ABSTRACT

MADISON NELL MOORE
Behavioral Changes Following Daily Practice of Saccade Tasks in Schizophrenia
(Under the Direction of JENNIFER MCDOWELL)

People with schizophrenia show impairment in tasks requiring executive control, like inhibition. A simple test of inhibition is the antisaccade task, which requires a glance towards the mirror image of a peripheral cue. The goal of this study is to determine how practicing the antisaccade task changes performance on that task and on related tasks known to assess executive control. Participants with schizophrenia (SZ) and healthy comparison subjects (NP) were assigned a single saccade task to practice daily - *either* antisaccades *or* prosaccades (glances towards a peripheral cue) - over a two-week period. Executive control was evaluated at pre- and post-test using two tasks: an ocular motor delayed response (ODR) task to measure changes due to practice on a different, but related, saccade task, and the Wisconsin Card Sorting Test (WCST) to evaluate whether changes in executive control could generalize beyond saccade tasks. Preliminary results suggest antisaccade practice resulted in modest antisaccade improvement for both NP and SZ groups. Prosaccade practice did not affect prosaccade performance (due to a ceiling effect in both groups). The NP antisaccade practice group showed improvement across both the saccade specific (ODR) and non-saccade specific (WCST) executive function tasks. The SZ practice groups show little evidence of change across time, with the exception of the SZ antisaccade practice group showing slightly better ODR performance and the SZ prosaccade group perhaps showing a slight decrease in performance on ODR. Initial results from this study suggest that saccadic performance is malleable within certain parameters. Specifically, it appears that behavior (and potentially its neural underpinnings) may be more malleable in healthy people than in people with schizophrenia and practice on one executive function task could potentially be associated with modest gains on related tasks. This result has implications for aiding or improving behavior and brain function using behavioral training techniques.

INDEX WORDS: Schizophrenia, Saccades, Antisaccades, Memory saccades, WCST

BEHAVIORAL CHANGES FOLLOWING DAILY PRACTICE OF SACCADE TASKS IN SCHIZOPHRENIA

by

MADISON NELL MOORE

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DEDICATION

To my family

With many thanks for their help, support, patience, and most of all, their love.

ACKNOWLEDGEMENTS

The completion of this thesis would not have been possible without the invaluable guidance of Dr. Jennifer McDowell. She not only served as my research mentor, but also challenged and encouraged me through my unique and rewarding undergraduate research experience, always focusing on helping me realize the products of my best efforts. Her help and support, as well as that of Dr. Brett Clementz, Mr. Benjamin Austin, Mr. Michael Amlung, and all the other members of the Clinical and Cognitive Neuroscience Laboratory enriched my experience and made my successes possible. For their time, their effort, their interest, and their friendship, I thank them all.

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CHAPTER 1
INTRODUCTION

Background and Significance

The plasticity of the human brain is a remarkable capacity that has implications for an enormous range of interests, from how we learn something new to how the brain can recover after injury. Of particular interest to the current study is the potential to develop behavioral therapies to assist individuals living with hypofrontality, or diminished functioning of the prefrontal cortex (PFC). The PFC mediates executive functions such as thinking ahead, inhibition, and cognitive flexibility in response to changing feedback. Illnesses affecting this area of the brain can greatly impair functioning, even on activities of daily life. Schizophrenia is such an illness, and it is hypothesized that hypofrontality is a key characteristic of the disease (Weinberger et al., 1994). Affecting approximately 1% of the population, schizophrenia is a disease for which behavioral therapy presents exciting possibilities for improvement in daily functioning.

In contrast to healthy individuals, people with schizophrenia exhibit a multitude of unusual symptoms and behaviors, as well as characteristic cognitive deficits. One system that affords relatively easy study and clear illustrations of these differences is the saccadic system. Saccades are small, rapid eye movements which involve the redirection of an individual’s gaze. These types of eye movements are a natural occurrence in all people, and are used daily for such tasks as focusing on an object, following a moving object, or visually orienting to a peripheral stimulus. Saccadic tasks can be characterized as requiring responses that are more 'automatic' to those that require more 'purposeful' movements (Leigh & Zee, 1999), and the study of the saccadic system has provided much information about brain activity in relation to more complicated motor movements (Dyckman, Camchong, Clementz, & McDowell, 2007; Dyckman & McDowell, 2005; McDowell et al., 2002).

The progression from prosaccades, rapid redirections of gaze to a peripheral stimulus which are simple and automatic, to the more complex antisaccades (or rapid redirections to the mirror image location of a stimulus, the same distance but opposite side of center) requires recruitment of more brain regions, specifically the PFC. Because of the nature of prosaccades, schizophrenia and normal participants perform similarly on this task (e.g. percent correct, correct reaction time; Fukushima et al., 1990; Clementz et al., 1994; McDowell & Clementz, 2001). The antisaccade task, however, requires mediation by the PFC and schizophrenia participants have been shown to make more errors on this task than normals (Fukushima et al., 1994; Thaker et al., 2000; Katsanis et al., 1997). Other studies have confirmed that this difference is not due to medications or the consequences of suffering from a chronic illness, because first degree relatives of schizophrenia participants show similar disruptions in performance on the antisaccade task (Crawford et al., 1998; McDowell et al., 1999; Thaker et al., 2000). Instead, this difference in performance is attributed to the hypofrontality of schizophrenia participants and the requirements placed on the PFC by antisaccade tasks (Pierrot-Deseilligny, 1994). In addition, previous evidence has shown that practice by normal participants on the antisaccade task can improve performance on that task (Dyckman & McDowell, 2005).

Based on this previous data, the current study raises the question of whether and how pro- and anti-saccade performance may change with practice across time in normal versus schizophrenia participants. Change in performance on the antisaccade task with practice may elucidate important information about the ways in which schizophrenia participants' behavioral performance on tasks requiring executive function can be modified over time. Other tasks that require executive functioning, such as an Ocular Motor Delayed Response Task (ODR) and the Wisconsin Card Sorting Test (WCST) are thought to be controlled by the same region of the PFC that mediates antisaccade performance (Baddeley, 1986; Goldman-Rakic, 1997). This relationship provides a chance to evaluate the potential for generalization of improvement from one task requiring executive functioning (the antisaccade task) to other tasks requiring executive function (ODR and WCST).

While it is not yet known if PFC functioning can be improved in such a way as to improve performance on the antisaccade task in schizophrenia participants, there is evidence to suggest that this is a reasonable hypothesis. Many skills can be enhanced with practice; normal participants can decrease their antisaccade error rates with practice (Dyckman & McDowell, 2005), and improvements on other executive function tasks in schizophrenia participants after practice have been reported as well (e.g. Rossell & David, 1997; Wykes et al., 2002). From these facts, it seems reasonable to suggest that daily practice of antisaccades could result in improved performance for patients with schizophrenia. If improvement on the antisaccade task and on other tasks of executive control is seen in the schizophrenia antisaccade practice group, it would raise the question of whether this improvement could represent a partial reversal of the hypofrontality and suggest that purposefully practicing executive control could be explored as a non-pharmacological means of improving activities of daily living.

Hypotheses

The hypotheses for the current study were as follows. First, among schizophrenia participants, behavioral performance following practice will show patterns similar to that documented in normal participants. Specifically, both schizophrenia and normal participants who practice prosaccades will show decreased latencies across time. Also, both schizophrenia and normal participants who practice antisaccades will show decreased antisaccade errors across time. Second, among antisaccade-practiced participants (both schizophrenia and normal), there will be the greatest improvement on other measures of executive function (i.e. ODR and WCST).

CHAPTER 2
MATERIALS AND METHODS

Overview:

The current study is part of a larger, ongoing NIH funded study with both a behavioral and an fMRI component. To date, eighteen schizophrenia participants (SZ) and sixteen normal participants (NP) have taken part in a twelve-day trial. After completing both a preliminary phone screening and an in-person interview conducted by two psychologists or highly trained graduate students, those participants who were then recruited for the study were assigned a single practice task, either antisaccades (SZ N = 9, NP N = 8) or prosaccades (SZ N = 9, NP N = 8). Participants came to the lab to practice their assigned tasks eight times, and on the first and last days of the trial (pre- and post-practice), all participants completed two executive functioning tasks: a) ODR, and b) WCST. The current participation represents approximately half of the goal for the final count of the study.

Participants:

Schizophrenia Participants (N=18, 33% Female, age M=34.8 years, SD=10.0) were recruited from the community through newspaper ads, the local AMI, and Advantage Behavioral Health. Each schizophrenia participant was interviewed using the SCID-IV to confirm diagnosis, establish length of illness, and generate a global assessment of functioning (GAF) score. Positive and negative symptoms were evaluated using the Scale for the Assessment of Negative Symptoms (SANS) and the Scale for the Assessment of Positive Symptoms (SAPS). In addition, schizophrenia participants brought their prescriptions to the lab so that names and doses could be recorded accurately. Only participants who had been on a stable dose of medication for two months and who did not undergo a change in medication through the two-week period of the study were included.

Normal Participants (N=16, 56% Female, age M=35.3 years, SD=11.7) were recruited from the community through newspaper ads and fliers posted at community facilities. They were interviewed using the SCID-IV NP to screen for Axis-I disorders.

All participants were right-handed (with the exception of one schizophrenia participant), free of serious physical health problems, absent of known neurological hard signs or history of head trauma, and free from contraindications for fMR imaging (eliminated from consideration if pregnant or claustrophobic; or for having any of the following: pacemaker, shrapnel or other metal, aortic clips, prosthesis, heart valve replacement, or IUD). Participants were screened for substance use disorders (SCID Section E) and potential participants were eliminated for meeting dependence criteria in the two months prior to the interview. The groups were comparable in race (SZ: 55.5% White, 27.8% Black/African American, 5.6% Hispanic, 11% Other; NP: 87.5% White, 6.3% Black/African American, 6.3% Hispanic, 0% Other) and education level (average education level: SZ = highschool, NP = part college) as well as age and gender.

The current study was reviewed and approved by the University of Georgia Institutional Review Board and met all the requirements for research involving human subjects. All participants provided informed consent (IRB approval # 2006-10382).

Practice Sessions:

During the two weeks of testing, participants reported daily to the Eye Tracking Laboratory (Rm. 629, UGA Psychology Building) for practice sessions (practice sessions #1–4 in week 1, and practice sessions #5-8 in week 2). Participants were pseudo-randomly assigned (to keep sex and age variables equivalent between groups) to either the pro- or anti-saccade practice conditions. Block designs were used for both task types, and three repetitions of the practice tasks were completed on each practice day. Participants were placed in a chin and cheek rest in a darkened room 70 cm from a flat color 21" monitor (NEC Multi Sync; NEC Ltd., Tokyo, Japan). Stimuli were generated, and timing and data collection were controlled using TEMPO (Reflective Computing, St. Louis, MO) *or* stimuli were generated by Presentation with timing and data collection controlled using EyeLink II, SR Research Ltd. Software (Osgoode, Ontario, Canada). Runs began with calibration trials to orient the eye tracker to the individual participants' eyes and saccades so as to standardize the data. Eye movements were recorded using an infrared eye movement monitor mounted on eye glass frames (either Eye Trak Model 310, Applied Science Laboratories, Waltham, MA *or* EyeLink II, SR Research Ltd., Osgoode, Ontario, Canada). Data was digitized (500 Hz), monitored continuously on a screen by researchers and saved to a hard drive for off-line analysis.

Practice Tasks:

Each run consisted of 13 blocks alternating between baseline and experimental conditions. The "prosaccade run" (Figure 1) alternated between blocks of fixation and blocks of seven prosaccade trials. The "antisaccade run" (Figure 2) alternated between blocks of fixation and blocks of seven antisaccade trials. Stimuli presented within a block consisted of a 1 degree filled circle that changed color (same luminance) to indicate task type and thus performance requirements. During the fixation block, the target (pink 1 degree circle) stayed at central fixation for 25600 ms plus a variable intertrial interval (ITI) of 2150-2650 ms and the participant was instructed to keep his or her eyes on the target. For the tasks, gap paradigms were selected because they result in more antisaccade errors (Fischer & Weber, 1996; McDowell & Clementz, 1997), thus preventing ceiling effects among normal participants.

During prosaccades, the target (yellow 1 degree circle) began at central fixation for the ITI. The target was then extinguished and 200 ms later (gap) reappeared at +/- 5 degrees or +/- 10 degrees for 1400 ms. The participant was instructed to follow the target as quickly and accurately as possible. This was repeated for a total of seven trials in each of the six experimental blocks, resulting in a total of 42 trials per task run (22 of +/- 5 degrees and 20 of +/- 10 degrees, half in each visual field). Reaction time and accuracy of the saccade were recorded.

During antisaccades, the same fixation target (a blue 1 degree circle) began at central fixation for the ITI. The target was once again extinguished and 200 ms later (gap) then reappeared at +/- 5 or 10 degrees for 1400 ms. Just as with the prosaccade tasks, this was repeated for a total of seven trials in each of the six experimental blocks, resulting in a total of 42 trials per task run (22 of +/- 5 degrees and 20 of +/- 10 degrees, half in each visual field). For the antisaccade task, the participant was instructed to look at the target only when it was in the middle of the screen, and to look to the mirror image of the target (same distance, opposite side of center) when the target moved to the side. A look to the peripheral stimulus was considered an error, and these errors were recorded, along with reaction time and accuracy of the antisaccade.

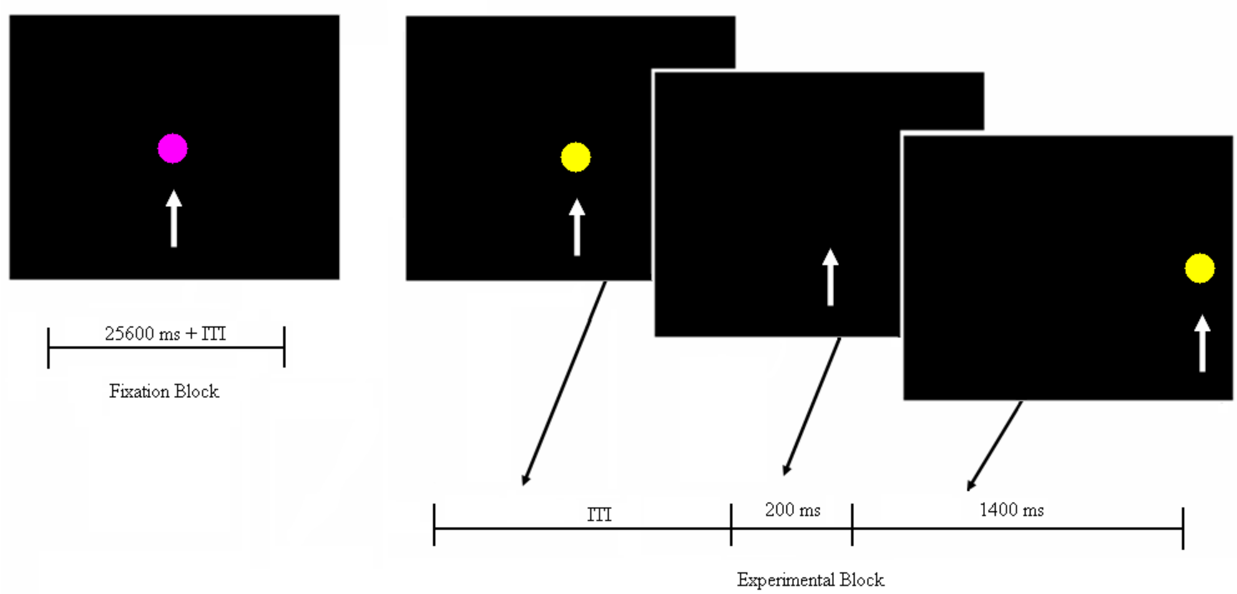

Figure 1: The Prosaccade Task requires a rapid redirection of gaze to the location of a peripherally presented cue. The black boxes represent screen shots across time (ms) with the stimuli as seen by the participants; white arrows represent the correct eye position at each time point, but are not present in the actual task. The task alternates between seven fixation blocks and six experimental blocks of seven trials each.

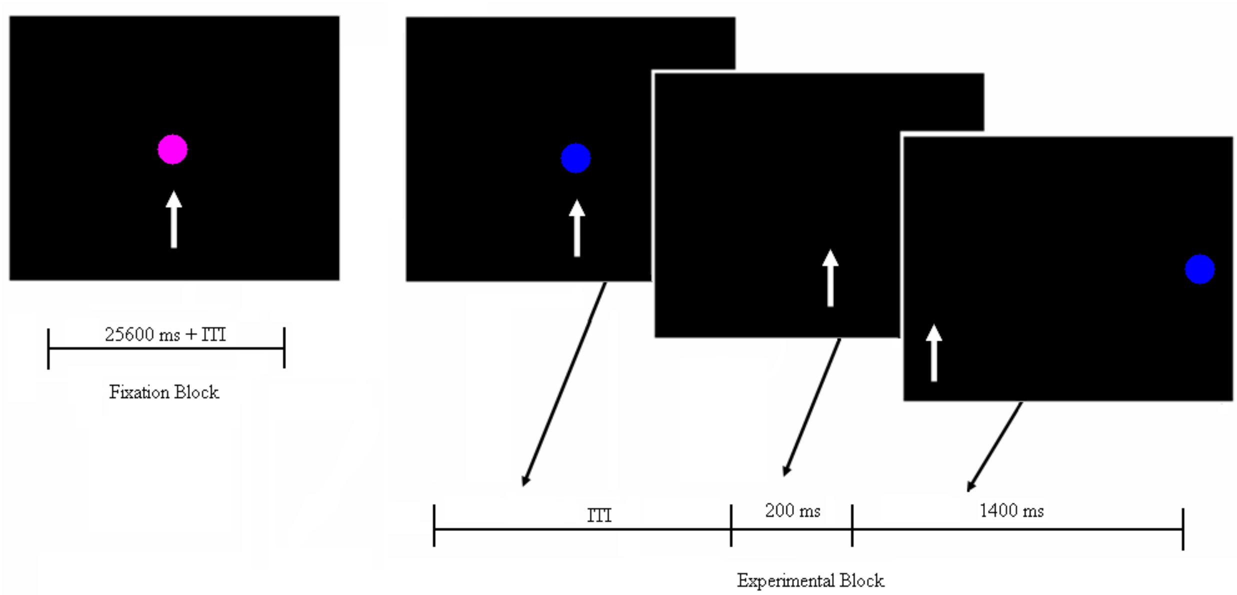

Figure 2: The Antisaccade Task requires a rapid redirection of gaze to the mirror image location (same distance, opposite side of the screen) of a peripherally presented cue. The black boxes represent screen shots across time (ms) with the stimuli as seen by the participants; white arrows represent the correct eye position at each time point, but are not present in the actual task. The task alternates between seven fixation blocks and six experimental blocks of seven trials each.

Executive Functioning Tasks:

ODR (Figure 3): The ODR task is an eye movement task which measures working memory and inhibition. Once again, participants were placed in a chin and cheek rest in a darkened room 70 cm from a flat color 21” monitor (NEC Multi Sync; NEC Ltd., Tokyo, Japan). As with the practice tasks, ODR stimuli were generated, and timing and data collection were controlled using TEMPO (Reflective Computing, St. Louis, MO) *or* stimuli were generated by Presentation with timing and data collection controlled using EyeLink II, SR Research Ltd. Software (Osgoode, Ontario, Canada). Eye movements were again recorded using an infrared eye movement monitor mounted on eye glass frames (either Eye Trak Model 310, Applied Science Laboratories, Waltham, MA *or* EyeLink II, SR Research Ltd., Osgoode, Ontario, Canada). Data was digitized (500 Hz), monitored continuously on a screen by researchers and saved to a hard drive for off-line analysis.

During the ODR task, 40 trials of the following were presented. At the beginning of the ODR task, a white cross was presented in the center of the screen for a variable intertrial interval (ITI) of 1250-1750 ms. Participants were instructed to keep their eyes fixated on this cross for the duration of its presentation. After the ITI, a peripheral cue was flashed for 100 ms at +/- 8 or 16 degrees, half in each visual field. Participants were instructed not to look at the peripheral cue when it was presented, but to remember its location. After the ensuing 4000 ms delay period, the central fixation cross was extinguished, and the participants had 1500 ms to generate an eye movement to the remembered location of the previously presented peripheral cue (a “memory saccade”). Any saccade generated prior to the removal of the central fixation cross was considered an error (an “anticipatory saccade”). Finally, the cue was presented again at the same location as before to reinforce or correct the participant’s memory saccade.

Trial by trial performance was scored using programs written in MATLAB (The Mathworks Inc., Natick, MA) by the PI. Memory-guided saccade accuracy as well as reaction time and the number of anticipatory saccades generated during the delay period were quantified.

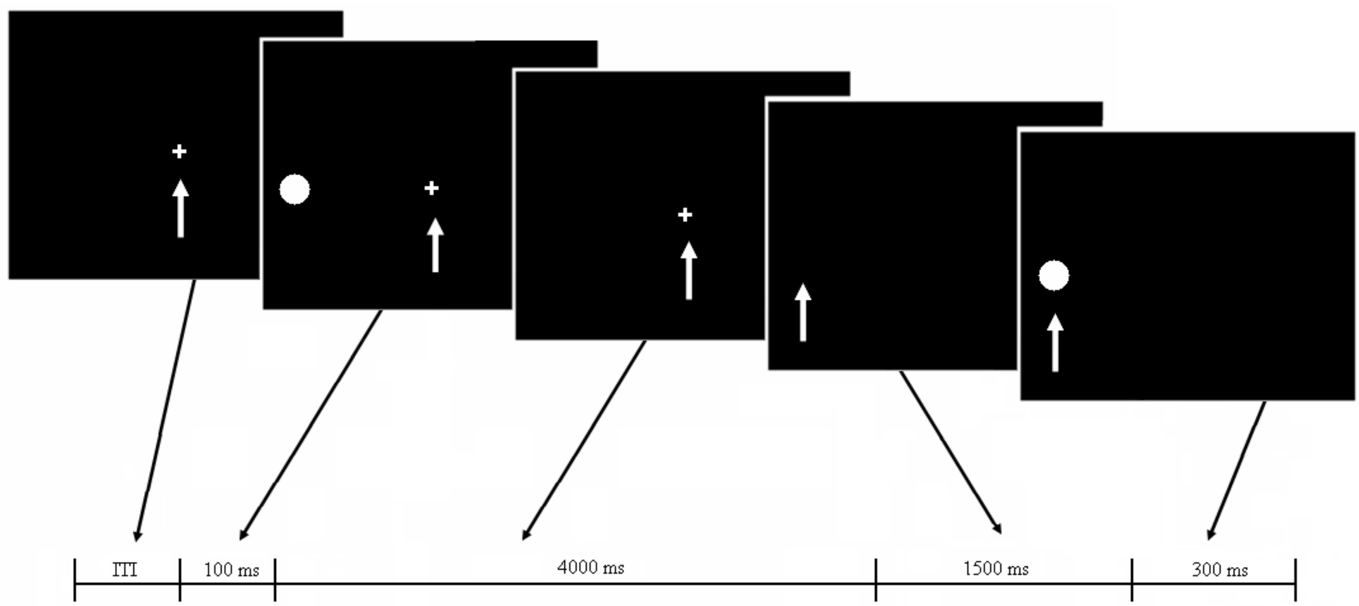

Figure 3: The ODR Task requires participants to remain fixated on the central cross throughout the presentation of a peripheral cue and the subsequent delay period. Following the extinguishing of the central cross, participants must generate a memory saccade (a saccade to the remembered location of the peripheral cue). A saccade prior to the removal of the central cross is an error termed an anticipatory saccade. The black boxes represent screen shots across time (ms) with the stimuli as seen by the participants; white arrows represent the correct eye position at each time point, but are not present in the actual task.

WCST (Figure 4)**:** The WCST is a complex task which requires abstract reasoning ability, cognitive flexibility in response to changing feedback, and inhibition. A computerized version of the WCST (Wisconsin Card Sorting Test®Computer Version 4 Research Edition (WCST:CV4™); Psychological Assessment Resources, Inc.) was administered on a desktop computer in the laboratory. Approximate time for completion of the test was 15-30 minutes.

At the start of the test, four cue cards appear at the top of the screen, one with each of the following combinations of numbers, colors, and shapes: one red circle, two green stars, three blue squares, four yellow crosses. In addition, there is a deck of 128 stimulus cards at the bottom corner, each with variations of numbers (1-4), colors (red, green, blue, or yellow), and shapes (circles, stars, squares, or crosses), presented one at a time throughout the test. The participants are instructed to match the bottom, stimulus card to one of the cue cards presented above; no other instructions are given. The test requires that the participants determine the correct sorting principle based on the computer feedback about the match they make. The first sorting principle is "color"; after the participant determines the sorting principle, the unstated goal is to make ten consecutive correct matches to that principle (color). After completion of the ten matches to color (the first "category completed"), the sorting principle changes without the participant's knowledge. The next sorting principle is "form" (shape), and after the participant again determines this sorting principle and makes ten consecutive correct matches, the category then changes to "number". The same pattern of sorting principles repeats once more, and the test is completed either when all six categories have been completed or when the participant runs out of cards to sort, whichever comes first. A participant's continuing to match to a previously correct sorting principle which has since changed is termed a "perseverative error". The WCST:CV4™ Scoring Program-Research Edition was used to assess perservative errors and number of categories completed.

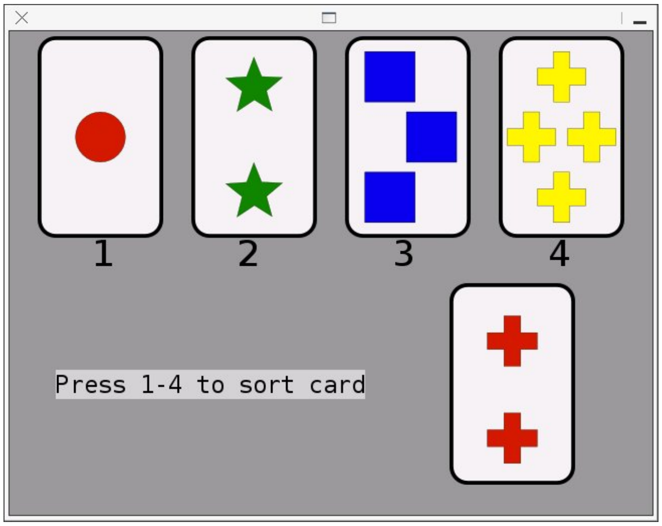

Figure 4: The Wisconsin Card Sorting Test requires participants to match the bottom stimulus cards to the top cue cards; no other instructions are given. In this example of a screen shot, the stimulus card could be matched to cue cards 1 (color), 2 (number), or 4 (shape). Upon matching the stimulus card to one of the cue cards, the computer provides feedback to the participant in the form of a message, either “Right” or “Wrong”. Ten consecutive correct matches compose a completed category, and continuing to match to a previously correct sorting principle once that principle is no longer in effect is termed a perseverative error.

Analyses of Eye Tracking Data:

All eye movement data from the laboratory practice sessions was scored by a researcher using programs written in MATLAB (The Mathworks Inc., Natick, MA) by the PI. After changing digital units to degrees of visual angle (based on the transform function of the calibration trials), data was low pass filtered. For the practice tasks, trials with blinks and trials with no saccades were eliminated. To be scored as a saccade, eye movements had to show the characteristic position and velocity profiles (Leigh & Zee, 1999) with reaction times greater than 90 ms (i.e. must be visually guided). Each event was scored for direction (correct or incorrect) and latency (reaction time in ms). For the ODR task, trials with blinks at 0 ms (coinciding with the presentation of the peripheral cue), trials with no saccades, and trials with final eye position data outside the range of the eye trackers were eliminated. An anticipatory saccade was defined as any saccade which occurred between 0 ms and 4180 ms (0-100 ms = cue presentation; 100-4100 ms = 4 second delay; 4100-4180 ms = reaction time necessary for a saccade to be visually guided as determined in Camchong et al, 2008), and memory saccades were defined as a saccade generated in the correct direction between 4180 ms and the end of the trial. Each event was scored for direction and latency (reaction time in ms).

CHAPTER 3
RESULTS

The current study reflects the behavioral component of an ongoing project whose primary aim is to understand the changes in behavioral performance and brain activity between schizophrenia and normal participants following daily practice of an eye movement task. Data will continue to be collected until the desired sample size of thirty schizophrenia participants and thirty normal participants has been reached. The following results reflect data from approximately half of the target goal of participants for this study and provide some interesting preliminary trends for consideration:

Practice Tasks Results:

Antisaccade practice did not result in a change in antisaccade percent correct in the schizophrenia practice group, but practice did result in a modest improvement in antisaccade percent correct in the normal practice group (Figure 5). Prosaccade practice resulted in no changes in prosaccade percent correct for either the schizophrenia group or normal group due to a ceiling effect in both groups (Figure 5).

Antisaccade practice did not result in a change in reaction time for either the schizophrenia group or the normal group, but prosaccade practice resulted in a decrease in reaction time for both groups (Figure 6).

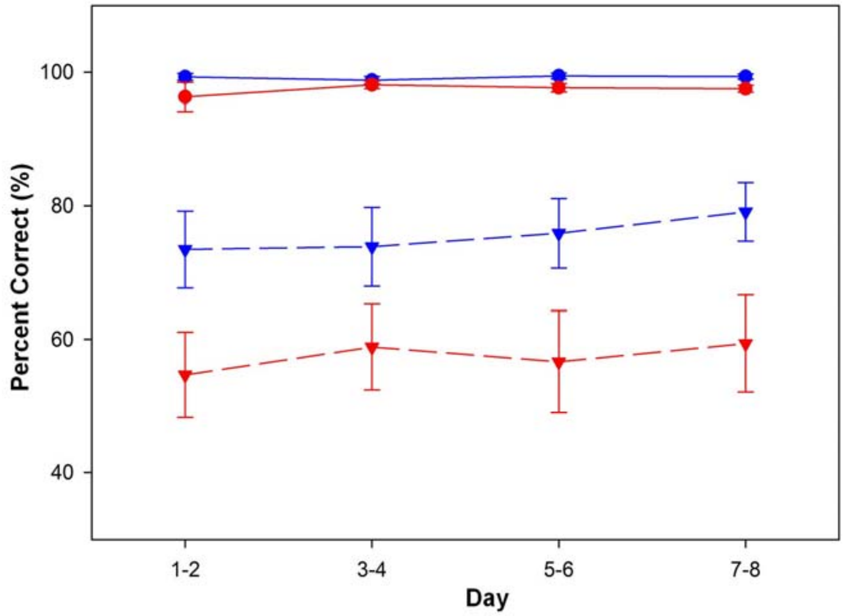

Figure 5. Percent of trials correct for antisaccades (dashed lines) and prosaccades (solid lines) for SZ (red) and NP (blue) across time. Data is collapsed across pairs of practice days. A correct trial was defined as a trial in which the participant looked to the correct location at presentation of the peripheral cue.

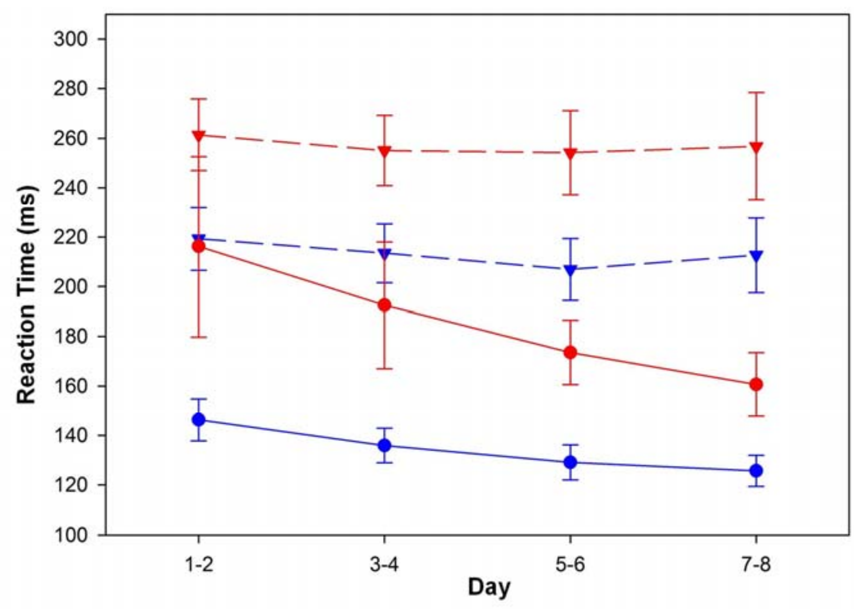

Figure 6. Correct reaction time for antisaccades (dashed lines) and prosaccades (solid lines) for SZ (red) and NP (blue) across time. Data is collapsed across pairs of practice days. Correct reaction time was calculated from the reaction times of correct trials.

ODR Results

Both antisaccade practice groups (schizophrenia and normal) showed a modest increase of percent correct trials on ODR. The schizophrenia prosaccade practice group showed no change on percent of trials correct on ODR, but the normal prosaccade practice group showed a modest increase (Figure 7).

The normal antisaccade practice group showed decreased anticipatory saccade generation on ODR, whereas the other groups showed relatively little change (Figure 8).

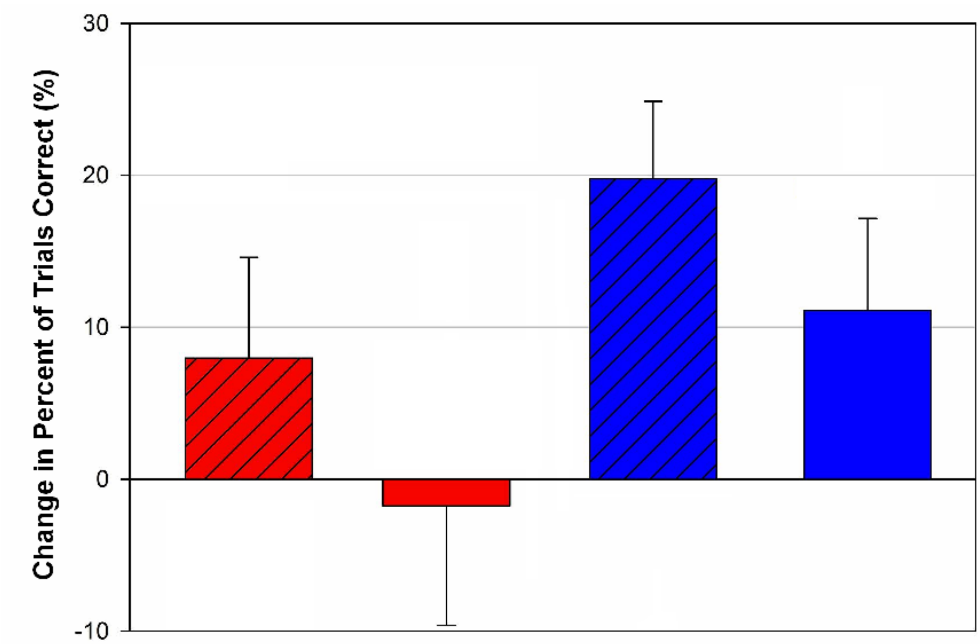

Figure 7. Change in percent of correct trials (time 2 minus time 1) on ODR for SZ (red) and NP (blue) antisaccade (crossed columns) and prosaccade (solid columns) practice groups. Positive values indicate more correct trials at time 2.

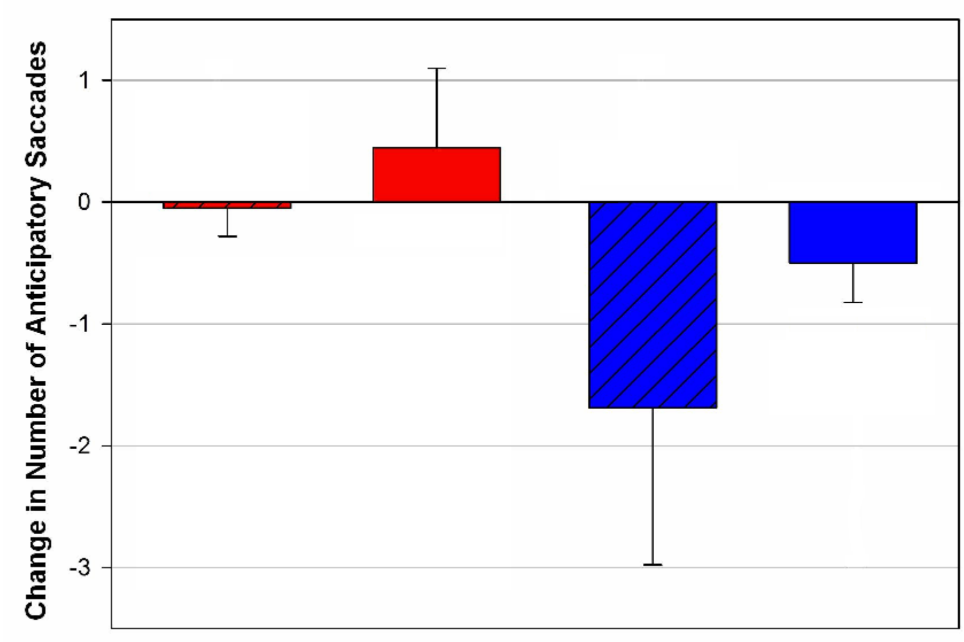

Figure 8. Change in anticipatory saccades (time 2 minus time 1) on ODR generated towards cue location during delay period for SZ (red) and NP (blue) antisaccade (crossed columns) and prosaccade (solid columns) practice groups. Negative values indicate fewer anticipatory saccades at time 2.

WCST Results

The normal antisaccade practice group was the only group to complete more categories from time one to time two (Figure 9). Neither schizophrenia practice group showed a change in perseverative errors, but the normal antisaccade practice group showed a decrease in these errors (Figure 10).

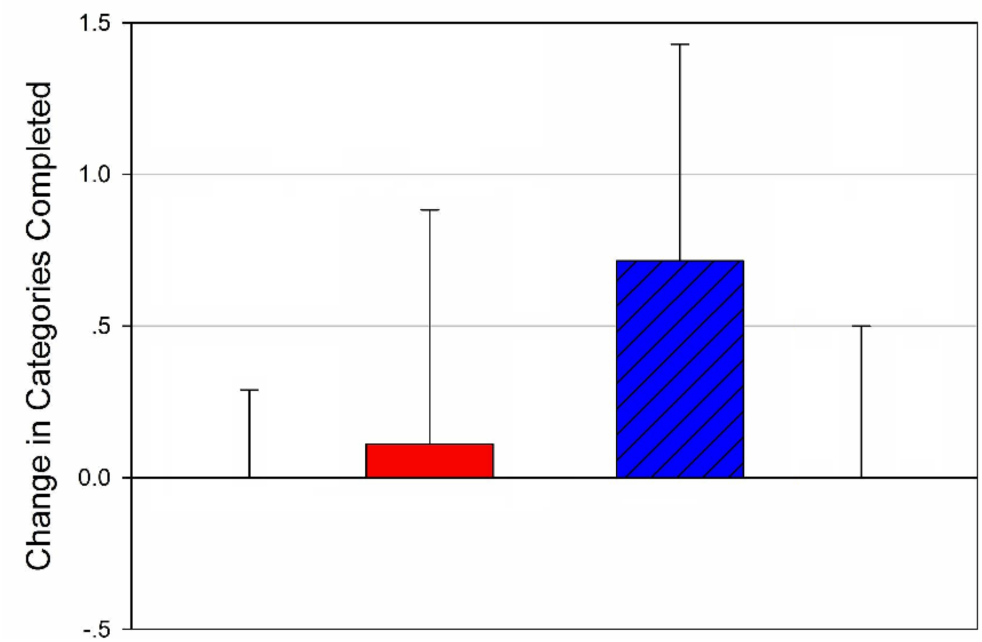

Figure 9. Change in categories completed (time 2 minus time 1) on WCST for SZ (red) and NP (blue) antisaccade (crossed columns) and prosaccade (solid columns) practice groups. Positive values indicate more correct categories at time 2.

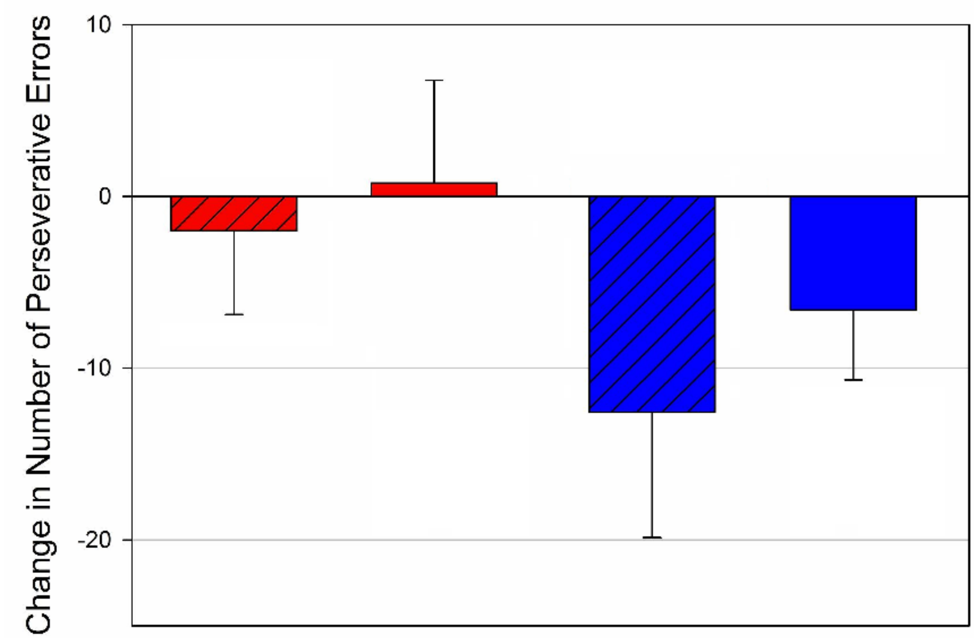

Figure 10. Change in perseverative errors (time 2 minus time 1) on WCST for SZ (red) and NP (blue) antisaccade (crossed columns) and prosaccade (solid columns) practice groups. Negative values indicate fewer perseverative errors at time 2.

CHAPTER 4
DISCUSSION

The prefrontal cortex (PFC) is the part of the brain that mediates executive functions, such as abstract thinking, cognitive flexibility, and inhibition. These functions are vital for the successful performance of tasks as simple as planning the day ahead or inhibiting an inappropriate action. For patients with schizophrenia, however, these tasks are not so simple. Hypofrontality, or a decrease in functioning of the PFC, is thought to be one of the characteristic cognitive deficits in schizophrenia that has strong implications for daily life. Even with the more obvious symptoms (such as auditory hallucinations) under control through medication, people with schizophrenia still feel the effects of their disease. With their executive functioning impaired, schizophrenia patients have difficulty successfully navigating through their daily lives.

Hypofrontality has been well documented in schizophrenia patients (Camchong et al., 2008) and one way in which this deficit has been revealed is through studies of saccadic circuitry. For example, it has been illustrated that schizophrenia participants perform at the same proficiency as normal participants on the prosaccade task (McDowell et al., 1999), but make more errors on the antisaccade task (Curtis et al., 2001; McDowell et al., 1999; Radant et al., 2006). This pattern is consistent with the evidence of PFC circuitry being dysfunctional in schizophrenia. Prior to the current study, however, there has been little work done to determine the malleability of antisaccade performance among schizophrenia participants or the potential for improvement on other tasks of executive function after practice of antisaccades. The current study was designed to provide schizophrenia participants with the necessary practice to allow for an evaluation of the malleability of antisaccade performance, as well as to explore the effects of this practice on other tasks of executive function.

Two tasks were selected to evaluate executive functioning. One, the ocular motor delayed response task (ODR), was selected because it is a saccade-specific executive function task and the other, the Wisconsin Card Sorting Test (WCST), was selected because it requires more generalized executive functioning. Because of the nature of these two tests, it is possible to examine the results and make conjectures as to the extent that improvement on the antisaccade task could generalize to other tasks of executive functioning. By looking at the results from the ODR, it is possible to evaluate generalization to a similar task. By looking at the results of the WCST, it is possible to evaluate the generalization to tasks that are more dissimilar to the practice task while still requiring the same neural underpinnings.

As a general pattern, the healthy participants who practiced antisaccades in this study appear to show consistent improvement across both the saccade specific (ODR) and non-saccade specific (WCST) executive function tasks. The schizophrenia practice groups show little evidence of change across time, with the exception of the schizophrenia antisaccade practice group showing slightly better ODR performance and the schizophrenia prosaccade practice group perhaps showing a slight decrease in performance on ODR. These initial results suggest that saccadic performance may be malleable within certain parameters. Specifically, it appears that behavior (and potentially its neural underpinnings) may be more malleable in healthy people than in people with schizophrenia. Although the gains are modest at this point, it is interesting to observe that practice on one executive function task could potentially be associated with gains on related tasks.

This result has implications for aiding or improving behavior and brain function using behavioral training techniques, especially in healthy individuals. In combination with the small changes seen for the schizophrenia antisaccade practice group, the small sample size to date and the relatively short practice regimen leaves the matter open as to whether similar improvements could be seen in schizophrenia patients, especially if a longer practice regimen were undertaken. In light of the hypofrontality that characterizes schizophrenia, it is likely that changes in performance on tasks mediated by the PFC may take longer to manifest than for normal participants. With an experimental design that incorporates more practice days over a longer period of time, it may be discovered that behavioral performance in schizophrenia patients is malleable to the same or greater degree than that in normal participants.

To date, approximately half of the desired sample size for this study has been collected and analyzed. With completion of the study and increase in the group sizes, it will be interesting to see what if any changes in these trends are seen. Of particular interest will be the schizophrenia antisaccade practice group. If continued or increased improvement on other tasks of executive control is seen in this group, it will raise the question of whether this improvement could represent a reversal of the hypofrontality in these participants. If this is the case, it would suggest that behavioral techniques that involve purposefully practicing executive control might be explored as a non-pharmacological means of improving activities of daily living for schizophrenia patients.

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