* = 0.27), however this group effect was reversed in the antisaccade task with adults with FASD (M = 27.69, SD = 3.79) making significantly more direction errors than adults without FASD (M = 15.15, SD = 1.84), (t(32) = 3.26, *p* = 0.0027, *d* = 0.25). This was the only outcome feature in which the group effect was different across the two tasks.

In the prosaccade task, adults with FASD had a significantly greater number of macrosaccades per trial (M = 2.79, SD = 0.30) than control adults without FASD (M = 1.83, SD = 0.083), (t(32) = 3.56, *p* = 0.0012) (Figure 4-6), suggesting that adults with FASD needed to make a greater number of saccades in each trial to move the eyes to the target. In support of this interpretation, the first angle offset (a measure of the error of the first saccade from the ideal path towards the target) was greater in adults with FASD (M = 3.25, SD = 0.36) compared with controls (M = 2.12, SD = 0.12), (t(33) = 3.46, *p* = 0.0015, *d* = 0.27)(Figure 4-7). The saccadic reaction time (SRT) was slower in adults with FASD (M = 179.6, SD = 7.38) compared with controls (M = 158.7, SD = 4.53), (t(32) = 2.53, *p* = 0.017, *d* = 0.17) (Figure 4-8). Finally, the coefficient of variation of saccade amplitude was significantly greater in adults with FASD (M = 13.22, SD = 1.13) compared to the control group (M = 10.11, SD = 0.75), (t(34) = 2.40, *p* = 0.022, *d* = 0.14) (Figure 4-9).

Similarly, in the antisaccade task adults with FASD also had a significantly greater number of macrosaccades (M = 3.4, SD = 0.29) compared with controls (M = 2.12, SD = 0.074), (t(31) = 4.97, *p* < 0.0001, *d* = 0.44) (Figure 4-6) and the first angle offset was greater in adults with FASD (M = 4.24, SD = 0.53) compared to controls (M = 2.61, SD = 0.13), (t(32) = 3.50, *p* = 0.0014, *d* = 0.28) (Figure 4-7). Adults with FASD exhibited a slower SRT (M = 285.4, SD = 13.23) compared to controls (M = 249.6, SD =5.24), (t(33) =2.78, *p* = 0.0092, *d* = 0.19) (Figure 4-8), and a greater coefficient of variation in saccade amplitude (FASD M = 28.03, SD = 2.19: Controls M = 17.72, SD = 1.26), (t(32) = 4.37, *p* = 0.0001, *d* = 0.37) (Figure 4-9).

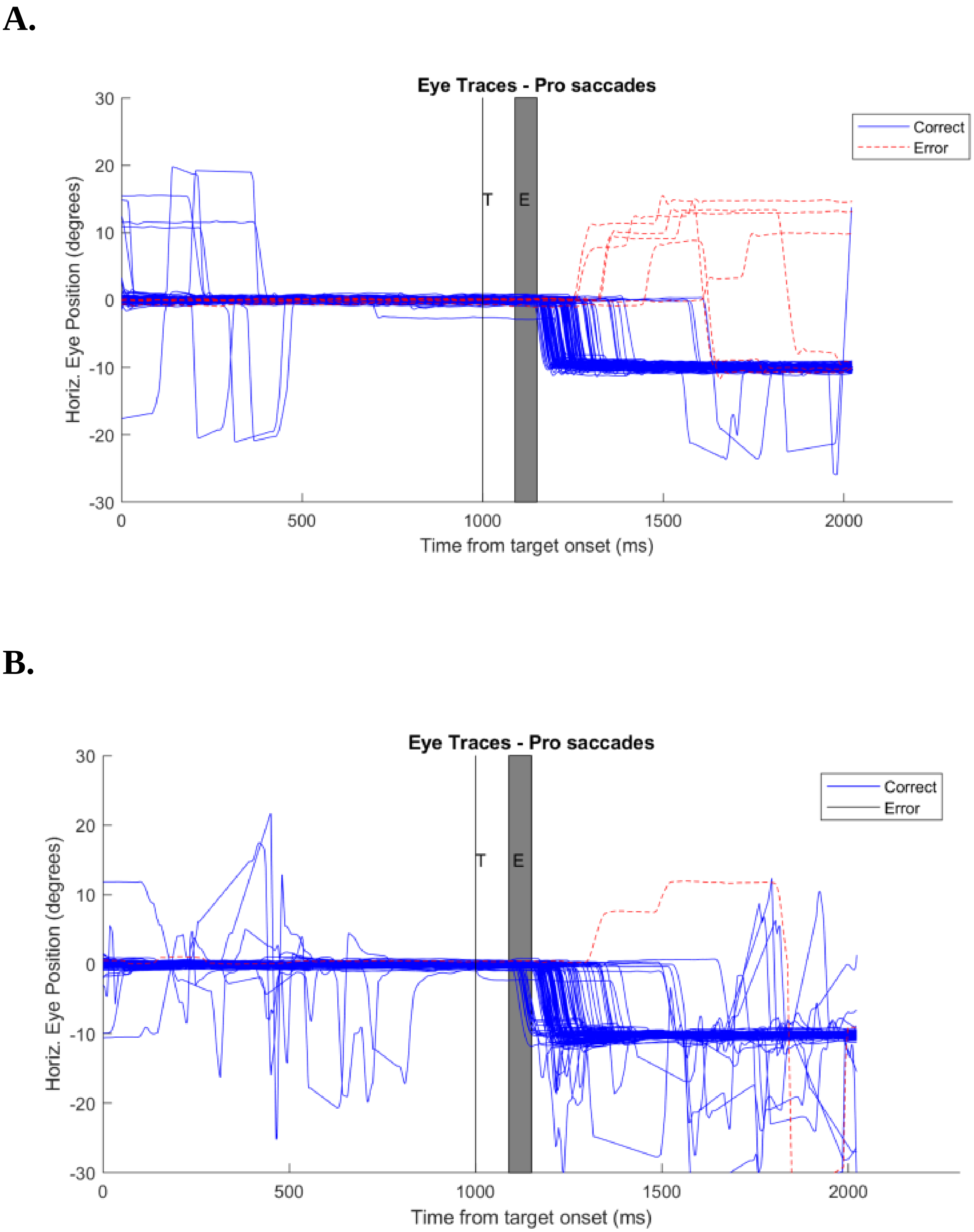

Figure 4-2. Prosaccade task eye traces of a participant with FASD in the CJS and Justice Control

(A) Prosaccade eye-traces of a justice-involved participant without FASD, **(B)** Prosaccade eye-traces of a justice-involved participant with FASD.

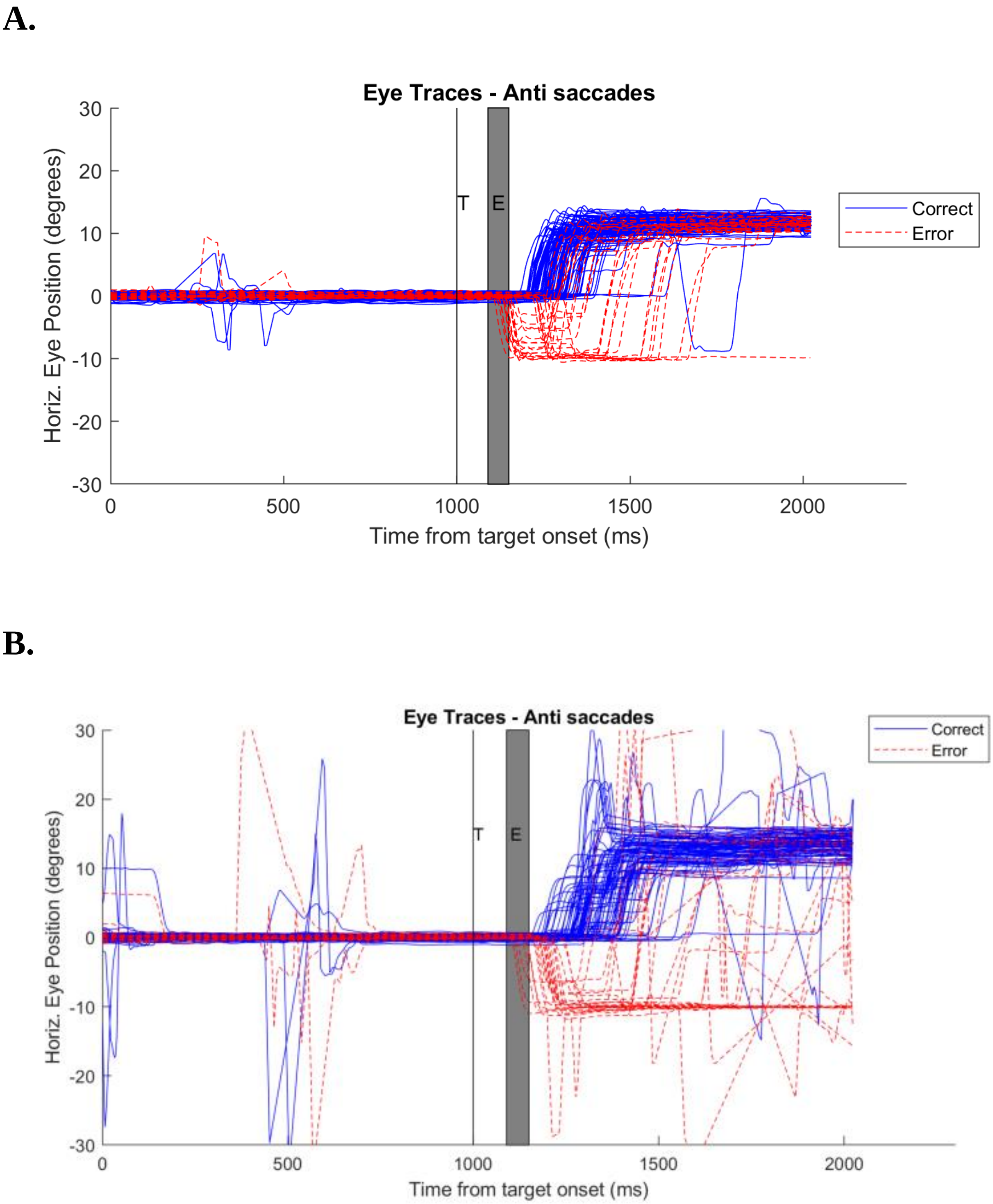

Figure 4-3. Antisaccade task eye traces of a participant with FASD in the CJS and Justice Control

(A) Antisaccade eye-traces of a justice-involved participant without FASD, **(B)** Antisaccade eye-traces of a justice-involved participant with FASD.

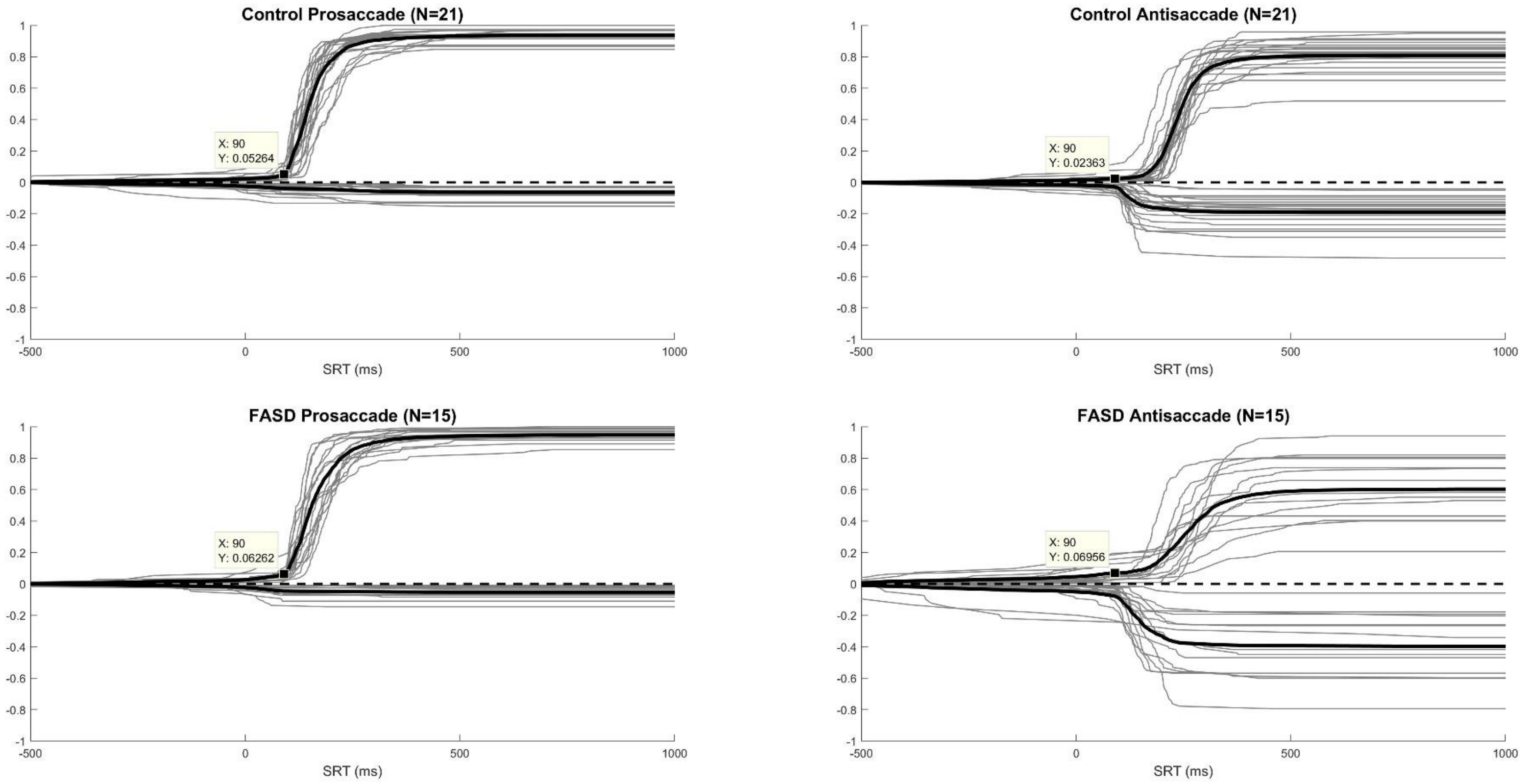

Figure 4-4. Average cumulative distributions of prosaccade and antisaccade tasks from each group.

Average cumulative distribution is displayed in the bold black line. Saccadic reaction time of 90 ms is marked on the distributions to indicate time at which reaction to “go signal” is appropriate.

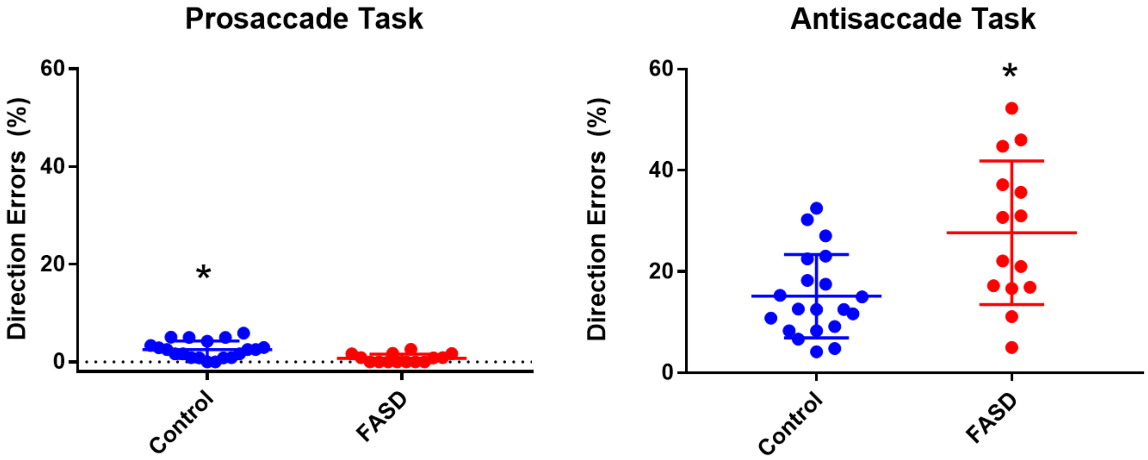

Figure 4-5. Direction errors in the prosaccade and antisaccade tasks.

Adults without FASD (blue circles) had a significantly greater percentage of direction errors (*p* = 0.0016) in the prosaccade task, but this was reversed in the antisaccade task, with adults with FASD showing a significantly greater percentage of direction errors (*p* = 0.0027). Bars represent mean and standard deviation.

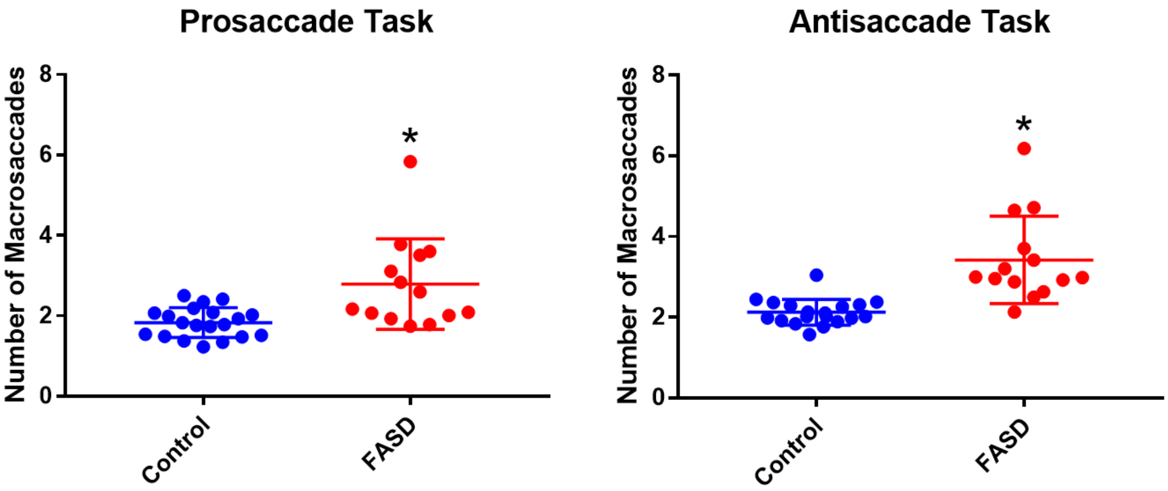

Figure 4-6. Number of macrosaccades per trial in the prosaccade and antisaccade tasks.

Adults with FASD (red circles) had a significantly greater number of macrosaccades per trial in both the prosaccade task ($p = 0.0012$) and the antisaccade task ($p < 0.0001$). Bars represent mean and standard deviation.

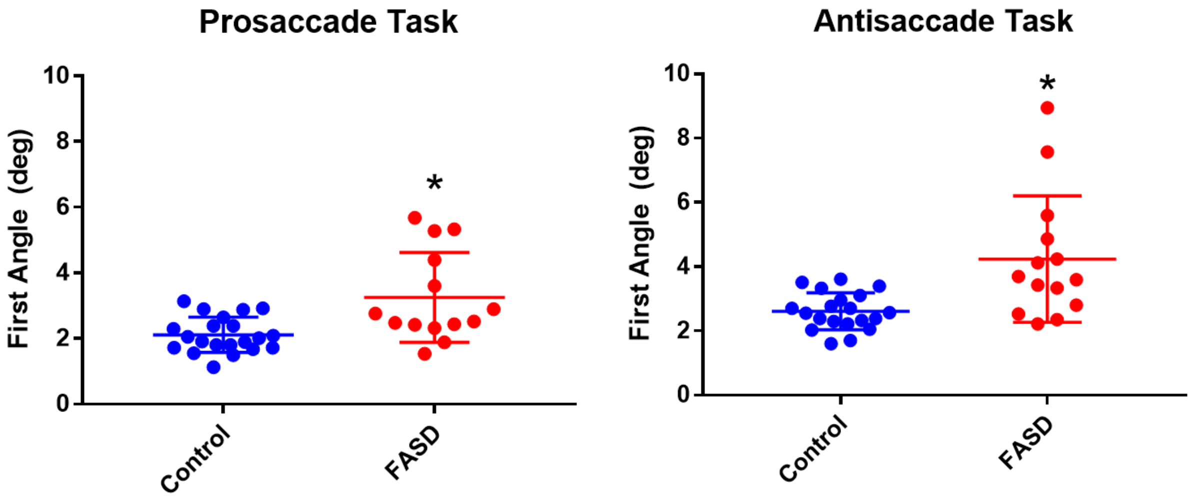

Figure 4-7. First angle offset in the prosaccade and antisaccade tasks.

Adults with FASD (red circles) had a significantly greater first angle offset in both the prosaccade task (*p* = 0.0015) and the antisaccade task (*p* = 0.0014). Bars represent mean and standard deviation.

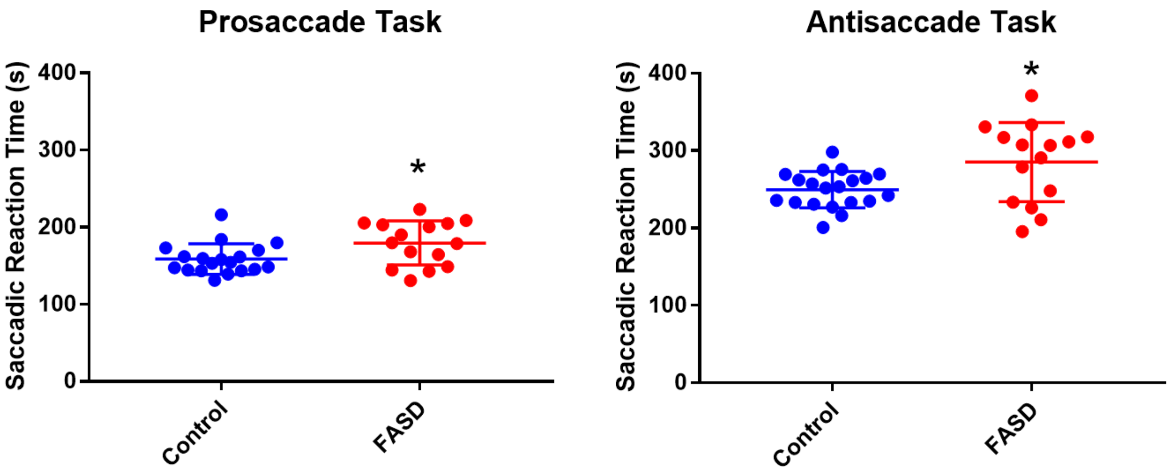

Figure 4-8. Saccadic reaction time in the prosaccade and antisaccade tasks.

Adults with FASD (red circles) had significantly slower saccadic reaction times in both the prosaccade task (*p* = 0.017) and the antisaccade task (*p* = 0.0092). Bars represent mean and standard deviation.

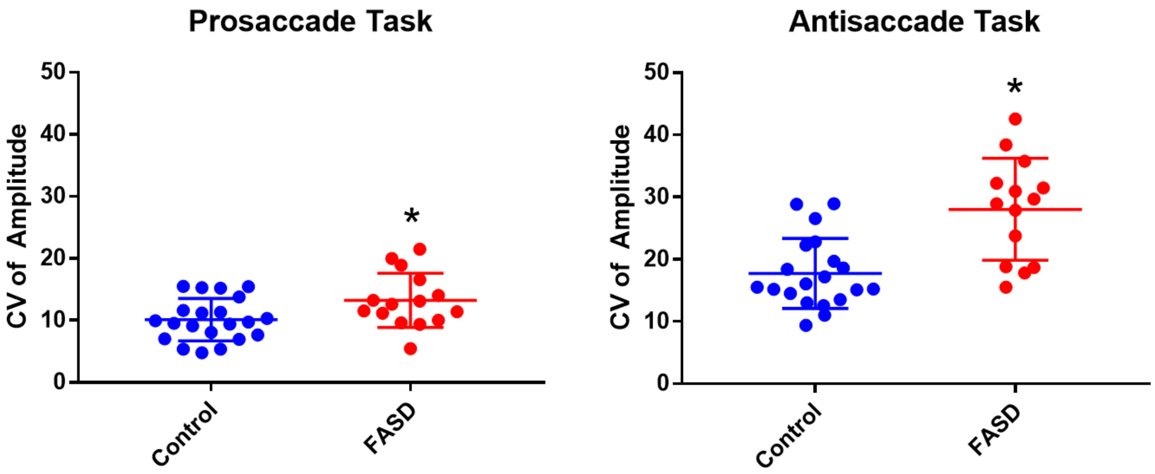

Figure 4-9. Coefficient of variation in saccade amplitude in the prosaccade and antisaccade tasks.

Adults with FASD (red circles) had significantly greater variability in saccade amplitude in both the prosaccade task (p = 0.022) and the antisaccade task (p = 0.0001). Bars represent standard deviation.

Table 4-1. Differences in prosaccade outcome features between adults with FASD and controls

Abbreviated table of eye movement features (outcomes) from the prosaccade task that are significantly different between adults with FASD and controls, organized by effect size.

Prosaccade Outcome Features	Control ($\bar{x}$ ± SEM)	FASD ($\bar{x}$ ± SEM)	p-value	Effect size (*d*)
End Point Error, Y axis	-0.25 ± 0.061	0.30 ± 0.10	<0.0001	0.42
SD of First Angle Offset	1.52 ± 0.074	2.57 ± 0.30	0.00	0.33
Number of Macrosaccades per Trial	1.83 ± 0.083	2.79 ± 0.30	0.00	0.28
Percent of Trials with Direction Errors	2.51 ± 0.40	0.73 ± 0.23	0.00	0.27
Number of Trials with Direction Errors	2.95 ± 0.47	0.86 ± 0.27	0.00	0.27
First Angle Offset	2.12 ± 0.12	3.25 ± 0.36	0.00	0.27
SD of End Point Error, Y axis	0.54 ± 0.044	1.18 ± 0.21	0.00	0.26
Number of Steps per Trial	0.20 ± 0.022	0.35 ± 0.047	0.00	0.25
Velocity of Saccades	352.8 ± 6.02	319.7 ± 8.67	0.00	0.25
Number of Direction Errors (Regular Saccades)	2.85 ± 0.49	0.86 ± 0.27	0.00	0.24

Table 4-2. Differences in prosaccade outcome features between adults with FASD and controls

Abbreviated table of eye movement features (outcomes) from the antisaccade task that are significantly different between adults with FASD and controls, organized by effect size.

Antisaccade Outcome Features	**Control ($\bar{x}$ ± SEM)**	**FASD ($\bar{x}$ ± SEM)**	**p-value**	**Effect size (*d*)**
CV of End Point Error, X axis	18.92 ± 1.13	32.2 ± 2.20	<0.0001	0.52
Percent of Trials with Corrective Saccades	90.41 ± 2.33	61.05 ± 5.00	<0.0001	0.50
Number of Macrosaccades per Trial	2.12 ± 0.074	3.4 ± 0.29	<0.0001	0.44
Velocity of Saccades	347.4 ± 7.11	281.5 ± 12.05	<0.0001	0.44
SD of End Point Error, X axis	1.99 ± 0.078	3.26 ± 0.27	<0.0001	0.44
Percent of Correct Trials	81.03 ± 2.04	55.78 ± 5.47	<0.001	0.41
Number of Correct Trials (Regular Saccades)	93.25 ± 3.15	57.8 ± 7.54	<0.0001	0.41
Number of Correct Trials	94.4 ± 3.03	59.07 ± 7.69	<0.0001	0.40
CV of Saccade Amplitude of Correct Trials	17.72 ± 1.26	28.03 ± 2.19	0.00	0.37
Number of Trials with Anticipatory Saccades	2.74 ± 0.65	10.29 ± 1.92	0.00	0.36

4.2.3 Outcome Features from the Memory-Guided Saccade Tasks

Eye movement behaviour collected from the 1-target, 2-target, and 3-target memory-guided tasks were used to investigate group differences between the adults with and without an FASD diagnosis. Selected outcomes from all three tasks were analyzed using a two-way repeated measures ANOVA with group (control, FASD) as the between-subject factor and task condition (1-target task, 2-target task, 3-target task) as the within-subject factor to compare the changes in performance as the task became progressively more difficult. The selected outcome features included correct trials (Figure 4-10), the frequency of timing errors (Figure 4-11), the path length accuracy (Figure 4-12), and the number of macrosaccades per trial (Figure 4-13). Similar to the anti-prosaccade task, these measures were selected because they represent features of saccade performance (attention, higher order cognitive processing and saccade accuracy) that were consistently found to differentiate adults with FASD from adults without FASD. An abbreviated list of the outcome features for these tasks, ranked by effect size, are reported in Table 4-3 for the 1-target memory-guided task, Table 4-4 for the 2-target memory-guided task, and Table 4-5 for the 3-target memory-guided task. The full lists of all eye-tracking performance outcomes are reported in Appendix C for the 1-target memory-guided task, Appendix D for the 2-target memory-guided task and Appendix E for the 3-target memory-guided task in Appendix 1.

Two-way repeated measures ANOVA of the percent correct trials revealed statistically significant main effects of group, $F(1,26) = 26.71$, $p < 0.0001$, and task condition, $F(2,52) = 68.86$, $p < 0.0001$, and a significant interaction between group and task condition ($F(2,52) = 4.287$, $p = 0.019$). Post-hoc multiple comparisons testing showed that the performance of adults with FASD and controls in the 1-target condition were not different from each other. Further, the performance of control was not different between the 1- and 2-target conditions of the task, but significantly dropped off in the 3-target condition. The interaction was driven by the fact that the performance of adults with FASD was worse in the 2-target condition compared to the 1-target condition. In addition, adults with FASD performed worse than controls in both the 2-target and 3-target conditions of the task. These data suggest that, whereas increasing task difficulty resulted in a decrease in the proportion of correct responses in both groups, individuals with FASD exhibited a relatively greater drop off in performance as the cognitive load (number of target locations being held in spatial working memory) increased.

Two-way repeated measures ANOVA of the frequency of all timing errors revealed a statistically significant main effect of group ($F(1,27) = 9.66$, $p = 0.0044$), but not task condition ($p > 0.5$), and there was no interaction between group and task condition (Fig. 3.11). These data suggest that, while adults with FASD made significantly more timing errors, increasing task difficulty did not influence the frequency of timing errors in the memory-guided saccade task.

Two-way repeated measures ANOVA of the path length accuracy did not show a statistically significant main effect of group $F(1,26) = 2.18$, $p = 0.15$, but it did for task condition ($F(2,52) = 66.86$, $p < 0.0001$), which reflects the fact that as the number of targets increased there was a greater difference between average path length and the ideal path length. There was also a significant interaction between group and task condition ($F(2,52) = 4.09$, $p = 0.022$), although visual inspection of the data suggests that the interaction was likely driven by 1-2 of the adults with FASD exhibiting relatively poorer performance selectively in the 2-target condition of the task.

Two-way repeated measures analysis of the number of macrosaccades per trial revealed statistically significant main effects of group ($F(1,28) = 5.55$, $p = 0.026$), and task condition ($F(2,56) = 163.6$, $p < 0.0001$). There was no interaction between group and task condition. The main effect of group suggests that adults with FASD made a greater number of macrosaccades per trial across the three conditions of the task. The main effect of task condition is not surprising: as the number of target locations that the participants is required to look towards increases, it makes sense for there to be a greater number of macrosaccades.

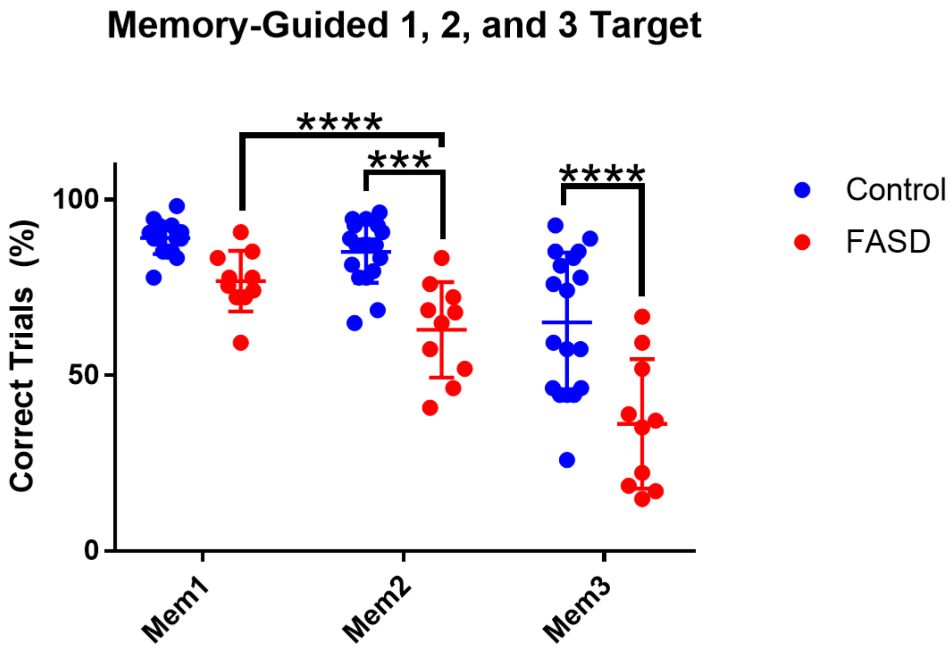

Figure 4-10. Correct trials in the memory-guided tasks.

There were significant main effects of group ($p < 0.0001$) and task condition ($p < 0.0001$), and a significant interaction between group and task condition ($p = 0.019$). The interaction was driven by a significant difference in percentage of correct trials between the 1-target and 2-target conditions for the FASD group ($p = 0.011$) that was not present in the control group ($p = 0.57$). Bars represent mean and standard deviation.

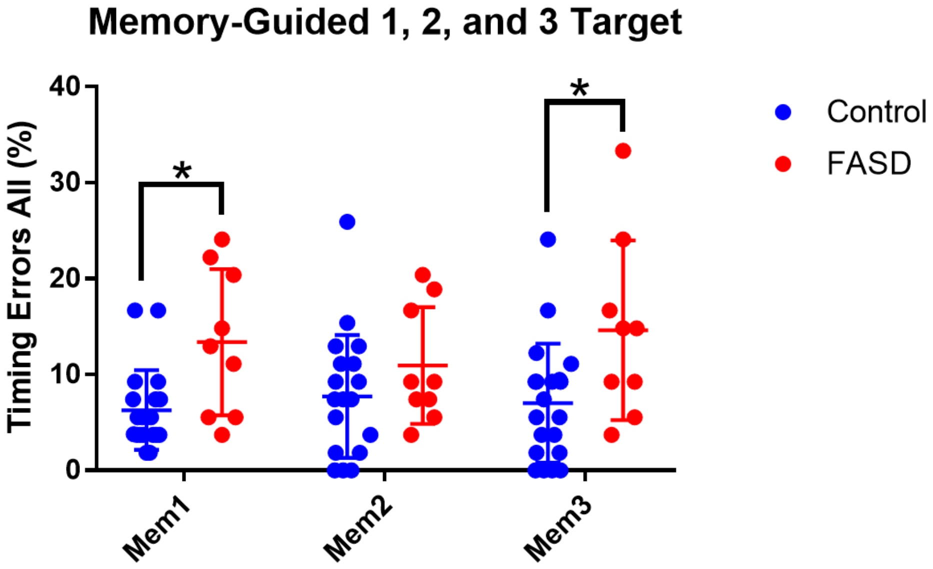

Figure 4-11. Timing errors in the memory-guided tasks.

There was a significant main effect of group ($p = 0.0044$) but not task condition ($p < 0.5$), and no significant interaction between group and task condition ($p = 0.28$). Bars represent mean and standard deviation. Adults with FASD exhibited a greater frequency of timing errors in the memory-guided task, especially in the 1- and 3-target conditions. Bars represent mean and standard deviation.

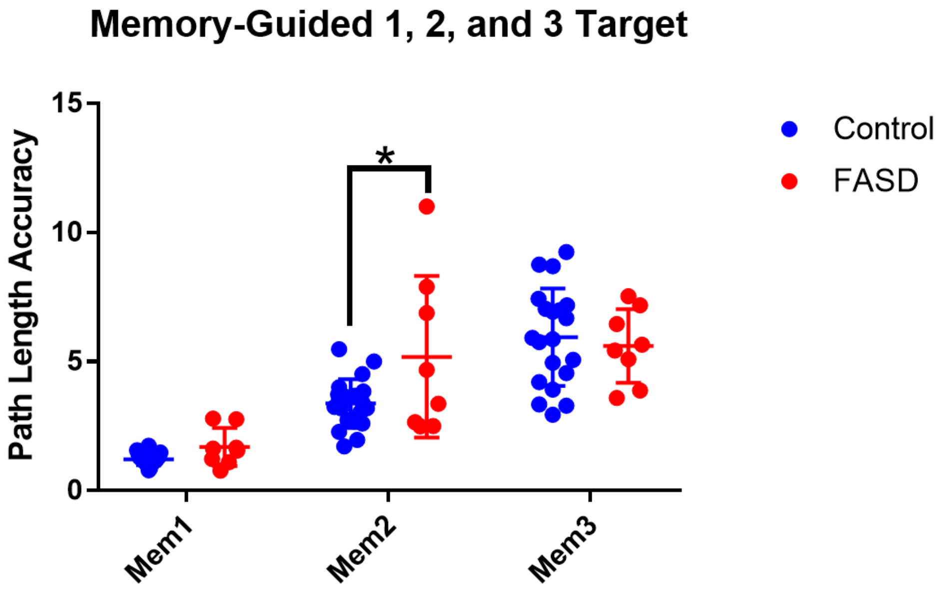

Figure 4-12. Path length accuracy in the memory-guided tasks.

There was not a significant main effect of group (*p* = 0.15), but there was for task (*p* < 0.0001) and for interaction (*p* = 0.022). Bars represent mean and standard deviation.

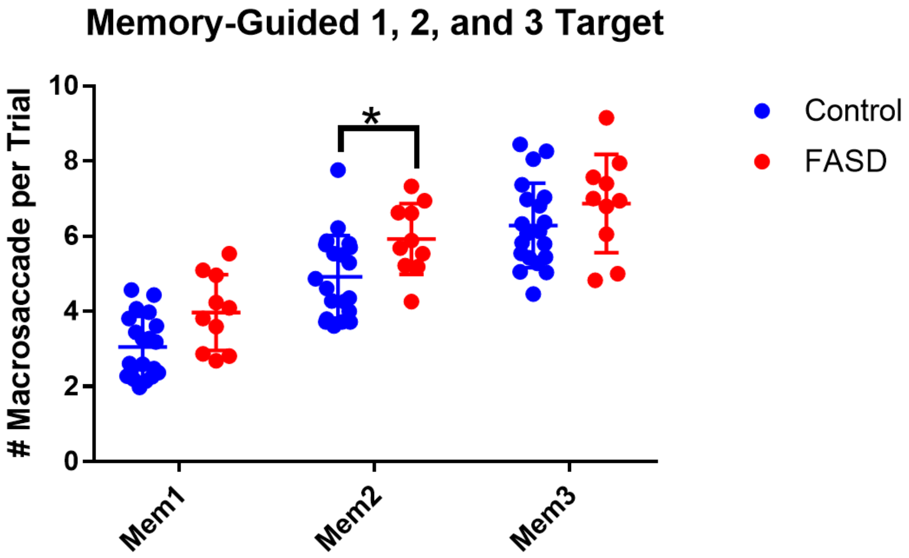

Figure 4-13. Number of macrosaccades per trial in the memory-guided tasks.

There were significant main effects of group (p = 0.026), and task condition (p < 0.0001), but no significant interaction between group and task condition (p = 0.43). Bars represent mean and standard deviation.

Table 4-3. Differences in the 1-target memory-guided task outcome features between adults with FASD and controls

Abbreviated table of eye movement features (outcomes) from the 1-target memory-guided task that are significantly different between adults with FASD and controls, organized by effect size.

Memory Guided 1-Target Task Outcome Features	**Control (x̄ ± SEM)**	**FASD (x̄ ± SEM)**	**p-value**	**Effect size (*d*)**
Number of Correct Trials	47.95 ± 0.56	40.91 ± 1.42	<0.0001	0.51
Percent of Correct Trials	88.88 ± 1.04	76.12 ± 2.56	<0.0001	0.51
Percent of Trials with Timing Errors Only	6.35 ± 0.88	15.13 ± 2.15	0.00	0.39
Percent of All Trials containing Timing Errors	6.35 ± 0.88	15.13 ± 2.15	0.00	0.39
Number of Trials with Timing Errors Only	3.43 ± 0.48	8.08 ± 1.14	0.00	0.38
Number of All Trials with Timing Errors	3.43 ± 0.48	8.08 ± 1.14	0.00	0.38
Path Length Accuracy of All Saccades, including Step Saccades	1.21 ± 0.048	1.85 ± 0.21	0.00	0.33
Saccade Threshold	13.93 ± 0.30	15.78 ± 0.41	0.00	0.30
Number of Macrosaccades per Trial	3.02 ± 0.18	4.23 ± 0.32	0.00	0.30
Number of No Fixation or Target Trials	0.81 ± 0.25	2.92 ± 0.65	0.00	0.29

Table 4-4. Differences in the 2-target memory-guided task outcome features between adults with FASD and controls

Abbreviated table of eye movement features (outcomes) from the 2-target memory-guided task that are significantly different between adults with FASD and controls, organized by effect size.

Memory Guided 2-Target Task Outcome Features	**Control (x̄ ± SEM)**	**FASD (x̄ ± SEM)**	**p-value**	**Effect size (*d*)**
Percent of Correct Trials	84.76 ± 1.94	59.4 ± 4.29	<0.0001	0.56
Number of All Trials containing No Saccade Errors	0.1 ± 0.084	1.55 ± 0.31	<0.0001	0.49
Percent of All Trials containing No Saccade Errors	0.34 ± 0.16	2.87 ± 0.58	<0.0001	0.49
Number of No Fixation or Target Trials	0.18 ± 0.084	1.64 ± 0.36	<0.0001	0.47
Percent of Trials with 2 Target Sequence Errors Only	4.60 ± 1.34	17.6 ± 2.89	<0.0001	0.41
Number of Trials with 2 Target Sequence Errors Only	2.48 ± 0.72	9.33 ± 1.54	<0.0001	0.40
Number of Correct Trials	43.86 ± 1.57	31.83 ± 2.40	0.00	0.37
First Saccade Accuracy to Second Target	3.02 ± 0.16	4.39 ± 0.36	0.00	0.34
Saccade Threshold	14.66 ± 0.32	17.2 ± 0.64	0.00	0.33
Percent of All Trials with 2 Target Sequence Errors	7.34 ± 2.31	23.48 ± 4.01	0.00	0.31

Table 4-5. Differences in the 3-target memory-guided task outcome features between adults with FASD and controls

Abbreviated table of eye movement features (outcomes) from the 3-target memory-guided task that are significantly different between adults with FASD and controls, organized by effect size.

Memory Guided 3-Target Task Outcome Features	**Control (x̄ ± SEM)**	**FASD (x̄ ± SEM)**	**p-value**	**Effect size (*d*)**
Percent of Correct Trials	60.82 ± 4.64	33.21 ± 5.68	0.00	0.30
Number of Correct Trials	32.71 ± 2.52	19.55 ± 2.85	0.00	0.26
Distance from Fixation Point to First Saccade Onset Position	0.58 ± 0.023	0.68 ± 0.026	0.01	0.21
Number of All Trials with 3 Target Sequence Errors	1.95 ± 0.60	5 ± 1.09	0.01	0.20
Percent of All Trials with 3 Target Sequence Errors	3.70 ± 1.16	9.30 ± 2.02	0.01	0.19
Number of Trials with 3 Target Sequence Errors Only	1.75 ± 0.53	4.18 ± 0.82	0.01	0.19
Percent of Trials with 3 Target Sequence Errors Only	3.31± 1.02	7.77 ± 1.51	0.02	0.18
Percent of All Trials containing Timing Errors	7.21 ± 1.33	14.07 ± 2.85	0.02	0.18
Saccade Threshold	15.13 ± 0.41	16.99 ± 0.66	0.02	0.17
Number of All Trials with 2 Target Sequence Errors	12.33 ± 1.69	19.25 ± 2.12	0.02	0.17

4.2.4 Errors in Performance Across the Two-Target and Three-Target Memory-Guided Tasks

Certain outcome measures cannot be obtained for the 1-target task (e.g., sequence errors). In these cases, the analysis of differences in eye movement behaviour between adults with FASD and controls was restricted to the 2-target, and 3-target conditions of the memory-guided saccade task. These outcomes were analyzed using a two-way repeated measures ANOVA with group (Control, FASD) as the between-subject factor and task condition (2-target, 3-target) as the within-subject factor to compare the changes in performance as the task became progressively harder. Those outcomes selected for presentation include the frequency of sequence errors (Figure 4-14) and proportion of all skip errors (Figure 4-15).

Two-way repeated measures ANOVA of the percent of sequence errors revealed statistically significant main effects of group ($F(1,28) = 10.07$, $p = 0.0036$), and task condition ($F(1,28) = 66.43$, $p < 0.0001$), but no interaction between group and task condition ($p = 0.81$) (Figure 4-14). These data suggest that adults with FASD had a higher frequency of sequence errors in the memory-guided saccade task and made a significantly greater percentage of sequence errors.

Two-way repeated measures ANOVA of the percent of all skip errors showed statistically significant main effects of group ($F(1,26) = 8.24$, $p = 0.0080$), and task condition ($F(1,26) = 28.3$, $p < 0.0001$), while the interaction effect approached significance ($p = 0.056$) (Figure 4-15). Skip errors occurred when participants failed to make a saccade to at least one of the targets presented in the trial. These data suggest that adults with FASD had a significantly greater frequency of skip errors and may have been more impaired than controls in the 3-target condition of the task.

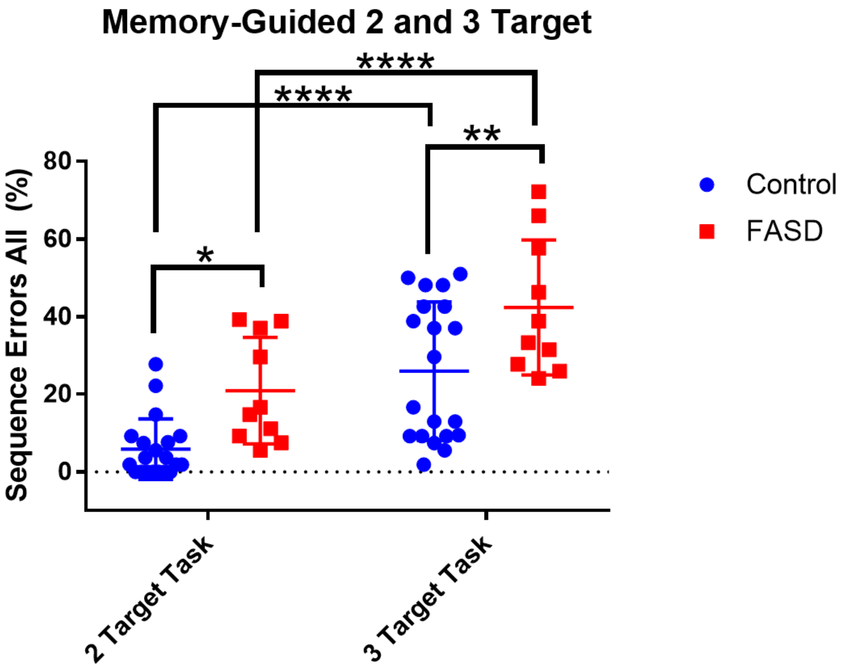

Figure 4-14. Sequence errors in the 2-target and 3-target memory-guided tasks.

There were significant main effects of group ($p = 0.0036$) and task ($p < 0.0001$), but no significant effect of interaction ($p = 0.81$). Bars represent mean and standard deviation.

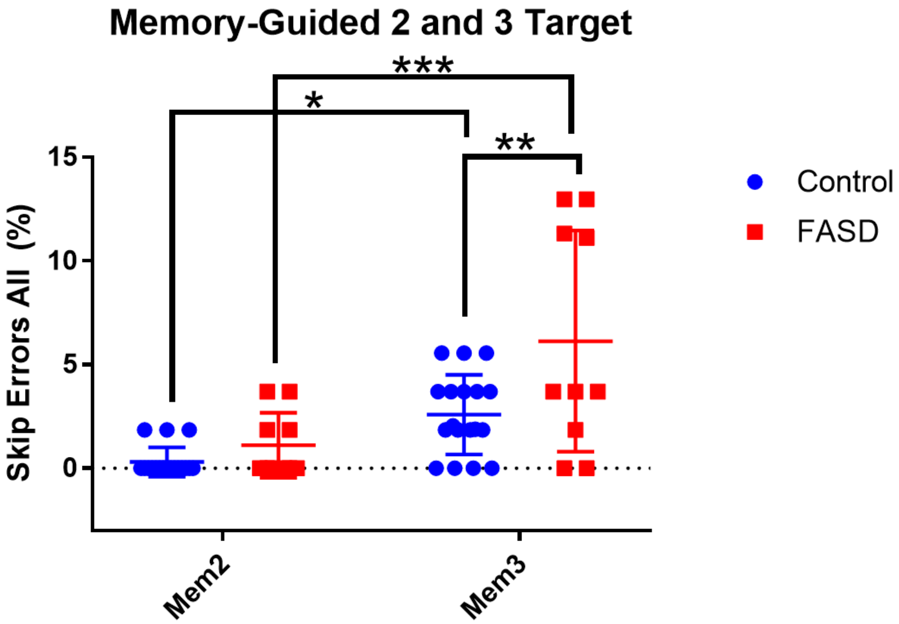

Figure 4-15. Skip errors in the 2-target and 3-target memory-guided tasks.

There were significant main effects of group (*p* = 0.0080) and task (*p* < 0.0001), and the interaction effect approached significance (*p* = 0.056). Bars represent mean and standard deviation.

Chapter 5

Discussion and Conclusion

5.1 Use of Structured Eye Movement Task Outcomes for Differentiating Adults with FASD

Previous studies have demonstrated that deficits in eye movement control can be used to differentiate children with FASD from typically developing control children (Green et al., 2009; Paolozza et al., 2014a; 2014b). The goal of the current study was to investigate whether adults with FASD exhibit similar differences in eye movement control, and whether adults with or without FASD in the CJS could be differentiated based on deficits in eye movement control. The longer-term goal is to develop low cost, high-throughput screening and assessment tools that can aid in the identification of individuals with FASD in the criminal justice system. Three structured eye-movement tasks, the prosaccade, antisaccade, and memory-guided (1-target, 2-target, and 3-target) tasks were administered using a portable Eyelink 1000 eye tracker. These tasks assess multiple domains of brain function, including sensorimotor integration, attention, response inhibition, and working memory. There is significant overlap between areas of the brain involved in eye movement control and areas known to be affected by PAE, including the dlPFC, FEF, and basal ganglia overlap, and lesions in these areas have been shown to cause deficits in performance of eye movement tasks (Munoz & Everling, 2004). In the current study, adults with FASD exhibited deficits in eye movement control across all three structured tasks in comparison to control adults. Notably, adults with FASD exhibited significant increases in both intra-subject and inter-subject variability in several outcome measures (e.g., saccade amplitude). Increasing task difficulty in the memory-guided saccade task revealed a differential vulnerability in adults with FASD. Somewhat surprisingly, adults in the CJS without FASD did not exhibit deficits in measures of executive function (e.g., response inhibition assessed in the antisaccade task) in comparison to community controls. Taken together, the results of this study support the notion that deficits in eye movement control may be a sensitive and specific biomarker of FASD in adults, including adults with FASD in the CJS.

Individuals with FASD are overrepresented in the CJS (Fast et al., 1999; MacPherson and Chudley, 2007). Adverse life outcomes of individuals with FASD such as mental health problems, social ineptness, substances use disorders, and being a victim of abuse put them at a higher risk for incarceration in the CJS (Streissguth et al., 2004). Individuals with FASD also exhibit deficits in memory, executive functioning, understanding cause and effect, and understanding and meeting social norms and expectations, which may play a role in their increased rates of incarceration (Popova et al., 2011; Streissguth et al., 2004). In 2013, Canadian courts acknowledged that individuals with FASD that become involved with the CJS may have difficulties understanding police-based arrest procedures, court etiquette, and related processes (Institute of Health Economics). In addition, individuals with FASD are more vulnerable to coercion or misunderstanding by multiple individuals in the justice system (e.g., police officers, corrections officers, parole officers, judges), leading to prolonged or repeated contact with the CJS (Fast and Conry, 2009; Moore and Green, 2004; Streissguth et al., 2004). Individuals with FASD are also vulnerable to making false confessions and agreeing to leading questions, as well as changing answers in response to negative feedback. For example, in one case a young adult with fetal alcohol syndrome (FAS) confessed to a double murder he could not have committed since at the time of the murders, he had been incarcerated (Fast and Conry, 2009).

Individuals need new treatments and sentencing that consider their needs. Introducing factors of structure, supervision and routine may be helpful when supporting individuals with FASD (Currie et al., 2016). Furthermore, the fundamental purpose of judicial sentencing is to denounce unlawful conduct, deter offenders and other persons from committing offences, separate offenders from society when necessary, assist in rehabilitating offenders, provide reparations for harm done to victims or to the community, and to promote a sense of responsibility in offenders and acknowledgement of the harm (Canadian Criminal Code, section 718). However, these principles may not be understood by individuals with FASD. High recidivism rates in individuals with FASD (Streissguth et al., 2004) suggest that the link between cause and effect may not be present. As a result, more effective treatments, sentencing, and training for sectors of the justice system may improve outcomes of individuals with FASD in the CJS.

In order to assess the reliability of these interventions, a method of identifying individuals with FASD in the CJS is needed. However, currently there are significant barriers to the rapid identification of individuals with FASD in the CJS context. The diagnostic process for FASD is lengthy, expensive, and involves a multidisciplinary team of health professionals. As a consequence of the low clinical capacity to assess individuals for FASD in Canada, screening every individual in the CJS using the Canadian Guidelines for FASD Diagnosis is not feasible. This situation has been recognized by the Justice partner in this study, who provided essential support for the project in the form of permissions and access to the correctional facility, help with recruitment, and a suitable space for conducting the experiments. The Justice partner will be a primary recipient of the new knowledge generated in this study.

5.2 Environmental Effects

One aspect that has not been adequately addressed in previous studies that examined eye movements in children with FASD was controlling for the effect of environment. The typically developing control children recruited to previous studies did not have the same demographic background as the children with FASD, including comorbidities and medications, home circumstances (the majority of children with FASD were living in foster or adoptive homes), and ethnicity (Green et al., 2009; Paolozza et al., 2014a; 2014b). Individuals with FASD are often exposed to difficult post-natal environments, including heavy parental alcohol use, maltreatment including physical and sexual child abuse and neglect (Smith et al., 2007; Werner, 1986), malnutrition (Fuglestad et al., 2013), and living in multiple placements (Smith et al., 2007). Many of these adverse early life experiences overlap with risk factors for criminal justice involvement, such as disruptions in education and substance abuse (Streissguth et al., 2004). In the current study, at least some of the environmental factors surrounding criminal justice involvement were controlled for by including a justice control group (adults with criminal justice involvement, but no FASD diagnosis). It was hypothesized that because adults with criminal justice system involvement often have difficulties with executive functioning skills, including response inhibition and working memory (Meijers et al., 2015), this population may exhibit deficits in eye movement control relative to a group of community control adults. However, the results of this study showed that this did not appear to be the case (Fig 4-1). Instead, adults with FASD were found to have significantly different eye movement control outcomes from adults without FASD, independent of whether or not the participants were currently involved with the justice system. These results suggest that, in adults without FASD in the CJS, the brain structures and circuits that underlie eye movement control are intact. Another possibility is that all of the data from participants in the justice control group (justice-involved without FASD) were collected in a corrections centre, resulting in participants maintaining a state of hypervigilance. This level of focus and control may have been reflected in the eye movement control outcomes. Taken together, the data presented in this thesis suggest that deficits in eye movement control in adults with FASD are more likely to be a result of the brain injury associated with prenatal alcohol exposure, and not a reflection of the environmental influences that led to CJS involvement. However, there is a strong probability that environmental factors interact with a history of prenatal alcohol exposure to determine the severity of outcomes. Future studies with a larger sample size and more extensive demographic information will be needed to address this question.

5.3 Group Differences Mirrored Previous Studies Investigating Children's Eye Movement Control

Many of the differences in eye movement control observed in adults with FASD mirrored group differences previously found in children with FASD, suggesting that these deficits may follow an individual from childhood to adulthood. The selected outcome features in this study included having a less accurate initial saccade towards the target (Figure 4-7), longer saccadic reaction time (Figure 4-8), and significantly more direction errors in the antisaccade task (Fig 4-5), and timing (Figure 4-11) and sequence errors (Figure 4-14) in the memory-guided tasks. Previous studies investigating eye movement control in children with FASD have found similar deficits (Green et al., 2009; Hemington & Reynolds, 2014; Paolozza et al., 2013; 2014a; 2014b). Some of these studies also correlated the deficits in eye movement control to psychometric tests, suggesting that eye movement outcomes assess similar domains of cognitive function (Paolozza et al., 2014a; 2014b). One study that included all three conditions in the memory-guided task (1-, 2-, and 3-targets) found that children with FASD also exhibited a greater proportion of trials with sequence errors in the 3-target conditions, and an increased frequency of incorrect trials in the 2- and 3-target conditions compared with typically developing controls (Hemington & Reynolds, 2014).

While previous studies have suggested that the deficits in eye movement control in children with FASD may be due to developmental delays, the presence of these same deficits in adults suggests that these deficits follow individuals with FASD through from childhood to adulthood and may be indicative of irreversible brain injury. In reviews of brain imaging studies, PAE has been shown to result in microcephaly and/or structural abnormalities in the basal ganglia, corpus callosum, cerebellum, hippocampus, and amygdala (Riley et al., 2004; Spadoni et al., 2007). It was also found that brain growth continued to be adversely affected long after the initial prenatal alcohol exposure insult, and that the brain regions most affected included the frontal and inferior parietal and perisylvian areas (Riley et al., 2004). In a mouse model with smaller but still clinically relevant doses of PAE, impairments in executive function processes including attention and working memory were seen to persist into adulthood (Marquardt et al., 2014). This is consistent with the response inhibition and executive function deficits specific to individuals with FASD and supports the findings that adults with FASD display similar deficits in eye movement control as children with FASD.

5.4 Increasing Task Difficulty Resulted in Increased Errors in Adults with FASD

While the prosaccade task is good for assessing sensorimotor integration and saccade metrics such as accuracy and main sequence, the antisaccade task is a good tool for assessing higher level cognitive processing including attention and response inhibition. In addition to inhibiting a reactive saccade towards a sudden peripheral stimulus, the antisaccade task requires the successful production of a saccade towards an internal representation of the target reflected in the equal and opposite direction from the stimulus. In addition, the use of the interleaved anti-prosaccade task required participants to be able to hold simple instructions in working memory (green fixation point indicates a prosaccade trial, red fixation point indicates an antisaccade trial) and maintaining attention to successfully complete the task. As hypothesized, adults with FASD had a greater percentage of direction errors in the antisaccade task (Figure 4-5). Interestingly, the control group showed a significantly greater percentage of direction errors in the prosaccade task than the adults with FASD. While it is unclear what drove this outcome, one possibility is that some community control participants were too relaxed during data collection and, in some cases, tried to maintain conversation while performing the task. However, if this were the case, these effects should have been observed across multiple outcome features. Instead, this difference may be due to a simple speed-accuracy trade-off: adults in the control group had a significantly faster SRT in the prosaccade task.

In the memory-guided task, the number of targets was sequentially increased in order to increase the difficulty of the task in a step-wise manner and assess the resulting changes in behaviour. This task assesses top-down control of internally-guided saccades and requires the integration of many executive functioning domains. The percentage of correct trials decreased as the number of targets increased, and this effect was greater on adults with FASD (Figure 4-10). While both groups made more errors in the 3-target condition than the 2-target condition, adults with FASD also made a greater proportion of sequence errors (Figure 4-14), than the control group. Sequence errors, as previously defined, are trials in which participants make movements towards targets in the wrong order. These errors indicate that adults with FASD have a greater difficulty in any or all of the following steps: (1) integration of the sensory input, (2) properly holding both the locations and the sequence of the targets in working memory, and (3) translating the memorized locations into motor movements that match both the order and locations of the targets. A similar pattern was also seen in the proportion of skip errors. Both groups made an increased proportion of skip errors going from the 2-target to the 3-target group, however adults with FASD were selectively impaired as they progressed from the 2-target to the 3-target task. Skip errors, as defined previously, are trials in which a participant bypasses a target while completing the task. Like the sequence errors, these errors indicate that adults with FASD had more difficulty using sensory input to dictate the proper motor sequence. Skip errors may also indicate a greater deficit in spatial working memory or attention than sequence errors due to a failure to encode the location of one of the targets.

A previous study recorded electroencephalograph (EEG) activity in children with FASD during the performance of the memory-guided saccade task. Like this study, the participants completed 1-, 2-, and 3-target conditions of the memory guided task in increasing order. This study found a reduction in alpha power specific to the FASD group during the 2- and 3-target conditions, and across all conditions, power decreased in children with FASD, but not control children (Hemington & Reynolds, 2014). This suggests that individuals with FASD may differ from controls in terms of the neural recruitment. That is, depending on the mnemonic load presented, individuals with FASD require greater neural resource engagement than controls to perform the same task.

5.5 Variability Outcomes were a Strong Indicator of Differences in Adults with FASD

One defining characteristic of individuals with FASD is variability in performance, both across different individuals, and within one individual, with repeated performances of the same task. In this study, new variability measures were created to assess whether quantitative differences existed in variability between participants with FASD and the control group. While the outcome measures from previous studies consisted of the average value across all trials for each participant, previous studies had qualitatively noted that the raw eye movement traces in individuals with FASD consistently showed greater variability than traces from control individuals (Paolozza et al., 2013). As a result, previous studies included a variability measure of the saccadic reaction time, and in fact found differences between children with FASD and typically-developing controls (Green et al., 2009). Greater variability was also qualitatively observed in the eye traces of participants with FASD in this study when compared to eye traces of control individuals in both the prosaccade (Figure 4-2) and antisaccade (Figure 4-3) tasks. As a result, additional outcome features quantifying the variability of some select outcome features were included in this study, and the full list is included in Appendix A – E. In particular, the selected outcomes included the coefficient of variation of saccade amplitude in the prosaccade and antisaccade tasks (Figure 4-9). Individuals with FASD showed a significantly greater variability in amplitude in both the prosaccade and antisaccade task. The greater variability in the prosaccade task seen in adults with FASD suggests that these individuals had deficits in sensorimotor integration, and as a result were worse at accurately hitting a visual target in the periphery. This is supported by the greater number of macrosaccades (Fig) and greater first angle offset (Fig), which are also reflections of saccade accuracy. The greater variability in amplitude seen in the antisaccade task in adults with FASD suggests deficits in aiming towards an internally represented target (participants were instructed to look towards an imaginary point in the opposite direction and equidistant from the peripheral target for the antisaccade task). Other outcomes that also showed adults with FASD had much greater variability in eye movement control included the coefficients of variation in saccadic reaction time and end point error along the horizontal axis in both the prosaccade and antisaccade tasks, and end point error along the vertical axis for the prosaccade task (Appendix A, Appendix B) These data strongly support the idea that variability in task performance should be routinely included in the battery of outcome measures when assessing individuals with FASD, as increased variability in itself may also be a defining feature of FASD.

Variability in presentation of FASD between different individuals is common. The symptoms presented in an individual depend on the amount and frequency of prenatal alcohol exposure, when along the developmental trajectory the alcohol exposure occurred, maternal nutrition, and the interplay of many complex environmental factors (May et al., 2013; Sulik, 2005). As a result, the inter-subject variability seen in eye movement control within the group of individuals with FASD was not unanticipated. However, intra-individual variability in performance across repeated tasks is also a defining feature for individuals with FASD. Intra-individual variability is defined as within-person variability on a single task across multiple sessions (MacDonald & Stawski, 2014). Recently, intra-individual variability has been investigated as a predictor of neural dysfunction. Increased intra-individual variability has been observed in groups with cognitive difficulties, including those with traumatic brain injuries (Hill et al., 2013), individuals with dementia (Macdonald et al., 2006), and children with attention deficit/hyperactivity disorder (ADHD) and other neurodevelopmental disorders (Guerts et al., 2008). It has also been noted as a common feature of FASD; one of the first studies investigating intra-individual variability in children with FASD found that they tended to be more variable in a go/no-go paradigm when compared to age-matched typically developing controls (Ali et al., 2017). Since children tend to be more variable in cognitive performance compared with adolescents and adults (Macdonald et al., 2006), it may be surprising that adults with FASD also showed increased variability in eye movement control as compared with controls. However, the intra-individual variability seen in eye movement control seems to be another indicator of deficits that exist past the developmental period, and like the parallel in deficits seen between children and adults with FASD, suggests that eye movement control deficits may be an indicator of brain injury.

5.6 Limitations

There are some limitations of this study that must be discussed. First, this study included a low number of participants. Due to this being a pilot study, the recruitment rates were not very high. There were only eight participants in the group of justice-involved individuals with FASD, and seven participants in the group of justice control individuals with FASD, resulting in a need to collapse the two groups. This prevented analyses to be run across all four groups. This also prevented investigation into the interaction of environmental factors and prenatal alcohol exposure and the effect on the severity of outcomes.

Secondly, due to time constraints, the free-viewing task and EEG data collected during the performance of the four eye-movement tasks were not analyzed. Previous studies using eye movement control outcome features as input fed into a machine learning algorithm to differentiate children with FASD from typically developing controls, have found that there tends to be a plateau in the ability of a classifier to identify children with FASD that occurs at around 80% (Thompson, 2017). This rate of identifying children with FASD would not be considered reliable in a clinical setting. This may be due to the fact that eye movement control on its own does not seem to contain enough data or power to be able to identify adults with FASD to a high degree of certainty. Part of this difficulty lies in the inter-individual variability in groups of individuals with FASD. In the previous work looking at building a reliable classifier, a few select individuals with FASD were consistently misclassified as control by the machine learning algorithm. This may be addressed by including additional outcome features or the free-viewing task and measures of EEG activity to improve the power of the classifier.

5.7 Future Directions

Due to time constraints, some data collected during this study were not included in the analysis. Future work should incorporate outcomes from the free-viewing eye movement task and the electroencephalography (EEG) data collected during the performance of the four eye movement tasks. This would allow for investigation of the underlying neural recruitment during the performance of the four eye movement tasks. Based on previous studies (Hemington & Reynolds, 2014; Tseng et al., 2013), the addition of these two measures would be expected to provide additional power towards differentiating between adults with FASD and controls. Inclusion of the free-viewing data would allow for a more robust dataset, including oculomotor-based and saliency-based outcomes that may further differentiate adults with FASD from the control group. A previous study using free-viewing eye movement data was able to differentiate between children with FASD, children with ADHD, and age-matched typically developing controls using these outcome features as input into a support vector machine at an overall accuracy of 77.3% (Tseng et al., 2013). EEG data has provided insight into neural recruitment with increasingly more difficult task conditions and may also offer a way of directly relating the eye movement behaviours to underlying neural activity across the two groups (Hemington & Reynolds, 2014).

Since variability outcomes have shown quantitative differences between adults with FASD and controls, investigating these outcomes in individuals with FASD may provide another avenue of eye-tracking that would differentiate the two groups. Intra-individual variability should be calculated for all outcome measures and included as another layer of data for differentiating between adults with FASD and controls.

5.8 Summary and Conclusions

The current thesis tested the following hypotheses:

1. Adults with FASD in the CJS will display significant differences in eye movement control compared with adults without FASD in the CJS.
2. Adults without FASD in the CJS will exhibit different patterns of eye movement control compared with community controls.

The results of this study suggest that criminal justice-involvement did not negatively affect eye movement control, and that the eye movement control of the justice-involved control group aligned closer to that of the community control group. However, adults with FASD (regardless of justice-involvement) did show significant differences in eye movement outcomes from the control group. This suggests that eye-tracking using the Eyelink 1000 may one day contribute to a rapid and inexpensive screening tool that could reliably identify individuals with FASD in the criminal justice system. This could lead to better outcomes for the individual, and society as a whole, by decreasing recidivism and creating treatment plans that can better address an individual with FASD.

The outcomes from this study show that group differences observed in children with FASD also exist in adults with FASD, suggesting that eye-movement control deficits are a result of brain injury due to prenatal alcohol exposure and not developmental delays. Results from this study also indicated that as the difficulty of a task increased (for example between prosaccade and antisaccade tasks and across the 1-, 2-, and 3-target conditions in the memory guided tasks), individuals with FASD became selectively impaired in their performance, as evidenced by greater error rates and decreased accuracy. Finally, individuals with FASD showed significant intra-individual variability in multiple outcome measures across the three structured eye movement tasks, which is consistent with variability being a defining characteristic of FASD.

Future studies will aim to investigate other saccadic eye movement measures and look at changes in EEG activity during performance of the eye movement tasks to investigate whether this may someday contribute to the development of a rapid, reliable screening tool for adults with FASD in the CJS.

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Appendix A

Prosaccade Outcome Features	**Control (x̄ ± SEM)**	**FASD (x̄ ± SEM)**	**p-value**	**Effect size (*d*)**
End Point Error, Y axis	-0.25 ± 0.061	0.30 ± 0.10	<0.0001	0.42
SD of First Angle Offset	1.52 ± 0.074	2.57 ± 0.30	0.00	0.33
Number of Macrosaccades[8] per Trial	1.83 ± 0.083	2.79 ± 0.30	0.00	0.28
Percent of Trials with Direction Errors	2.51 ± 0.40	0.73 ± 0.23	0.00	0.27
Number of Trials with Direction Errors	2.95 ± 0.47	0.86 ± 0.27	0.00	0.27
First Angle Offset[1]	2.12 ± 0.12	3.25 ± 0.36	0.00	0.27
SD of End Point Error, Y axis	0.54 ± 0.044	1.18 ± 0.21	0.00	0.26
Number of Steps per Trial[9]	0.20 ± 0.022	0.35 ± 0.047	0.00	0.25
Velocity of Saccades[1]	352.8 ± 6.02	319.7 ± 8.67	0.00	0.25
Number of Direction Errors (Regular Saccades[4])	2.85 ± 0.49	0.86 ± 0.27	0.00	0.24
Percent of Trials with Step Saccades[9]	19.37 ± 2.14	32.85 ± 4.29	0.00	0.23
Saccade Threshold[7]	15.17 ± 0.29	17.62 ± 0.89	0.00	0.22
SD of End Point Error, Y axis (absolute value)	0.43 ± 0.071	0.73 ± 0.15	0.05	0.21
Number of Viable Trials[10]	118.9 ± 0.46	114.1 ± 1.98	0.01	0.20
SD of SRT	52.2 ± 2.63	68.94 ± 6.26	0.01	0.19
Number of Trials with Step Saccades[9]	22.74 ± 2.54	36.5 ± 4.97	0.01	0.19
Skew 1[2]	14274 ± 351.2	12570 ± 566.3	0.01	0.19
Maximum Saccadic Acceleration	24995 ± 581.1	22256 ± 892.7	0.01	0.18
CV of End Point Error, X axis	10.46 ± 0.88	14.97 ± 1.56	0.01	0.18
SRT of Correct Trials (Regular Saccades[4])	189.2 ± 2.46	203.9 ± 5.78	0.01	0.18
SRT of Correct Trials	158.7 ± 4.53	179.6 ± 7.38	0.02	0.17
Percent of Blinks per Trials	1.70 ± 0.26	3.18 ± 0.58	0.02	0.16
Number of No Fixation or Target Trials	0.65 ± 0.33	4.14 ± 1.68	0.02	0.15
Distance from Fixation Point to Saccade Onset Position[1]	0.65 ± 0.032	0.84 ± 0.084	0.02	0.15
CV of Saccade Amplitude of Correct Trials	10.11 ± 0.75	13.22 ± 1.13	0.02	0.14

Prosaccade Outcome Features	**Control ($\bar{x}$ ± SEM)**	**FASD ($\bar{x}$ ± SEM)**	**p-value**	**Effect size (*d*)**
Drift Base in the Y Axis	0.42 ± 0.020	0.65 ± 0.11	0.03	0.14
CV of First Angle Offset	73.45 ± 2.01	80.97 ± 2.91	0.04	0.14
Number of Lost Trials	0 ± 0	0.57 ± 0.31	0.03	0.13
SD of End Point Error, X axis	1.00 ± 0.080	1.33 ± 0.14	0.04	0.13
Skew 2[2]	8913 ± 224.7	7994 ± 392	0.04	0.13
Amplitude of Correct Trials	9.74 ± 0.090	9.30 ± 0.21	0.04	0.12
CV of SRT	32.84 ± 1.32	38.58 ± 2.7	0.05	0.12
CV of End Point Error, Y axis	2.22 ± 161.4	515.6 ± 189.8	0.05	0.12
Drift Base in the X Axis	0.39 ± 0.027	0.54 ± 0.084	0.07	0.10
Minimum Saccadic Acceleration	-20987 ± 642.5	-18732 ± 1051	0.06	0.10
SD of Saccade Amplitude of Correct Trials	0.97 ± 0.067	1.16 ± 0.079	0.08	0.09
Number of No Detected Saccade Trials	0.35 ± 0.17	1 ± 0.36	0.08	0.09
SRT of False Corrective Trials	384.3 ± 50.51	498.2 ± 49.79	0.13	0.09
Percent of Saccades with an Amplitude ≤ 7.2 °[13]	2.32 ± 0.60	5.116 ± 1.76	0.10	0.08
End Point Error, X axis	9.74 ± 0.089	9.38 ± 0.22	0.10	0.08
End Point Error, Y axis (absolute value)	0.54 ± 0.041	0.68 ± 0.11	0.16	0.06
CV of End Point Error, Y axis (absolute value)	78.84 ± 7.41	94.99 ± 8.23	0.16	0.06
Number of False Start Trials[12]	0.26 ± 0.13	0.53 ± 0.19	0.24	0.04
Number of Correct Trials	105 ± 1.75	101.7 ± 2.62	0.28	0.04
Percent of False Corrective Trials	1.14 ± 0.20	1.56 ± 0.36	0.29	0.03
Percent of Trials with Corrective Saccades	85.15 ± 3.69	90.54 ± 3.61	0.32	0.03
Percent of Trials with Anticipatory Saccades[6]	7.02 ± 1.10	8.68 ± 1.27	0.33	0.03
Number of Correct Trials (Express Saccades[5])	42.95 ± 4.70	35.4 ± 6.03	0.32	0.03
Number of False Corrective Trials	1.25 ± 0.23	1.67 ± 0.39	0.33	0.03
SRT of Correct Trials (Express Saccades[5])	119.9 ± 1.08	121.4 ± 1.32	0.39	0.02
Percent of Correct Trials (Express Saccades[5])	41.07 ± 4.56	35.2 ± 5.43	0.41	0.02
Percent of Correct Trials (Regular Saccades[4])	58.93 ± 4.56	64.8 ± 5.43	0.41	0.02
Skew Index[11]	0.27 ± 0.022	0.25 ± 0.020	0.46	0.02
Percent of Direction Error Trials (Express Saccades[5])	1.85 ± 1.85	0 ± 0	0.54	0.02

Prosaccade Outcome Features	**Control ($\bar{x}$ ± SEM)**	**FASD ($\bar{x}$ ± SEM)**	**p-value**	**Effect size (*d*)**
Percent of Direction Error Trials (Regular Saccades[4])	98.15 ± 1.85	100 ± 0	0.54	0.02
Percent of Trials with Express Saccades[5]	40.05 ± 4.50	34.88 ± 5.38	0.46	0.02
Number of Trials with Anticipatory Saccades[6]	8.25 ± 1.31	9.43 ± 1.26	0.54	0.01
Number of Trials with Corrective Saccades	6.05 ± 0.91	5.27 ± 1.00	0.57	0.01
SRT of Direction Errors (Regular Saccades[4])	299.8 ± 13.21	309.7 ± 13.5	0.65	0.01
SRT of All Direction Errors	295 ± 12.86	304.5 ± 14.91	0.67	0.01
Duration of Correct Saccades from Saccade Onset to Saccade Offset[2]	66.15 ± 1.47	65.3 ± 1.71	0.71	0.00
Percent of False Start Trials[12]	0.38 ± 0.19	0.46 ± 0.17	0.74	0.00
Initial Trajectory of Well Behaved Saccades[3]	6.69 ± 0.47	6.95 ± 0.81	0.77	0.00
CV of Initial Trajectory	1.01 ± 0.051	1.03 ± 0.064	0.79	0.00
SD of Initial Trajectory	7.12 ± 0.57	7.32 ± 1.04	0.86	0.00
Number of Correct Trials (Regular Saccades[4])	62.1 ± 4.93	63.27 ± 5.87	0.88	0.00
Percent of Correct Trials	90.14 ± 1.22	90.4 ± 1.33	0.89	0.00
SRT of Corrective Trials	271 ± 19.13	268.6 ± 24.97	0.94	0.00
Number of Direction Errors (Express Saccades[5])	--	--	--	--
SRT of Direction Errors (Express Saccades[5])	--	--	--	--

Appendix B

Antisaccade Outcome Features	**Control ($\bar{x}$ ± SEM)**	**FASD ($\bar{x}$ ± SEM)**	**p-value**	**Effect size (*d*)**
CV of End Point Error, X axis	18.92 ± 1.13	32.2 ± 2.20	<0.0001	0.52
Percent of Trials with Corrective Saccades	90.41 ± 2.33	61.05 ± 5.00	<0.0001	0.50
Number of Macrosaccades[8] per Trial	2.12 ± 0.074	3.4 ± 0.29	<0.0001	0.44
Velocity of Saccades[1]	347.4 ± 7.11	281.5 ± 12.05	<0.0001	0.44
SD of End Point Error, X axis	1.99 ± 0.078	3.26 ± 0.27	<0.0001	0.44
Percent of Correct Trials	81.03 ± 2.04	55.78 ± 5.47	<0.001	0.41
Number of Correct Trials (Regular Saccades[4])	93.25 ± 3.15	57.8 ± 7.54	<0.0001	0.41
Number of Correct Trials	94.4 ± 3.03	59.07 ± 7.69	<0.0001	0.40
CV of Saccade Amplitude of Correct Trials	17.72 ± 1.26	28.03 ± 2.19	0.00	0.37
Number of Trials with Anticipatory Saccades[6]	2.74 ± 0.65	10.29 ± 1.92	0.00	0.36
SD of Saccade Amplitude of Correct Trials	1.85 ± 0.090	2.56 ± 0.16	0.00	0.35
Percent of Trials with Anticipatory Saccades[6]	2.46 ± 0.56	13.66 ± 3.37	0.00	0.30
SD of First Angle Offset	1.95 ± 0.096	3.71 ± 0.58	0.00	0.28
Saccade Threshold[7]	15.13 ± 0.25	17.91 ± 0.88	0.00	0.28
First Angle Offset[1]	2.61 ± 0.13	4.24 ± 0.53	0.00	0.28
Maximum Saccadic Acceleration	24955 ± 576.1	20800 ± 1162	0.00	0.27
Percent of Saccades with an Amplitude ≤ 7.2 °[13]	6.83 ± 1.90	22.44 ± 4.82	0.00	0.26
Number of Direction Errors (Regular Saccades[4])	7.429 ± 1.11	16.29 ± 2.72	0.00	0.26
Number of Steps per Trial[9]	0.13 ± 0.019	0.27 ± 0.041	0.00	0.26
Percent of Trials with Direction Errors	15.15 ± 1.84	27.69 ± 3.79	0.00	0.25
SD of SRT	54.54 ± 4.12	81.83 ± 8.15	0.00	0.25
End Point Error, Y axis	-0.30 ± 0.066	0.15 ± 0.14	0.00	0.24
Percent of Trials with Step Saccades[9]	12.98 ± 1.83	25.24 ± 3.64	0.00	0.24
SRT of Correct Trials (Regular Saccades[4])	247.8 ± 4.62	287.3 ± 12.73	0.00	0.24
Percent of Blinks per Trials	1.62 ± 0.26	3.14 ± 0.43	0.00	0.24
Skew 1[2]	14167 ± 339.6	11911 ± 692.2	0.00	0.23

Antisaccade Outcome Features	**Control ($\bar{x}$ ± SEM)**	**FASD ($\bar{x}$ ± SEM)**	**p-value**	**Effect size (*d*)**
SD of End Point Error, Y axis	0.73 ± 0.078	1.48 ± 0.27	0.00	0.23
Number of No Detected Saccade Trials	0.4 ± 0.24	1.86 ± 0.44	0.00	0.23
Number of No Fixation or Target Trials	0.95 ± 0.42	11.21 ± 4.55	0.00	0.23
Number of Trials with Direction Errors	17 ± 2.07	30.73 ± 4.40	0.00	0.22
CV of SRT	22.06 ± 1.45	29.96 ± 2.28	0.00	0.22
SRT of Correct Trials	249.6 ± 5.24	285.4 ± 13.23	0.01	0.19
Number of Viable Trials[10]	117.8 ± 0.97	106 ± 5.06	0.01	0.19
Percent of False Corrective Trials	0.70 ± 0.20	2.15 ± 0.63	0.02	0.18
Drift Base in the Y Axis	0.43 ± 0.025	0.66 ± 0.10	0.02	0.17
Number of False Corrective Trials	0.71 ± 0.18	1.8 ± 0.43	0.01	0.16
SRT of Corrective Trials	278.4 ± 13.84	339.2 ± 20.52	0.02	0.16
Drift Base in the X Axis	0.38 ± 0.024	0.88 ± 0.25	0.02	0.15
Minimum Saccadic Acceleration	-17396 ± 616.6	-14915 ± 804.4	0.02	0.15
Distance from Fixation Point to Saccade Onset Position[1]	0.65 ± 0.033	0.81 ± 0.064	0.02	0.15
Skew 2[2]	7172 ± 161.8	6346 ± 343.4	0.03	0.15
Number of Trials with Step Saccades[9]	15.16 ± 2.25	24.86 ± 4.04	0.03	0.14
End Point Error, Y axis (absolute value)	0.66 ± 0.049	0.90 ± 0.11	0.04	0.13
Skew Index[11]	0.34 ± 0.017	0.29 ± 0.016	0.04	0.13
Percent of Direction Error Trials (Regular Saccades[4]**)**	46.4 ± 6.79	65.15 ± 5.10	0.05	0.11
Percent of Direction Error Trials (Express Saccades[5]**)**	53.6 ± 6.79	34.85 ± 5.10	0.05	0.11
SD of End Point Error, Y axis (absolute value)	0.73 ± 0.078	1.05 ± 0.19	0.09	0.09
End Point Error, X axis	10.76 ± 0.35	9.73 ± 0.53	0.10	0.08
Number of Lost Trials	0.15 ± 0.15	0.93 ± 0.53	0.11	0.08
Amplitude of Correct Trials	10.55 ± 0.31	9.70 ± 0.46	0.12	0.07
CV of End Point Error, Y axis (absolute value)	85.12 ± 8.19	101.8 ± 7.85	0.17	0.06
Number of Trials with Corrective Saccades	17.2 ± 1.95	22.07 ± 3.07	0.17	0.06
SRT of All Direction Errors	154.9 ± 7.46	170.5 ± 8.85	0.19	0.05
CV of First Angle Offset	75.31 ± 2.41	81.67 ± 4.64	0.19	0.05
SD of Initial Trajectory	6.20 ± 0.45	7.82 ± 1.41	0.25	0.04

Antisaccade Outcome Features	**Control ($\bar{x}$ ± SEM)**	**FASD ($\bar{x}$ ± SEM)**	**p-value**	**Effect size (*d*)**
Percent of False Start Trials^{12}	0.26 ± 0.090	0.47 ± 0.17	0.25	0.04
Number of False Start Trials^{12}	0.3 ± 0.10	0.53 ± 0.19	0.26	0.04
CV of Initial Trajectory	0.87 ± 0.025	0.93 ± 0.053	0.27	0.04
SRT of Correct Trials (Express Saccades^{5})	118.9 ± 7.08	124.2 ± 6.20	0.59	0.03
Percent of Trials with Express Saccades^{5}	10.53 ± 1.92	13.86 ± 2.63	0.30	0.03
Number of Direction Errors (Express Saccades^{5})	8.632 ± 1.52	10.86 ± 2.07	0.38	0.02
Percent of Correct Trials (Express Saccades^{5})	0.71 ± 0.37	1.33 ± 0.64	0.38	0.02
Percent of Correct Trials (Regular Saccades^{4})	99.29 ± 0.37	98.67 ± 0.64	0.38	0.02
Initial Trajectory of Well Behaved Saccades^{3}	6.83 ± 0.36	7.63 ± 1.02	0.40	0.02
CV of End Point Error, Y axis	-110.2 ± 60.46	-547.8 ± 758.2	0.51	0.01
Duration of Correct Saccades from Saccade Onset to Saccade Offset^{2}	72.35 ± 1.55	70.88 ± 3.27	0.66	0.01
SRT of Direction Errors (Regular Saccades^{4})	199.6 ± 6.66	202.5 ± 9.03	0.79	0.00
SRT of False Corrective Trials	376.8 ± 75.03	387.8 ± 47.83	0.90	0.00
SRT of Direction Errors (Express Saccades^{5})	116.5 ± 1.75	116.6 ± 2.15	0.98	0.00
Number of Correct Trials (Express Saccades^{5})	0.65 ± 0.33	0.64 ± 0.27	0.99	7.54E-06

Appendix C

Memory Guided 1-Target Task Outcome Features	**Control ($\bar{x}$ ± SEM)**	**FASD ($\bar{x}$ ± SEM)**	**p-value**	**Effect size (d)**
Number of Correct Trials	47.95 ± 0.56	40.91 ± 1.42	<0.0001	0.51
Percent of Correct Trials	88.88 ± 1.04	76.12 ± 2.56	<0.0001	0.51
Percent of Trials with Timing Errors Only	6.35 ± 0.88	15.13 ± 2.15	0.00	0.39
Percent of All Trials containing Timing Errors	6.35 ± 0.88	15.13 ± 2.15	0.00	0.39
Number of Trials with Timing Errors Only	3.43 ± 0.48	8.08 ± 1.14	0.00	0.38
Number of All Trials with Timing Errors	3.43 ± 0.48	8.08 ± 1.14	0.00	0.38
Path Length Accuracy of All Saccades, including Step Saccades	1.21 ± 0.048	1.85 ± 0.21	0.00	0.33
Saccade Threshold[7]	13.93 ± 0.30	15.78 ± 0.41	0.00	0.30
Number of Macrosaccades per Trial	3.02 ± 0.18	4.23 ± 0.32	0.00	0.30
Number of No Fixation or Target Trials	0.81 ± 0.25	2.92 ± 0.65	0.00	0.29
Drift Base in the Y Axis	0.86 ± 0.085	1.61 ± 0.27	0.00	0.25
SRT to First Target	368.6 ± 9.32	420.4 ± 16.14	0.01	0.23
Drift Base in the X Axis	0.76 ± 0.079	1.21 ± 0.16	0.01	0.21
Percent of All Trials containing No Saccade Errors	0.37 ± 0.17	0.93 ± 0.50	0.01	0.18
Number of All Trials containing No Saccade Errors	0.2 ± 0.092	0.5 ± 0.27	0.01	0.18
First Angle Offset of First Saccade	5.18 ± 0.23	6.76 ± 0.70	0.01	0.18
Number of Lost Trials	0 ± 0	0.42 ± 0.23	0.02	0.16
Number of Viable Trials[10]	54 ± 0	53.58 ± 0.23	0.02	0.16
First Saccade Accuracy to First Target	1.93 ± 0.10	2.45 ± 0.23	0.02	0.16
Number of Step Saccades per Trial[9]	0.37 ± 0.032	0.50 ± 0.053	0.03	0.15
SD of SRT to First Target	172.2 ± 11.62	212.8 ± 11.2	0.03	0.14
SD of First Saccade Accuracy to First Target	1.28 ± 0.075	1.56 ± 0.14	0.06	0.11
Distance from Fixation Point to First Saccade Onset Position	0.50 ± 0.019	0.56 ± 0.030	0.08	0.10
CV of SRT to First Target	44.17 ± 1.98	49.8 ± 2.69	0.10	0.09
Overall Accuracy of Last Saccade	1.51 ± 0.060	1.74 ± 0.14	0.11	0.08
Skew 1[2] to First Target	11597 ± 412.4	10436 ± 601.8	0.12	0.08

Memory Guided 1-Target Task Outcome Features	Control (x̄ ± SEM)	FASD (x̄ ± SEM)	p-value	Effect size (*d*)
Percent of Blinks per Trial	1.05 ± 0.22	1.63 ± 0.32	0.14	0.07
CV of First Saccade Accuracy to First Target	0.65 ± 0.022	0.74 ± 0.076	0.15	0.07
Percent of Trials with Step Saccades[9]	31.98 ± 2.71	38.41 ± 3.29	0.15	0.07
Amplitude to First Target	9.47 ± 0.16	9.07 ± 0.34	0.23	0.05
Percent of Trials with False Start Errors Only	4.08 ± 0.55	5.45 ± 1.41	0.30	0.04
Percent of All Trials containing False Start Errors	4.08 ± 0.55	5.45 ± 1.41	0.30	0.04
Number of Trials with False Start Errors Only	2.2 ± 0.30	2.92 ± 0.75	0.31	0.03
Number of All Trials containing False Start Errors	2.2 ± 0.30	2.92 ± 0.75	0.31	0.03
Duration of Saccade to First Target	73.24 ± 1.85	77.74 ± 4.75	0.31	0.03
Number of Trials with Step Saccades[9]	17.25 ± 1.47	19.45 ± 1.48	0.34	0.03
SD of Accuracy of Closest Saccade to First Target	0.87 ± 0.050	0.94 ± 0.088	0.47	0.02
Maximum Saccadic Acceleration to First Target	21961 ± 886.4	20826 ± 1553	0.50	0.02
Initial Trajectory of Well Behaved Saccades	17.51 ± 0.82	17.51 ± 0.82	0.59	0.01
Velocity of Saccade to First Target	303.7 ± 11.12	294.7 ± 23.42	0.69	0.01
Accuracy of Closest Saccade to First Target	1.50 ± 0.069	1.54 ± 0.11	0.75	0.00
CV of Closest Saccade to First Target	0.57 ± 0.018	0.56 ± 0.024	0.79	0.00
Minimum Saccadic Acceleration to First Target	-16500 ± 1134	-16018 ± 1756	0.81	0.00
Skew Index[11] to First Target	0.27 ± 0.016	0.27 ± 0.020	0.90	0.00
Skew 2[2] to First Target	6732 ± 357.2	6779 ± 606.9	0.94	0.00
Percent of Trials with No Saccade Errors Only	--	--	--	--
Number of Trials with No Saccade Errors Only	--	--	--	--

Appendix D

Memory Guided 2-Target Task Outcome Features	**Control ($\bar{x}$ ± SEM)**	**FASD ($\bar{x}$ ± SEM)**	**p-value**	**Effect size (*d*)**
Percent of Correct Trials	84.76 ± 1.94	59.4 ± 4.29	<0.0001	0.56
Number of All Trials containing No Saccade Errors	0.1 ± 0.084	1.55 ± 0.31	<0.0001	0.49
Percent of All Trials containing No Saccade Errors	0.34 ± 0.16	2.87 ± 0.58	<0.0001	0.49
Number of No Fixation or Target Trials	0.18 ± 0.084	1.64 ± 0.36	<0.0001	0.47
Percent of Trials with 2 Target Sequence Errors Only	4.60 ± 1.34	17.6 ± 2.89	<0.0001	0.41
Number of Trials with 2 Target Sequence Errors Only	2.48 ± 0.72	9.33 ± 1.54	<0.0001	0.40
Number of Correct Trials	43.86 ± 1.57	31.83 ± 2.40	0.00	0.37
First Saccade Accuracy to Second Target	3.02 ± 0.16	4.39 ± 0.36	0.00	0.34
Saccade Threshold[7]	14.66 ± 0.32	17.2 ± 0.64	0.00	0.33
Percent of All Trials with 2 Target Sequence Errors	7.34 ± 2.31	23.48 ± 4.01	0.00	0.31
Number of All Trials with 2 Target Sequence Errors	3.96 ± 1.25	12.42 ± 2.11	0.00	0.30
Path Length Accuracy of All Saccades, including Step Saccades	3.56 ± 0.24	6.11 ± 0.93	0.00	0.26
Drift Base in the X Axis	0.55 ± 0.043	0.84 ± 0.093	0.00	0.26
CV of Closest Saccade to Second Target	0.56 ± 0.017	0.70 ± 0.048	0.00	0.25
Percent of All Trials with Skip Errors	0.29 ± 0.16	1.90 ± 0.57	0.00	0.25
Number of All Trials with Skip Errors	0.16 ± 0.086	1 ± 0.30	0.00	0.25
Drift Base in the Y Axis	0.62 ± 0.064	0.95 ± 0.088	0.00	0.24
SRT to First Target	368.1 ± 10.32	432.4 ± 20.46	0.00	0.23
First Angle Offset of First Saccade	6.53 ± 0.37	9.08 ± 0.93	0.00	0.23
SD of SRT to First Target	177.5 ± 8.22	232 ± 18.99	0.00	0.23
First Saccade Accuracy to First Target	2.38 ± 0.16	3.16 ± 0.22	0.01	0.21
Number of Step Saccades per Trial[9]	1.00 ± 0.10	1.52 ± 0.16	0.01	0.20
Number of All Trials with Timing Errors	3.52 ± 0.55	6.25 ± 0.91	0.01	0.20
Percent of Trials with Skip Errors Only	0.29 ± 0.16	1.61 ± 0.56	0.01	0.19
Number of Trials with Skip Errors Only	0.16 ± 0.086	0.85 ± 0.30	0.01	0.18
Accuracy of Closest Saccade to Second Target	1.86 ± 0.075	2.33 ± 0.19	0.01	0.18

Memory Guided 2-Target Task Outcome Features	**Control (x̄ ± SEM)**	**FASD (x̄ ± SEM)**	**p-value**	**Effect size (*d*)**
Overall Accuracy of Last Saccade	1.96 ± 0.084	2.43 ± 0.20	0.02	0.17
SD of First Saccade Accuracy to Second Target	2.62 ± 0.23	3.62 ± 0.33	0.02	0.17
Percent of Trials with False Start Errors Only	2.87 ± 0.38	1.40 ± 0.40	0.02	0.16
Distance from Fixation Point to First Saccade Onset Position	0.55 ± 0.031	0.69 ± 0.052	0.02	0.15
SD of Accuracy of Closest Saccade to Second Target	1.12 ± 0.10	1.56 ± 0.19	0.03	0.15
Number of Macrosaccades per Trial	5.01 ± 0.25	5.91 ± 0.27	0.03	0.14
Percent of All Trials containing Timing Errors	7.44 ± 1.31	11.68 ± 1.67	0.06	0.11
Number of Trials with False Start Errors Only	1.55 ± 0.21	0.92 ± 0.26	0.07	0.09
SD of SRT to Second Target	241.5 ± 12.47	279.1 ± 19.25	0.10	0.08
SD of Accuracy of Closest Saccade to First Target	1.01 ± 0.055	1.19 ± 0.12	0.12	0.08
SD of First Saccade Accuracy to First Target	1.57 ± 0.16	1.95 ± 0.16	0.15	0.07
Amplitude to First Target	9.15 ± 0.20	8.63 ± 0.30	0.14	0.07
Skew 1[2] to Second Target	12774 ± 530.3	11507 ± 671.6	0.15	0.06
Amplitude to Second Target	14.27 ± 0.34	13.31 ± 0.63	0.15	0.06
CV of First Saccade Accuracy to First Target	0.61 ± 0.023	0.68 ± 0.051	0.16	0.06
CV of SRT to First Target	48.99 ± 1.49	52.74 ± 2.32	0.16	0.06
Duration of Saccade to Second Target	84.65 ± 2.73	90.96 ± 3.74	0.18	0.06
Percent of Blinks per Trial	1.49 ± 0.35	2.28 ± 0.53	0.21	0.05
Accuracy of Closest Saccade to First Target	1.79 ± 0.089	1.97 ± 0.15	0.30	0.04
CV of SRT to Second Target	24.46 ± 0.92	26.13 ± 1.30	0.30	0.03
Velocity of Saccade to Second Target	360.8 ± 11.5	337 ± 22.81	0.31	0.03
Percent of Trials with Timing Errors Only	6.34 ± 1.07	8.27 ± 1.51	0.30	0.03
Number of Trials with Timing Errors Only	3.41 ± 0.58	4.42 ± 0.81	0.31	0.03
Skew Index[11] to First Target	0.28 ± 0.011	0.26 ± 0.018	0.35	0.03
Skew 2[2] to Second Target	6903 ± 313	6359 ± 537.4	0.36	0.03
Skew 1[2] to First Target	11100 ± 469.4	10362 ± 737.3	0.38	0.02
Minimum Saccadic Acceleration to First Target	-15522 ± 1013	-17130 ± 1691	0.39	0.02
SRT to Second Target	965.7 ± 44.68	1022 ± 56.07	0.46	0.02
CV of Closest Saccade to First Target	0.57 ± 0.023	0.60 ± 0.037	0.45	0.02

Memory Guided 2-Target Task Outcome Features	**Control (x̄ ± SEM)**	**FASD (x̄ ± SEM)**	**p-value**	**Effect size (*d*)**
Initial Trajectory of Well Behaved Saccades	17.78 ± 0.66	18.72 ± 1.25	0.47	0.02
Skew 2^2 to First Target	6438 ± 363	6885 ± 524.1	0.47	0.02
Percent of Trials with Stop Errors Only	0.34 ± 0.16	0.54 ± 0.28	0.50	0.01
Percent of All Trials with Stop Errors	0.34 ± 0.16	0.54 ± 0.28	0.50	0.01
Minimum Saccadic Acceleration to Second Target	-18345 ± 1269	-19962 ± 2463	0.52	0.01
Percent of Trials with Step Saccades[9]	67 ± 3.87	70.8 ± 4.86	0.54	0.01
Number of Trials with Stop Errors Only	0.18 ± 0.084	0.27 ± 0.14	0.56	0.01
Number of All Trials with Stop Errors	0.18 ± 0.084	0.27 ± 0.14	0.56	0.01
Number of All Trials containing False Start Errors	1.64 ± 0.23	1.42 ± 0.31	0.58	0.01
Number of Trials with Step Saccades[9]	36.05 ± 2.06	37.77 ± 2.70	0.61	0.01
Percent of All Trials containing False Start Errors	3.04 ± 0.43	2.66 ± 0.61	0.61	0.01
Maximum Saccadic Acceleration to Second Target	26413 ± 1361	25253 ± 2076	0.63	0.01
Duration of Saccade to First Target	73.61 ± 2.45	75.12 ± 4.45	0.75	0.00
Number of Lost Trials	0.14 ± 0.10	0.091 ± 0.091	0.77	0.00
Number of Viable Trials[10]	53.86 ± 0.10	53.91 ± 0.091	0.77	0.00
CV of First Saccade Accuracy to Second Target	0.79 ± 0.047	0.78 ± 0.056	0.85	0.00
Skew Index[11] to Second Target	0.28 ± 0.014	0.29 ± 0.021	0.85	0.00
Velocity of Saccade to First Target	282.3 ± 10.75	283.4 ± 17.56	0.95	0.00
Maximum Saccadic Acceleration to First Target	22020 ± 1154	22027 ± 1645	1.00	4.075E-07
Percent of Trials with No Saccade Errors Only	--	--	--	--
Number of Trials with No Saccade Errors Only	--	--	--	--

Appendix E

Memory Guided 3-Target Task Outcome Features	**Control ($\bar{x}$ ± SEM)**	**FASD ($\bar{x}$ ± SEM)**	**p-value**	**Effect size (*d*)**
Percent of Correct Trials	60.82 ± 4.64	33.21 ± 5.68	0.00	0.30
Number of Correct Trials	32.71 ± 2.52	19.55 ± 2.85	0.00	0.26
Distance from Fixation Point to First Saccade Onset Position	0.58 ± 0.023	0.68 ± 0.026	0.01	0.21
Number of All Trials with 3 Target Sequence Errors	1.95 ± 0.60	5 ± 1.09	0.01	0.20
Percent of All Trials with 3 Target Sequence Errors	3.70 ± 1.16	9.30 ± 2.02	0.01	0.19
Number of Trials with 3 Target Sequence Errors Only	1.75 ± 0.53	4.18 ± 0.82	0.01	0.19
Percent of Trials with 3 Target Sequence Errors Only	3.31± 1.02	7.77 ± 1.51	0.02	0.18
Percent of All Trials containing Timing Errors	7.21 ± 1.33	14.07 ± 2.85	0.02	0.18
Saccade Threshold[7]	15.13 ± 0.41	16.99 ± 0.66	0.02	0.17
Number of All Trials with 2 Target Sequence Errors	12.33 ± 1.69	19.25 ± 2.12	0.02	0.17
Percent of All Trials with 2 Target Sequence Errors	22.99 ± 3.14	35.89 ± 4.02	0.02	0.17
Amplitude to Second Target	14.01 ± 0.40	12.42 ± 0.58	0.03	0.16
Drift Base in the X Axis	0.64 ± 0.074	1.01 ± 0.16	0.03	0.16
Amplitude to First Target	8.83 ± 0.23	7.92 ± 0.36	0.04	0.14
SD of Accuracy of Closest Saccade to Third Target	1.14 ± 0.047	1.38 ± 0.13	0.04	0.14
CV of Closest Saccade to Second Target	0.57 ± 0.027	0.67 ± 0.046	0.05	0.13
Drift Base in the Y Axis	0.64 ± 0.064	0.94 ± 0.15	0.04	0.13
Velocity of Saccade to Second Target	352.5 ± 13.64	303.9 ± 19.96	0.05	0.13
SRT to First Target	374.5 ± 12.7	427.6 ± 27.64	0.05	0.12
Skew Index[11] to Second Target	0.29 ± 0.016	0.23 ± 0.026	0.05	0.12
Number of All Trials with Timing Errors	3.86 ± 0.71	6.44 ± 1.13	0.06	0.12
First Saccade Accuracy to Second Target	2.98 ± 0.16	3.60 ± 0.32	0.06	0.12
Skew 1[2] to Second Target	13023 ± 546.7	11132 ± 895.1	0.07	0.11
Amplitude to Third Target	14.69 ± 0.40	13.47 ± 0.48	0.07	0.11
Number of All Trials with Stop Errors	2.05 ± 0.36	3.1 ± 0.41	0.09	0.10
Percent of All Trials with Stop Errors	3.81 ± 0.67	5.75 ± 0.75	0.09	0.10

Memory Guided 3-Target Task Outcome Features	**Control (x̄ ± SEM)**	**FASD (x̄ ± SEM)**	**p-value**	**Effect size (*d*)**
Number of Trials with Timing Errors Only	1.9 ± 0.45	3.18 ± 0.60	0.10	0.09
Percent of Trials with Timing Errors Only	3.55 ± 0.83	5.94 ± 1.12	0.10	0.09
SRT to Second Target	921.4 ± 30.84	1019 ± 55.96	0.11	0.09
Velocity of Saccade to Third Target	365.1 ± 14.74	327.1 ± 16.49	0.11	0.08
First Angle Offset of First Saccade	7.76 ± 0.43	8.91 ± 0.69	0.15	0.07
SD of Accuracy of Closest Saccade to Second Target	1.23 ± 0.063	1.44 ± 0.15	0.15	0.07
Percent of Trials with Skip Errors Only	1.76 ± 0.34	2.81 ± 0.81	0.17	0.07
Skew 1[2] to First Target	10978 ± 528.5	9656 ± 805.4	0.17	0.07
Number of Trials with Skip Errors Only	0.95 ± 0.18	1.5 ± 0.43	0.18	0.06
Percent of All Trials with Skip Errors	3.63 ± 0.93	6.13 ± 1.69	0.17	0.06
Number of All Trials with Skip Errors	1.95 ± 0.50	3.3 ± 0.91	0.17	0.06
Skew 2[2] to Third Target	6893 ± 365.7	6041 ± 524.7	0.18	0.06
Initial Trajectory of Well Behaved Saccades	19.3 ± 0.88	17.27 ± 0.99	0.18	0.06
Percent of All Trials containing No Saccade Errors	0.37 ± 0.17	0.93 ± 0.50	0.20	0.06
Number of All Trials containing No Saccade Errors	0.2 ± 0.092	0.5 ± 0.27	0.20	0.06
Percent of Trials with Stop Errors Only	2.05 ± 0.50	3.27 ± 0.80	0.18	0.06
Number of Trials with Stop Errors Only	1.1 ± 0.27	1.75 ± 0.43	0.19	0.06
Number of Lost Trials	0.05 ± 0.05	0.25 ± 0.18	0.20	0.05
Number of Viable Trials[10]	53.95 ± 0.05	53.75 ± 0.18	0.20	0.05
Skew 1[2] to Third Target	12951 ± 578.4	11707 ± 865.2	0.23	0.05
Accuracy of Closest Saccade to Second Target	2.22 ± 0.11	2.45 ± 0.15	0.24	0.05
Maximum Saccadic Acceleration to Second Target	24707 ± 1103	22570 ± 1430	0.26	0.05
SD of First Saccade Accuracy to Third Target	2.47 ± 0.20	2.08 ± 0.23	0.26	0.04
Skew 2[2] to First Target	6286 ± 347.1	5601 ± 520.1	0.27	0.04
Number of Macrosaccades per Trial	6.37 ± 0.25	6.85 ± 0.38	0.28	0.04
SD of First Saccade Accuracy to Second Target	2.31 ± 0.20	2.71 ± 0.34	0.29	0.04
SD of Accuracy of Closest Saccade to First Target	1.19 ± 0.087	1.37 ± 0.19	0.31	0.04
CV of Closest Saccade to Third Target	0.51 ± 0.018	0.54 ± 0.019	0.35	0.03
Skew Index[11] to First Target	0.27 ± 0.014	0.25 ± 0.018	0.35	0.03

Memory Guided 3-Target Task Outcome Features	**Control ($\bar{x}$ ± SEM)**	**FASD ($\bar{x}$ ± SEM)**	**p-value**	**Effect size (*d*)**
Velocity of Saccade to First Target	277.1 ± 13.48	258.3 ± 14.76	0.38	0.03
Duration of Saccade to Third Target	83.75 ± 3.04	88.46 ± 4.05	0.37	0.03
Skew Index[11] to Third Target	0.29 ± 0.020	0.32 ± 0.02	0.39	0.03
Percent of Trials with Step Saccades[9]	81.45 ± 2.64	77.65 ± 3.46	0.39	0.02
Number of Trials with Step Saccades[9]	43.7 ± 1.37	41.75 ± 1.90	0.40	0.02
Percent of Blinks per Trial	1.24 ± 0.25	1.61 ± 0.46	0.45	0.02
Number of No Fixation or Target Trials	0.3 ± 0.13	0.5 ± 0.27	0.45	0.02
SD of SRT to Third Target	313 ± 13.03	292.6 ± 28.52	0.46	0.02
Number of All Trials containing False Start Errors	0.85 ± 0.23	1.17 ± 0.37	0.45	0.02
Percent of All Trials containing False Start Errors	1.60 ± 0.44	2.18 ± 0.69	0.45	0.02
SD of SRT to First Target	182.1 ± 13.21	200.9 ± 25.05	0.47	0.02
Number of Step Saccades per Trial[9]	1.42 ± 0.11	1.56 ± 0.16	0.47	0.02
Maximum Saccadic Acceleration to Third Target	25367 ± 1255	24051 ± 1238	0.50	0.02
SD of First Saccade Accuracy to First Target	1.87 ± 0.15	2.05 ± 0.24	0.50	0.02
CV of First Saccade Accuracy to Third Target	0.71 ± 0.047	0.65 ± 0.049	0.50	0.02
Accuracy of Closest Saccade to First Target	2.09 ± 0.11	2.25 ± 0.25	0.53	0.01
Number of Trials with 2 Target Sequence Errors Only	10.33 ± 1.48	11.75 ± 1.61	0.54	0.01
Path Length Accuracy of All Saccades, including Step Saccades	6.12 ± 0.44	5.69 ± 0.54	0.56	0.01
Percent of Trials with 2 Target Sequence Errors Only	19.26 ± 2.75	21.83 ± 2.97	0.55	0.01
Minimum Saccadic Acceleration to Third Target	-16381 ± 868.8	-17237 ± 1488	0.60	0.01
CV of SRT to Third Target	20.62 ± 0.60	19.94 ± 1.88	0.67	0.01
Duration of Saccade to First Target	72.53 ± 2.87	74.59 ± 3.88	0.68	0.01
CV of First Saccade Accuracy to First Target	0.59 ± 0.024	0.61 ± 0.045	0.69	0.01
Maximum Saccadic Acceleration to First Target	20666 ± 1128	19933 ± 1334	0.69	0.01
Minimum Saccadic Acceleration to Second Target	-15646 ± 687.9	-16258 ± 1593	0.69	0.01
First Saccade Accuracy to First Target	3.00 ± 0.17	3.11 ± 0.25	0.71	0.01
Accuracy of Closest Saccade to Third Target	2.25 ± 0.096	2.19 ± 0.13	0.72	0.00
First Saccade Accuracy to Third Target	3.32 ± 0.16	3.22 ± 0.25	0.72	0.00
SRT to Third Target	1480 ± 50.25	1507 ± 76.98	0.77	0.00

Memory Guided 3-Target Task Outcome Features	**Control ($\bar{x}$ ± SEM)**	**FASD ($\bar{x}$ ± SEM)**	**p-value**	**Effect size (*d*)**
CV of SRT to Second Target	26.06 ± 0.94	26.56 ± 2.17	0.81	0.00
CV of First Saccade Accuracy to Second Target	0.72 ± 0.044	0.74 ± 0.055	0.83	0.00
Duration of Saccade to Second Target	79.2 ± 2.21	79.97 ± 2.83	0.84	0.00
CV of Closest Saccade to First Target	0.56 ± 0.028	0.57 ± 0.024	0.85	0.00
SD of SRT to Second Target	248.2 ± 11.56	245.5 ± 26.4	0.92	0.00
CV of SRT to First Target	47.69 ± 2.52	47.27 ± 3.76	0.92	0.00
Overall Accuracy of Last Saccade	2.41 ± 0.091	2.42 ± 0.14	0.94	0.00
Percent of Trials with False Start Errors Only	0.59 ± 0.25	0.62 ± 0.35	0.94	0.00
Number of Trials with False Start Errors Only	0.32 ± 0.13	0.33 ± 0.19	0.94	0.00
Minimum Saccadic Acceleration to First Target	-16007 ± 1251	-15866 ± 1437	0.94	0.00
Skew 2[2] to Second Target	6535 ± 262.8	6525 ± 492.5	0.98	0.00
Percent of Trials with No Saccade Errors Only	--	--	--	--
Number of Trials with No Saccade Errors Only	--	--	--	--

[1] See Panel A of Figure 3-2_

[2] See Panel B of Figure 3-2_

[3] Well-behaved saccades are saccades without extraordinary high velocities. These saccades are < 800 °/s. Anything above this velocity is impossible for saccades in the range of 10 ° and indicates bad eye tracking, blinking, or another unusual event. See Panel A of Figure_

[4] Regular saccades are defined as saccades where saccade onset starts at __ ms after go signal.

[5] Express saccades are defined as saccades where saccade onset starts at __ ms after go signal.

[6] Anticipatory saccades as defined as saccades that start in the anticipation epoch (saccade onset starts less than 90 ms after go signal); refer to Panel B of Figure_

[7] Saccade threshold calculation depends on first finding the mode of the fixation signal per trial (fixation is defined as any period where the speed is < 50 °/s, with no blinks). Saccade threshold is defined as the mode of fixation + 2* the standard deviation of the fixation. Saccades are detected as any time the speed is above this threshold for 5 or more consecutive sample points.

[8] Macrosaccades are defined as saccades ≥ 2 °

[9] Step Saccades are defined as saccades < 2 deg!

[10] Viable trials are trials that were not ignored due to lost eye tracking or other factors

[11] Skew index is calculated by: (skew1 - skew2)/(skew1 + skew2)

[12] False start trials are defined as viable trials where fixation was broken but reacquired before the trial proceeded normally.

[13] A saccadic amplitude of 7.2 ° is 2 standard deviations away from the mean amplitude of control participants