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Validation of a new method for neurobehavioral testing of oculomotor function

Author
Turner, Travis Henry

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Validation of a New Method for Neurobehavioral Testing of Oculomotor Function.

A dissertation submitted in partial satisfaction of the requirements for the

Degree of Doctor of Philosophy

in

Clinical Psychology

by

Travis Henry Turner

Committee in charge:

University of California, San Diego

Professor Gregory G. Brown, Chair
Professor Jody Corey-Bloom
Professor Eric Granholm

San Diego State University

Professor Sandra Marshall, Co-Chair
Professor Jörg E. Matt

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The Dissertation of Travis Henry Turner is approved, and it is acceptable in quality and form for publication on microfilm.

Co-Chair

Chair

University of California, San Diego

San Diego State University

2007

DEDICATION

This dissertation, and the research that lies both behind and ahead of it, I dedicate to the patients with Huntington's disease and their family members who gave so generously of their time to participate in my studies. May this work contribute towards developing better treatments and finding a cure.

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VITA

1998	Bachelor of Science, University of Pittsburgh
1999-2001	Psychology Technician, University of Pennsylvania
2001-2006	Graduate Research Assistant, University of California, San Diego
2003-2004	Graduate Teaching Assistant, Psychology Department, San Diego State University
2004-2005	Course Instructor, Psychology Department, San Diego State University
2002-2003	Student Therapist, San Diego State University Psychology Clinic
2003-2004	Student Therapist, Substance Abuse and Mental Illness Clinic, San Diego VAMC
2004-2005	Student Therapist, Neuropsychology Clinic, San Diego VAMC
2005-2006	Student Therapist, Neuropsychology Laboratory, University of California, San Diego
2006-2007	Psychology Intern, Charleston Consortium Psychology Internship Training Program (Medical University of South Carolina and the Ralph H. Johnson VAMC)
2007	Doctor of Philosophy in Clinical Psychology, San Diego State University and the University of California, San Diego

PUBLICATIONS

Turner, T.H., Yanagi, M.A., Brown, G.G., & Drummond, S.P.A. Total Sleep Deprivation's Effects on Component Processes of Verbal Working Memory. (Neuropsychology, in press)

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FIELDS OF STUDY

Major Field: Clinical Psychology

Studies in Clinical Neuropsychology
Professors Gregory G. Brown, Mark Bondi, Vincent Filoteo, Michael Caliguiri, Dean Delis, Robert K. Heaton

Studies in Research Design and Statistical Analysis
Professors Georg E. Matt and Scott C. Roesch

ABSTRACT OF THE DISSERTATION

Validation of a New Method
for Neurobehavioral Testing of Oculomotor Function.

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Travis Henry Turner

Doctor of Philosophy in Clinical Psychology

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Abnormal saccadic and smooth pursuit eye movements have been identified in a number of neuropsychiatric, neurodegenerative, and brain injured patient groups. Characteristics of these eye movements have shown value for differential diagnosis, tracking change with treatment, understanding brain-behavior relationships, and developing endophenotype models of diseases with genetic components. However, complications involved with traditional eye-tracking equipment preclude oculomotor assessment in many clinical and research applications. To facilitate evaluation of saccadic and smooth pursuit eye movements, a computerized battery of behavioral tests was developed and standardized. The tests provide quantitative measurements and can be administered independently of eye-tracking equipment. Smooth pursuit eye movements are assessed by a test of visual velocity discrimination. Saccadic eye movements are assessed by a series of tests that measure visuoperceptual ability without eye movement, latency of eye movements to visual targets, latency to disengage visual attention, and ability to inhibit saccades.

Test validity was examined via the multi-trait, multi-method correlation matrix in a sample of 60 healthy persons. Participants completed the tests while eye movements were tracked at 250Hz using digital video eye-tracking equipment. The tests were found to elicit the intended eye movements. Split-half reliability ranged from 0.65 to 0.97. Construct validity of the saccade tests was supported by hypothesized differences in performances across tests. Convergent validity was evidenced by statistically significant correlations within-traits between behavioral and related eye-tracking measures. Although within-trait correlations were stronger than between-trait correlations, discriminant validity was not supported by formal statistical testing. A second study explored clinical utility of the tests. A sample of 11 patients with Huntington's disease (HD) was compared to an age-matched sample of 12 healthy persons. As expected, the HD group performed worse on all saccade tests. Results suggested that saccade disinhibition in HD is independent of reduced oculomotor efficiency. Furthermore, saccade slowing and disinhibition may follow different courses with respect to age of onset and disease progression.

Findings from these studies support the validity of the tests in assessment of smooth pursuit and saccades. Future studies examining validity and diagnostic utility in other patient groups, age-based norm development, and potential improvements to test design are discussed.

INTRODUCTION

Background

Investigation of oculomotor functioning (i.e., tracking of eye movements) has become an important component in clinical neuropsychological examinations and many research programs. The majority of investigations (including all those cited in this dissertation) have focused on two types of eye movements: smooth pursuit and saccadic eye movements. Smooth pursuit eye movements involve slow and fluid adjustments of the eye to keep the fovea (center of eye with optimal acuity) focused on a particular target. Saccadic movements involve quick, drastic adjustments to match fovea position with a target.

Clinical findings: Abnormal eye movements in a clinical population were first reported in schizophrenia patients in 1908 by Difendorf and Dodge (as cited in Sweeney, Levy, & Harris, 2002). For over 60 years, these findings were largely ignored in the literature until the mid-1970's when Holzman et al (1973; 1974) "rediscovered" the phenomenon. Since then, a large corpus of literature has supported and further explicated the nature of oculomotor abnormalities in schizophrenia with a remarkable degree of consistency. As noted in a review by Sweeney and colleagues (Sweeney et al., 2002), oculomotor deficits, particularly for saccadic movements, have been consistently reported across experimental procedures (e.g., types of stimuli, number of trials, timing, etc.), clinical differences in patient samples (e.g., acutely psychotic, first episode, chronically ill, etc.), and degree of treatment naiveté (i.e., degree of exposure to typical and atypical antipsychotics and other psychotropic medications). Interestingly, oculomotor abnormalities in unaffected first degree relatives of schizophrenia patients have also been widely reported (Clementz & Sweeney, 1990).

Since the schizophrenia studies, eye movements have been examined in a host of other neuropsychiatric populations, with various abnormalities reported in Huntington's Disease (for review see Lasker & Zee, 1997), HIV infection (Currie et al., 1988; Sweeney et al., 1991), autism (Minshew, Luna, & Sweeney, 1999), Tourette's syndrome (Narita et al., 1997; Segawa, 2003), bipolar depression (for review see Sweeney et al., 2002), Alzheimer's Dementia (e.g., Flechtner & Sharpe, 1986; Shafiq-Antonacci, Maruff, Masters, & Currie, 2003), Parkinson's Disease (e.g., Vidailhet et al., 1994; Crawford et al., 2002), and obsessive-compulsive disorder (e.g., Clementz, Farber, Lam & Swerdlow, 1996; Rosenberg, et al., 1997). Eye-tracking impairments have been demonstrated subsequent to traumatic brain and spino-cerebellar injury (for review see Heitger, Anderson & Jones, 2002), related to reading impairments (for review see Kulp & Schmidt,1996), and characterized as a consequence of normal aging (e.g., Spooner, Sakala & Baloh, 1980; Nieuwenhuis et al., 2000). Eye movements are also examined as indicators of intoxication (e.g., Wegner & Fahle, 1999) and for management of medication side effects (e.g., Broerse, Crawford, & den Boer, 2002).

Neurological systems: Given the variety of disease states wherein oculomotor disturbances are observed, it is not surprising that a convergence of findings implicates a widely distributed neurological system that includes cortical, diencephalic, mesencephalic, and cerebellar structures. In the cortex, the frontal eye fields (ca. precentral gyrus and sulcus), supplementary eye fields (anterior to sensorimotor area), the parietal eye field (ca. intraparietal sulcus), and the dorsolateral prefrontal cortex have been implicated (for review see Pierrot-Deseilligny et al., 2002). The basal ganglia are thought to play crucial roles in the initiation and inhibition of eye movements in response to stimuli (Isa & Kobayashi, 2004). Subcortical structures include the mediodorsal thalamus and its connections with the superior colliculus (Sommer & Wirtz, 2004).

It is generally well accepted that there is significant overlap in neuroanatomical structures involved with smooth pursuit and saccades; however, there are certain brain regions that may be unique to each. Perhaps because more paradigms have been developed to study saccadic movements, there is a more comprehensive understanding of the neurological systems linked to their execution. Specific linkages include the dorsolateral prefrontal cortex and basal ganglia with inhibition of saccades, the parietal eye fields for reflexive, visually-guided saccades, the supplementary eye fields for sequencing movements, and regions of the frontal eye fields for memory-guided saccades (for review see Pierrot-Deseilligny et al., 2002). For smooth pursuit eye movements, the dorsal visual pathway, including the medial and medial superior temporal lobe seem to be uniquely involved, as does a separate sub-region of the frontal eye field (Klauzlis, 2004; Rosano et al., 2002). Studies of primates suggest that regions of the cerebellum and pons may be specific to smooth pursuit (Straumann & Haslwanter, 2001). Taken together, current findings from the literature suggest that smooth pursuit and saccadic eye movements recruit some unique cortical structures for their execution, but tend to share most diencephalic, mesencephalic, and cerebellar subcortical systems. However, given the tremendous complexity of the visual system, it is likely that more sophisticated oculomotor studies of patient groups (e.g., spino-cerebellar ataxia, corticobasal degeneration, etc.) and further advancements in functional brain imaging will identify unique non-cortical structures in the near future.

Oculomotor assessment: In clinical settings, assessment of eye movements is often performed by a neurologist or neuropsychologist using bedside techniques and qualitative ratings. While this approach can be useful in performing general surveys and detecting gross abnormalities, it has been shown to lack the sensitivity necessary to detect more subtle disturbances (Heitger, Anderson, & Jones, 2002). There are several psychophysical methodologies that have been developed to provide quantitative measures of eye movements for use in research. The most commonly used techniques are infrared limbus detection, scleral search coils, and digital video eye-tracking. All of these methods are capable of capturing eye position data with excellent spatial resolution at frequencies of 500Hz or greater (Imai et al, 2005; Traisk F, Bolzani R, Ygge, 2006). However, with scleral search coils, subject discomfort associated with placement of the coil on the eye is frequently reported, and infrared limbus detection requires subjects to remain near motionless while the experiment takes place.

Regardless of the method employed, maintenance of eye-tracking equipment and the technical support to administer protocols and analyze data can be prohibitively expensive for clinicians and researchers whose primary area of investigation is not the visual system. Furthermore, there is considerable controversy surrounding data analytic procedures, especially for evaluation of smooth pursuit, with some researchers employing a qualitative approach (e.g., Keefe et al., 1997) and others insisting on quantitative measures (e.g., Ross et al., 1998; Avila, McMahon, Elliott, & Thaker, 2002). As noted by Braff (1998), there are also questions regarding which quantitative measures are most appropriate for identifying oculomotor abnormalities that are reflective of neurological abnormalities.

A convenient, affordable, and reliable means of assessing oculomotor function would be a valuable tool to neuropsychology clinicians and researchers. The ideal tool would provide functional measures of both smooth pursuit and saccadic eye movements. To enable dissociation between various psychiatric and neurological conditions affecting specific types of saccadic eye movements, the battery would provide multiple measures of saccadic behavior including:

1) Latency of saccade to novel stimuli (i.e., express saccades), shown to be impaired in patients with a lesion to the superior colliculus or parietal eye field (Leigh & Kennard, 2004).
2) Ability to disengage from visual fixation (i.e., reflexive saccade), shown to be impaired in patients with Tourette's (LeVasseur, Flanagan, Riopelle, and Munoz, 2001) and with ethanol intoxication (Vassallo & Abel, 2002).
3) Ability to inhibit eye movements (i.e., anti-saccade), shown to be impaired in schizophrenia (Sweeney et al., 2002), Huntington's disease (e.g., Blekher et al., 2004) and Tourette's syndrome (Farber, Swerdlow, & Clementz, 1999).

The entire procedure should be brief (e.g., less than 30 minutes) to avoid examinee fatigue. It would also be well-integrated with other cognitive tests and independent of specialized testing equipment and data analysis software packages. Furthermore, the tests would provide outcome data in meaningful quantitative psychometric units. While several experimental tasks assessing eye movements have been designed to address specific questions in eye-tracking studies (described in detail below), at the present time, there are no published behavioral tests for the purpose of oculomotor assessment.

To this end, a new battery of behavioral tests has been developed. Smooth pursuit eye movements are assessed by a test of visual velocity discrimination. Saccadic eye movements are assessed by a series of tests that measure visuoperceptual ability without eye movement, latency of eye movements to visual targets, latency to disengage visual attention, and ability to inhibit saccades. In their current state, the tests employ a simple stepped-ramp design to measure a discrimination threshold. They are administered via PC computer on standard CRT monitors at a standardized viewing distance of 57cm using PowerPoint® software for the smooth pursuit test, and E-Prime© software for the saccade tests. Performance on the smooth pursuit test is hand-scored, while the saccade tests are scored through an automated program. Depending upon ability level, the entire protocol lasts between 20 and 30 minutes.

Study Overview

The purpose of the present research is to assess concurrent validity of the new oculomotor test battery. In Study 1, the validity of the tests will be examined in a sample of healthy persons. To accomplish this aim, subjects will take the battery while having their eye movements recorded using the EyeLink© video-based eye-tracking system at Eye-Tracking, Inc. Eye-tracking data will be analyzed to determine whether the tests elicit the intended types of eye movement. The multi-trait, multi-method approach will be used to compare test performances and standard measures of oculomotor functioning obtained using eye-tracking equipment. An additional test of construct validity for the saccade tests will involve comparisons between performances based on the theoretical bases of the tests. In Study 2, validity of the tests will be established by their ability to distinguish a sample of Huntington's patients, a group with well-documented oculomotor abnormalities, from age-matched healthy controls. Here, impaired performance on the saccade tests, but not the smooth pursuit test, is expected. Specific hypotheses and planned statistical analyses for Study 1 and Study 2 are detailed in the Methods section below.

Development of Smooth Pursuit Test

Velocity discrimination: Tasks requiring visual velocity discrimination have been used to measure smooth pursuit. Previous velocity discrimination tasks have used moving sine-wave gratings to measure thresholds. The targets to measure smooth pursuit eye movements used moving sine-wave gratings to obtain a velocity discrimination threshold hypothesized to reflect functioning of the smooth pursuit system. Typically, subjects are first shown a "baseline" grating that moves at a certain speed, and instructed to compare the baseline to a series of items that move either faster or slower. While such designs have been useful for discriminating some patient groups (e.g., Chen et al., 1999a) and demonstrating a correlation between task performance and smooth pursuit eye-tracking data (Chen et al., 1999b), they rely heavily on spatial working memory. The use of smooth pursuit eye movements while viewing the gratings has not been established, and it is reasonable to suggest that the task evokes the optokinetic response or can be performed passively by keeping the fovea fixed and allowing the gratings to simply pass by. Thus, this paradigm is not appropriate for the current application.

Acuity: Another task for smooth pursuit has been developing by Haarmeier and Thier (1999) using Landolt C optotype stimuli. These stimuli are small circular targets with a “c” inscribed in the center. In their study using these stimuli, a blank circular target moved across the visual field at a fixed rate and a small "c" was briefly displayed in the center of the target at a random position. Subjects were then asked which direction the "c" was facing (forward or backward). Because high acuity is required to make the determination, it was found that subjects must use smooth pursuit eye movements to keep their fovea on the target (Haarmeier & Their, 1999). To establish a functional threshold for smooth pursuit, it is conceivable that target speed might be increased until performance reaches chances levels. Unfortunately, because the rate and vector of target is held constant across a trial, target position is predictable and saccadic movements would be elicited with increased target rates. Thus, the design is not well suited for establishing a functional threshold or other quantitative measurement of smooth pursuit.

Acceleration / deceleration: Recently, a test designed to provide a psychophysical performance measure of smooth pursuit suitable for CRT presentation was developed by Gegenfurtner and colleagues (Gegenfurtner, Xing, Scott, & Hawken, 2004). In this task, an achromatic Gaussian vignetted patch of sinusoidal grating moved across a neutral background from either the left or right side towards the center. At a random point during the movement, the speed of the patch either increased or decreased for 200 or 1000 ms. With a baseline speed of 4 degrees of visual angle per second, the researchers found an average speed discrimination threshold of 0.28 degrees per second in a sample of four participants. Through simultaneous recording of oculomotor movements, the researchers demonstrated that smooth pursuit eye movements were elicited by the stimuli and that overall oculometric and psychometric performances were correlated. Additionally, perceptual errors (in stimulus assessment) were not correlated with oculomotor deviance (i.e., mismatch between ocular and target speed) for individual trials. From this finding, the authors concluded that the motor and perceptual system share similar constraints, but act independently and are subject to unique sources of error. It should be noted that the conclusion that oculomotor and visual perceptual systems act independently stands in contrast to a large body of literature (e.g., Watamaniuk & Heinen, 2003; Watamaniuk & Heinen, 1999; Beutter & Stone, 2000; Krauzlis & Stone, 1999) that has consistently shown perception of speed, direction, and acceleration to guide both smooth pursuit and saccadic eye movements for tracking stimuli.

Regardless of the accuracy of their conclusions, the task developed by Gegenfurtner and colleagues makes a substantial contribution towards developing a behavioral measure of oculomotor function. However, the feature of predictable stimulus movement associated with the task makes it sub-optimal as a stand-alone tool for the assessment of smooth pursuit. The authors reported in detail their effort to remove saccade activity from the data for their analysis of eye movements. This suggests that saccades commonly occurred (although a proportion of observations reflecting saccadic movements was not provided), despite instructing participants to "follow the target as closely as possible with eye movements." Given that the targets always moved in a predictable vector, it seems reasonable that participants may have employed predictive saccadic eye movements during speed changes to make discriminations. Because an analysis comparing eye movements made during target speed perturbation with eye movements made during constant speed was not performed, this concern cannot be dismissed. It is therefore possible that the lack of reported correlation between oculometric measurement and psychophysical perceptual performance in this study may be due to the elicitation of saccade activity by the task.

Smooth Pursuit Test

The smooth pursuit test used in this study was designed to provide a psychophysical measurement of smooth pursuit eye movements without the confounds of the task designs described above. It involves minimal spatial working memory demands, allows for the estimation of a functional threshold, and contains features (described below) that limit the use of saccadic eye movements for performance.

The smooth pursuit test shows two moving circular targets, one light and one dark, moving in a random-walk pattern across a mid-gray background. Both targets move at a constant rate, but one target always moves faster than the other. The average velocity of the two discs is 4 degrees of visual angle per second. This speed is with the range commonly used in smooth pursuit task designs (as in the Gegenfurtner design) and is well below the limit of accurate smooth pursuit in humans, ca. 30 degrees per second (Lisberger, Morris, & Tychsen, 1987). Vector changes are random from a flat distribution, but constrained to +/- 23 degrees from the previous vector with a mean change of 0. Additionally, a virtual "corral" was programmed to contain the stimuli on the screen by increasing the probability of vector changes returning towards the center of the visual field when the target reaches a position 25% of the field away from the center. The contrast between the targets and background is well above sensitivity threshold (+/- 25% in Michelson units) to avoid confounds with basic visual-perceptual abilities. Each trial consists of a six second mpeg movie wherein one of the discs moves faster than the other. After the movie is finished, the subject is asked to report which disc has moved faster. The Octave ® script for creating the velocity discrimination stimuli is attached as Appendix A.

For optimal efficiency, subjects first complete a Branching test. This test begins with a block of eight items comparing disks that move at velocities differing by approximately 4 degrees/second. The ratio of light to dark correct responses (i.e., faster moving disk) is split evenly within each block. The difference between the velocity of the disks decreases in steps of 0.25 degrees/second (split evenly between the faster and slower disc) until the subject is unable to accurately detect the faster disc (6/8 correct or more within a block). Based on the failure point of this test, the subject is then branched to a follow-up test wherein greater fidelity of performance ability can be measured.

In the follow-up test, stimuli are presented in blocks of 8 items with a difference in rate of .025 degrees/second less than last successfully achieved step from the Branching test. The test proceeds over steps of .025 degrees/second until the subject is unable to identify at least 6/8 of targets within a block ($p = 0.144$), or identifies 6/8 targets in two consecutive blocks. The last level successfully performed is considered the subject's achievement level. In the event that two consecutive blocks of 6/8 accuracy occurs, achievement level is estimated between the two blocks (e.g., failure between levels 7.7 and 7.8 would be scored as 7.75). Test achievement level can be converted to a psychophysical velocity discrimination threshold for minimum difference in target speed by the following equation:

Velocity discrimination threshold (deg. visual angle / sec) = 2.27 – 0.25 x Level

It is hypothesized that in order for the subject to discriminate the faster moving disc, he/she must:

1. Follow each target using smooth pursuit because the directions of the targets are unpredictable.
2. Mentally compute and compare a velocity for each disc based on the amount of eye movements required to track the targets.
3. Employ saccadic movements to "jump" between targets. These saccadic movements are not likely to be directly related to test performance, as saccade distance between targets moving in a random-walk pattern cannot be used to estimate differential velocity.

Subjects must also be able to sustain attention for the duration of the test, switch attention between discs, and avoid perseverative errors. Importantly, because both targets are displayed simultaneously, spatial working memory demands are reduced.

Standard Smooth Pursuit Task

Although not intended to be a part of the battery, a task displaying stimuli for assessing smooth pursuit eye movement in the traditional manner has also been developed for validation of the velocity discrimination threshold as a measure of smooth pursuit. Subjects view mpeg stimuli that move at a sinusoidally varying rate in horizontal and vertical paths, and at a constant rate in an orbital path. For each type of movement, five 20-second mpeg stimuli are shown. Angular target rate ranges from 1 to 5 degrees of visual angle per second in 1 degree / second intervals; this covers the range of target speeds used in velocity discrimination and extends through the range typically examined in studies of smooth pursuit.

At speeds greater than 1.5 degrees visual angle per second, target movement begins to appear “jumpy” when the mpeg file is played using standard software. This effect is due to increased distance between target locations from frame to frame. To avoid this confound, two motion sub-samples of the target are drawn on each frame. The centers of the sub-samples are 90% and 80% of the position change from the previous location. The contrast between the trailing comets and background are 75 and 50 percent respectively of the target contrast. This effect is shown in Figure 1. The Octave® scripts used to create the different baseline stimuli are all generally similar; the script used to create the Orbital stimuli is attached as Appendix B.

The standard smooth pursuit tasks are administered while eye movements are tracked using digital video eye-tracking equipment. Gain, perhaps the commonly used quantitative measure of smooth pursuit accuracy (computed as the average foveal rate divided by target rate), will be the primary outcome measure. Additionally, the number of anticipatory saccades and the number and amplitude of “catch-up” saccades (made when fovea position becomes mismatched with target position) are also be analyzed.

Development of Saccade Tests

Reading: Several tests have been developed to assess saccadic eye movements in relationship to reading skills. The Developmental Eye Movement test (Garzia, Richman, Nicholson, & Gaines, 1990), is perhaps the most widely used

(Rouse, Nestor, Parot, & DeLand, 2004), is the only that does not confound performance with memory demands, and allows a clinician to account for rapid-naming ability when performing an assessment. An additional benefit of this test is that performance measures for horizontal and vertical saccadic movements can be derived. Unfortunately, there are also major confounds including verbal naming ability and motor speed, that limit the interpretation of results in many clinical populations. Furthermore, a recent study of the Developmental Eye Movement test in the original target population (elementary school aged children) indicated that test-retest reliability is too low to offer diagnostic utility. Thus, this test and its general design seem inappropriate for study of oculomotor impairment in neuropsychiatric populations.

Guided Visual Exploration: The Guided Visual Exploration test (Reischies, Gaebel, Mielewczyk, & Frick, 1988) measures visuospatial, visual scanning, and visuomotor abilities. During administration, subjects are shown a piece of paper with arrows connected to circles, and are instructed to follow the arrows from circle to circle until the arrow points to a number. When the subject reaches the number, he or she states it aloud and the response time (from beginning of display) and accuracy are recorded. Impaired performance on the guided visual exploration test with respect to time and errors have been observed in patient groups with known visual scanning, visuoperceptual, and oculomotor deficits. (Reischies, et al, 1988; Lang, Reischies, Majer, & Daum, 1999).

In a study examining psychometric properties of the guided visual exploration test in healthy persons (Reischies & Berghofer, 1995), males showed better performance than females in terms of time and / or error rate across all age groups ranging from 16-24 to 55-91 years. This gender difference highlights the significant visuospatial component embedded in test performance, as such gender differences have not been found in healthy persons for any oculomotor measure from eye-tracking research (e.g., Fujiwara, Kunita, Toyama, 2000; Nyberg, Wahlstrom, Backstrom, & Poromaa, 2004; Ettinger, Hejda, Flak, Corr, 2005) except in older adults (Hutton, Nagel, & Loewenson, 1983). Because performance on the guided visual exploration test reflects a composition of cognitive, visual, and perceptual components, it does not provide a suitable substitution for traditional eye-tracking measures of saccadic eye movements.

Saccade tests.

The tests for assessment of saccades described in this dissertation are designed to minimize visuospatial demands and control for basic visuoperceptual processing. There are 4 subtests: a baseline test for Fixation, a latency test for express saccades (Express), a latency test for reflexive saccades that requires disengaging visual attention (Reflexive), and a test for ability to inhibit reflexive saccades to a distracting stimulus and make volitional anti-saccades to a target (AntiSaccade). The primary visual stimulus used in the saccade tests is the previously described Landolt C optotype. As demonstrated by Haarmeier and Their (1999), foveal acuity is required to identify orientation of a visually presented “c”. In all of the tests, the subjects is asked to focus for 1500ms on a central fixation point, a black circle subtending 1’ of visual angle with the letter “c” inscribed in the center. After a delay of 1500ms, a target stimulus with either a forward or backward facing “c” appears for a brief period of time. After the presentation, the subject indicates whether the “c” remained facing forward (i.e., gap facing right) or flipped to face backwards (gap facing left) by pressing a button on the computer keyboard. Due to the small size of the gap in the “c” (approximately 0.25 degrees of visual angle), foveal vision is required for discrimination of direction. It should be noted that a masking stimuli is displayed for 25ms immediately following target presentation so as to prevent subjects from responding based on retinal afterimages.

Fixation test: In the baseline Fixation test, the target stimulus appears in the same position as the fixation point; thus, no oculomotor movement is required (see Figure 2a). The amount of time that the target is presented decreases in a stepwise fashion in increments of 50ms from 400ms to 50ms, with four stimuli presented per step (ergo, odds of perfect performance of a step by chance 1/16, $p = 0.0625$). Orientation of the “c” is evenly split within blocks. In a pilot study with a sample of five participants (ages 25 to 53 years), all subjects demonstrated perfect performance on even the most difficult level of the Fixation test. The purpose of the Fixation test is to rule out potential confounds of bradycognition, attention deficit, perseverative responding, and general visual dysfunction (e.g., acuity, contrast sensitivity) in clinical populations to ensure that test results are specific to the assessment of saccadic eye movements.

Express and Reflexive tests: The Express and Reflexive saccade tests follow the same general design as the Fixation test, with the addition of 10 degrees of visual angle difference between target location (i.e., where the forward or backward-facing “c” is presented) and central fixation point, thereby necessitating oculomotor movement (see Figure 2b). For each trial, target location is randomly assigned to one of eight cardinal positions. The first three blocks consist of 6 items with presentation times of 500, 450, and 400 ms respectively. These blocks are primarily intended to serve as practice. The remaining 11 blocks contain 8 stimuli with a stimulus presentation time decreasing in 25ms increments from 325ms to 75ms. Within each block, targets are presented randomly without replacement in one of eight cardinal positions from the central fixation point. Criteria for determining thresholds are identical to the smooth pursuit test. In the Express test, the fixation point disappears 200ms before the target is presented, allowing for assessment of express saccades. During the Reflexive test, the fixation point remains, requiring the subject to disengage visual attention before a saccade to the target can be made. For both tests, the minimum stimulus presentation time wherein the subject is able to perform beyond chance level should coincide with latency of the eyes to reach the target.

AntiSaccade test: The AntiSaccade test is similar to the Express test in that the central fixation point disappears, and the target appears in one of eight cardinal positions 10º visual angle away from the center. However, prior to presentation of the target, a black circle appears in the cardinal position opposite to the location where the target will be presented (see Figure 2c). As with typical anti-saccade task designs, presentation time for the distractor and target are equivalent, and the distractor disappears when the target is presented. Upon presentation of the distractor in the periphery, the subject is instructed to move his or her eyes to the opposite area of the screen. For the AntiSaccade test, threshold measurement begins at presentation time of the distractor, rather than target. Failure to inhibit movement to the distractor necessitates a change in eye position twice as far in distance (as from the central fixation point) to match foveal position with location of the target for accurate responding, and is therefore expected to impair performance.

Discrimination threshold on the AntiSaccade test should thus coincide with latency of eyes to reach the target and reflect ability to inhibit saccades towards the distractor.

Summary of Tests and Measures

Smooth pursuit eye movements are assessed with a test for visual velocity discrimination. This test returns a threshold for the minimum difference in velocity (degrees of visual angle per second) between two moving discs that can accurately be detected. Saccadic eye movements are assessed using a series of tests that require foveal vision to make accurate perceptual judgments about targets. Over the course of the saccade tests, presentation time of the target decreases until a threshold for minimum presentation time with accurate perceptual judgment is established. This threshold (ms) reflects latency of the eyes to reach the target position. The Fixation test presents targets in the center of the screen, and therefore involves no eye movement. This test is designed to detect possible problems involving visuoperceptual abilities that would confound tests of saccades. The Express test presents targets in the periphery of the screen, requiring saccadic eye movements. The Reflexive test is similar to the Express test, except that a fixation point remains, requiring the subject to disengage visual fixation before looking at the target. The AntiSaccade test requires subjects to inhibit saccadic eye movement towards a visual distractor and make a volitional saccade to the target.

STUDY 1: TEST PERFORMANCES & EYE-TRACKING MEAURES

Methods

Aim

The general aim of this study is to establish validity of the tests in healthy persons. To accomplish this, a sample of healthy persons will complete the battery of tests and the standard smooth pursuit task while eye movements are recorded using digital video eye-tracking. Test performances will be compared to eye-tracking measures. Traditional eye-tracking criterion measures from the standard smooth pursuit task include gain, saccade frequency (saccades per second), and amplitude of catch-up saccades. From the saccade tests, eye movements will be analyzed to determine latency for the eye to reach the target (ms). Additionally, the percent of trials in which an individual makes a saccade to the distractor during the AntiSaccade test will be examined.

Hypotheses

Smooth pursuit during velocity discrimination: It is hypothesized that velocity discrimination between the two targets in the smooth pursuit test requires smooth pursuit eye movement; therefore, the test is expected to elicit smooth pursuit eye movement. Because it is expected that stimuli will also elicit fixation activity and saccades, a formal hypothesis is not made regarding the percentage of time that participants will use smooth pursuit eye movements while performing the tests.

Saccade test performance differences: Reduced latency for Express saccades relative to Reflexive saccades has been consistently demonstrated in studies of saccadic eye movements (Leigh & Kennard, 2004). Therefore, reduced latency of eye position to target is expected for the Express relative to Reflexive test, as is discrimination threshold measured by the tests. With regards to the AntiSaccade test, previous studies using the anti-saccade design have demonstrated that healthy persons frequently make saccades towards distractors (ca. 30-80% of trials), and inhibiting movement towards a visual distractor increases latency to initiate movement in the opposite direction (Hallett, 1978). Therefore, the presence of the distractor in the AntiSaccade test is expected to result in larger mean target latency and discrimination thresholds than found in the Express or Reflexive tests.

Convergent and discriminant validity: Smooth pursuit test performance is expected to be associated with traditional smooth pursuit eye movement metrics from the standard smooth pursuit task. Saccade test performance is expected to be associated with measures of saccadic movement. For all the tests, lower discrimination threshold values reflect better performance; for all eye-tracking measures except gain, lower values also reflect better performance. Thus, all correlations except velocity discrimination threshold from the smooth pursuit test and gain should be positive. In addition to a relationship between discrimination threshold and target latency, lower discrimination thresholds on the AntiSaccade test are also expected to have a direct correlation with the percent of trials wherein saccades to the distractor are observed. The expected correlations between behavioral and related eye-tracking measures are hypothesized to be stronger than relationships between behavioral and unrelated eye-tracking measures. The multi-trait, multi-method approach will be used to examine convergent and discriminant validity for the oculomotor tests against a minimum correlation of +/- 0.33 ($\alpha<0.01$). The matrix corresponding to the hypothesized relationships is illustrated in Table 1.

Composition of AntiSaccade test performance: For the AntiSaccade test, the mechanism by which saccades to the distractor are expected to impair discrimination of target orientation is through increasing latency of the fovea to reach the target. To examine this hypothesis, 95% confidence intervals will be constructed around mean target latency and probability of a correct response for trials with and without a saccade to the distractor. Because accuracy is expected to decline with decreasing stimulus presentation time over the course of the AntiSaccade test, separate comparisons will be made at each level.

Target latency composition: The latency for eye position to reach the target in the Express and Reflexive tests can be thought of as a combination of latency for initial movement and speed of saccade:

Target Latency = latency for initial movement + (saccade velocity / distance to target). Discrimination threshold, as measured by performance, should also reflect this combination. An exploratory analysis will be conducted to determine the extent to which discrimination threshold and latency for eye position to reach the target in the Express and Reflexive tests are based on initial latency and saccade velocity. Note that the presence of saccades to the distractor, which occur intermittently and are variable with respect to distance, confounds this relationship in the AntiSaccade test.

Sample

A sample of 60 participants, comprised of 48 undergraduate psychology students from San Diego State University and 12 volunteers over 30 years of age from the community were included in the analysis. Undergraduates were recruited via the university's on-line Experimetrix website and earned experimental credit hours to be applied towards their psychology classes. Community volunteers were recruited through flyers posted on Craig's List website, http://sandiego.craigslist.org/vol/, and in public areas surrounding the university area. Community participants were compensated $20 to cover time and travel costs. All subjects provided written informed consent to prior to participating in the study protocol.

Complete data sets were obtained from all 12 community participants (100%) and 48 out of 64 undergraduates participants (75%). Six data sets were unusable due to technical difficulties with eye-tracking equipment, seven data sets were not used in the analysis because the tests were administered out-of-order, and one was not used because data were missing. Data from two subjects were not used because of excessive blinks and body movement throughout administration of the protocol. Of the 16 subjects excluded, only the person with missing data was excluded due to problems acquiring behavioral data (experimenter error).

An anonymous self-report neuropsychological history questionnaire was given to all participants to characterize the sample. Six participants reported current treatment with anti-depressant medications (Celexa, Prozac, Zoloft and Effexor); one of these participants was also taking Lithium, and another was concurrently taking Xanax. Seventeen participants reported past or current treatment for psychological problems. No participants reported having a family member with a diagnosis of schizophrenia. Two subjects reported dyslexia, and one subject reported past treatment for attention deficit disorder. One subject reported problems with pupillary constriction and sensitivity to light, and two subjects reported diagnosis and treatment of migraine headaches. Eleven participants reported past history of head injury that resulted in a concussion. Fourteen participants reported past use of marijuana; of these, two participants reported using within the past 48 hours. One subject reported remote poly-substance use and problems with alcohol use. No subjects reported use of alcohol within the 24 hours preceding the experiment. Twenty participants reported consumption of caffeinated beverages within the past two hours. On a scale ranging from 1 (very tired) to 10 (very awake), the mean rating after completing the entire protocol was 5.9 (*SD* = 2.17).

Protocol

Participants were seated directly in front of the computer monitor at a measured distance of 57cm (surface of eye to midline of screen). The EyeLink II tracking headset was fitted to each participant to minimize discomfort and shifting. All participants were instructed to avoid touching the headset or cameras during the study, and to notify the administrator if the equipment became uncomfortable. Gaze position relative to the computer was calibrated to 9 points (compensating for head position) within standard parameters defined as "good" by the EyeLink© software (i.e., max error < 1 degree visual angle). Data were collected at a rate of 250 measurements per second. The entire setup process typically took between 3 and 6 minutes.

All participants completed the smooth pursuit standard task immediately after equipment calibration, when body position relative to the monitor was closest to 57cm. For all tests, on-screen instructions were first read by the participant, and comprehension was confirmed by the experimenter prior to administration. After the baseline task, the velocity discrimination test for smooth pursuit (branching and follow-up) was given. The administrator operated the keyboard and recorded responses on a score sheet (see Appendix C) throughout both of these tests. Following the smooth pursuit test, all participants completed the Fixation test. For all saccade tests, participants entered their own responses on the keyboard. To control for potential order effects, participants next completed either the Express (n=33) or Reflexive (n=27) test. Assignment to order condition alternated. Following completion of both the Express and Reflexive tests, the AntiSaccade test was administered. This test was always administered last to reduce confusion regarding instructions. Upon completion of all tests, the eye-tracking headset was removed and subjects were allowed privacy to complete the neuropsychological history questionnaire.

Analysis of Eye Tracking Data

The test paradigms developed for this study were intended to be used independently of eye-tracking equipment. Thus, eye movement analysis programs designed for use in other eye-tracking studies were not appropriate for deriving the eye-tracking criterion measures in this study. Therefore, a series of analysis scripts was developed and refined specifically for analyzing the eye-tracking data. Given the variety of paradigms, study aims, and equipment specifications, this is not an uncommon practice in eye-tracking research.

All eye position data were analyzed in their raw state, without the use of smoothing or filtering procedures that are often employed in other eye-tracking research programs. A smoothing procedure that averaged eye positions would reduce the advantages of high frequency sampling for detecting the onset of saccades and artificially create fixation from an indeterminate background. The use of high or low-pass filters would obscure the presence of microsaccades, especially in the velocity discrimination data where their discrimination from smooth pursuit is critical to the hypotheses in question. As detailed in Appendix D, there are, however, portions of various algorithms that examine neighborhood observations to compensate for non-linear saccades and reduce noise to allow for the discrimination of smooth pursuit activity from fixation.

Previous research has shown that many individuals have a dominant eye that can be quickly identified in a bedside examination of relative location accuracy for monocular versus binocular vision. The non-dominant eye has been shown to have longer latency for horizontal saccades, and may be less accurate in tracking targets than the dominant eye (Oishi, Tobimatsu, Arakawa, Taniwaki, & Kira, 2005). Thus, although data was acquired from both eyes, data from the dominant eye was analyzed for test validation purposes.

Only observations acquired during test-related activity were examined. To accomplish this, the EyeLink II system recorded two time-synchronized data files. A schematic for the equipment used in this study is provided in Figure 3. The first file, hereon referred to as the position file, contained x-y coordinates and pupil size for each eye for every 4ms interval for the duration of the entire experiment (including set-up and time between tests). An event file was also recorded that contained a list of keystrokes with event times corresponding to the eye position data. The event file was filtered in Excel® so that it contained only information relevant to the beginning and end of each trial for every test. An unexpected interface problem between the EyeLink© software for recording keystrokes and the E-Prime© software for running the saccade tests encumbered synchronization of eye position data to test trials. Although a solution was reached, it was known prior to statistical analysis that the criterion measure of target latency would be subject to a degree of error, ranging from approximately 1 to 17ms (*M*=7, *SD*=4) for the saccade tests. The details of this problem and its solution are provided in Appendix E.

The event and position files were read into MATLAB® for analysis of the eye-tracking data. Eye position data corresponding to each trial were plotted and visually inspected to ensure proper alignment of the two files. Exemplar cases for each test are summarized in Figure 4. For the standard smooth pursuit task, the expected eye position traces were observed for all subjects for all trials. Eye position traces resembled movements that would be made while tracking the random-walk targets in the velocity discrimination test on the majority of trials. Activity resembling fixation was observed for the Fixation test, and periods of fixation followed by saccades towards a target were observed for the saccade tests. Upon confirmation of proper alignment, oculomotor metrics were extracted for each test. Attached as Appendices F-M are the corresponding MATLAB® scripts, composed specifically for this study, for performing all data processing and analysis.

Summary scores for each test (see Appendix N) were extracted from the eye-tracking data and imported into an Excel® workbook containing demographic information, medical history, and behavioral data. All items from the smooth pursuit test and the standard smooth pursuit stimuli were included in derivation of summary scores. For the Fixation test, averages were taken from all except the first item, where extreme variability in eye movement was observed as subjects learned the test design. For the Express, Reflexive, and

AntiSaccade tests, scores were derived from trials where an eye movement towards the target was detected. Data from trials where the participant made an anticipatory eye movement towards the target prior to the actual presentation of the target were excluded from summary scores. Of the 114 items in the saccade tests, an average of 94 items (SD=13.7) were summarized for the Reflexive test, 78 (SD=16. 2) for the Express test, and 70 (SD=13.4) for the AntiSaccade test. Item exclusion for each test by type is provided in Table 2.

Results

Data Diagnostics

Distribution properties: Prior to hypothesis testing, primary behavioral and eye-tracking measures were explored with respect to central tendency. Descriptive statistics are summarized in Table 3. Skewness and kurtosis estimates were evaluated against a z-statistic of +/- 1.96. The distribution of Fixation performance was negatively skewed and leptokurtotic around a mean of 98% correct. For all other measures, mean and median values were found to be very similar, and no observations were at floor or ceiling levels. However, most measures were not normally distributed. Distributions of discrimination thresholds from the Express and Reflexive tests were positively skewed and leptokurtotic. The distribution of AntiSaccade discrimination threshold was positively skewed. Velocity discrimination yielded a multimodal distribution. This finding was further explored in a separate section below. Of the eye-tracking measures, only saccade frequency during smooth pursuit (saccades per second) was normally distributed. Amplitude of catch-up saccades during smooth pursuit was positively skewed and leptokurtotic. Target latency distributions for all saccade tests were negatively skewed. Distributions of target latency for the Reflexive and Express tests were leptokurtotic, and distribution of saccades to the distractor during the AntiSaccade test was platykurtotic.

Univariate outliers were screened using box and whisker plots, with whiskers defined at 1.5 times the interquartile range. Plots for behavioral measures are provided in Figure 5; plots for eye-tracking measures are in Figure 6. Outliers were identified as cases with a score 1.5 to 3 times the interquartile range from the median score, while extreme cases were identified as cases with a score more distal than 3 times the interquartile range from the median. One or more outlier cases were found on all behavioral measures and most eye-tracking measures. Extreme cases were found for Fixation, Express discrimination threshold, amplitude of catch-up saccades, and target latency for the Reflexive test. With few exceptions, outliers represented poor performance. Additionally, most outlier cases represented individuals with only one outlier score. However, subject #57 (61 year old male) had outlier scores representing poor performance on all saccade test measures and AntiSaccade target latency, while subject #50 (21 year old male) had outlier scores representing poor performance for velocity discrimination threshold, Express discrimination threshold, Gain, and amplitude of catch-up saccades.

Because the main hypotheses of this study involved associations between behavioral and eye-tracking measures, data were also screened for multivariate outliers that would impact the strength of correlations. Cook's D for each individual was generated through linear regression analysis and used as the indicator of influence. Using the standard Cook's D value of 1.0 to identify cases whose exclusion from the analysis would result in substantial changes to the regression coefficients, no multivariate outliers were detected in any of the predicted relationships between measures. Scatterplots are provided below in the section where the correlations are examined.

Internal Consistency: For the behavioral measures, internal consistency was assessed by examining split-half (odd-even) correlation coefficients. For the saccade tests, it was not appropriate to include items administered beyond the participant's discrimination threshold, as these responses were by definition at chance-level and would only contribute random noise to the measurement. Therefore, responses on items at the first level of failure and above were included in calculating split-half performance. For the velocity discrimination, all administered items were included, as the test was discontinued by the examiner upon establishing threshold. As outlined in Table 4, internal consistency (Spearman-Brown corrected) was found to be in the high range for the velocity discrimination (r=.92), Express (r=.92), Reflexive (r=0.95), and AntiSaccade (r=.97) tests. Although presentation time of the target decreased over the course of the Fixation test (500ms to 50ms), no performance decline was observed; therefore, all 36 items were included in analysis of internal consistency. Perhaps due to a ceiling effect for overall performance, internal consistency was found to be lower (r=.65) for this test. The use of Fixation performance as a covariate was not indicated by statistically significant changes in results for any of the analyses relating to primary hypotheses.

For standard smooth eye-tracking measures, Cronbach's alpha was employed to examine reliability of gain, saccade rate, and saccade amplitude. For each, 20 measures (5 horizontal, 5 vertical, 10 orbital) were included in the estimate.

Reliability was found to be in the high range for smooth pursuit Gain (α=.94) and saccade frequency (α=.96), while reliability for catch-up saccade amplitude was in the moderate range (α=.76). Cronbach's alpha was also estimated to examine reliability for the measurement of fixation observations made during the Fixation test. Here, reliability was found to be in the high range (α=.90). Reliability estimates for eye-tracking measures relevant to the saccade tests (i.e., target latency for the Express, Reflexive, and AntiSaccade tests and number of saccades to the distractor during the AntiSaccade test) were calculated using the same technique applied to the behavioral measures. It should be noted that the reliability estimates for the saccade tests in Table 4 are most likely inflated by the systematic person-person error associated with the interface problem between E-Prime© and the EyeLink II software.

Order Effects: Independent sample t-tests were performed to explore order effects on the behavioral and eye-tracking measures. Inflated Type-I error rates were controlled using the Steele and Torrie adaptation of Tukey's Method (1960) for creating 95% confidence intervals of differences between groups of unequal sample sizes. The only statistically significant difference found was for Reflexive discrimination threshold, where participants who completed the Reflexive test before the Express Test had lower Reflexive discrimination thresholds (mean difference = -19ms, 95% CI: [-34, -3]). No order-group differences with respect to age, date of testing, unusual cases, or other factors were found that could explain this finding.

Demographic effects: Possible gender differences on the behavioral and eye-tracking measures were also explored using independent sample t-tests. After applying the Steele and Torrie correction, a significant difference favoring men was found for gain [.01, .10]. Men and women were not significantly different on any other measure. A correlation analysis was conducted to investigate whether age was associated with performance. For the behavioral measures, age was not correlated with velocity discrimination threshold or Fixation performance. Statistically significant relationships were found between age and discrimination thresholds from the Express ($r=.387$, $p=0.002$), Reflexive ($r.492$, $p<0.0005$), and AntiSaccade tests ($r=.566$, $p<0.0005$); however, age was not correlated with any of the corresponding eye-tracking measures. Because the final education attainment of the undergraduate sample was indeterminate, the relationship between education and performance was examined in the community sample. No statistically significant relationships were found.

Intercorrelations: An exploratory analysis of intercorrelations for behavioral (Table 5) and eye-tracking (Table 6) variables was performed to examine shared and unique components of the measurements. Velocity discrimination threshold was found to be associated with discrimination thresholds from the Express ($r=.312$), Reflexive ($r=.301$), and AntiSaccade tests ($r=.290$), but not with Fixation performance. Improved Fixation was associated with lower discrimination thresholds from all saccade tests. These relationships were difficult to interpret given the highly skewed distribution of Fixation performance. As shown in the Table 5, positive relationships ranging from $r=.517$ to $r=.587$ were found between saccade tests. In sum, individuals who performed well on one oculomotor test tended to perform well on the other tests; however, saccade discrimination thresholds were more strongly associated with one another than with velocity discrimination threshold from the test of smooth pursuit.

With regards to eye-tracking measures, a pattern emerged wherein relationships were observed within, but not between traits. For smooth pursuit measures, improved gain was associated with reduced frequency of saccades (r=-.808), and smaller amplitude of catch-up saccades (r=-.402). A weaker relationship was found between saccade frequency and amplitude of catch-up saccades (r=.272). A between-domain relationship was observed between amplitude of catch-up saccades and AntiSaccade target latency (r=.290). Target latency measures from the saccades tests were associated with one another. Percent of trials with a saccade to the distractor during the AntiSaccade test was not associated with any other eye-tracking measure.

Tests of Primary Hypotheses

Smooth pursuit during velocity discrimination: Eye-tracking data obtained during velocity discrimination were examined to determine the relative percentage of time performing smooth pursuit versus fixation and saccade. As seen in Figure 7, half of the observations were identified as Fixation. The next most frequent activity was smooth pursuit (32%), followed by major saccade (15%), and micro saccade (2%). Blinks comprised approximately 1% of the observations. Smooth pursuit activity was observed for every trial for every subject (range: [7%, 79%]); the minimum average percentage of smooth pursuit observations was 21%, and the maximum was 40%. An exploratory analysis was performed to examine intercorrelations between eye movement observations, and to determine whether velocity discrimination threshold was associated with percentages of time performing each of these activities. As can be seen in Table 7, inverse relationships were found between fixation and major saccade, smooth pursuit, and blink observations. Increased smooth pursuit eye movement observations were associated with increased major saccade observations. Smaller velocity discrimination thresholds (i.e., better performances) were associated with larger percentages of fixation time. These results support the hypothesis that velocity discrimination recruits smooth pursuit eye movements; however, increased smooth pursuit activity during the test was not found to be associated with improved performance.

Saccade test performance differences: Hypotheses regarding differences in discrimination and target latency across saccade tests were tested using paired sample t-tests. Type-I error was controlled using the Bonferroni method (α=.025) for statistical significance testing of two a priori comparisons (Reflexive vs. Express and AntiSaccade vs. Reflexive) in two families of analyses (behavioral and eye-tracking data). Discrimination threshold was significantly higher for the Reflexive over the Express test ($t(59)=5.84$, $p<.0005$; 97.5% CI: [12ms, 28ms]), and AntiSaccade discrimination threshold was in turn significantly higher than Reflexive discrimination threshold ($t(59)=23.93$, $p<.0005$; 97.5% CI: [192ms, 233ms]). The same pattern was found for the eye-tracking data, where target latency was significantly longer for the Reflexive than Express test ($t(59)=6.43$, $p<.0005$; 97.5% CI: [18ms, 37ms]), and AntiSaccade target latency was significantly longer than Reflexive target latency ($t=-25.39$, $p<.0005$; 97.5% CI: [151ms, 181ms]). Figure 8 illustrates the distributions of discrimination threshold; Figure 9 illustrates the distributions of target latency. Although mode values differ, there is a noticeable similarity in the patterns of distribution between discrimination threshold and target latency.

A follow-up analysis was conducted to determine the number of participants where the patterns for difference in mean scores was observed. Distributions of differences are provided in Figure 10 for Reflexive versus Express comparison, and

Figure 11 for AntiSaccade versus Reflexive comparison. A minority of subjects had differences in the opposite direction for Reflexive versus Express discrimination threshold (10/60) and target latency (8/60). Of the subjects that had lower Reflexive discrimination threshold, one of these subjects also had lower Reflexive target latency, and five subjects had less than 25ms difference between Reflexive and Express target latencies. None of the subjects with lower Reflexive target latencies had more than 25ms difference in discrimination thresholds. The difference between discrimination thresholds was statistically significant in both order groups (Express first = 25ms, 95% CI: [17, 34]; Reflexive first = 13, 95% CI: [2, 23]). The 95% confidence interval for the difference between order groups was [0, 27].

For AntiSaccade versus Reflexive discrimination thresholds, no subjects had a pattern of difference in the opposite direction of the means. Difference scores were created for AntiSaccade minus Reflexive discrimination threshold, and AntiSaccade minus Reflexive target latency. A correlation analysis between these difference scores revealed a statistically significant relationship (r=.295, p=.011, 95% CI: [.044, .511]), suggesting that differences in discrimination threshold are mirrored by differences in target latency. Although this correlation is not particularly large, it should be noted that the upper limit is restricted by observed validity correlations.

The results of these inter-test comparisons suggest that the tests are performing in the manner intended by design. Differences in target latency indicate that the Express test is generating the fastest saccades, followed by the Reflexive design which requires disengaging visual attention from the fixation point, and lastly the AntiSaccade design, where visual distractors increase target latency. The expected differences in discrimination threshold suggest that the tests are also providing unique behavioral measurements.

Convergent validity: Correlation coefficients reported in the multi-trait, multi-method matrix (Table 8) were corrected for attenuation due to error in measurement. Given that reliability estimates are believed to be inflated for the saccade tests, the attenuation correction may not be sufficient. Generally, the expected correlations between behavioral and eye-tracking measures were found, and correlations not connected with hypotheses were absent. From the smooth pursuit test, velocity discrimination threshold showed the expected negative correlation with gain (r=-.510, 99% CI: [-.718, -.219]) and saccade frequency (r=.363, 99% CI: [.040, .617]). Statistically significant relationships were not found between amplitude of catch-up saccades and any behavioral measure. As expected, velocity discrimination threshold was not associated with any saccade measurement. Express discrimination threshold was the only behavioral measure not associated with any smooth pursuit or saccade measurement. Reflexive discrimination threshold showed the expected correlation with Reflexive target latency (r=.457, 99% CI: [.152, .683]); however, it was also associated with AntiSaccade discrimination threshold and saccades to the distractor. AntiSaccade discrimination threshold showed the hypothesized association with both AntiSaccade target latency (r=.463, 99% CI: [.159, .689]) and saccades to distractor (r=.423, 99% CI: [.110, .659]). The only statistically significant correlation observed across smooth pursuit and saccade domains was a weak relationship between Reflexive discrimination threshold and gain (r=.343, 99% CI: [.017, .603]). No relationships were observed wherein better behavioral measures were associated with worse eye-tracking measures. It should also be noted that neither logarithmic transformations nor rank-ordering of the positively skewed behavioral data improved convergent correlations.

Discriminant validity: Formal statistical testing of discriminant validity was performed using the method described by Meng, Rosenthal, and Rubin (1992) for comparing correlated correlation coefficients. Here, the strength of hypothesized convergent associations between behavioral and eye-tracking measures (i.e., those in framed cells from Table 8) were compared to between-trait relationships that were not hypothesized (i.e., column-wise relationships not framed in Table 8). Amplitude of catch-up saccades and measures from the Express test were not included in this analysis, as no statistically significant between-method relationships were observed. The comparisons are outlined in Table 9. The convergent correlation between velocity discrimination threshold and gain was stronger than correlations with eye-tracking measures from the AntiSaccade test (target latency: $z=-2.69$, $p=.004$; saccades to distractor: $z=2.09$, $p=.018$). The hypothesized correlations between velocity discrimination threshold and saccade frequency was not significantly stronger than relationships with eye-tracking measures from the saccade tests. The correlation between Reflexive discrimination threshold and target latency was significantly stronger than the correlation with AntiSaccade saccades to distractor ($z=-2.38$, $p=.008$), but not significantly stronger than the correlations with gain or saccade frequency. Neither of the convergent correlations involving AntiSaccade discrimination threshold were significantly stronger than relationships with other smooth pursuit or saccade eye-tracking measures. In sum, the present discriminant validity tests do not indicate that the behavioral tests provide measures that are specific to the hypothesized eye-tracking measures.

Convergent validity for Express test: As described in the Methods section and Appendix E, difficulties regarding alignment of eye position data with event timing for the saccade tests subjected the criterion measure of target latency to an unknown and variable degree of error. Nevertheless, the expected correlations were found for the Reflexive and AntiSaccade test. For reasons unknown, a correlation was not found between the behavioral and eye-tracking measures from the Express test. Because the expected mean differences (relative to the Reflexive test) in behavioral and eye-tracking measures were found, the problem with synchronization of position file with event timing was further explored.

Three subgroups (n=20) were created based on ranked differences between observed Reflexive and Express target latency. The rationale for this division is that event and eye position data files may have been better aligned for some individuals than others with respect to the Express test, and this could be discerned by examining differences between Reflexive and Express target latency values. Because larger differences are expected by theory and previous findings in the literature, the group composed of individuals with the largest differences in target latency may be considered those with the best alignment. Importantly, this method is not inherently biased towards placing individuals into groups based on behavioral measures. Target latency differences ranged from –39 to 11ms in the first group, 11 to 36ms in the second group, and 39 to 139ms in the third group. No significant group differences were found for Express discrimination threshold. The third group had significantly shorter mean Express target latency than the first (mean difference = -38ms, $t(38)=3.23$, $p=.003$) and second group (mean difference = -29, $t(38)=3.19$, $p=.003$). However, values of Express target latency in the third group span the distribution of the entire sample, avoiding problems associated with restriction of range in the group of primary interest. As shown in Figure 12, no relationship between Express discrimination threshold and target latency was found in the first or second group. The third group, with ostensibly the best alignment, showed a statistically significant relationship (r=.48, p=.017). This finding lends support to the hypothesis of an association between behavioral and eye-tracking measures, and convergent validity of the Express test.

<u>Composition of AntiSaccade test performance:</u> As hypothesized, target latency for trials with a saccade to the distractor were longer (8ms, 95% CI: [6, 10]), and probability of a correct response was lower (.04, 95% CI: [.037, .043]). Figure 13 depicts target latency difference between trials with and without saccades to the distractor at each stimulus presentation time level of the AntiSaccade test; Figure 14 depicts difference in probability by level. Target latency was significantly reduced in trials without a saccade to the distractor at levels 1000ms, 800ms, 700ms, 650ms, 600ms, 500ms, 450ms, and 400ms. Importantly, target latency was significantly longer (mean difference = 12ms, 95% CI: [10, 13[) for trials with a saccade to the distractor over the observed range of discrimination thresholds (700 to 300ms). The only level with reduced target latency for trials with a saccade to the distractor was 200ms (95% CI: [1, 26]).

Probability of a correct response was significantly lower for trials with a saccade to the distractor at levels 900ms, 800ms, 700ms, 550ms, 500ms, 400ms, 200ms, and 150ms. Over the observed range of discrimination thresholds, probability of a correct response was significantly lower for trials with a saccade to the distractor (mean difference = .04, 95% CI: [.03, .05]). The only level with greater probability of a correct response for trials with a saccade to the distractor was 250ms (95% CI: [.009, .098]). Although a causal model cannot be confirmed, these results generally support the hypothesis that saccades to the distractor result in longer target latency and reduced probability of accurate discrimination.

Composition of Express and Reflexive target latency: An exploratory analysis was conducted to determine the extent to which latency for initial movement and velocity of saccades contributed towards latency for eyes to reach the target and discrimination threshold in the Express and Reflexive tests. Figure 15 compares distributions for initial latency of movement; Figure 16 compares saccade velocities. Latency for initial movement was significantly shorter for the Express versus Reflexive test (mean difference = 27 ms, 95% CI: [17, 36]), and Express saccade velocity was faster than Reflexive saccade velocity (mean difference = 5.7 deg / sec., 95% CI: [2.4, 8.9]). These findings are in keeping with lower discrimination thresholds, and shorter target latency for the Express over Reflexive test.

As shown in Table 10, relationships between target latency and latency of initial movement were approximately collinear for the Express (r=.991) and Reflexive test (r=.988). Correlations between target latency and saccade velocity were weak for the Express test (r=-.296) and non-significant for the Reflexive test. Saccade velocity was not correlated with discrimination threshold in either test. Across tests, a stronger correlation between saccade velocities (r=.786) versus latency for initial movement was found (r=.296). In sum, these findings suggest that individual differences in latency of eyes to reach the target are primarily driven by individual differences in latency of initial movement. Consequently, performance on the Express and Reflexive test primarily reflects latency for saccades. Across test designs where ability to disengage visual attention is manipulated, saccade velocity is more stable than latency of initial movement.

Follow-up Analyses: Convergent Correlations

Velocity discrimination: To explore the nature of the observed correlations between behavioral and eye-tracking measures, scatterplots were created. Figure 17 illustrates the relationships between velocity discrimination threshold and the related smooth pursuit eye-tracking measures. Subject #50, while not identified as a multivariate outlier with influence on the regression surface via Cook's D, clearly stands out from the rest of the distribution with respect to velocity discrimination threshold and gain. Without subject #50, the adjusted correlation coefficients are reduced for velocity discrimination and gain ($r=-.413$) and saccade rate ($r=.334$), but remain significant at the established $p<.01$ level.

Saccade tests: If the eye position and event timing files are properly aligned, and accurate discrimination of the target is dependent on the fovea being focused on the target (as hypothesized), a 1:1 relationship can be expected. As can be seen in Figure 18, the observed relationship (dashed line) did not approximate the theoretical 1:1 relationship (solid black line) for any of the tests. Because the relationship between behavioral and eye-tracking measures for the Express was not statistically significant, such a relationship could not be expected. For the Reflexive and AntiSaccade tests, where discrimination threshold and target latency were correlated, this was a possibility. The equations matching target latency (ms) to discrimination threshold are given by:

Reflexive target latency = 196 + 0.37 x (Reflexive discrimination threshold)

AntiSaccade target latency = 320 + 0.29 x (AntiSaccade discrimination threshold).

A global mismatch between eye position and event timing would impose an error with respect to the constant in the equation, but not the regression coefficient. One possibility is that the deviation of the regression coefficient from 1 reflects event-timing errors that vary subject-subject; alternatively, the assumption that perceptual discrimination of the target is dependent on foveal position matching target position can be questioned.

The intersection point of the observed and theoretical trend also bears upon interpretation of test scores. In the Express and Reflexive test, note that almost all observations lie above the theoretical line, and the intersection point is towards the upper end of discrimination threshold (313ms for the Reflexive test). For the AntiSaccade test, the points are distributed almost evenly above (60%) and below (40%) the theoretical line, and the intersection point is close to the means (448ms). Thus, for the average healthy person, AntiSaccade discrimination threshold typically approximates that individual's target latency with an error that could be an over or underestimation, while Reflexive discrimination threshold consistently underestimates target latency.

Follow-up Analyses: Internal Psychometric Properties

Velocity discrimination: Examination of velocity discrimination thresholds (Figure 19) revealed relative peaks at 0.375, 0.275, and 0.188 degrees per second. Theoretically, item difficulty increases in a linear fashion with each level as the difference in speeds between targets decreases. Furthermore, probability of correct response should be equivalent within level. However, due to random movement characteristics of the stimuli, it is possible that some items are in fact significantly different with respect to difficulty than expected for their level. To investigate whether certain items generated more incorrect responses than others, the percent of participants responding correctly to each item was examined. Figure 20 shows a scatterplot of observed item difficulty by discrimination threshold. It should be noted that the number of responses per item varies (average = 15.3, SD = 6.0), as each subject is administered a series of items tailored to his or her performance.

As expected, a linear trend was observed where percent of correct responses increases as the difference between target velocities increases (r=.52). One item from discrimination level 0.375 stands out as being much more difficult than the other items in the set. This item may explain some of the peak in the distribution of velocity discrimination threshold at this level; however, one difficult item alone cannot drive performance, as discontinuation criteria require at least three incorrect responses within a level or two incorrect responses in two consecutive levels. Furthermore, the mean difficulty level for these items is almost identical to the value predicted by the linear trend. At 0.275, another relatively difficult item was found. In this case, the mean difficulty of the level is slightly above the linear trend (i.e., easier than expected); therefore, if the item were removed, the relative difficulty of the level would be even more deviant. Interestingly, the local minimum in the distribution at level 0.325 corresponds with items that are of a highly consistent difficulty level and a mean difficulty that is closely matched with the overall linear trend. Thus, aberrant items cannot explain the non-normal distribution in velocity discrimination thresholds.

<u>Saccade target latency</u>: An exploratory analysis was conducted to determine whether target latency values varied over the course of the saccade tests. Recall

that, unlike the velocity discrimination test for smooth pursuit, participants responded to all items from the saccade tests. However, the entire sample cannot be used to generate mean target latency values because not all subjects made a saccade to the target for every trial. The mean number of participants making a saccade to the target for a given item was 43.8 (SD=9.4) and not significantly different across tests or different over test levels to an extent that would impact estimates. However, very few subjects made a saccade to the target for items at the two most difficult levels of the AntiSaccade test (mean=13.6, SD=6.0). Therefore, estimates made at this level do not represent all participants.

Figure 21 depicts the relationship between mean target latency and test level (i.e., stimulus presentation time) for the Express, Reflexive, and AntiSaccade tests. First, observe that target latency is significantly longer for the AntiSaccade versus Reflexive test over all common stimulus presentation time levels (except 150ms), and Reflexive target latency is significantly longer than Express target latency over all test levels. Second, note that there is only a small change in mean target latency over increasing levels of difficulty for the Express and Reflexive test, while there is a very strong and consistent linear change in target latency over the course of the AntiSaccade test. The linear trends for the Express and Reflexive test accounted for 7% ($p=.004$) and 20% ($p<.0005$) of the variance in target latency respectively, while the linear trend for AntiSaccade accounted for 88% ($p<.0005$) of the variance in target latency. The equations for matching target latency (ms) with test level are given by:

Express target latency = 240 + 0.02 x (Express ms level)

Reflexive target latency = 263 + 0.04 x (Reflexive ms level)

AntiSaccade target latency = 302 + 0.24 x (AntiSaccade ms level)

Note that these equations are only applicable to predictions within the range actually observed, and should not be used for extrapolations.

Although the linear trends are statistically significant, the regression coefficients associated with the Express and Reflexive trends were very small. Over the entire range of items administered (i.e., 500ms to 75ms), a difference of only about 15ms in target latency should be expected for either test. Thus, the relationships for the Express and Reflexive tests bear minimal implications with regards to test mechanics. As can be readily seen in Figure 21, the relationship is not trivial for the AntiSaccade test. Applied, the regression coefficient predicts a drop of about 96ms between the highest (700ms) and lowest (300ms) discrimination thresholds. This represents about two standard deviations in AntiSaccade target latency (SD=52ms). Thus, it appears that participants make an appreciable reduction in latency to reach the target as difficulty increases over the course of the AntiSaccade test, but not the Reflexive or Express.

<u>Impact of saccades to the distractor:</u> An exploratory analysis was performed to determine if incidence of saccades to distractor varied over AntiSaccade test level. As illustrated in Figure 22, incidence of saccades to the distractor varies by test level. On initial trials with long stimulus presentation times, participants made saccades to the distractor on about 62% of the trials. After approximately 6 trials, when presentation time was reduced to 900ms, participants made less saccades to the distractor. However, when presentation time was reduced below 650ms, the frequency of saccades to the distractor began increasing at a linear rate, reaching approximately 88% by the last difficulty level. With the first level excluded as a learning period, a count-weighted regression analysis showed a statistically

significant linear relationship ($t(104)=-8.42$, $p<.0005$, $R^2=.40$) between AntiSaccade test level and probability of a saccade to the distractor. The equation is given by:

Probability(saccade to distractor) = .782 - .0003 x (AntiSaccade ms level)

The regression coefficient probably has some bearing on test mechanics, as the estimated difference in probability of a saccade to the distractor between the highest and lowest observed discrimination thresholds is about 0.12, representing about half the standard deviation in proportion of trials with a saccade to the distractor (SD=.21).

STUDY 2: DISCRIMINATORY POWER OF TESTS

Methods

Aim

The general aim of this study is to examine the ability of the tests to distinguish a patient group with known oculomotor abnormalities from an age-matched sample of healthy controls.

Hypotheses:

Group comparisons on behavioral tests: Patients with Huntington's Disease (HD) have delayed initiation of saccades towards visual targets and pronounced difficulty inhibiting saccades towards visual distractors. Although abnormal smooth pursuit eye movements have been reported in patients with Huntington's Disease (Collewijn, Went, Tamminga, & Vegter-Van der Vlis 1988; Oepen, Mohr, Willmes, Thoden 1985), the preponderance of published literature suggests minimal, if any, impairment in this domain until very late stages of disease progression (Lasker & Zee, 1997). Furthermore, the neurological systems most affected by HD (i.e., basal ganglia) have not been characterized as a part of the smooth pursuit system. Therefore, the patient group was expected to have velocity discrimination thresholds similar to the healthy normal group on the smooth pursuit test, and perform worse than the healthy normal group on the Express, Reflexive, and AntiSaccade tests. Independent sample t-tests were used to make the group comparisons between tests.

Saccade disinhibition in HD: Because saccade disinhibition is a hallmark feature of HD, it was expected that the Huntington's patients would show impaired performance on the AntiSaccade test beyond what would be expected due to general oculomotor slowing. To test this hypothesis, an analysis of covariance was performed that examined group differences on the AntiSaccade test after controlling for performance on the Reflexive test.

Sample

A sample of 11 patients (7 male, 4 female) was recruited through the UCSD Huntington's Disease Center of Excellence at the University of California, San Diego to complete the behavioral oculomotor test battery. All participants gave written informed consent to participate in the study. Patients carried a clinical diagnosis of HD and a had family history of HD or a CAG repeat expansion of 37 or greater. Mean UHDRS (Huntington's Study Group, 1996) motor subscale score was 35.6 (SD = 12.1); UHDRS Stroop scores were 42.8 (SD = 12.8) for Color, 60.8 (SD = 17.5) for Word, and 29.2 (SD = 10.0) for Color-Word. Average age of onset was 36.2 (SD = 9.6), duration of illness (was 7.2 years (SD = 3.2).

The mean age of the patient group was 43 years (SD = 12.5, [26, 60]). Average education achievement was 14.9 years (SD = 3.0, [12,20]). No volunteers were excluded from participation. The HD patient group was compared to the previously described sample of 12 adult volunteers from the community. Independent sample t-tests indicated that the groups were not significantly different with respect to age, education, or composition by gender.

<u>Protocol</u>

To avoid floor effects, easier versions of the saccade tests were programmed. These versions contained the same number of trials, with stimulus presentation times extended to 700ms for the Fixation, Express, and Reflexive tests, and 1400ms for the AntiSaccade test. If the participant was unable to successfully respond to the first several trials of the regular version of the test, the adapted version was given. If the participant was then able to successfully complete the adapted version, the regular version of the test was re-administered. In total, one participant required administration of the adapted Express and Reflexive test, another participant required the adapted Reflexive test, and two participants were given the adapted AntiSaccade test.

All testing was done in a private examination room at the UCSD clinical trials building. In addition to occasional use of adapted versions of the tests, there were three differences in the way the tests were administered for the patient versus the previously described control group. First, as described earlier, digital video eye-tracking was not performed while patients completed the tests. Second, responses on the saccade tests were entered by the researcher so as to minimize errors associated with executive and motor dysfunction in HD. Finally, if the administrator observed chance-level performance, the tests were discontinued approximately 8 trials after patients reported guessing. This was done to make the testing experience less taxing for the patients so that optimal performance could be obtained on the entire battery of tests.

Results

Primary Hypothesis Tests

Group comparisons on behavioral tests: Differences in performance between the HD patient and healthy control group on the oculomotor battery were examined using independent sample t-tests. Inflated Type-I error rate associated with multiple a-priori comparisons was controlled using the Bonferroni method of protection (5 comparisons, $\alpha=.01$). Because variances between groups were grossly unequal for Velocity, Express, and Reflexive performance (see Table 11), separate variance estimates were used for these comparisons. The patient group was found to have significantly worse discrimination thresholds on all saccade tests (Express: $t(21)=3.95$, $p=.001$; Reflexive: $t(21)=2.95$, $p=.008$; AntiSaccade: $t(1,21)=4.62$, $p<.0005$). Although a trend favoring healthy controls was observed, the group difference in velocity discrimination threshold from the smooth pursuit test fell short of statistical significance ($t(21)=2.03$, $p=.056$). Figure 23 illustrates the differences between groups on the saccade tests. The groups showed very similar performance on the Fixation test. Furthermore, inclusion of Fixation performance as a covariate did not result in statistically significant changes for any of the primary hypothesis tests detailed below.

Given the observed differences in means, a linear discriminant function analysis was performed to examine the utility of the saccade tests in predicting group membership. Prior probabilities were based on group size, and separate group covariance matrices were used. In the initial model, Express, Reflexive, and AntiSaccade discrimination threshold were entered as predictors. The linear discriminant function generated by the analysis was significant ($X^2(3)=14.85$, $p=.002$).

Overall, 91.3% of the subjects were correctly classified, with one misclassification in each group. Examination of the standardized canonical correlation coefficients showed Express (r=.365) and AntiSaccade discrimination thresholds (r=.701) to be strong predictors of group membership.

The refined model included only Express (r=.416) and AntiSaccade discrimination thresholds (r=.69) as predictors ($X^2(2)=15.22$, $p<.0005$). Subject classification based on this model was identical to the first (91.3% success), with the same two subjects misclassified. Further examination revealed the misclassified patient to be the youngest participant (30 years old) and the misclassified healthy control to be the oldest participant (61 years old). Based on these findings, a final model was developed that included age as a predictor. The addition of age improved overall model fit ($\Delta X^2(1)=6.92$, $p=.009$), and all predictors were statistically significant. However, overall predictive utility of the model did not improve (91.3%), as the patient remained misclassified and correct classification of the older healthy control was offset by incorrect classification of a younger control (37 years old) with a relatively poor AntiSaccade discrimination threshold (650 ms).

Saccade disinhibition in HD: As seen in study 1, performance on the AntiSaccade test was related to both saccade latency and ability to inhibit saccades to the distractor. To determine whether the impairment in AntiSaccade performance was related to the gross oculomotor slowing or disinhibition of saccades, a third linear regression analysis was conducted. The analysis first controlled for Reflexive discrimination threshold, then added the group term, then an interaction term of group x Reflexive discrimination threshold. In the first step, Reflexive discrimination threshold was found to be a statistically significant predictor of AntiSaccade performance (t(20)=2.84, R^2=.387, p=.01). In the second step, the addition of the group term resulted in a statistically significant increase in the proportion of variance explained (ΔR^2=.19, t(20)=-3.01, p=.007, η^2 =.34). The interaction term in the third step fell short of statistical significance at the α=0.05 level (ΔR^2=.067, t(19)=1.89, p=.074, η^2 =.17). An examination of the scatterplot depicted in Figure 24 strongly implicates the existence of an important group difference in the relationship between Reflexive and AntiSaccade discrimination thresholds. If examined independently, the relationship between the two discrimination thresholds is stronger in the healthy control group (r=.75, p=.0017), than in the HD group (r=.38, p=.12). These findings suggest that impaired performance on the AntiSaccade test in the HD groups cannot be explained by oculomotor slowing alone, and is likely due to the additive effect of saccade disinhibition.

Exploratory Analyses

Saccade performance and age: Linear regression analysis was used to determine whether the rate of change in Reflexive discrimination threshold with age differed between groups. In the first model, significant main effects were found for both group (t(20)=-3.49, p=.002) and age (t(20)=-2.60, p=.017). Together, age and group accounted for 43% of the variance. The interaction term fell short of statistical significance at the α=0.05 level (ΔR^2=.09, t(19)=2.02, p=.058, η^2 =.18); however, the scatterplot depicted in Figure 25a suggests the existence of an important difference in the relationship between age and Reflexive discrimination threshold. This difference implies that basic oculomotor reaction time declines more rapidly with advancing age in patients with Huntington's Disease than in healthy persons.

The same linear regression analysis was performed to investigate group and age effects on AntiSaccade discrimination threshold. Again, both group (t(20)=-5.68, p<.0005) and age (t(20)=3.70, p=.001) were statistically significant predictors. Here, however, the interaction term did not approach statistical significance and did not contribute towards variance explained in discrimination threshold (ΔR^2=.01). The near-parallel slopes of the group trendlines through the scatterplot of age versus AntiSaccade discrimination in Figure 25b illustrates the similarity in relationships. Interpreted, these findings suggest that saccade disinhibition increases with age at the same rate for both healthy persons and those with HD; however, at some point in development or disease progression the patients sustain a "hit" that results in worse performance.

Saccades and clinical measures: Given the apparent differential effects of age on Reflexive and AntiSaccade discrimination thresholds in HD, an exploratory analysis was performed to determine whether UHDRS motor score, UHDRS Stroop scores, or duration of illness were interrelated. The relationship between age and duration of illness was statistically significant (r=.62, p=.044). No relationships were found between duration of illness and oculomotor measures; however, an unexpected negative correlation between duration of illness and UHDRS motor score was found (r=-.66, p=.027). This finding may be due to decrease in chorea (a heavily-weighted component of UHDRS motor) with disease progression. Stroop Color was negatively correlated with Reflexive discrimination threshold (r=-.60, p=.038) and Stroop Word was negatively correlated with AntiSaccade discrimination threshold (r=-.71, p=.015). The correlation between Stroop Color-Word and AntiSaccade fell short of statistical significance (r=-.53, p=.096). The relationship between UHDRS motor scores and saccade measures after controlling for the effects of age revealed a statistically significant relationship between UHDRS motor scores and Reflexive (r=.75, p=.013), but not Antisaccade discrimination thresholds (r=.30, n.s.). This finding suggests that global motor dysfunction is related to oculomotor slowing, but not saccade disinhibition.

A final examination was performed to explore possible clinical factors that might have influenced individual test performances in the HD group. Specifically, two cases (5 and 11) with apparent influence on the regression surface relating Reflexive to AntiSaccade performance (as illustrated in Figure 24) were examined in more closely. Case number 5, a male with good Reflexive and poor AntiSaccade performance, was found to be average relative to the rest of the HD sample with regards to age, number of CAG repeats, duration of illness, and Stroop scores. However, this individual was one of the four patients currently taking anti-psychotic medication (Clozaril). Case number 11, a male with poor Reflexive and average AntiSaccade performance was also not unusual with regards to clinical measures; however, he was also taking antipsychotic medication (Seroquel). One of the other individuals taking antipsychotic medication (Zyprexa) showed average Reflexive and poor AntiSaccade performance; the other individual taking antipsychotic medication (Seroquel, Haldol, and Neurontin) showed performance relative close to the regression surface. Given these results, a summary statement regarding interactions between medication and saccade test performances in Huntington’s disease cannot be made at this time.

DISCUSSION

Summary of Findings

The results from the present study support the use of smooth pursuit and saccade tests in the assessment of oculomotor functioning. In study 1, velocity discrimination was found to elicit smooth pursuit in all subjects, and clear evidence of saccade activity was observed for all subjects while taking the saccade tests. Internal consistency estimates were high for all tests. Differences in discrimination threshold distributions between saccade tests supported hypotheses regarding the type of saccade each test was designed to elicit and assess. These differences in discrimination thresholds were mirrored by differences in target latency distributions. Convergent validity of the velocity discrimination, Reflexive, and AntiSaccade tests were established through significant correlations between discrimination thresholds and standard eye-tracking metrics. Evidence for convergent validity of the Express test was found within a subset of subjects believed to have more accurate standard eye-tracking measures. Discriminant validity was qualitatively observed through greater strength in predicted associations between behavioral and eye-tracking measures. However, formal statistical testing of correlated correlations did not consistently support discriminant validity for any of the behavioral measures. Performance on the AntiSaccade test was found to reflect both target latency and incidence of saccades to the distractor; Reflexive and Express tests were determined to primarily reflect latency of initial saccadic movement.

Results from study 2 support the discriminatory power of the tests to distinguish healthy persons from patients with Huntington's Disease (HD). HD patients were expected to show performance similar to healthy persons on the smooth pursuit and Fixation tests, and perform worse on the saccade tests. As expected, HD patients performed well above chance and similar to healthy controls on the Fixation test, and worse than healthy controls on all saccade tests. The linear discriminant function based on Express and AntiSaccade discrimination thresholds was found to be effective in distinguishing HD patients from healthy controls. Although not statistically significant, a trend was observed towards a difference between healthy controls and HD patients on the smooth pursuit test. This unexpected finding suggests that either smooth pursuit eye movements were impaired in the sample of HD patients, or velocity discrimination also draws upon functioning of the saccade system. Performance differences between groups on the AntiSaccade test remained after controlling for basic oculomotor speed using Reflexive discrimination threshold. Furthermore, a strong relationship between AntiSaccade and Reflexive discrimination threshold was found for healthy controls, but not HD patients, indicating that one or more additional factors was driving performance in the patient group. Given that AntiSaccade discrimination threshold was found to be related to both target latency and saccades to the distractor in study 1, these findings suggest that the AntiSaccade test is sensitive to oculomotor disinhibition in a clinical population. Finally, performances on the saccade tests generally corresponded in a reasonable manner with UHDRS measures, as Reflexive discrimination threshold was associated with UHDRS motor scores, while AntiSaccade discrimination threshold showed a trend towards a relationship with Stroop inhibition.

Velocity Discrimination

The non-normal distributions of velocity discrimination threshold in the current sample of healthy persons was not expected and cannot be readily explained through item analysis nor demographic features. It is possible that the observed multi-modal distribution is simply chance sampling of a normal distribution, and a larger sample would yield a normal distribution. If the observed distribution shape was replicated, the validity of velocity discrimination as a measure of the integrity of the smooth pursuit eye movement system would be questioned, as multi-modal distributions for standard smooth pursuit measures have not been reported in the literature.

During velocity discrimination, some subjects articulated specific strategies such as, “watching the distance between discs when they moved in the same direction,” “focusing in the center and using peripheral vision,” and, “following only one disc.” One explanation for an observed multimodal distribution of a latent variable that is normally distributed is that strategic approaches to the test vary within the sample. In this case, some individuals develop an effective strategy to make discriminations, whereas others do not. A strategy based on employing fixation is supported by the data, as a large percentage of fixation activity (50%) was observed while performing the test, and a small but non-negligible correlation between velocity discrimination threshold and number of fixation observations was found.

It seems reasonable that employing a strategy would influence performance, and the ability to develop an effective strategy would likely be determined by cognitive functioning not related to the oculomotor system. Furthermore, the ability to develop an effective strategy could be all-or-none. Thus, velocity discrimination thresholds would represent the combined product of multiple latent traits (i.e., smooth pursuit and strategy), and separate, perhaps overlapping, distributions would be found for the different strategy groups. Within strategy groups, variability would be explained by differences in the smooth pursuit eye movement system. Correlations between velocity discrimination thresholds and performances on tests of visuospatial, problem-solving, and abstraction abilities would support this hypothesis. If such relationships were found, the velocity discrimination threshold as a measure of smooth pursuit functioning would need to be corrected for performance on the related test(s).

Saccade tests

The kurtotic and skewed distributions of the saccade tests were likely due to the restricted demographics of the current sample. In a similar way, the observed validity correlation coefficients in the current study are likely to be limited by restriction of range due to the narrow age range in the majority of the sample, and the inclusion of only healthy normal persons. A repetition of study 1 using a patient group with known oculomotor abnormalities, such as schizophrenia, would improve the probability of detecting relationships between the behavioral and eye-tracking measures. This would be especially helpful for assessing discriminant validity, where less correlation would be expected across oculomotor domains (i.e., smooth pursuit and saccades) due to differential impact of the neuropsychiatric condition(s).

The saccade tests appear to provide unique measurements for specific types of saccades, and their clinical utility is likely maximized when all tests are administered. As demonstrated in study 2, a clinical population was able to perform the baseline Fixation test at a level comparable to healthy controls. This test allows critical investigators to control or discount the impact of other cognitive processes that might bear on saccade test performance. The Express discrimination threshold can be thought of as a measure for maximal saccade response efficiency. When compared to the Express discrimination threshold, Reflexive discrimination threshold reflects the impact of disengaging visual fixation. Such a comparison could be useful when studying populations such as Tourette's syndrome (LeVasseur et al, 2001), and ethanol intoxication (Vassallo & Abel, 2002). Reflexive discrimination threshold, in turn, provides a comparison for AntiSaccade discrimination threshold to determine the impact of the distractor on performance. In this capacity, the Reflexive is superior to the Express test, as disengaging from visual fixation in the Reflexive test and inhibiting saccades towards the distractor in AntiSaccade test both require additional time. Therefore, the difference between discrimination thresholds is more likely to reflect saccades to the distractor.

Saccade latency is a commonly reported measure in the literature. If a 1:1 relationship between discrimination threshold and target latency had been observed in study 1, a minor adjustment (based on average difference between target latency and latency for movement, ca. 10ms) could allow discrimination thresholds to be used interchangeably with latency. It is quite possible that without the timing synchronization problem between E-Prime® and the eye-tracking data, a near 1:1 relationship would have been found. It is not known whether future versions of E-Prime® or EyeLink® software will improve compatibility. However, a simple modification to the E-Prime® script could record a time-stamp for stimulus presentation that would be more accurate than the response page time stamp used in this study. Until a 1:1 relationship has been convincingly demonstrated, users of the saccade tests should use discrimination thresholds as proxy for latency with arbitrary units.

The findings that target latency decreases and probability of a saccade to the distractor increases as the AntiSaccade test becomes more difficult were not expected. With regards to target latency, it is possible that participants moved their eyes towards the target only as fast as necessary to make the discrimination. This seems unlikely, however, given that target latency was relatively consistent throughout the Express and Reflexive tests. A more plausible explanation is that the extended presence of the distractor at easier levels (recall the presentation time of the distractor matched presentation time of the target) retarded volitional saccades to the target. The change in rate of saccades to the distractor may be due to increasing challenge of the test at difficult levels where an immediate response is required. In this case, the demand for an immediate response impedes ability to inhibit a reflexive, counter-productive response. If such a phenomenon exists, the finding may have implications for inhibition testing in other modalities. For example, the commonly observed ceiling effect in the go no-go test design might be reduced by requiring increasingly faster responding.

Previous studies showing independence of the neurological systems involved with saccade inhibition and oculomotor reaction time are supported by the differential impact of HD on AntiSaccade and Reflexive discrimination thresholds that was observed in study 2. In addition to providing evidence for validity of the saccade tests, the results have implications with respect to disease progression in HD. For the AntiSaccade test, the similar slopes with different intercepts for age and discrimination threshold between healthy persons and HD patients suggest that a dramatic neurological insult occurs prior to formal diagnosis and treatment. In a 2004 study, Blekher and colleagues found no differences on anti-saccade eye-tracking measures (saccades to the distractor or latency for anti-saccade) between a sample of presymptomatic gene carriers for HD versus a cohort comprised of gene-negative siblings. Taken together, these results suggest that a dramatic change in ability to inhibit saccades occurs very proximal to the time of symptom onset. Thus, the AntiSaccade test may be particularly useful in longitudinal studies of individuals at-risk for phenoconversion. Such studies could also help determine whether oculomotor disinhibition was associated with, or had a diagnostic advantage over, the Stroop components of the UHDRS.

Reflexive discrimination threshold appears to increase much more rapidly with advancing age for persons with HD. However, this relationship is difficult to interpret given that duration of illness was inversely related to UHDRS motor scores and not associated with Reflexive performance. One possibility is that HD patients begin to experience a progressive slowing of saccades prior to phenoconversion. Two recent studies using similar methodology have yielded mixed findings regarding slowing of reflexive saccades in presymptomatic gene carriers for the disease, where Blekher and colleagues (2004) found a difference relative to gene-negative siblings, while Golding and colleagues did not (2006). Another possibility is that the degree of oculomotor slowing that occurs at time of symptom onset is proportional to an individual's age. This finding would be in keeping with the current finding of an association between Reflexive discrimination threshold and UHDRS motor scores and a study by Siesling and colleagues (Siesling, van Vugt, Zwinderman, Kieburtz, & Roos, 1998) showing greater decline in UHDRS motor scores over a 1-year period for individuals with older age of onset. Both explanations for the observed effect of age on the Reflexive test in HD could be examined through longitudinal testing of individuals at-risk for phenoconversion repeated over regular intervals (ca. 1 year).

Future Studies

The relationship between age and test performances should be characterized in a larger and more age-diverse sample. The residuals between thresholds and standard eye-tracking measures should be examined for heteroscedasticity to determine whether convergent validity for the tests holds across the age spectrum. Patient groups should also perform the tests while eye-tracking measures are collected to ascertain convergent validity. Test-retest reliability in both healthy and patient groups should be examined to determine the stability of the measures and assess practice effects.

Application of the saccade tests could also be helpful for understanding behavioral disinhibition in other clinical populations. Comparisons between performance on the AntiSaccade test and other cognitive (e.g., Stroop, Hayling sentence completion, go no-go, etc.) and psychophysical (pre-pulse inhibition) measures of disinhibition could help determine whether a common neurological substrate was implicated across clinical groups, domains, and testing modalities. Additionally, the relationship between basic oculomotor disinhibition and clinically-significant behavioral disinhibition could be assessed. Such studies would be informative in neuropsychiatric populations with characteristic impulsivity and disinhibition features.

The sensitivity and specificity of velocity discrimination threshold as a measure of smooth pursuit eye movement in a clinical population has not been established. Specificity of the test is questioned by results from the current study, where a trend towards a significant difference between the HD patient and control group suggests that additional cognitive and oculomotor functionality are required. This finding would be tempered by results from follow-up studies showing that standard smooth pursuit eye-tracking metrics (e.g., gain, frequency of saccades, etc.) were also impaired in the sample. An investigation comparing velocity discrimination to saccade measures in patients with lesions in the area around the inferior temporal sulcus (i.e., the human analogue of the medial superior temporal area in the macaque monkey) would be useful in establishing specificity.

Perhaps the most effective way of examining the sensitivity and specificity of the smooth pursuit and saccade tests would be to repeat the protocol from study 1 with a sample of patients with various spino-cerebellar degenerative diseases. Such patients are frequently observed to have both impairment for both types of eye movements (e.g., Moschner, Perlman, & Baloh, 1994; Gaymard, Pierrot-Deseilligny, Rivaud, & Velut, 1993). However, relative levels of impairment have previously been shown useful in differential diagnosis (Ceravolo et al, 2002; Wessel, Moschner, Wandinger, Kömpf, & Heide, 1998; Thier, Bachor, Faiss, Dichgans, & Koenig, 1991) and identification of phenotype subgroups (Buttner et al, 1999; Burk et al, 1999; Klostermann, Zuhlke, Heide, Kompf, & Wessel, 1997). A heterogeneous sample of patients with spino-cerebellar involvement (e.g., spino-cerebellar ataxia, Friedreich's ataxia, idiopathic cerebellar atrophy, olivopontocerebellar atrophy, etc.) would likely produce a wide distribution of standard eye-tracking and behavioral measures.

Convergent and discriminant correlations between behavioral and eye-tracking measures in this group would provide support for the validity of the tests in a clinical population. Patients showing relatively circumscribed impairment for either smooth pursuit or saccadic eye-tracking measures could be further examined to determine whether the behavioral data also suggested a circumscribed impairment. Diagnostic membership in oculomotor subgroups could also be examined through linear discriminant functional analysis to assess the utility of the tests in clinical differentiation.

As described earlier, a large body of literature has documented oculomotor abnormalities in schizophrenia patients and unaffected family members. Impaired smooth pursuit eye movements in clinically unaffected family members have also been related to various genetic and biological markers (for review, see Keri & Janka, 2004). However, results from recent studies examining the utility of anti-saccade measures as potential indicator of genetic liability for schizophrenia have been mixed. A meta-analysis by Levy and colleagues (Levy et al, 2004) suggested that studies documenting impaired anti-saccade performance tended to use non-symmetrical inclusion and exclusion criteria for family members and healthy controls. The authors concluded that anti-saccade measures may not be useful in identifying clinically unaffected carriers of genes for schizophrenia. Because of their portability and ease of administration, the smooth pursuit and saccade tests lend themselves towards application in large-scale studies that could better evaluate whether oculomotor markers represent a useful component in multidimensional endophenotype models of schizophrenia. This study would also be useful in evaluating the discriminatory power of the test battery for identifying the oculomotor abnormalities (i.e., saccade disinhibition and impaired smooth pursuit) that have previously been reported in schizophrenia.

Although impaired smooth pursuit and saccadic eye movements have been frequently reported as a consequence of traumatic brain injury (TBI), there are currently no published studies examining these eye movements as a consequence of concussion. The potential utility of the smooth pursuit and saccade tests in assessment of concussions is supported by a recent study (Suh, Kolster, Sarkar, McCandliss, & Ghajar, 2006) that found smooth pursuit impairments in patients with mild TBI. However, another study examining saccade latency and anti-saccade error rate determined that these measures were not sensitive to mild TBI (Crevits, Hanse, Tummers, & Van Maele, 2000). If the tests were found to be sensitive to the effects of concussion, their application in management of sport-related concussion could be valuable for guiding return-to-play and tracking changes in liability for neurocognitive impairment with repeated injuries.

The general form of the saccade tests assesses latency of saccades averaged over eight cardinal trajectories from the center; however, the tests can easily be adapted to compare saccade latencies by direction. This flexibility would be particularly useful in assessing patients with suspected progressive surpanuclear palsy (PSP), where latency for horizontal versus vertical saccades could be compared. Discriminating PSP from other atypical parkinsonian syndromes is often difficult, as the diseases share common behavioral features and histologies (Feany, Mattiace, Dickson, 1996). Although slowing of vertical saccades is a hallmark feature, qualitative bedside examinations of oculomotor functioning lack the sensitivity to discriminate patients with PSP until late in disease progression (Leigh & Riley, 1999). Thus, use of the tests in clinical assessments may improve diagnostic accuracy for this group.

The saccade tests could also be modified to generate separate scores for saccades to the left and right of the fixation point. This modification could be useful in assessing laterality effects of stroke, where previous eye-tracking studies have yielded conflicting results regarding the extent to which latency is prolonged for saccades contralateral to the affected hemisphere (e.g., Catz, Ron, Ring, Solzi, & Korczyn, 1994; Pierrot-Deseilligny, Rivaud, Gaymard, & Agid, 1991). The ease of administration and scoring of behavioral data from the saccade tests (relative to standard eye-tracking data) would facilitate the collection of samples large enough to adequately address this question in a notoriously heterogenous clinical population. In a similar way, asymmetry of Parkinson's Disease (PD) presentation could be explored. Only two studies can be found in the literature that investigate the relationship between laterality of global motor symptoms and laterality of oculomotor dysfunction in PD: 1) A 2001 study by Ventre-Dominey, Dominey, & Broussolle that documented increased latency for saccades in PD when coupled with pointing using the more severely affected hand; and, 2) A study by O'Sullivan and colleagues (O'Sullivan et al, 2003) that found no lateralitalized effects on fixation measures following unilateral pallidotomy in PD. Therefore, in addition to examining the utility of the saccade tests as a tool for assessment of PD, such an investigation would contribute towards understanding of the role of the basal ganglia circuitry in modulating saccades.

The neurological structures supporting performances of the smooth pursuit and saccade tests are hypothesized to be the same as those involved in smooth pursuit and saccadic eye movements, respectively. This hypothesis could be tested in functional brain imaging studies, where healthy persons would complete the tests while undergoing functional MRI. As described in the introduction, unique cortical and shared cerebellar and subcortical activation would be expected for the smooth pursuit and saccade tests. Comparisons between healthy persons and patient populations could determine whether differences in recruitment of neurological systems were associated with performance deficits. Only minor adaptations to the tests that are unlikely to threaten validity (i.e., magnet synchronization and inclusion of resting periods) would be required to perform such studies. However, special measures may be required to reduce motion artifacts related to head movements while subjects perform the saccade tests.

It is believed that all subjects who participated in the current study put forth their best effort, and that test performances and eye-tracking measures are not related to effort. In previous studies examining other domains of cognitive functioning, workload has been related to pupil dilation, where greater workload is associated with increased pupil dilation. Although not used in the present analyses, pupilometry data were acquired throughout Study 1. Eye-Tracking, Inc. has developed, validated, and patented a reliable technique for estimating the Index of Cognitive Activity (ICA) based on pupil dilation as measured by the EyeLink® II system. This technique could be employed to examine ICA over the course of test administration to test the following hypotheses regarding the impact of effort on performance:

1. For the vast majority of participants, the overall pattern of pupillary constriction and dilation reflects attentive cognitive effort to perform the tests.

2. Level of ICA is higher while subjects are performing tests than while resting between tests.
3. ICA increases as test difficulty increases.
4. Greater effort is elicited by the AntiSaccade than Express or Reflexive test during early trials, but approaches similar levels when an individual's discrimination threshold is reached.
5. Larger changes in ICA over the course of administration are not associated with improved discrimination thresholds in the smooth pursuit and saccade tests.
6. Degree of difficulty-dependent change in ICA (slope over test) is not associated with reduced target latency in the saccade tests (i.e., latency of saccades not based on effort).

Additionally, examination of pupillometry data could shed light on test summaries scores that represented univariate outliers.

Limitations and Improvements

The protocol for study 1 was developed to mirror applications of the tests in clinical and research assessment environments where formal eye-tracking equipment is not available. This feature makes behavioral measurement errors from the validity study comparable to those in applied usage. A consequence of this design decision was that a chin rest was not employed to keep the participants head at a fixed distance from the screen throughout the study. Measurement error by deviation from 57cm is plotted in Figure 26. It seems possible that being closer to screen might improve velocity discrimination, as the difference in target speed with respect to degrees of visual angle per second would increase. For example, given the average velocity discrimination threshold of 0.28 degrees per second at 57cm, being 10cm closer to the screen would increase the difference in target speed by about 0.06 deg/second (about two-thirds of the standard deviation in healthy normal subjects); sitting 10cm further from the screen would decrease the difference in target speed by about 0.04 deg/second (about one-half the standard deviation). These errors may be partially mitigated by increasing difficulty in velocity discrimination (Masson, Mestre, & Stone, 1999) and reduced smooth pursuit gain (Haarmeier & Their, 1999) at higher mean target speeds. Within the context of study 1 and study 2, all participants who made visible movements towards or away from the screen were repositioned and reminded to remain at the fixed distance. Such procedures would need to be maintained in future clinical studies for assured comparability of measurements.

It is not known whether being closer or further from the screen would improve performance on the saccade tests. Decreasing distance to the screen would improve acuity and improve the probability that a saccade that fell short of matching target position would still place the fovea close enough to allow accurate discrimination. However, decreasing distance to the screen would also result in an increase in the degrees of visual angle for the eye to travel to reach the target. In this case, a position 10cm closer to the screen would increase center to target distance from 10 to 12.2 degrees of visual angle; 10cm further from the screen would reduce the distance to about 8.5 degrees. Regardless of the net effect, standardized distance from the screen should be maintained during test administration to minimize error in measurement.

Several subjects reported that they were occasionally able to perform the velocity discrimination by comparing the change in distance between the discs when the discs followed similar paths. One potential modification to address this problem would be to have the stimuli follow concentric orbits based on unique elliptical parameters and random sinusoidal variance, as depicted in Figure 27. As in the random-walk design, each stimulus would have a unique, randomly-determined path for the faster and slower moving disk. Although the targets follow mathematically-determined orbits, smooth pursuit eye movements would be demanded for accurate tracking because the trajectory incorporates a substantial unpredictable component. The major advantages over the current design are smoother motion features and the ability to mechanically separate targets and vectors (via different starting points) throughout a stimulus presentation. This may reduce the likelihood that subjects would observe changes in distance between targets to make velocity discriminations. A potential drawback is the possibility that subjects would make rapid saccades between targets instead of smooth pursuit eye movements to make the discrimination.

One interesting and unexpected finding was that the mean (0.29 deg/sec) and median (0.28 deg/sec) velocity discrimination threshold in healthy subjects were essentially identical to the mean velocity discrimination threshold of 0.28 degrees per second reported by Gegenfurtner and colleagues (2003). These researchers used a completely different type of stimuli (single Gaussian vignetted patch) and task design (detection of speed perturbation in horizontal movement) but a common mean target velocity (4 deg/sec) and viewing distance (57cm). It is therefore possible that velocity discrimination threshold in healthy persons is relatively robust within a given range of base velocity, and any of the alterations described above would return minimal changes in measurements. Nevertheless, empirical data would be required to assess the impact of alterations to stimulus characteristics.

Fully-automated administration of the smooth pursuit test would represent a major improvement over the current format. This would reduce the possibility of incorrect scoring and help to standardize administration. Ideally, both the smooth pursuit and saccade tests would run on the same platform. At the present time, E-Prime® is not able to display mpeg or other dynamic stimulus (e.g., AVI, WMV, etc.) formats. However, the software developers state that E-Prime® version 2 will have this ability when it is released in the summer of 2006. It is unlikely that such an adaptation would jeopardize the validity of the tests for assessing healthy persons. However, in assessment of patient groups, the administrator would still need to enter responses to avoid problems associated with perseverative responding and psychomotor dysfunction.

Several improvements could be made to the structure of the saccade tests that would significantly improve the fidelity of measurement. First, current versions of the tests present a fixed set of 114 items that cover a wide range of discrimination thresholds. The data obtained in this study show that for healthy controls, many of these items are not necessary (i.e., too easy or too hard), while in patient groups, the standard range is not adequate (too hard). An easy refinement would be to alter the stimulus presentation times so that levels outside the range of thresholds observed in this study were not sampled. With this approach, separate versions for populations with oculomotor impairments would still need to be created. Alternatively, an adaptive testing paradigm could be employed to ascertain thresholds more efficiently.

Adaptive testing was not employed in the current study because a standard set of eye-tracking data was needed to conduct analyses regarding test mechanics. Although not eloquent, E-Prime® does allow for changes to be made to scripts that would enable adaptive testing using the established discontinuation criteria.

Another improvement that could be made to the saccade tests would be to display target stimuli oriented to the left, right, up, and down. This change would not alter the underlying construct, but would decrease the probability of chance-level correct response to 25%. With this change, the number of items per level could be reduced from 8 to 5 (allowing 2 incorrect responses) and fidelity of measurement would remain the same ($p=.016$). Unfortunately, current limitations of monitor refresh rates (+/- 12.5ms) preclude improving fidelity of discrimination threshold below 25ms intervals through tighter stimulus presentation times.

Ideally, an intuitive, graphical user interface (GUI) would allow researchers and clinicians to design test parameters and structure for specific assessment purposes. Such a GUI cannot be easily programmed using the E-Prime® platform at this time. The best solution given current limitations would be to program several different versions of the test based on expected applications (such as those discussed above), and incorporate a very wide range of stimulus presentation times (e.g., 3000ms to 200ms for the AntiSaccade, 2000ms to 100ms for the Express and Reflexive) from which the adaptive testing paradigm could sample. Researchers interested in employing the smooth pursuit and saccade tests in their studies are encouraged to contact the author for the most recent version of the tests.

In conclusion, the results from this dissertation project support the further development of the present oculomotor battery. In their current form, the behavioral tests appear to provide valid measures of smooth pursuit and saccadic eye movements. The tests also show promise as a diagnostic and research tool in patient groups with known oculomotor abnormalities. The next steps in development of the battery involve implementation of the test improvements discussed above and further validation in additional clinical and healthy populations. Pending results from this work, the collection of age-based normative data would make the test battery appropriate for use in clinical neuropsychological examinations.

FIGURES

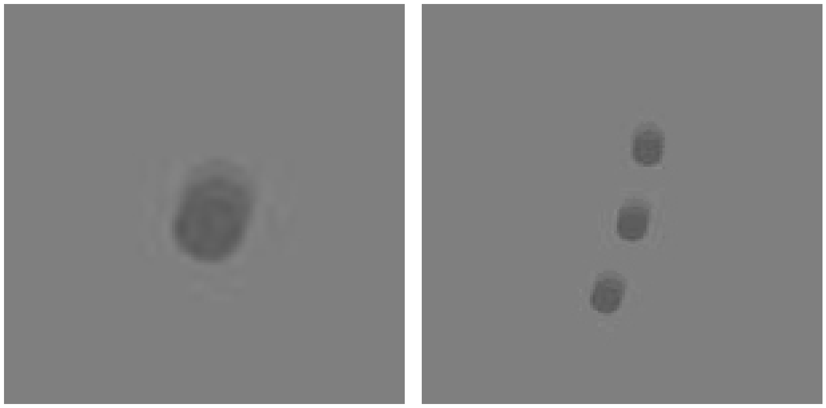


Figure 1. Use of motion sub-samples in SPEM baseline stimuli. The two sub-samples are visible in Image #1, which is an enlargement of the target. Image #2 is an overlay of three consecutive frames, where the distance between the sub-samples and previous target location can be observed.

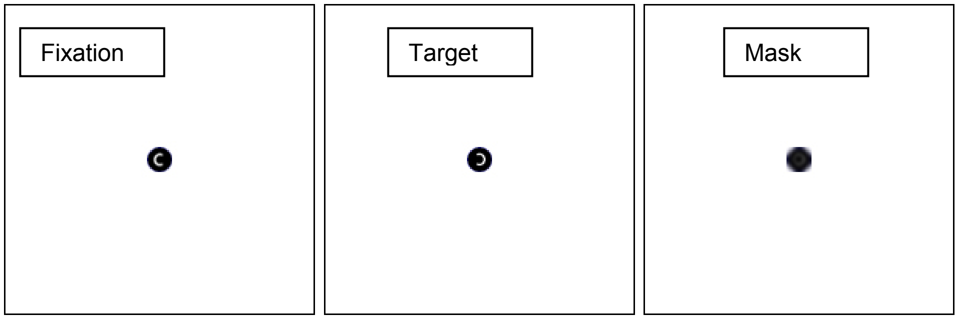


Figure 2a. Sequence of screen images from the Fixation test.

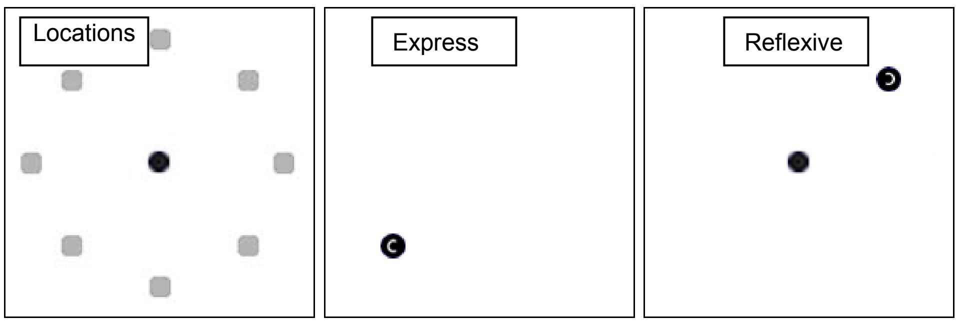


Figure 2b. Express and Reflexive saccade test. In the Express test, the central fixation point disappears 200ms prior to presentation of the target; In the Reflexive test, the fixation point remains throughout.

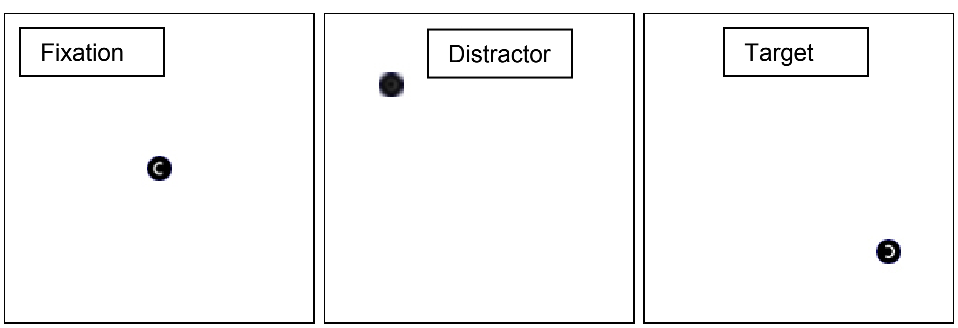


Figure 2c. Anti-Saccade test. A distractor stimuli is presented in the opposite corner of the screen from where the target will appear prior to presentation of the target. Subjects are instructed to look for the target in the region opposite from the distractor.

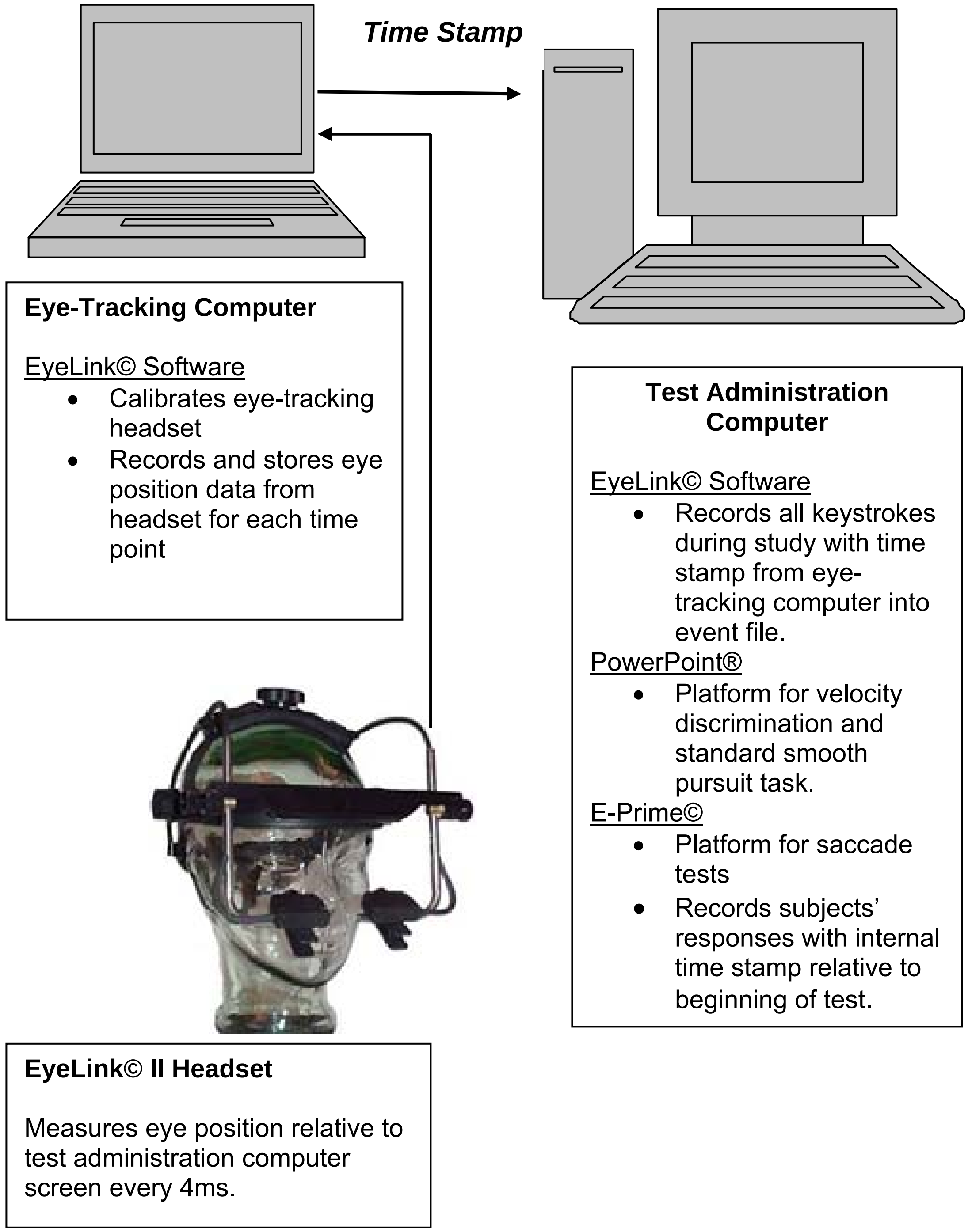


Figure 3. Equipment and software schematic. A time stamp relative to the eye-tracking data was recorded into the event file for all keystrokes and mouse clicks made on the test administration computer except while E-Prime© was running.

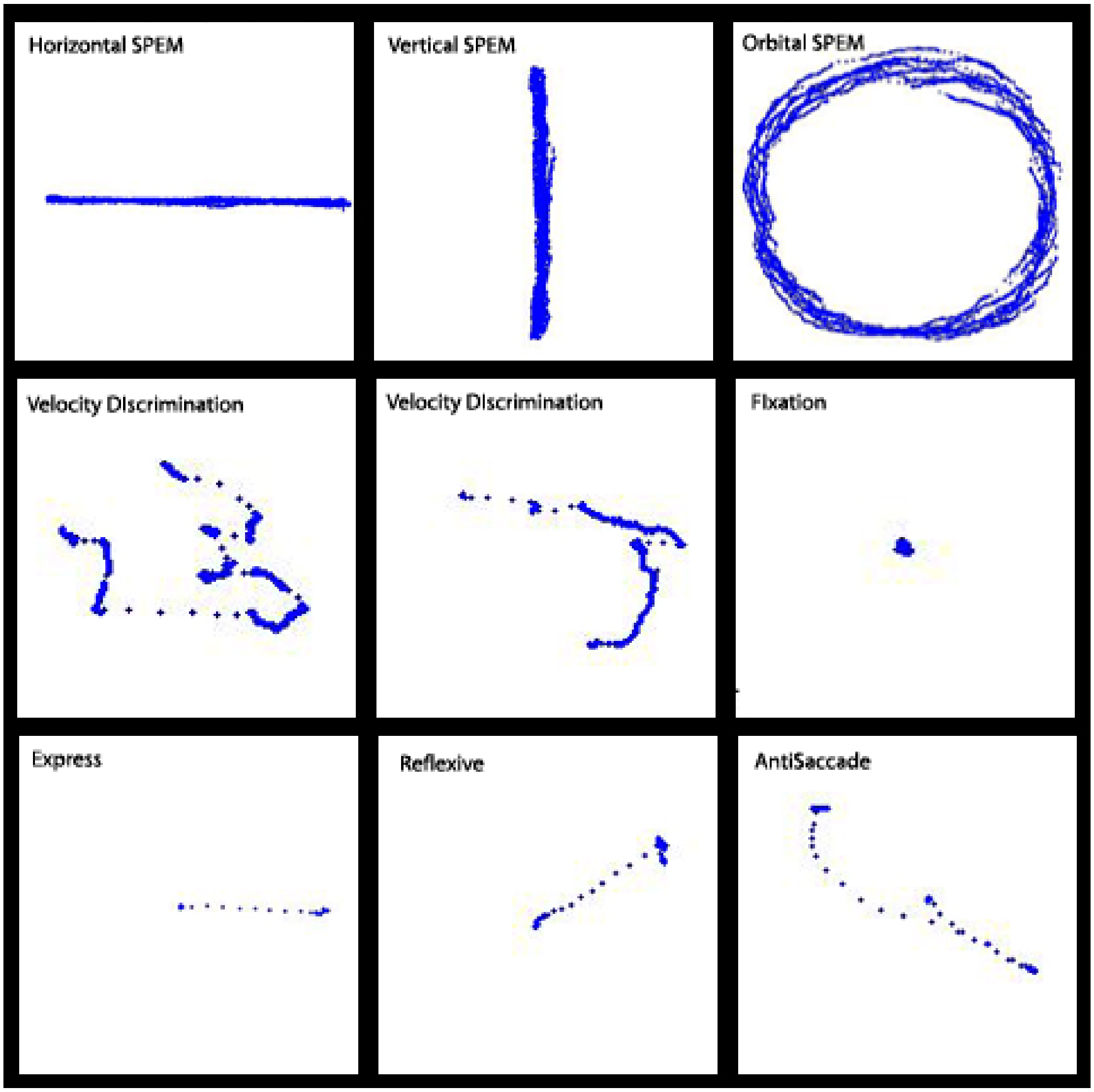


Figure 4. Example eye position traces for the tests (not to common scale).

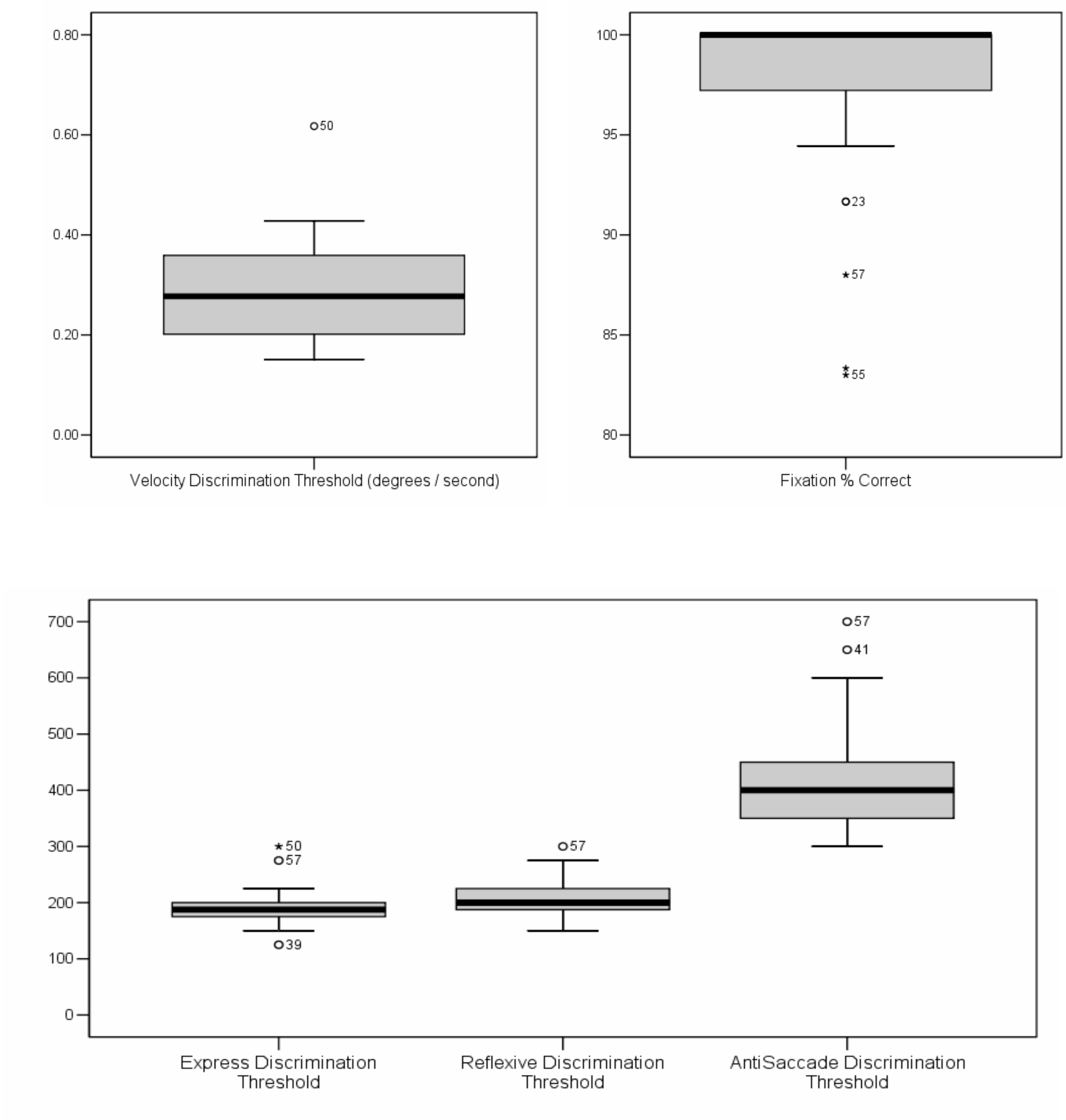


Figure 5. Box-plots for primary behavioral measures, with whiskers at +/- 1.5 times the interquartile range from the median. Outliers (1.5 – 3 times interquartile range) are identified by circles, extreme cases (3^+ x interquartile range) by stars.

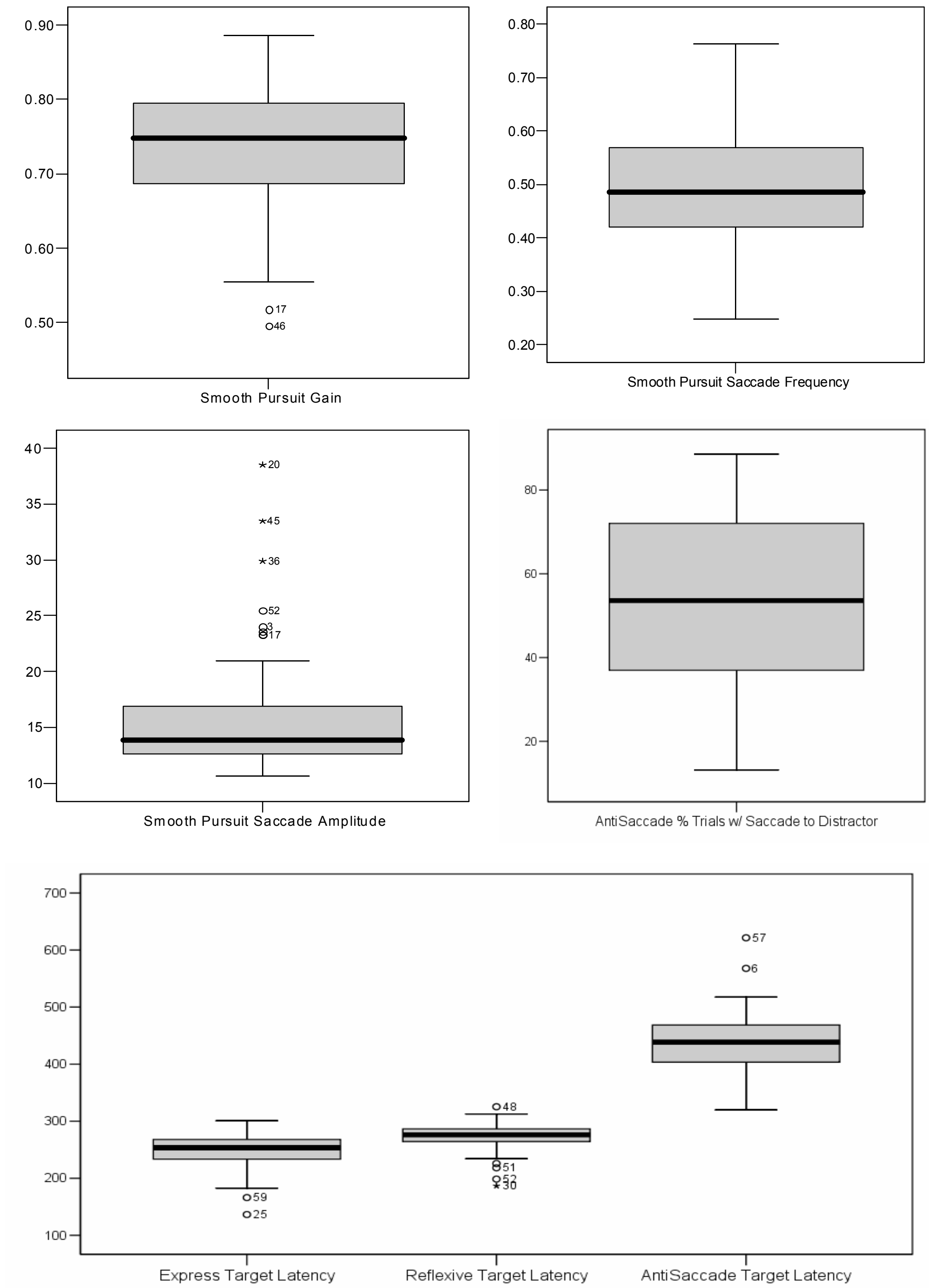


Figure 6. Boxplots for primary eye-tracking measures.

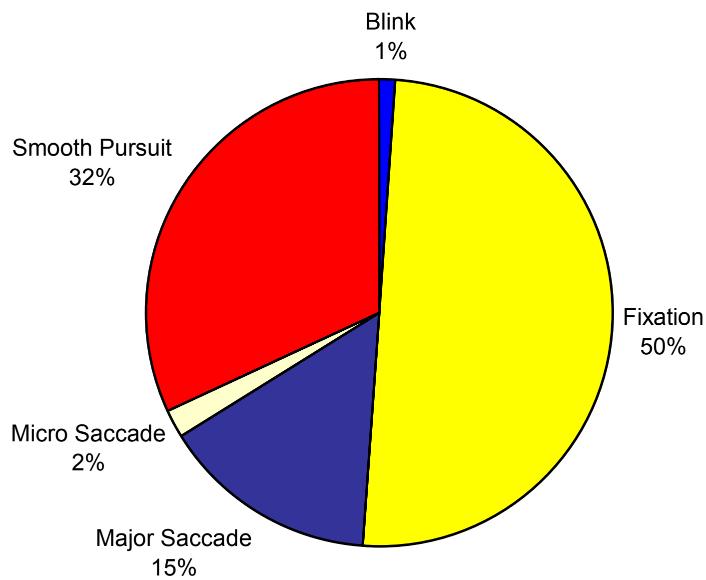


Figure 7. Breakdown of eye movements made during velocity discrimination.

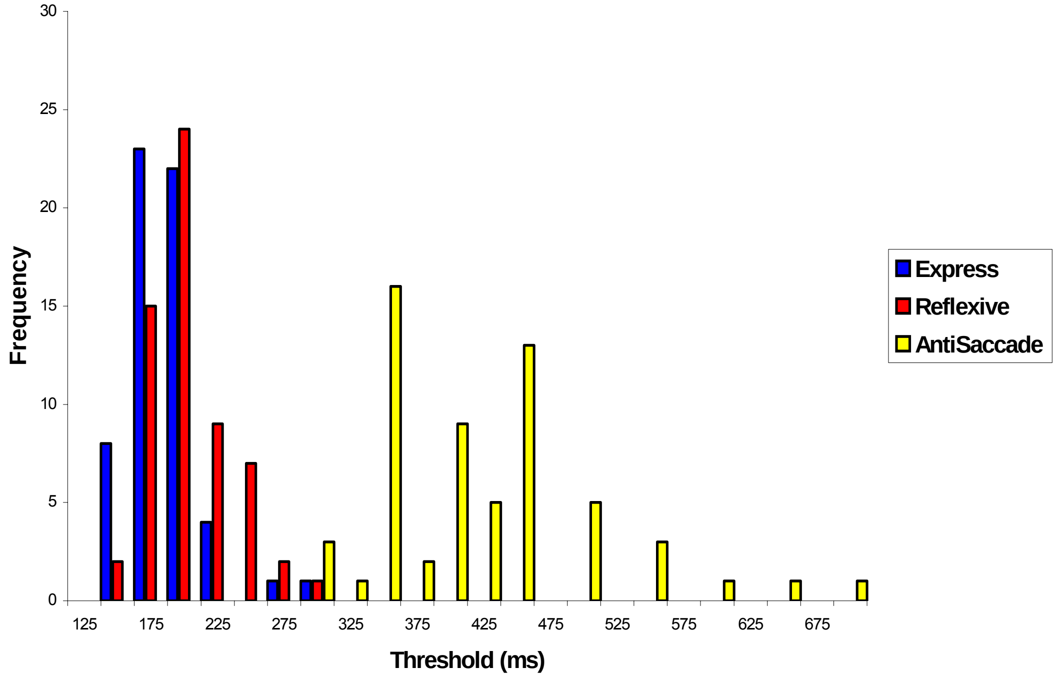


Figure 8. Distributions of discrimination thresholds for the saccade tests.

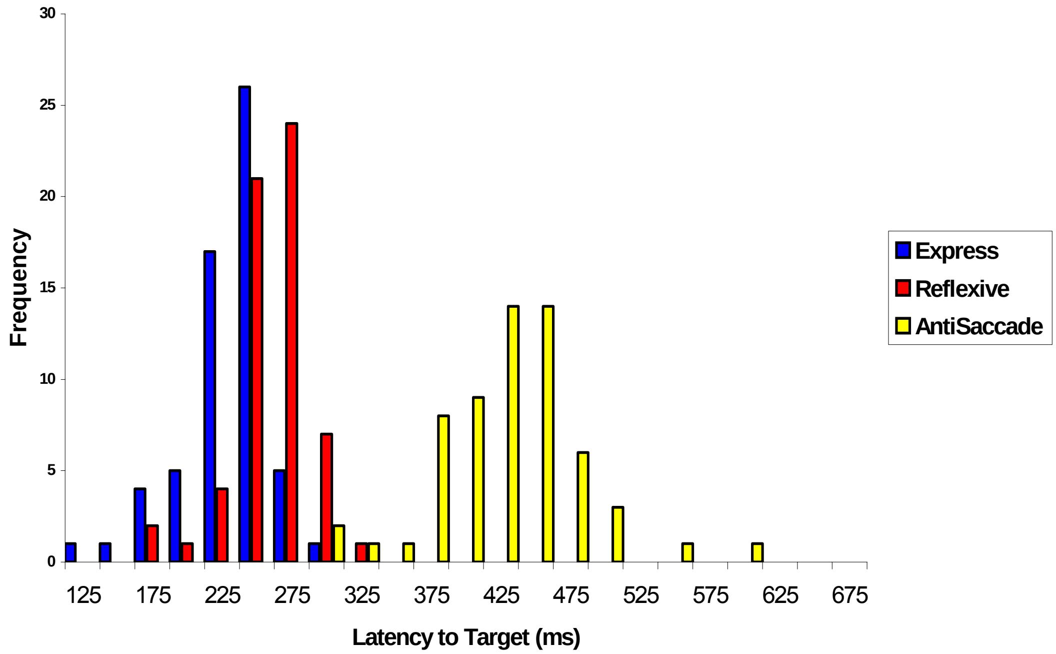
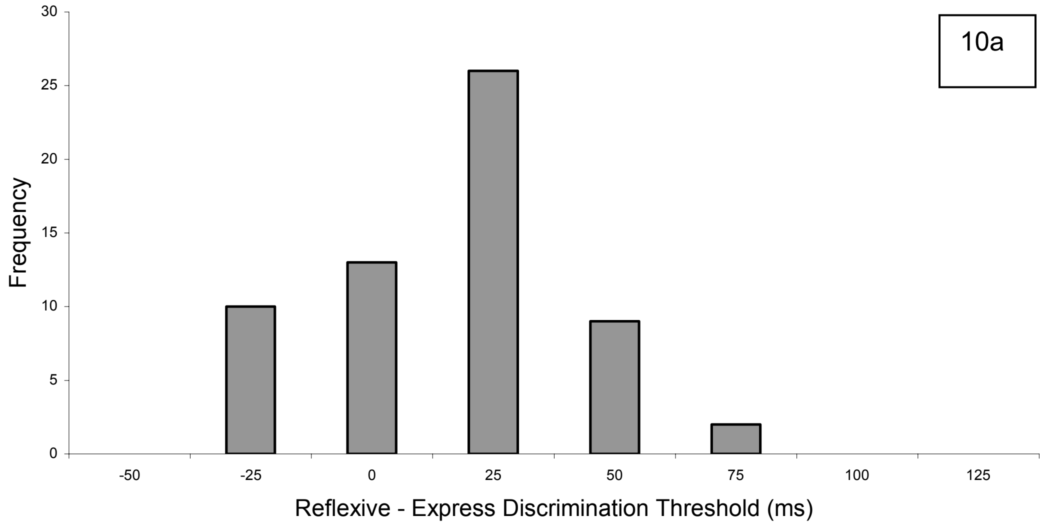


Figure 9. Distributions of mean latency for eyes to reach target in the saccade tests.



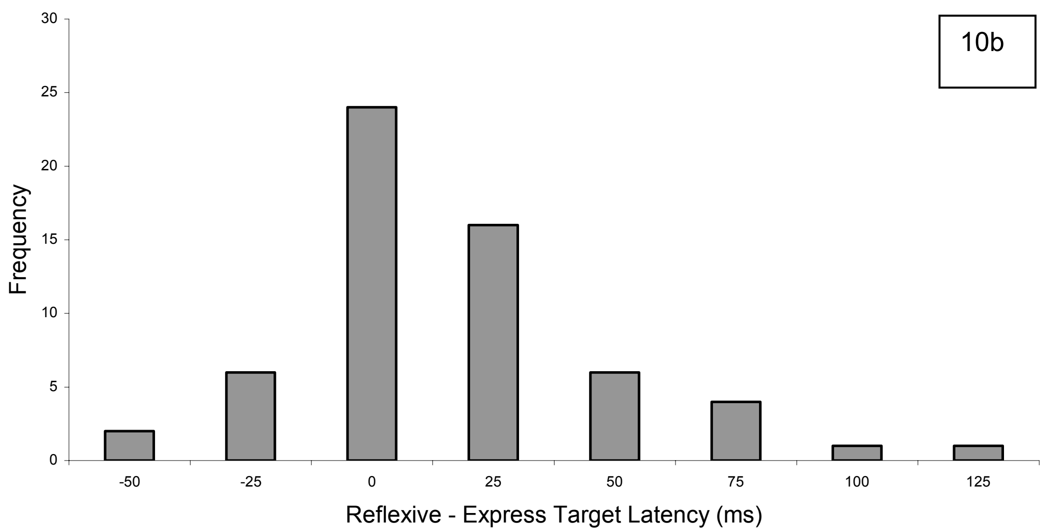


Figure 10. Distributions of differences for Reflexive versus Express discrimination threshold (10a) and latency for eye movement to target (10b).

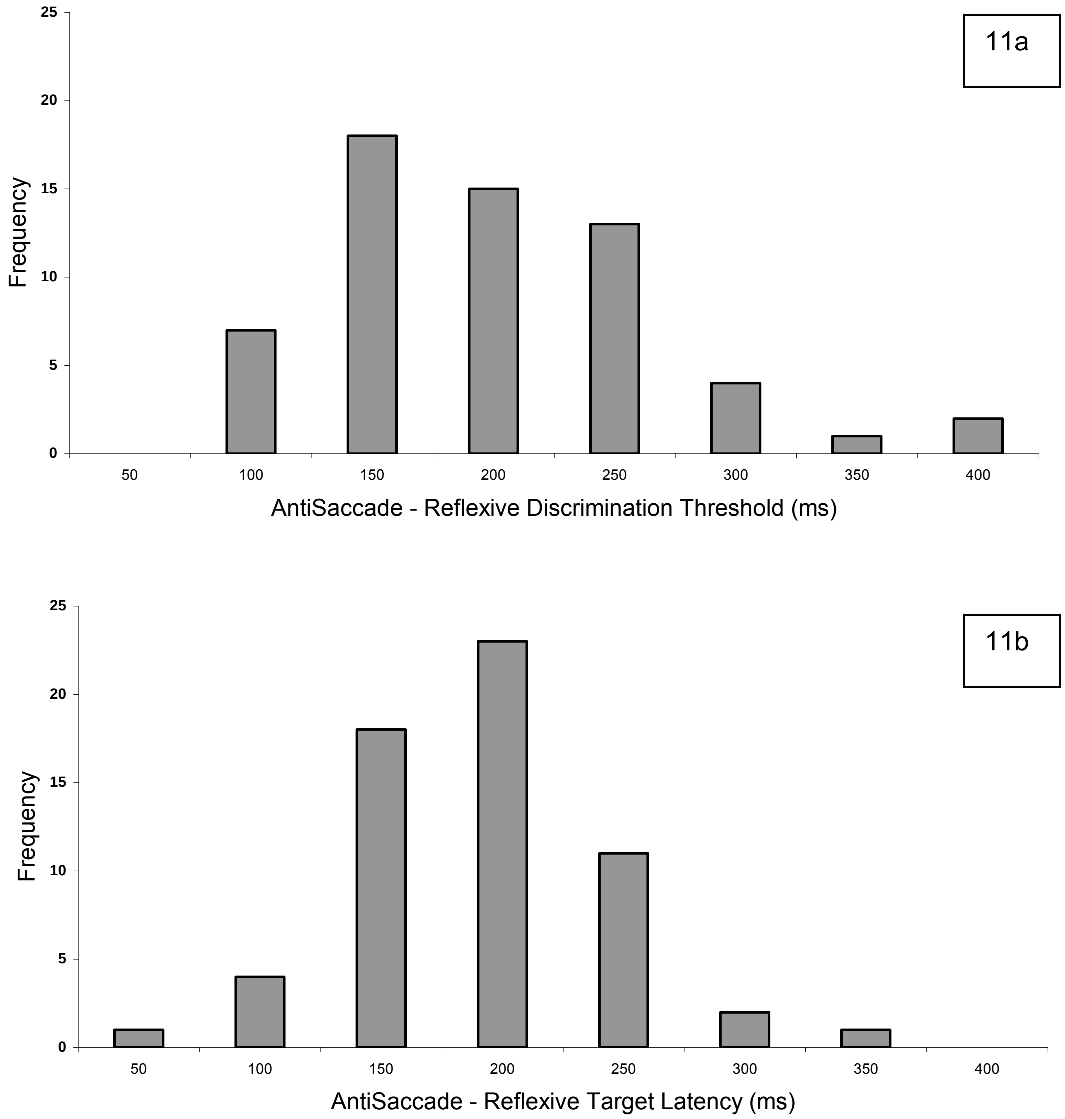


Figure 11. Distributions of differences for AntiSaccade versus Reflexive discrimination threshold (11a) and latency for eye movement to target (11b).

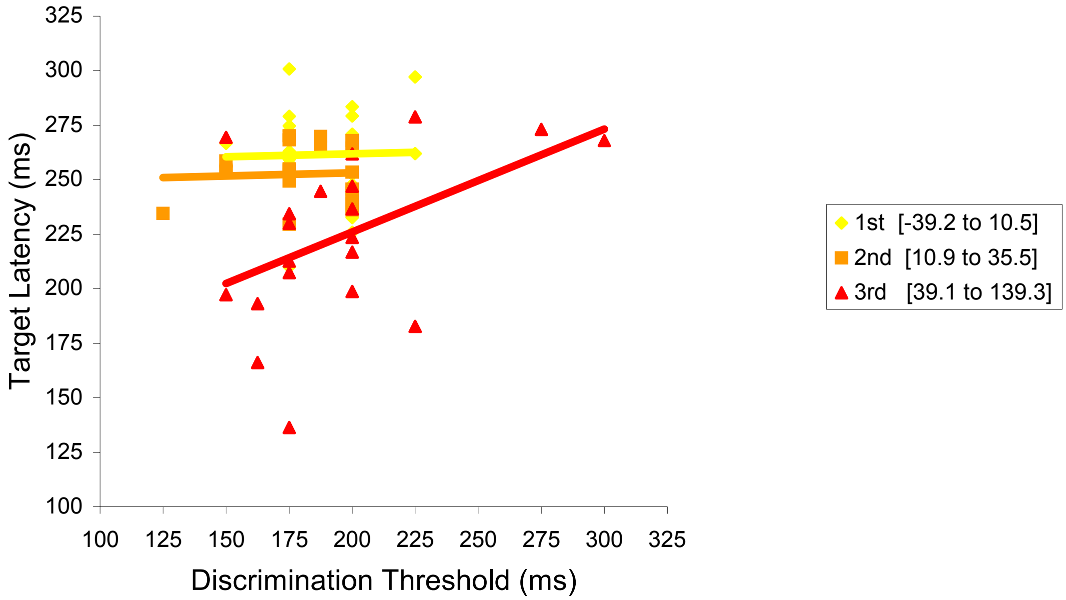


Figure 12. Scatterplot with linear trends of relationships between Express discrimination threshold and target latency for three subgroups (n=20) based on ranked differences between observed Reflexive and Express target latency.

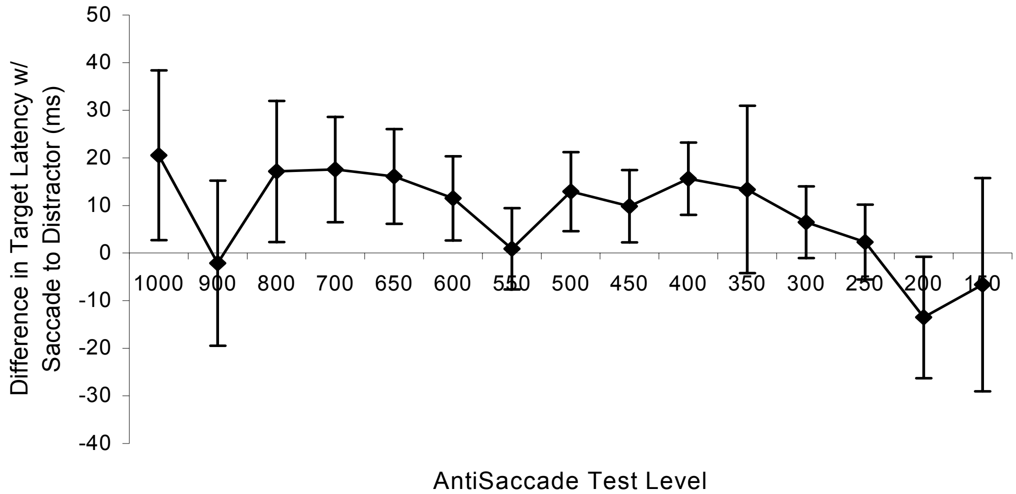


Figure 13. Impact of a saccade to the distractor on target latency for the AntiSaccade test.

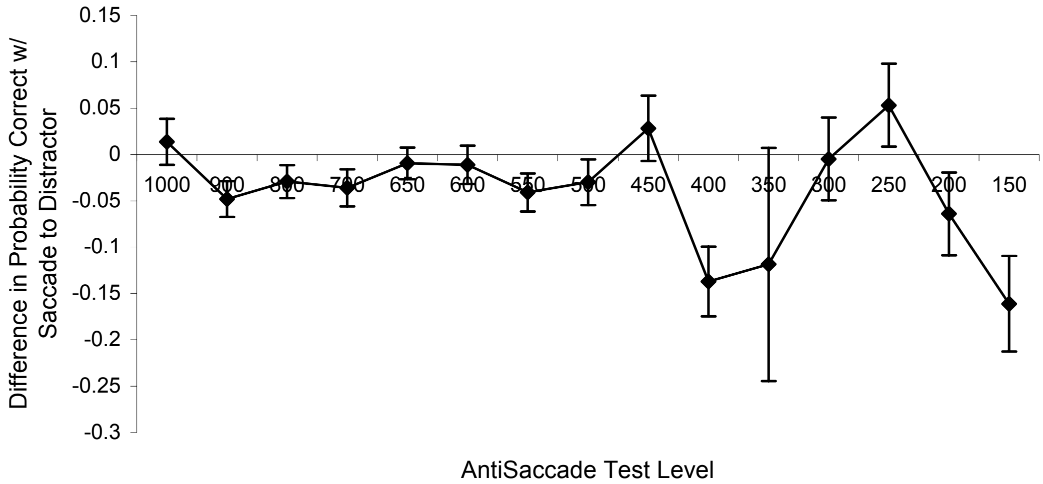


Figure 14. Impact of a saccade to the distractor on probability of a correct response (b) for the AntiSaccade test.

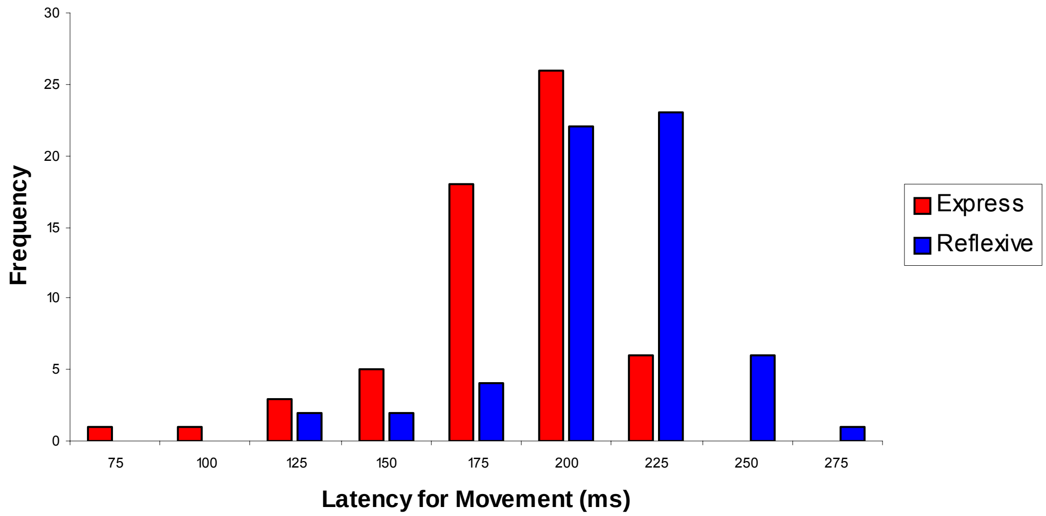


Figure 15. Distributions of initial latency for movement for Express and Reflexive tests.

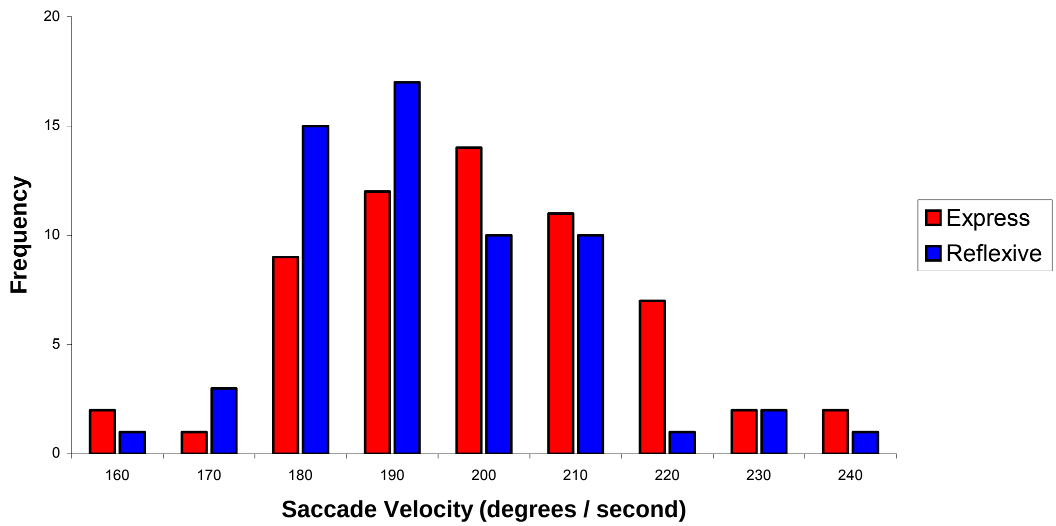


*Figure 16***.** Distributions of saccade velocity for Express and Reflexive tests

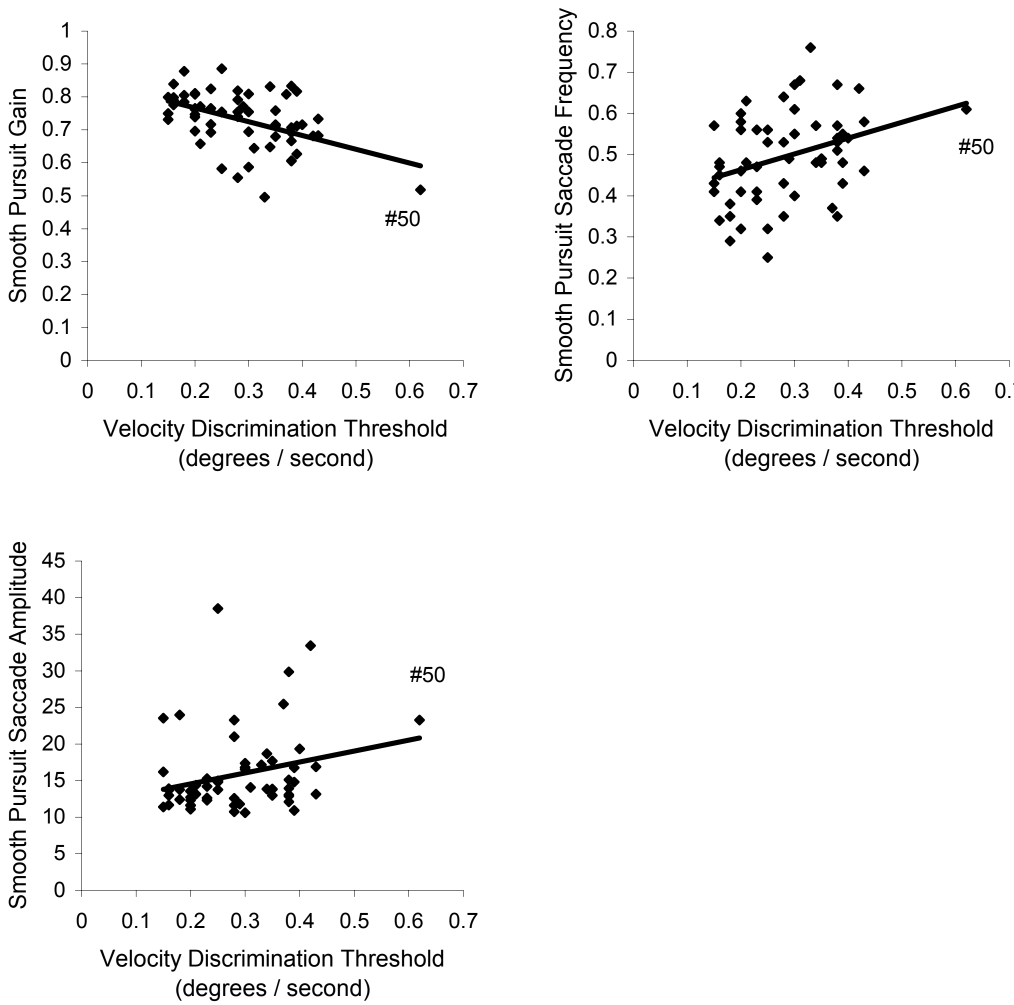


Figure 17. Scatterplots for velocity discrimination threshold and related smooth pursuit measures.

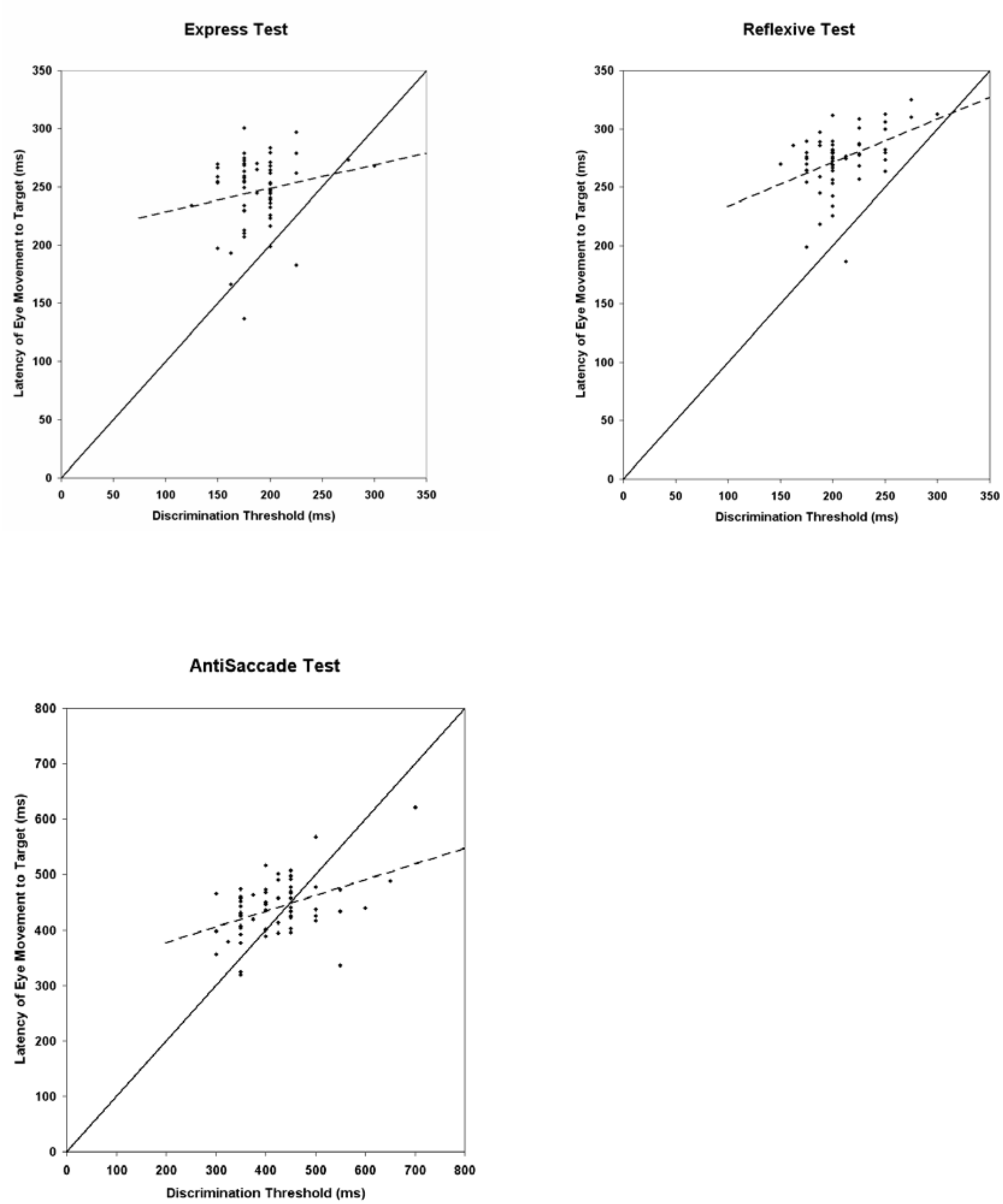


Figure 18. Relationship between discrimination threshold and latency of eye movements to reach target. The solid line represents a theoretical 1:1 relationship; the dashed line represents the observed linear relationship.

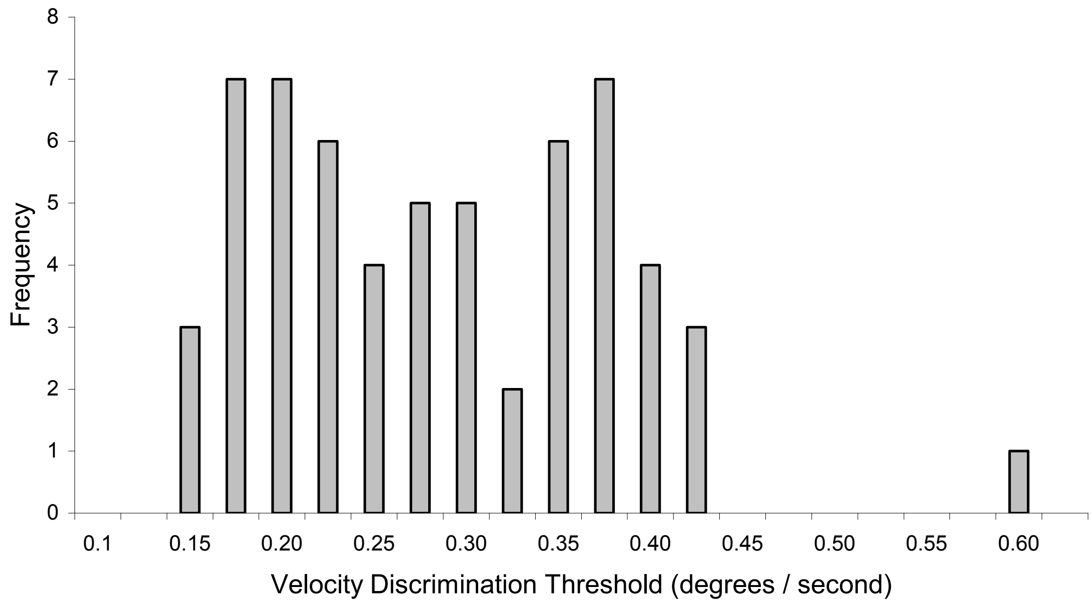


Figure 19. Distribution of velocity discrimination thresholds.

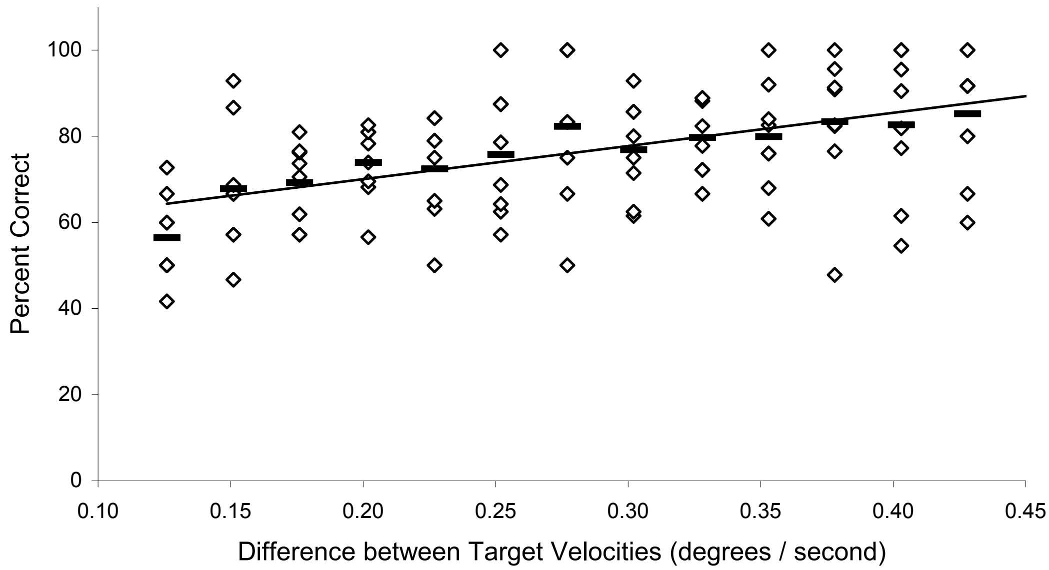


Figure 20. Observed difficulty at each level of velocity discrimination. Individual items are indicated by a hollow diamond, mean difficulty is shown with a solid horizontal line, and the linear trend is indicated by the solid line.

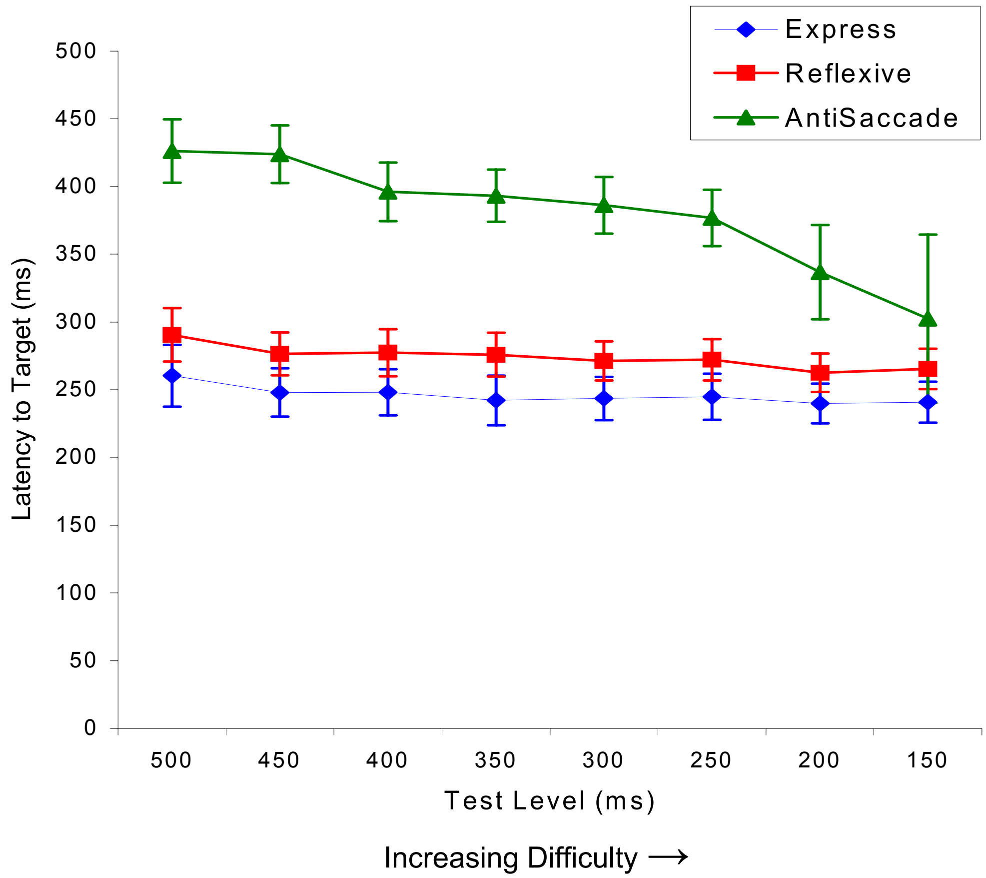


Figure 21. Latency for fovea to reach target for common difficulty levels of the saccades tests. Error bars represent 95% confidence intervals.

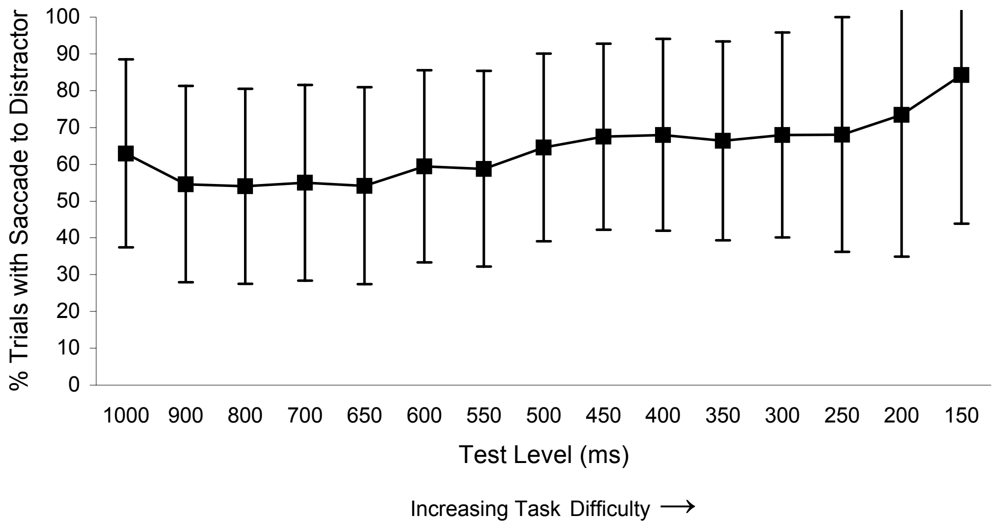


Figure 22. Incidence of saccades made to the distractor stimulus by AntiSaccade test level. Error bars represent 95% confidence intervals.

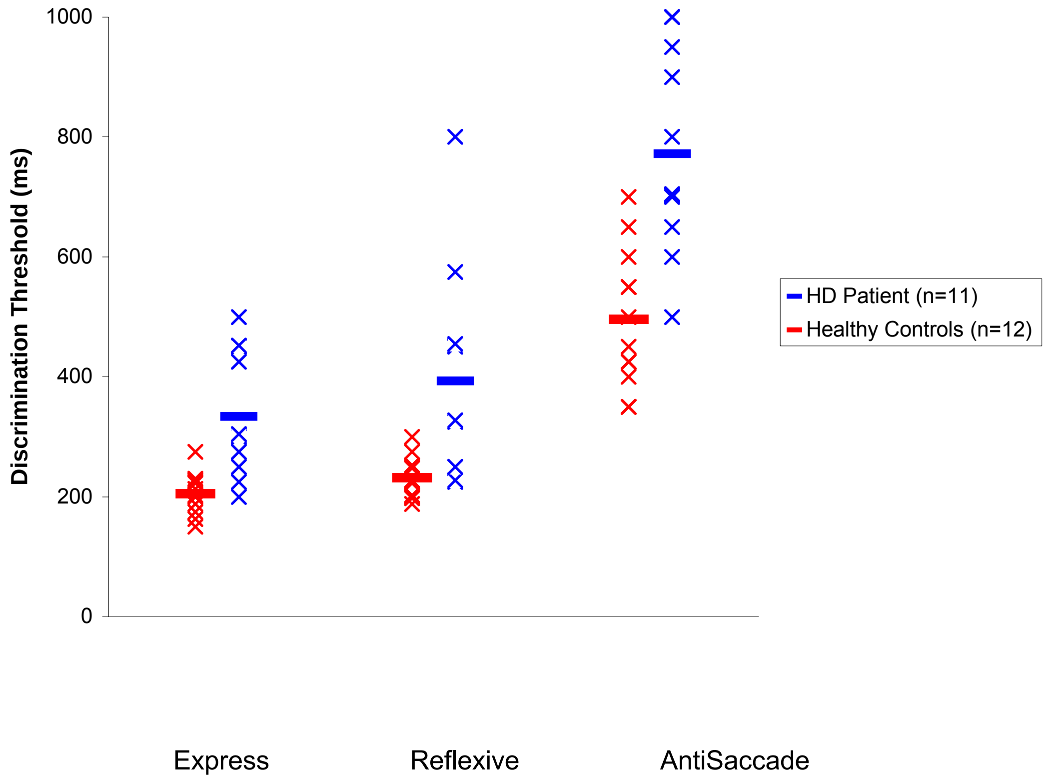


Figure 23. Discrimination thresholds on the saccade tests by group. Means are indicated by a solid line, individual cases are denoted by an ‘x’.

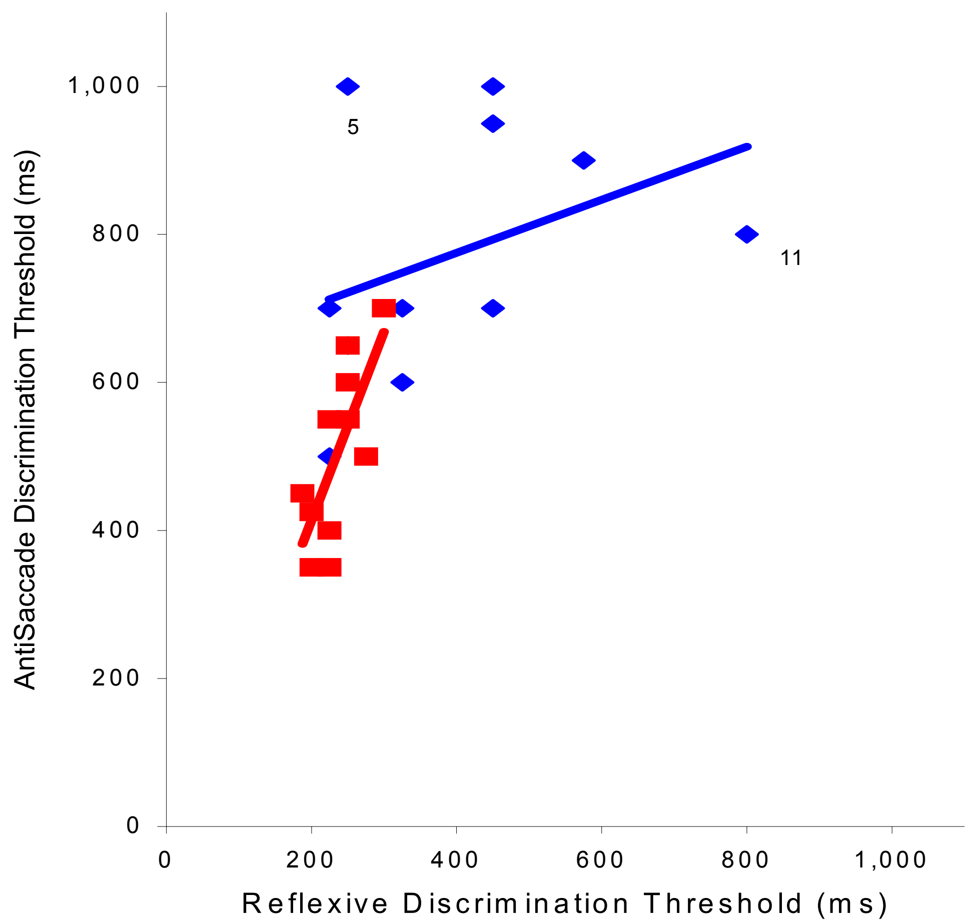
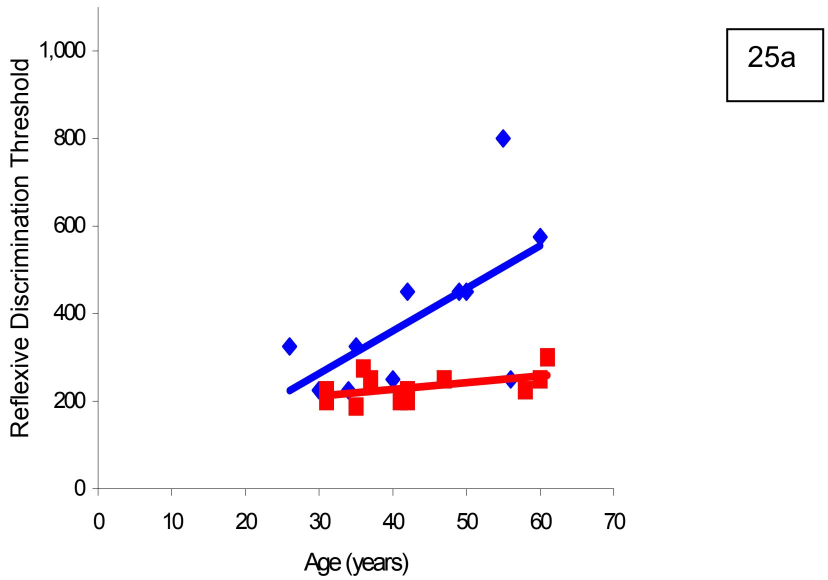


Figure 24. Scatterplot of relationships between Reflexive and AntiSaccade discrimination thresholds for the healthy control (red) and HD patient group (blue). Two patients cases with apparent influence on the regression surface are labeled by number.



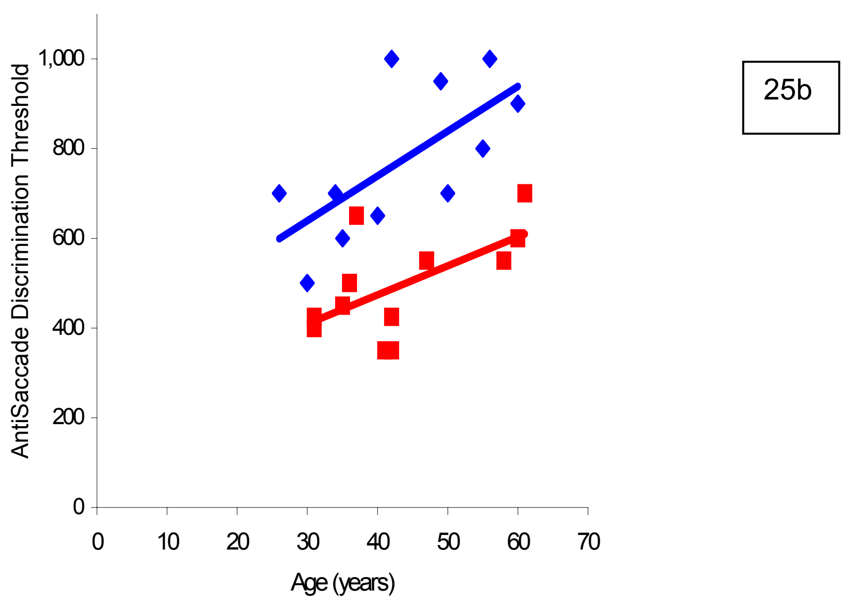


Figure 25. Scatterplots of relationships for age versus Reflexive and AntiSaccade discrimination threshold in healthy controls (red) and HD patients (blue).

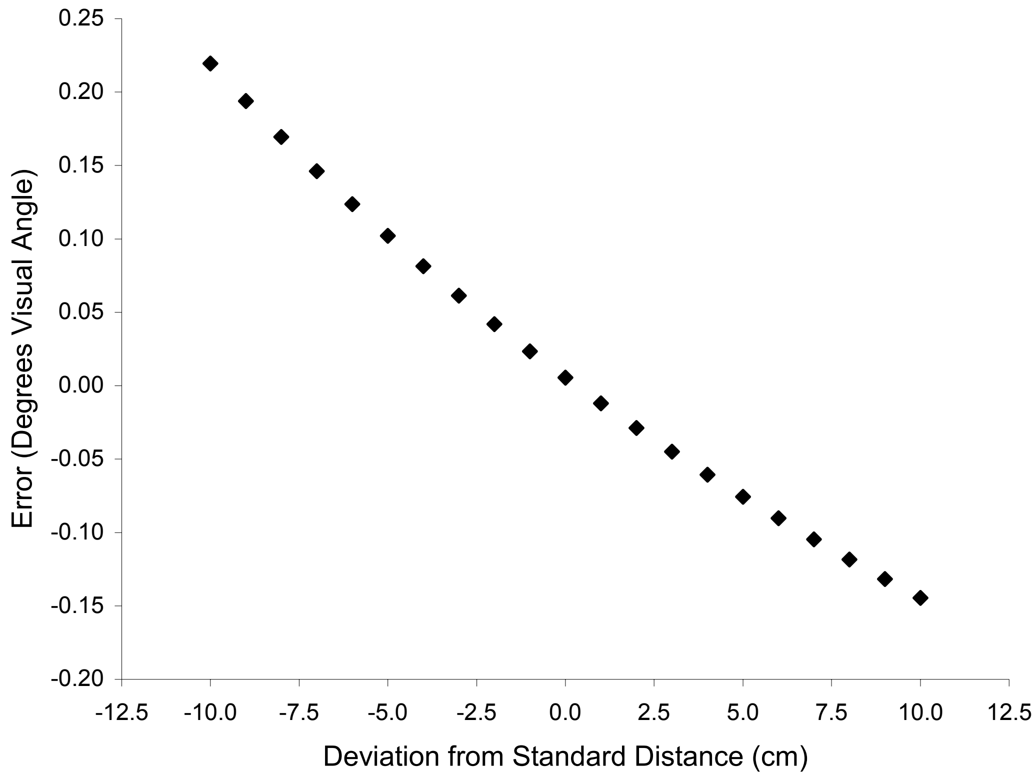


Figure 26. Amount of error in eye-tracking measures by deviation from the standard distance of 57cm. The equation for relating degrees of visual angle per centimeter of screen based on distance from screen is given by:

Visual Angle (degrees) = 180 x (tan(1 / distance from screen)) / pi

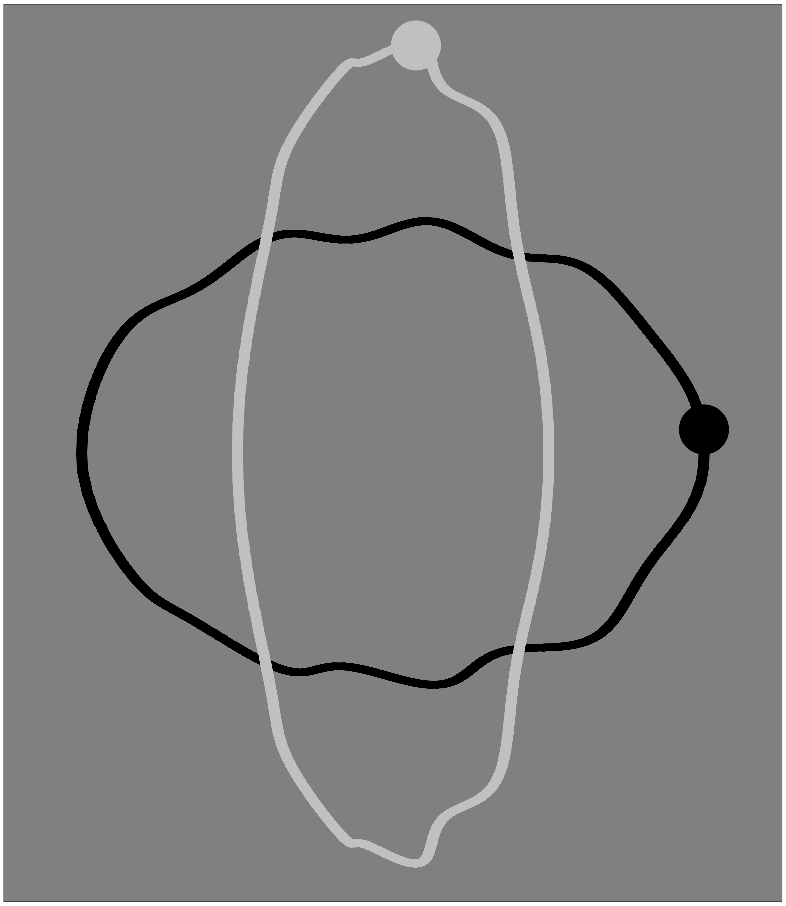


Figure 27. Paths of light and dark discs with concentric orbits based on unique elliptical parameters and random sinusoidal variance.

TABLES

Table 1.

Matrix for testing convergent and discriminant validity. Primary correlations for convergent validity are boxed.

Measure	Velocity Discrimination Threshold	Express Discrimination Threshold	Reflexive Discrimination Threshold	AntiSaccade Discrimination Threshold
Smooth Pursuit Gain	negative	-	-	-
Smooth Pursuit Saccades / Second	positive	-	-	-
Smooth Pursuit Saccade Amplitude	positive	-	-	-
Express Latency to Target	-	positive	-	-
Reflexive Latency To Target	-	-	positive	-
AntiSaccade Latency to Target	-	-	-	positive
AntiSaccade Saccades to Distractor	-	-	-	positive

Table 2.

Mean percent of items (SD) excluded from movement analysis by criteria.

Criteria	Reflexive	Express	AntiSaccade
No Saccade	8.8 (6.3)	11.4 (7.1)	19.5 (5.0)
Anticipatory Saccade	8.6 (5.8)	20.1 (7.1)	18.6 (6.7)

Table 3.

Descriptive statistics for primary outcome measures.

Source	Measure	Mean	SD	Median	Range
Behavioral	Velocity Discrimination Threshold (deg /sec)	0.29	0.09	0.28	[.15, .62]
	Fixation % Correct	98	4	100	[83, 100]
	Express (ms)	188	28	188	[125, 300]
	Reflexive (ms)	208	30	200	[150, 300]
	AntiSaccade (ms)	421	82	400	[300, 700]
Eye-Tracking	Smooth Pursuit Gain	0.73	0.08	0.75	[0.5, 0.89]
	Smooth Pursuit Saccades / Second	0.50	0.11	0.49	[0.25, 0.76]
	Smooth Pursuit Saccade Amplitude (a.u.)	15.81	5.52	13.8	[10.6, 38.5]
	Express Target Latency (ms)	246	31	253	[136, 300]
	Reflexive Target Latency (ms)	274	26	276	[187, 325]
	AntiSaccade Target Latency (ms)	439	52	438	[319, 621]
	AntiSaccade % trials w/ Saccades to Distractor	53	21	54	[13, 89]

Table 4.

Internal consistency for primary outcome measures.

Source	Measure	# items	Method	Reliability Estimate
Behavioral	Velocity	24	odd-even	0.92
	Fixation % Correct	36	odd-even	0.65
	Express (ms)	variable	odd-even	0.92
	Reflexive (ms)	variable	odd-even	0.95
	AntiSaccade (ms)	variable	odd-even	0.97
Eye-Tracking	Smooth Pursuit Gain	20	Cronbach's Alpha	0.94
	Smooth Pursuit saccades / second	20	Cronbach's Alpha	0.96
	Smooth Pursuit saccade amplitude	20	Cronbach's Alpha	0.76
	Fixation % fixation obs	35	Cronbach's Alpha	0.90
	Express target latency (ms)	variable	odd-even	0.98
	Reflexive target latency (ms)	variable	odd-even	0.93
	AntiSaccade target latency (ms)	variable	odd-even	0.96
	AntiSaccade % trials w/ saccades to distractor	variable	odd-even	0.94

Table 5.

Intercorrelations between behavioral measures.

Measure	Fixation	Express	Reflexive	AntiSaccade
Velocity Discrimination	-.176	.312*	.301*	.290*
Fixation		-.495**	-.295*	-.289*
Express			.584**	.517**
Reflexive				.587**

** = significant at p<.05 level; ** = significant at p<.01 level

Table 6.

Intercorrelations between eye-tracking measures

Measure	Smooth Pursuit Saccade Frequency	Smooth Pursuit Saccade Amplitude	Express Latency to Target	Reflexive Latency To Target	AntiSaccade Latency to Target	AntiSaccade Saccades to Distractor
Smooth Pursuit Gain	-.808**	-.402**	-.175	-.183	-.202	-.155
Smooth Pursuit Saccade Frequency		.272*	.246	-.002	.114	.127
Smooth Pursuit Saccade Amplitude			.132	.076	.290*	.12
Express Latency to Target				.303*	.395**	.021
Reflexive Latency To Target					.316*	.023
AntiSaccade Latency to Target						.067

** = significant at p<.05 level; ** = significant at p<.01 level

Table 7.

Intercorrelations between performance and eye-tracking measures during velocity discrimination.

Measure	Fixation	Major Saccades	Micro Saccades	Smooth Pursuit	Blinks
Velocity Discrimination Threshold	-.277*	.254	.087	.201	.161
Fixation		-.836**	.027	-.897**	-.480**
Major Saccades			-.265	.618**	.325*
Micro Saccades				.014	-.163
Smooth Pursuit					.177

** = significant at p<.05 level; ** = significant at p<.01 level

Table 8.

Correlations for convergent and discriminant test validity (r>.33, p<.01). The primary correlations for convergent validity are boxed.

Measure	Velocity Discrimination Threshold	Express Discrimination Threshold	Reflexive Discrimination Threshold	AntiSaccade Discrimination Threshold
Smooth Pursuit Gain	-.510	-	-.343	-
Smooth Pursuit Saccades / Second	.363	-	-	-
Smooth Pursuit Saccade Amplitude	-	-	-	-
Express Latency to Target	-	-	-	-
Reflexive Latency To Target	-	-	.457	-
AntiSaccade Latency to Target	-	-	.375	.463
AntiSaccade Saccades to Distractor	-	-	.331	.423

Table 9.

Statistical testing of dependent correlations for discriminant validity.

Behavioral	Convergent Correlation	vs Discriminant Correlation	z	Probability
Velocity Discrimination Threshold (VDT)				
	Smooth Pursuit Gain	Reflexive Target Latency	-1.35	ns
	Smooth Pursuit Gain	AntiSaccade Target Latency	-2.69	p=.004
	Smooth Pursuit Gain	AntiSaccade Saccades to Distractor	-2.09	p=.018
	Smooth Pursuit Saccade Freq.	Reflexive Target Latency	0.38	ns
	Smooth Pursuit Saccade Freq.	AntiSaccade Target Latency	1.47	ns
	Smooth Pursuit Saccade Freq.	AntiSaccade Saccades to Distractor	1.05	ns
Reflexive Discrimination Threshold (RDT)				
	Reflexive Target Latency	Smooth Pursuit Gain	-0.69	ns
	Reflexive Target Latency	Smooth Pursuit Saccade Freq.	-1.44	ns
	Reflexive Target Latency	AntiSaccade Target Latency	-0.52	ns
	Reflexive Target Latency	AntiSaccade Saccades to Distractor	-2.38	p=.008
AntiSaccade Discrimination Threshold (ASDT)				
	AntiSaccade Target Latency	Smooth Pursuit Gain	-1.25	ns
	AntiSaccade Target Latency	Smooth Pursuit Saccade Freq.	-1.39	ns
	AntiSaccade Target Latency	Reflexive Target Latency	-0.95	ns
	AntiSaccade Saccades to Distractor	Smooth Pursuit Gain	-0.93	ns
	AntiSaccade Saccades to Distractor	Smooth Pursuit Saccade Freq.	-1.11	ns
	AntiSaccade Saccades to Distractor	Reflexive Target Latency	-0.54	ns

Table 10.

Correlations between behavioral and eye-tracking components of the Reflexive and Express tests.

Measure	Express Target Latency	Express Latency of Movement	Express Saccade Velocity	Reflexive Disc. Threshold	Reflexive Target Latency	Reflexive Latency of Movement	Reflexive Saccade Velocity
Express Discr. Threshold	0.184	0.167	-0.166	0.584**	0.178	0.178	-0.026
Express Target Latency		0.991**	-0.296*	0.198	0.303*	0.29*	-0.091
Express Latency of Movement			-0.167	0.171	0.293*	0.296*	0.014
Express Saccade Velocity				-0.222	-0.121	0.001	0.786**
Reflexive Discr. Threshold					0.43**	0.419**	-0.072
Reflexive Target Latency						0.988**	-0.103
Reflexive Latency of Movement							0.052

* significant at p<.05 level

** significant at p<.01 level

Table 11

Descriptive statistics for Huntington's Disease patient (n=11) and age-matched healthy control group (n=12) on oculomotor tests.

Measure		Mean	SD	Median	Range
Velocity Discrimination (deg / sec)	Controls	0.30	0.09	0.31	[.15, .43]
	Patients	0.41	0.16	0.38	[.25, .83]
Fixation % Correct	Controls	98	6	100	[83, 100]
	Patients	96	3	97	[92, 100]
Express (ms)	Controls	188	34	207	[150, 275]
	Patients	334	103	300	[200, 500]
Reflexive (ms)	Controls	208	34	225	[187.5, 300]
	Patients	393	178	325	[225, 800]
AntiSaccade (ms)	Controls	421	115	475	[350, 700]
	Patients	773	169	700	[500, 1000]

Appendix A: Velocity Discrimination Stimulus Script

```
% This octave (or matlab) script generates an mpeg file showing two circular targets moving in
a random path at constant velocity for use in the Velocity Discrimination test.
function [] = velocity(speed1,speed2,size,length,filename);
sp1 = num2str([speed1]);
sp2 = num2str([speed2]);
outfile = ([(filename),'.mpg']);   % Name of the mpeg file to be created

% Dimensions of the movie
nrows = size;        % Number of rows in each frame
ncols = size;        % Number of columns in each frame
nfram = (length*30);% Number of frames
nsub  =   3;         % Number of motion samples per frame

% Description of the objects
bkg   = [0.5 0.5 0.5];     % Background color

% Disk 1 parameters
color1 = [0.75 0.75 0.75];     % Disk color
dirac1 = .4;             % Maximum angle change per step, in radians
veloc1 = speed1;              % Velocity, in percent of screen per step

% Disk 2 parameters
color2 = [0.25 0.25 0.25];     % Disk color
dirac2 = .4;             % Maximum angle change per step, in radians
veloc2 = speed2;             % Velocity, in percent of screen per step

% Some other parameters
aar = 2.0;             % Radius of antialiasing psf
xc0 = 0.50 * ncols;     % Center of the universe
yc0 = 0.50 * nrows;
rmx = 0.25 * nrows;     % Radius of containment circle
rmd = 5;              % Variance multiplier outside containment

% Coordinate mesh for computations
[xx, yy] = meshgrid(1:ncols, 1:nrows);

% Disk 1: initial conditions
dir1 = 0.0;
xc1 = 0.40 * ncols;
yc1 = 0.50 * nrows;
rc1 = nrows/40;

% Disk 2: initial conditions
dir2 = 0.0;
xc2 = 0.60 * ncols;
yc2 = 0.50 * nrows;
rc2 = nrows/40;

% Loop over the frames
for t = 1:nfram
printf("Frame %d:  ", t); fflush(stdout);
```

```
% Draw the background
        printf("drawing..."); fflush(stdout);
        red = bkg(1)*ones(nrows, ncols);
        grn = bkg(2)*ones(nrows, ncols);
        blu = bkg(3)*ones(nrows, ncols);
% Disk 1: equations of motion
        out = (xc1-xc0)*cos(dir1) + (yc1-yc0)*sin(dir1);
        r = sqrt((xc1-xc0)^2+(yc1-yc0)^2);
        if (r > rmx && out > 0)
                dir1 = dir1 + rmd*dirac1*(rand()-0.5);
        else
                dir1 = dir1 + dirac1*(rand()-0.5);
        end
        xc1 = xc1 + veloc1 * ncols * cos(dir1);
        yc1 = yc1 + veloc1 * nrows * sin(dir1);
% Disk 1:drawing
        mask = zeros(nrows, ncols)
        rad = sqrt((xx-xc1).^2 + (yy-yc1).^2);
        mask = mask + max(0.0, min(1.0, (rc1-rad)./aar));
        cmask = 1.0-mask;
        red = cmask.*red + mask.*color1(1);
        grn = cmask.*grn + mask.*color1(2);
        blu = cmask.*blu + mask.*color1(3);

% Disk 2: equations of motion
        out = (xc2-xc0)*cos(dir2) + (yc2-yc0)*sin(dir2);
        r = sqrt((xc2-xc0)^2+(yc2-yc0)^2);
        if (r > rmx && out > 0)
                dir2 = dir2 + rmd*dirac2*(rand()-0.5);
        else
                dir2 = dir2 + dirac2*(rand()-0.5);
        end
        xc2 = xc2 + veloc2 * ncols * cos(dir2);
        yc2 = yc2 + veloc2 * nrows * sin(dir2);
% Disk 2: drawing
        mask = zeros(nrows, ncols);
        rad = sqrt((xx-xc2).^2 + (yy-yc2).^2);
        mask = mask + max(0.0, min(1.0, (rc2-rad)./aar));
        cmask = 1.0-mask;
        red = cmask.*red + mask.*color2(1);
        grn = cmask.*grn + mask.*color2(2);
        blu = cmask.*blu + mask.*color2(3);

% Write this frame to a temporary image file
        printf("saving..."); fflush(stdout);
        fname = sprintf("frame-%04d.ppm", t);
        writeppm(fname, red, grn, blu);
        printf("done.\n"); fflush(stdout);
end

% Specialize the generic mpeg param file
cmd = sprintf("sed 's/@nframes@/%04d/' mover.param.in | sed 's/@outfile@/%s/' >
mover.param", nfram, outfile);
```

```
system(cmd);

% Convert to mpeg and delete temporary image files
system("mpeg_encode mover.param")
system("rm frame-*.ppm");
```

Appendix B: Orbital Stimulus Script

```
% This octave (or matlab) script generates an mpeg file showing a
% single ball moving in a circular path at constant or dynamic velocity.
function [] = orbit(speed,numorb);
nrows = 600;       % Number of rows in each frame
ncols = 600;       % Number of columns in each frame
nsub  = 3;       % Number of motion samples per frame
norbits = numorb;      %Number of orbits in movie
radius = .4;       %percent of screen for radius
contrast = .25;
c1 = (contrast/2);

% Description of the background
bkg  = [(.5) (.5) (.5)];     % Background color

% Disk parameters
color1 = [(.5-c1) (.5-c1) (.5-c1)];     % Disk color
veloc = speed;             % Velocity, in revolutions per second
accel = 0;            %change in velocity, in revolutions per second squared
rveloc = 0;               %change in radius of disk, in percent of screen per step
raccel = 0;          %change in change of radius of disk, in percent of screen per step

% Disk 1: initial conditions
inity = ncols/2;
initx = (nrows/2)+(radius);
dsksize = .01;               %percentage of #cols

preffile = 'orbit';   % Name of the mpeg file to be created
xvp = num2str(veloc);
outfile = ([(preffile), "_v", (xvp), ".mpg"]);

% Coordinate mesh for computations; order of arguments not what is expected!
[xx, yy] = meshgrid(1:ncols, 1:nrows);
dsksize = dsksize*ncols;
rc1 = dsksize;
aar = 1;             % Radius of antialiasing psf
nfram =  30*(norbits / veloc);
start = (radius*nrows);
inity = nrows/2;
initx = ncols/2;
xc1=inity;
yc1=inity;
rc1=1;

% Loop over the frames
for t = 0:nfram
        printf("Frame %d:  ", t); fflush(stdout);
        printf("drawing..."); fflush(stdout);
        red = bkg(1)*ones(nrows, ncols);
        grn = bkg(2)*ones(nrows, ncols);
        blu = bkg(3)*ones(nrows, ncols);
        oxc1=xc1;
```

```
        oyc1=yc1;
        orc1=rc1;
        xchange=cos((t*norbits)/(nfram/2/3.141));
        ychange=sin((t*norbits)/(nfram/2/3.141));
        xc1 = initx+(start*xchange);
        yc1 = inity+(start*ychange);
        rc1 = (dsksize + (t * rveloc * dsksize) + (t * t * raccel * dsksize));
        difx = .1 * (xc1-oxc1);
        dify = .1 * (yc1-oyc1);
        difr = .1 * (rc1-orc1);
%Disk: drawing, with sub-sampling for motion blur
        mask = zeros(nrows, ncols);
        for is = 0:(nsub);
                backstep = is - nsub;
                dark = (is/nsub);
% adjusts blurring to new-weighted average of old and new positions
                ixc = xc1 + (backstep * difx);
                iyc = yc1 + (backstep * dify);
                irc = rc1 + (backstep * difr);
                rad = sqrt((xx-ixc).^2 + (yy-iyc).^2);
                shape = min((dark), (irc-rad));
                mask = max(0, shape);
                cmask = 1 - mask;
                red = cmask.*red + mask.*color1(1);
                grn = cmask.*grn + mask.*color1(2);
                blu = cmask.*blu + mask.*color1(3);
        end
% Write this frame to a temporary image file
        printf("saving..."); fflush(stdout);
        fname = sprintf("frame-%04d.ppm", t);
        writeppm(fname, red, grn, blu);
        printf("done.\n"); fflush(stdout);
end

% Specialize the generic mpeg param file
cmd = sprintf("sed 's/@nframes@/%04d/' mover.param.in | sed 's/@outfile@/%s/' >
mover.param", nfram, outfile);
system(cmd);
% Convert to mpeg and delete temporary image files
system("mpeg_encode mover.param")
system("rm frame-*.ppm");
```

Appendix C: Velocity Discrimination Scoresheet

Velocity discrimination - 1

*For Branching, if subject does not achieve at least 6/8 in a block, stop & go to level in indicated.
If subject acheives level 7, proceed to block 8
**For task, If subject achieves first 5 correct, proceed to next block
**For task, discontinue if less than 6/8 correct in one block, or 6/8 correct in 2 consecutive blocks

Branching						level 1				level 2				level 3			
1_1	L		6_1	D		1_1	D	6_1	L	1_1	D	6_1	D	1_1	D	6_1	D
1_2	D		6_2	L		1_2	L	6_2	D	1_2	L	6_2	L	1_2	L	6_2	D
1_3	D		6_3	L		1_3	L	6_3	L	1_3	D	6_3	D	1_3	L	6_3	L
1_4	L		6_4	L		1_4	L	6_4	D	1_4	D	6_4	L	1_4	D	6_4	L
1_5	D		6_5	L		1_5	D	6_5	D	1_5	L	6_5	D	1_5	L	6_5	L
1_6	D		6_6	D		1_6	D	6_6	L	1_6	L	6_6	L	1_6	D	6_6	D
1_7	L		6_7	D		1_7	D	6_7	D	1_7	D	6_7	D	1_7	D	6_7	D
1_8	L	**D1**	6_8	D	**D6**	1_8	L	6_8	L	1_8	L	6_8	L	1_8	L	6_8	L
2_1	D		7_1	D		2_1	L	7_1	D	2_1	L	7_1	D	2_1	L	7_1	L
2_2	D		7_2	L		2_2	L	7_2	D	2_2	L	7_2	L	2_2	L	7_2	L
2_3	L		7_3	D		2_3	D	7_3	L	2_3	L	7_3	L	2_3	L	7_3	L
2_4	L		7_4	D		2_4	L	7_4	D	2_4	D	7_4	D	2_4	D	7_4	D
2_5	D		7_5	L		2_5	D	7_5	L	2_5	D	7_5	L	2_5	D	7_5	D
2_6	D		7_6	L		2_6	D	7_6	L	2_6	D	7_6	D	2_6	D	7_6	D
2_7	L		7_7	D		2_7	D	7_7	L	2_7	L	7_7	D	2_7	D	7_7	D
2_8	L	**D2**	7_8	L	**D7**	2_8	L	7_8	D	2_8	D	7_8	L	2_8	L	7_8	L
3_1	L					3_1	L	8_1	L	3_1	D	8_1	L	3_1	D	8_1	L
3_2	D					3_2	D	8_2	D	3_2	D	8_2	L	3_2	L	8_2	L
3_3	L					3_3	L	8_3	D	3_3	L	8_3	D	3_3	D	8_3	D
3_4	L					3_4	L	8_4	L	3_4	L	8_4	D	3_4	D	8_4	D
3_5	D					3_5	L	8_5	L	3_5	L	8_5	D	3_5	L	8_5	D
3_6	L					3_6	D	8_6	D	3_6	D	8_6	D	3_6	L	8_6	L
3_7	D					3_7	D	8_7	L	3_7	D	8_7	L	3_7	D	8_7	L
3_8	D	**D3**				3_8	D	8_8	D	3_8	L	8_8	L	3_8	L	8_8	D
4_1	L					4_1	L	9_1	D	4_1	L	9_1	L	4_1	D	9_1	D
4_2	D					4_2	D	9_2	D	4_2	L	9_2	D	4_2	L	9_2	D
4_3	D					4_3	L	9_3	L	4_3	L	9_3	L	4_3	D	9_3	L
4_4	D					4_4	D	9_4	L	4_4	D	9_4	D	4_4	L	9_4	D
4_5	D					4_5	L	9_5	L	4_5	D	9_5	L	4_5	L	9_5	D
4_6	L					4_6	D	9_6	D	4_6	D	9_6	D	4_6	D	9_6	L
4_7	L					4_7	L	9_7	D	4_7	D	9_7	L	4_7	D	9_7	L
4_8	L	**L4**				4_8	D	9_9	L	4_8	L	9_8	D	4_8	L	9_8	L
5_1	D					5_1	D	10_1	L	5_1	D	10_1	L	5_1	D	10_1	D
5_2	D					5_2	D	10_2	D	5_2	D	10_2	L	5_2	D	10_2	L
5_3	L					5_3	L	10_3	L	5_3	L	10_3	L	5_3	L	10_3	D
5_4	D					5_4	D	10_4	D	5_4	L	10_4	D	5_4	L	10_4	L
5_5	L					5_5	L	10_5	L	5_5	D	10_5	D	5_5	L	10_5	L
5_6	L					5_6	D	10_6	D	5_6	L	10_6	D	5_6	L	10_6	D
5_7	L					5_7	L	10_7	D	5_7	D	10_7	D	5_7	D	10_7	L
5_8	D	**L5**				5_8	L	10_8	L	5_8	L	10_8	L	5_8	D	10_8	D

Velocity Discrimination - 2

* If subject achieves first 5 items correct, proceed to next level
** Discontinue if subject does not respond correctly to at least 6/8 items in 2 consecutive levels.

level 4

1_1	L	6_1	L
1_2	L	6_2	L
1_3	D	6_3	D
1_4	L	6_4	L
1_5	D	6_5	L
1_6	D	6_6	D
1_7	L	6_7	D
1_8	D	6_8	D
2_1	L	7_1	D
2_2	L	7_2	L
2_3	D	7_3	D
2_4	D	7_4	D
2_5	L	7_5	L
2_6	D	7_6	D
2_7	L	7_7	L
2_8	D	7_8	L
3_1	D	8_1	L
3_2	L	8_2	L
3_3	D	8_3	L
3_4	L	8_4	D
3_5	D	8_5	D
3_6	L	8_6	L
3_7	L	8_7	D
3_8	D	8_8	D
4_1	L	9_1	L
4_2	D	9_2	L
4_3	D	9_3	D
4_4	D	9_4	L
4_5	L	9_5	L
4_6	L	9_6	D
4_7	L	9_7	D
4_8	D	9_8	D
5_1	L	10_1	L
5_2	L	10_2	D
5_3	D	10_3	L
5_4	D	10_4	D
5_5	D	10_5	D
5_6	D	10_6	D
5_7	L	10_7	L
5_8	L	10_8	L

level 5

1_1	L	6_1	L
1_2	D	6_2	D
1_3	D	6_3	L
1_4	D	6_4	L
1_5	L	6_5	L
1_6	L	6_6	D
1_7	D	6_7	D
1_8	L	6_8	D
2_1	D	7_1	L
2_2	D	7_2	D
2_3	L	7_3	L
2_4	L	7_4	L
2_5	L	7_5	D
2_6	L	7_6	D
2_7	D	7_7	L
2_8	D	7_8	D
3_1	L	8_1	D
3_2	D	8_2	L
3_3	D	8_3	L
3_4	L	8_4	D
3_5	L	8_5	D
3_6	L	8_6	D
3_7	D	8_7	L
3_8	D	8_8	L
4_1	L	9_1	D
4_2	L	9_2	D
4_3	D	9_3	D
4_4	L	9_4	L
4_5	L	9_5	L
4_6	D	9_6	L
4_7	D	9_7	L
4_8	D	9_8	D
5_1	D	10_1	D
5_2	L	10_2	L
5_3	D	10_3	D
5_4	L	10_4	L
5_5	L	10_5	D
5_6	D	10_6	D
5_7	L	10_7	L
5_8	D	10_8	L

level 6

1_1	D	6_1	L
1_2	L	6_2	L
1_3	D	6_3	D
1_4	D	6_4	L
1_5	L	6_5	L
1_6	L	6_6	D
1_7	L	6_7	D
1_8	D	6_8	D
2_1	L	7_1	L
2_2	D	7_2	D
2_3	L	7_3	L
2_4	D	7_4	D
2_5	D	7_5	L
2_6	L	7_6	D
2_7	L	7_7	L
2_8	D	7_8	D
3_1	D	8_1	D
3_2	L	8_2	D
3_3	L	8_3	D
3_4	D	8_4	L
3_5	L	8_5	L
3_6	D	8_6	L
3_7	L	8_7	L
3_8	D	8_8	D
4_1	L	9_1	D
4_2	L	9_2	L
4_3	D	9_3	L
4_4	D	9_4	D
4_5	D	9_5	L
4_6	L	9_6	L
4_7	L	9_7	D
4_8	D	9_8	D
5_1	L	10_1	D
5_2	L	10_2	L
5_3	L	10_3	D
5_4	D	10_4	L
5_5	D	10_5	L
5_6	D	10_6	L
5_7	D	10_7	D
5_8	L	10_8	D

level 7

1_1	L	6_1	L
1_2	L	6_2	L
1_3	D	6_3	D
1_4	L	6_4	L
1_5	D	6_5	L
1_6	D	6_6	D
1_7	L	6_7	D
1_8	D	6_8	D
2_1	L	7_1	D
2_2	D	7_2	L
2_3	L	7_3	D
2_4	D	7_4	D
2_5	L	7_5	L
2_6	L	7_6	D
2_7	D	7_7	L
2_8	D	7_8	L
3_1	D	8_1	L
3_2	L	8_2	L
3_3	L	8_3	L
3_4	D	8_4	D
3_5	D	8_5	D
3_6	D	8_6	L
3_7	L	8_7	D
3_8	L	8_8	D
4_1	L	9_1	L
4_2	L	9_2	L
4_3	D	9_3	D
4_4	L	9_4	L
4_5	D	9_5	L
4_6	D	9_6	D
4_7	L	9_7	D
4_8	D	9_8	D
5_1	L	10_1	L
5_2	D	10_2	D
5_3	L	10_3	L
5_4	D	10_4	D
5_5	D	10_5	D
5_6	D	10_6	D
5_7	L	10_7	L
5_8	L	10_8	L

level 8

1_1	L	6_1	D
1_2	D	6_2	L
1_3	D	6_3	L
1_4	L	6_4	D
1_5	D	6_5	D
1_6	L	6_6	L
1_7	L	6_7	D
1_8	D	6_8	L
2_1	L	7_1	D
2_2	L	7_2	L
2_3	L	7_3	L
2_4	D	7_4	D
2_5	L	7_5	L
2_6	D	7_6	L
2_7	D	7_7	D
2_8	D	7_8	D
3_1	L	8_1	D
3_2	D	8_2	L
3_3	L	8_3	L
3_4	D	8_4	D
3_5	D	8_5	D
3_6	D	8_6	D
3_7	L	8_7	L
3_8	L	8_8	L
4_1	D	9_1	L
4_2	D	9_2	D
4_3	L	9_3	L
4_4	L	9_4	D
4_5	D	9_5	L
4_6	D	9_6	L
4_7	L	9_7	D
4_8	L	9_8	D
5_1	D	10_1	L
5_2	L	10_2	D
5_3	D	10_3	L
5_4	L	10_4	L
5_5	L	10_5	L
5_6	D	10_6	D
5_7	L	10_7	D
5_8	D	10_8	D

Appendix D: Eye-Tracking Analysis

Standard Smooth Pursuit Stimuli

The purpose of the script to analyze eye movements made while viewing the standard smooth pursuit stimuli was to calculate gain of smooth pursuit movement, identify anticipatory and catch-up saccades, calculate the amplitude of catch-up saccades, and count the number of observations identified as smooth pursuit. Only eye movements in the direction of the stimulus were analyzed for the horizontal and vertical trials, while separate measurements were obtained for movements in the horizontal and vertical directions for the orbital task.

The first step in the analysis was to exclude observations obtained during blinks, which were identified by missing pupil data. The next step was to determine the range of movement traveled by the stimuli in degrees of visual angle relative to the subject. Although each subject was positioned 57cm from the computer monitor, movement (e.g., shifting in chair, leaning forward and backward, etc.) was often observed during administration of the protocol. Therefore, a single mathematically defined stimulus amplitude, applied universally, would include an indeterminate amount of error for each subject. To overcome this problem, the amplitude of stimulus movement was approximated for each trial by taking the top and bottom 99^{th} percentile (of 5000 observations) for observed eye position along the given axis. From this, the rate of actual target movement (relative to the subject) at each instant, the maximum rate of movement, and the mean rate over the course of the stimulus presentation were calculated.

To distinguish smooth pursuit from saccade activity, a cut point was determined based on the maximal rate of the target. Although smooth pursuit movement is physiologically limited to the rate of the pursued target, the cut point was set at twice the maximum target rate to account for errors in mpeg frame playback rate, screen refresh rate, and eye position measurement. All observations below the cut point were included for analysis of smooth pursuit movement, all observations greater than 2 times the cut point were marked as saccades, and all observations in between were considered indeterminate and excluded from further analysis. This method is in keeping with the approach described by Gegenfurtner and colleagues (2003). Gain for each trial was calculated by taking the mean rate of all observed smooth pursuit activity and dividing by the actual rate of the target. Visual examination of time series plots showed eye movements to be closely matched to targets with respect to amplitude of movement, time, and velocity.

Saccade activity was further parsed to count the number of anticipatory and catch-up saccades events. If the average rate of the 8 observations (i.e., 32ms) following the end of the saccade series was less than half the mean rate of the stimulus (thereby indicating fixation), an anticipatory saccade was counted; if the average rate was greater than half the mean rate of the stimulus (indicating resumption of smooth pursuit tracking behavior), a catch-up saccade was counted. Counts obtained via visual inspection of time plots for horizontal, vertical, and orbital data corresponded to counts generated by this algorithm.

Velocity Discrimination

Eye movements made during trials 61 through 78 of the smooth pursuit branching test and all trials from the follow-up test were assessed for:

1. Number of blinks
2. Number of fixation observations & periods
3. Number of major saccade observations & events
4. Number of probable microsaccades
5. Conservative estimate of smooth pursuit observations (see above)
6. Mean, median, and standard deviation of velocity for smooth pursuit eye movements.

Blinks were excluded as described above. The distance between consecutive observations was calculated to determine type of eye movement activity. Saccade activity was identified by instantaneous changes that were greater than 1.5 interquartile distances from the median change for each trial. Non-saccade activity was then examined to distinguish fixation from smooth pursuit.

Fixation: Initially, a cut point separating fixation from smooth pursuit was hard-set to 0.5 degrees of visual angle per second, the value utilized by EyeLink© software. However, this cut point failed to identify smooth pursuit activity visible in a trace plot in velocity discrimination and the slower standard smooth pursuit stimuli. Visual inspection of distributions of observed instantaneous velocities did not reveal the presence of a clear smooth pursuit-fixation cut point (i.e., two modes at the lower end of the distribution). Adjustment of the cut point to lower values led to identification of smooth pursuit activity during the Fixation test, a physiological impossibility. The most probable reason that an ideal cut point based on instantaneous rate could not be established is that the slower moving stimuli did not elicit tracking rates that were markedly different from slow drifts in foveal position during the Fixation test in the face of eye position measurement error. To overcome this problem, each point was analyzed with respect to absolute distance traveled over a 36ms period. If movement over this time period amounted to more than 1 degree of visual angle per second (the slowest rate of stimulus movement), smooth pursuit was identified. This method helped reduce the impact of temporally short foveal drifts and increased the likelihood that position measurement errors would cancel out. In a cursory examination of data sets from three participants, the algorithm provided favorable results, as it primarily identified smooth pursuit activity during the standard smooth pursuit standard task and fixation during the Fixation test.

Microsaccades: Eye movement vector information was also incorporated into identification of smooth pursuit movement. Because smooth pursuit eye movement is by definition smooth, consecutive movements with drastic vector changes cannot represent smooth pursuit. Visual inspection of time series plots from pilot data showed the occasional presence of such drastic changes, most likely reflective of microsaccades occurring within a series of eye movements otherwise within the range of smooth pursuit. The most straightforward manner for including eye movement vector information was to generate predictive positions based on linear extrapolation of the previous two positions for all eye movements that fall within the range of smooth pursuit. (Note that a 3-point arcical extrapolation would not fit the two-point vector-change parameter of the stimuli.) During smooth pursuit, each measurement should fall within a specified radius of its predicted position. Exploratory analysis evaluated the mean, median, cut-off value for saccades, and previous value for position change as potential candidates for the radius. Visual examination of position trace plots suggested that the cut-off value for saccades determined by the data for each trial optimized sensitivity and specificity.

Saccade Tests

The same algorithm was used to process eye tracking data from the Express and Reflexive tests. For every trial, 800ms of fixation were observed. The number of observations for saccade activity depended on the presentation time of the target, ranging from 75ms to 500ms. An additional 40ms of observations were included to allow for errors in stimulus presentation time and measurement of saccades occurring after the target had been replaced by the backward mask. Thus, the total amount of observation time analyzed for each trial ranged from 915ms to 1340ms.

A loop function began at the start of each time series and calculated the difference between consecutive observations. Maximal sensitivity and specificity for distinguishing saccades towards a target from fixation activity (determined via visual inspection of position trace plots) was achieved with a cut-point 5 interquartiles from the median distance. This cut distance was then adjusted (via division of square root of 2) to detect changes in both x and y coordinate space.

A second loop function examined each distance in the x and y dimensions to identify onset of saccades. Fixation activity (i.e., observations with changes less than the cut) was recorded as 0. Changes in the x and y dimensions greater than the absolute value of the cut score were recorded as 1 if positive, and –1 if negative. This information could then be used to determine time of onset and vector of any saccade. Vector information is critical for the analysis, since only saccades towards targets (not those made towards the keyboard, clock, or elsewhere) are pertinent to the analysis. These vectors were then compared with the actual target location to determine whether test-relevant saccadic activity had occurred.

Visual inspection revealed occasional observations of saccades towards targets that did not fall neatly along the trajectory line. Furthermore, within a clear saccadic movement series, there were occasionally distance observations smaller than the cut. These anomalies were most likely due to errors in eye position measurement. Thus, a second loop was used to smooth the vector data, such that if 4 of 5 consecutive observations contained the same value, all 5 observations were assigned that value.

The algorithm then returned to the beginning of the time series and searched for two consecutive saccades towards the target location. The beginning of the first saccade was identified as latency for movement. The algorithm then continued until saccade activity had ceased, suggesting that the subject's foveal position had reached the target. The number of observations prior to this point indicated target latency. Amplitude of the first saccade and average velocity of the saccade was also extracted. Additionally, saccadic movements not directed towards the target were recorded. These measures were stored for each trial of the test. Trials in which no saccade towards the target and trials in which anticipatory saccades reached the target prior to stimulus presentation (i.e., before 800ms or the 200th observation) were also recorded. Latency and velocity measures for the early saccades (i.e., those before target presentation) were not included in subsequent analyses.

The algorithm for analyzing eye position data for the AntiSaccade test followed the same procedure as the Express and Reflexive tests with regards to distinguishing saccades from fixation and smoothing of vector data. One minor difference is that 800ms of fixation were observed, followed by presentation time of the distractor (75ms to 500ms), presentation time of the target (75ms to 500ms), and 40ms of mask presentation. However, an important additional step utilized vector data to determine whether a saccade towards the distractor stimulus was made.

For the Fixation test, eye position data were analyzed to determine whether and to what extent the subject remained fixated on the target during each presentation. The general algorithm followed the same procedure as the saccade tests with respect to observation period and identification of saccades, except that the cut distance was set more conservatively (i.e., 1.5 times the interquartile range) so that minor saccadic deviations from the center would be detected.

Specificity of smooth pursuit algorithm.

A database was also developed to examine the specificity of the algorithm used to detect smooth pursuit. For this, counts for each type of observed eye movement (e.g., fixation, smooth pursuit, saccade, etc.) were summarized from the all standard smooth pursuit items, the first 30 items of velocity discrimination, all but the first item of the Fixation test, and 60 items from the middle of the Express, Reflexive, and AntiSaccade tests. As described earlier, the algorithm was developed to maximize discrimination of smooth pursuit eye movements from fixation, such that smooth pursuit would not be found by the algorithm during administration of the saccade tests. The primary index of specificity for smooth pursuit eye movement was the ratio of

Fixation over the sum of smooth pursuit and fixation, where a value of 1 would indicate that the algorithm did not misidentify any fixation. The algorithm produced an average specificity of 0.73 (SD=0.09) for the Fixation test, 0.65 (SD=0.11) for the Reflexive test, 0.65 (SD=0.11) for the Express test, and 0.63 (SD=0.11) for the AntiSaccade test.

Because the primary question is distinguishing fixation from smooth pursuit, the Fixation specificity is most relevant to interpretation of eye movement counts from the smooth pursuit test. To adjust for the probable detection of false positive smooth pursuit during velocity discrimination, each individual's average smooth pursuit count was multiplied by his or her Fixation specificity. The resulting number was then divided by the total observations per trial to obtain a conservative estimate of the percent of time that each subject followed the targets using smooth pursuit eye movements.

Appendix E. Eye-Tracking Interface Problem

The EyeLink© software is capable of recording keystroke times with respect to eye-tracking data while running nearly any type of software; however, because E-Prime© commandeers the Windows environment of while running an experiment, keystrokes were recorded haphazardly and with incorrect time stamps. The only keystroke that could accurately link eye-tracking data was the command (F7) to compile and run the test. Thus, inter-subject deviations in compilation time and actual stimulus presentation time over the course of the test could not be precisely determined. However, output from the E-Prime© program provides time stamping for presentation of the response page (i.e., the condition after stimulus has presented and the subject is asked to indicate whether he or she observed a flipped target). This time stamp is relative to the completion (not initiation) of compilation, and is theoretically accurate to within +/- 13 ms (due to screen refresh rate error) for each stimulus presentation. Inspection of the E-Prime data files (i.e., values of reaction times, inter-trial intervals, total test time) suggested that the tests were being executed properly by the test administration computer, and behavioral measures would not be impacted by the eye-tracking interface problem.

Given these limitations, eye movement data from the saccade tests were identified for each epoch based on the E-Prime© time stamps for responses. These time stamps were used to create a window in the eye position data during which visual stimuli (i.e., fixation point and target) were believed to be presented for each trial. Visual inspection of eye position traces based on this approach showed logical congruence for all subjects, where a number of observations suggesting central fixation, followed by saccades towards a target were observed. Unfortunately, random errors in compilation time between subjects obfuscate the ability to precisely determine the number of fixation observations prior to initiation of saccade towards a target; therefore, latency of movement and latency to reach target were subjected to a degree of error.

To characterize the extent of the error, a Monte Carlo simulation was performed wherein script compilation time was measured over 60 iterations for each test. Measurements were made using a stopwatch based on the computer's internal processing clock. The stopwatch was programmed using the .NET 2.0 framework in Visual Studio, and is theoretically accurate to measurements at or below the millisecond level, even while being run in an active Windows environment. Further Details regarding the functional specifications of this stopwatch can be found at http://msdn2.microsoft.com/en-us/library/system.diagnostics.stopwatch.aspx. The stopwatch examined compilation time for all E-Prime tests on the same machine used in the study under conditions similar to those during the experiment. Mean compilation times and variability were found to be similar across tasks: Fixation *M*=7.3ms, *SD*=3.8, range [1, 15]; Express *M*=6.5, *SD*=3.3, range [1,13]; Reflexive *M*=7.13, *SD*=3.6, range [1,15]; AntiSaccade *M*=7.6, *SD*=3.7, range [1, 17]. This degree of error does not preclude analysis of eye-tracking data; however, it results in an overestimation of internal consistency estimates for target latency, and an attenuation of convergent correlations with discrimination threshold.

Appendix F: Primary Eye-Tracking Analysis Script

```
% This is the primary eye-tracking data analysis script.
% It is called from the command line (or batch file) and analyzes data from all tasks.
% A single file is written out with movement statistics for each trial as '<subj>.txt_new.txt'
% Input arguments are case sensitive.

function [ALLMAT]=MOVEPROCESS(positionfile,efile,eye,review)
global eventfilename
global REFLEXMAT
global EXPRESSMAT
global ANTIMAT
global FIXMAT
global SPEMMAT
global VELOCITYMAT
global VELEND
global NOSPEMMAT

%positionfile contains eyeposition data in standard format from eyelink

% eventfile contains event information in the following format:
% col1 = task
% col2 = item
% col3 = accuracy (1= correct; 2=incorrect)
% col4 = starttime
% col5 = endtime

% eye: 1=left; 2= right

% review: 1=visual inspect data for each trial ; 0=skip review process

% example syntax: MOVEPROCESS('9000.txt','9000_event.txt',2,1)

eventfilename=positionfile;
display(['eye position and event data loading...']);
positionfile=load(positionfile,'-ascii');
eventfile=load(efile,'-ascii');
display(['eye position and event data loaded']);

ALLMAT=zeros(2000,13);

%This calls the function to visually inspect data, if called for
if review=1;
   REVIEW(positionfile,eventfile,eye);
else
end

%This function processes the SPEM standard-metric tasks
[SPEMMAT]=SPEMPROCESS2(positionfile,eventfile,eye);
for allloop=1:15
   for spemloop=1:12
      ALLMAT(allloop,spemloop)=SPEMMAT(allloop,spemloop);
   end
```

```
end
display(['SPEM data processed and written to file']);

[FIXMAT]=FIXPROCESS(positionfile,eventfile,eye);
for allloop=201:236
   for sacloop=1:7
      ALLMAT(allloop,sacloop)=FIXMAT(allloop-200,sacloop);
   end
end
display(['FIXATION data processed']);

[REFLEXMAT]=REFLEXPROCESS(positionfile,eventfile,eye);
for allloop=301:414
   for sacloop=1:6
      ALLMAT(allloop,sacloop)=REFLEXMAT(allloop-300,sacloop);
   end
end
display(['REFLEXIVE SACCADE data processed']);

[EXPRESSMAT]=EXPRESSPROCESS(positionfile,eventfile,eye);
for allloop=501:614
   for sacloop=1:6
      ALLMAT(allloop,sacloop)=EXPRESSMAT(allloop-500,sacloop);
   end
end
display(['EXPRESS SACCADE data processed']);

[ANTIMAT]=ANTIPROCESS(positionfile,eventfile,eye);
for allloop=701:814
   for sacloop=1:8
      ALLMAT(allloop,sacloop)=ANTIMAT(allloop-700,sacloop);
   end
end
display(['ANTI SACCADE data processed']);

taskend=size(eventfile,1);

[NOSPEMMAT]=MOVEPARSE(positionfile,eventfile,eye);
for allloop=1001:(1000+taskend)
   for nospemloop=1:12
      ALLMAT(allloop,nospemloop)=NOSPEMMAT(allloop-1000,nospemloop);
   end
end

ofile=([(eventfilename),'_new.out']);
dlmwrite(ofile,ALLMAT,'\t');

display([(eventfilename),' completed.']);
```

Appendix G: Visual Inspection Script

%This program is used to visually examine eye-tracking data from the Oculomotor battery. It can be run independently, but is called by MOVEPROCESS.m by default.

```
function []=REVIEW(positionfile,eventfile,eye);

%Avoids re-loading data into MATLAB if called by MOVEPROCESS.m
if positionfile=[]
            eventfilename=positionfile;
            display(['eye position and event data loading...']);
            positionfile=load(positionfile,'-ascii');
            eventfile=load(eventfile,'-ascii');
            display(['eye position and event data loaded']);
else
end

%This section reviews data from the Standard SPEM task
if eye==1;
   x=3;
   y=4;
   pup=5;
else
   x=6;
   y=7;
   pup=8;
end

for SPEMLOOP=1:15
   start=eventfile(SPEMLOOP,4);
   tempx=zeros(5000,1);
   tempy=zeros(5000,1);
   for SPEMITEM=1:5000
      tempx(SPEMITEM,1)=positionfile(start+SPEMITEM-1,x);
      tempy(SPEMITEM,1)=positionfile(start+SPEMITEM-1,y);
   end
   if eventfile(SPEMLOOP,1)==1
      type='horizontal'
   else
      if eventfile(SPEMLOOP,1)==2
         type='vertical'
      else
         type='orbital'
      end
   end
   item=eventfile(SPEMLOOP,2)
   figure(1)
   plot(tempx,tempy,'MarkerSize',2,'Marker','o','MarkerFaceColor','k','LineStyle','none')
   xlim([0 800]);
   ylim([0 800]);
   display('If the image above appears to contain measurements representing the titled plot,
press Return to continue')
```

```
display ('Otherwise, make a note of the bad image, then press Return to continue or Press
CTRL + C to discontinue')
   pause
end

%This section reviews data from the VELOCITY task

number_of_events=size(eventfile);
number_of_events=number_of_events(1);

% This subsection determines the location of velocity data & the number of
% stimuli
i=0;
for VELLOCLOOP=16:number_of_events
   check=eventfile(VELLOCLOOP,1);
   if check==4;
      i=i+1;
   else
      if check==5;
         i=i+1;
      else
      end
   end
end

VELEND=i+15;
for VELOCITYLOOP=16:(VELEND)
   start=eventfile(VELOCITYLOOP,4);
   tempx=zeros(1000,1);
   tempy=zeros(1000,1);
   for VELOCITYITEM=1:1000
      tempx(VELOCITYITEM,1)=positionfile(start+VELOCITYITEM-1,x);
      tempy(VELOCITYITEM,1)=positionfile(start+VELOCITYITEM-1,y);
   end
   if eventfile(VELOCITYLOOP,1)==4
      type='branching'
   else
      type='task'
   end
   item=eventfile(VELOCITYLOOP,2)
   acc=eventfile(VELOCITYLOOP,3)
   figure(1)
   plot(tempx,tempy,'Marker','o','MarkerSize',2,'MarkerFaceColor','k','LineStyle','none')
   xlim([0 800]);
   ylim([0 800]);
   display('If the image above appears to contain measurements representing Velocity Task
Activity, press Return to continue')
   display ('Otherwise, make a note of the bad image, then press Return to continue or Press
CTRL + C to discontinue')
   pause
end
```

```
%This section reviews data from the Latency task
LATEND=VELEND+36;
for LATLOOP=(VELEND+1):(LATEND)
   startevent=eventfile(LATLOOP,4);
   endevent=eventfile(LATLOOP,5);
   LOOPLENGTH=(endevent-startevent);
   tempx=zeros(LOOPLENGTH,1);
   tempy=zeros(LOOPLENGTH,1);
   for LATITEM=1:LOOPLENGTH
      tempx(LATITEM,1)=positionfile(startevent+LATITEM-1,x);
      tempy(LATITEM,1)=positionfile(startevent+LATITEM-1,y);
   end
   display('Fixation')
   acc=eventfile(LATLOOP,3)
   eventfile(LATLOOP,2)
   plot(tempx,tempy,'MarkerSize',2,'Marker','o','MarkerFaceColor','k','LineStyle','none')
   xlim([0 800]);
   ylim([0 800]);
   display('If the image above appears to contain measurements representing Fixation Task
Activity, press Return to continue')
   display ('Otherwise, make a note of the bad image, then press Return to continue or Press
CTRL + C to discontinue')
   pause
end

%This section reviews data from the reflexive task
REFEND=LATEND+114;
for LATLOOP=(LATEND+1):(REFEND)
   startevent=eventfile(LATLOOP,4);
   endevent=eventfile(LATLOOP,5);
   LOOPLENGTH=(endevent-startevent);
   tempx=zeros(LOOPLENGTH,1);
   tempy=zeros(LOOPLENGTH,1);
   for LATITEM=1:LOOPLENGTH
      tempx(LATITEM,1)=positionfile(startevent+LATITEM-1,x);
      tempy(LATITEM,1)=positionfile(startevent+LATITEM-1,y);
   end
   display('REFLEX')
   eventfile(LATLOOP,2)
   acc=eventfile(LATLOOP,3)
   plot(tempx,tempy,'MarkerSize',2,'Marker','o','MarkerFaceColor','k','LineStyle','none')
   xlim([-1000 1000]);
   ylim([-1000 1000]);
   axis off
   display('If the image above appears to contain measurements representing Reflexive Task
Activity, press Return to continue')
   display ('Otherwise, make a note of the bad image, then press Return to continue or Press
CTRL + C to discontinue')
   pause
end

%This section reviews data from the express task
EXPEND=REFEND+114;
```

```
for LATLOOP=(REFEND+1):(EXPEND)
   startevent=eventfile(LATLOOP,4);
   endevent=eventfile(LATLOOP,5);
   LOOPLENGTH=(endevent-startevent);
   tempx=zeros(LOOPLENGTH,1);
   tempy=zeros(LOOPLENGTH,1);
   for LATITEM=1:LOOPLENGTH
      tempx(LATITEM,1)=positionfile(startevent+LATITEM-1,x);
      tempy(LATITEM,1)=positionfile(startevent+LATITEM-1,y);
   end
   display('EXPRESS')
   acc=eventfile(LATLOOP,3)
   eventfile(LATLOOP,2)
   plot(tempx,tempy,'MarkerSize',2,'Marker','o','MarkerFaceColor','k','LineStyle','none')
   xlim([-1000 1000]);
   ylim([-1000 1000]);
   axis off
   display('If the image above appears to contain measurements representing Express Task
Activity, press Return to continue')
   display ('Otherwise, make a note of the bad image, then press Return to continue or Press
CTRL + C to discontinue')
   pause
end


%This section reviews data from the reflexive task
ANTIEND=EXPEND+114;
for LATLOOP=(EXPEND+1):(ANTIEND)
   startevent=eventfile(LATLOOP,4);
   endevent=eventfile(LATLOOP,5);
   LOOPLENGTH=(endevent-startevent);
   tempx=zeros(LOOPLENGTH,1);
   tempy=zeros(LOOPLENGTH,1);
   for LATITEM=1:LOOPLENGTH
      tempx(LATITEM,1)=positionfile(startevent+LATITEM-1,x);
      tempy(LATITEM,1)=positionfile(startevent+LATITEM-1,y);
   end
   display('ANTISACCADE')
   acc=eventfile(LATLOOP,3)
   eventfile(LATLOOP,2)
   plot(tempx,tempy,'MarkerSize',2,'Marker','o','MarkerFaceColor','k','LineStyle','none')
   xlim([-1000 1000]);
   ylim([-1000 1000]);
   axis off
   display('If the image above appears to contain measurements representing AntiSaccade
Activity, press Return to continue')
   display ('Otherwise, make a note of the bad image, then press Return to continue or Press
CTRL + C to discontinue')
   pause
end
```

Appendix H: Smooth Pursuit Standard Task Analysis Script

```
%This function is called by MOVEPROCESS and analyzes data from the Smooth Pursuit
standard tasks.
%Data returned to file '<subj>.txt_new.txt' beginning at row 1 reflect the following:
%(1)=horizontal gain
%(2)=horizontal anticipatory saccades
%(3)=horizontal catch-up saccades
%(4)=amplitude of horizontal catch-up saccades (averaged over trial)
%(5)=number of observations identified as horizontal smooth pursuit
%(6)=number of blinks
%(7)=vertical gain
%(8)=vertical anticipatory saccades
%(9)=vertical catch-up saccades
%(10)=amplitude of vertical catch-up saccades (averaged over trial)
%(11)=number of observations identified as vertictal smooth pursuit
%(12)=number of blinks

%NOTE: data are only analyzed in the relevant domain (e.g., no vertical analysis for horizontal
stimuli)

function [SPEMMAT]=SPEMPROCESS(positionfile,eventfile,eye);
global eventfilename
global SPEMMAT

event=1;
SPEMMAT=zeros(15,12);


% positionfile contains eyeposition data in standard format from eyelink

% eventfile contains event information in the following format:
% col1 = task
%col2 = item
%col3 = accuracy (1= correct; 2=incorrect)
%col4 = starttime
%col5 = endtime

%order: 1=reflexive first; 2=express first

%eye: 1=left; 2= right

%DATALOADING
%positionfile=load(positionfile,'-ascii');
%eventfile=load(eventfile,'-ascii');


if eye==1;
   x=3;
   y=4;
   pup=5;
else
   x=6;
```

```
   y=7;
   pup=8;
end

%This section processes the data from the horizontal stimuli

i=2; %This accounts for twice the distance traveled in a cycle
for HORLOOP=1:5
   start=eventfile(HORLOOP,4);
   posx=zeros(5000,1);
   numblinks=0;
   for SPEMITEM=1:5000
      if positionfile(start+SPEMITEM-1,x+2) > 0
         posx(SPEMITEM,1)=positionfile(start+SPEMITEM-1,x);
      else
         numblinks=numblinks+1;
      end
   end
   posx=nonzeros(posx);
   temp=sort(posx);
   temp2=size(temp);
   temp2=temp2(1);
   tempmax=temp(round(temp2*.99));
   tempmin=temp(round(temp2*.01));
   obsdistance=(tempmax-tempmin);
   ratx=zeros(1,1);
   raty=zeros(1,1);
   actposx=zeros(temp2,1);
   actratx=zeros((temp2-1),1);
   actposx=zeros(temp2,1);
   actratx=zeros((temp2-1),1);
   anticipatory=0;
   catchup=0;
   for actualloop=1:temp2 %This loop calculates the actual target rate and position at each
measurement
      change=1+cos(-pi+(i*pi*2*actualloop)/5000);
      change=(change/pi)*(obsdistance)*(pi/2);
      actposx(actualloop)=(tempmax-change);
   end
   for actratloop=2:(temp2-1)
      actratx(actratloop,1)=abs((actposx(actratloop)-actposx(actratloop-1)));
   end
   maxrat=max(actratx)*2;
   meanrat=mean(actratx);
   j=1;
   cup=0;
   as=0;
   asreset=0;
   cupreset=0;
   cupdist=0;
   for SPEMITEM2=2:(temp2-8) %This loop determines rate at each observation
      rat=abs((posx(SPEMITEM2)-posx(SPEMITEM2-1)));
      if rat <= maxrat
```

```
        ratx(j,1)=rat;
        asreset=0;
        cupreset=0;
        j=j+1;
      else %This counts anticipatory and catchup saccade events
        if rat >= (2*maxrat);
            for fl=1:8
            f(fl)=abs((posx(SPEMITEM2+1)-posx(SPEMITEM2)));
               f(fl)=abs((posx(SPEMITEM2+2)-posx(SPEMITEM2+1)));
            f(fl)=abs((posx(SPEMITEM2+3)-posx(SPEMITEM2+2)));
            f(fl)=abs((posx(SPEMITEM2+4)-posx(SPEMITEM2+3)));
            f(fl)=abs((posx(SPEMITEM2+5)-posx(SPEMITEM2+4)));
            f(fl)=abs((posx(SPEMITEM2+6)-posx(SPEMITEM2+5)));
            f(fl)=abs((posx(SPEMITEM2+7)-posx(SPEMITEM2+6)));
            f(fl)=abs((posx(SPEMITEM2+8)-posx(SPEMITEM2+7)));
            favg=mean(f);
            fmax=max(f);
          end
          if fmax <= (2*maxrat)
            if favg <= (meanrat/2);
              if asreset==0
                as=as+1;
                asreset=1;
              else
              end
            else
              if favg <= maxrat
                if cupreset==0
                                  cupdist=cupdist+abs(rat);
                cup=cup+1;
                cupreset=1;
                else
                end
              else
              end
            end
          else
          end
        else
        end
      end
    end
    SPEMCOUNT=j;
    gain=(mean(ratx)/mean(actratx));
    cupamp=(cupdist/cup);
    i=i+2;
    SPEMMAT(HORLOOP,1)=gain;
    SPEMMAT(HORLOOP,2)=as;
    SPEMMAT(HORLOOP,3)=cup;
    SPEMMAT(HORLOOP,4)=cupamp;
    SPEMMAT(HORLOOP,5)=SPEMCOUNT;
    SPEMMAT(HORLOOP,6)=numblinks;
  end
```

```
%This section processes the data from the vertical stimuli

i=2; %This accounts for twice the distance traveled in a cycle
for VERLOOP=6:10
   numblinks=0;
   start=eventfile(VERLOOP,4);
  posx=zeros(5000,1);
   posy=zeros(5000,1);
   for SPEMITEM=1:5000
      if positionfile(start+SPEMITEM-1,y+1) > 0
         posy(SPEMITEM,1)=positionfile(start+SPEMITEM-1,y);
      else
         numblinks=numblinks+1;
      end
   end
   posx=nonzeros(posx);
   posy=nonzeros(posy);
   temp=sort(posy);
   temp2=size(temp);
   temp2=temp2(1);
   tempmax=temp(round(temp2*.99));
   tempmin=temp(round(temp2*.01));
   tempmean=temp(round(temp2/2));
   obsdistance=(tempmax-tempmin);
   ratx=zeros(1,1);
   raty=zeros(1,1);
   actposy=zeros(temp2,1);
   actraty=zeros((temp2-1),1);
   actposy=zeros(temp2,1);
   actraty=zeros((temp2-1),1);
   anticipatory=0;
   catchup=0;
   for actualloop=1:temp2 %This loop calculates the actual target rate and position at each
measurement
      change=sin(-pi+(i*pi*2*actualloop)/5000);
      change=(change/pi)*(obsdistance)*(pi/2);
      actposy(actualloop)=(tempmean-change);
   end
   for actratloop=2:(temp2-1)
      actraty(actratloop,1)=abs((actposy(actratloop)-actposy(actratloop-1)));
   end
   maxrat=max(actraty)*2;
   meanrat=mean(actraty);
   j=1;
   cup=0;
   as=0;
   cupdist=0;
   asreset=0;
   cupreset=0;
   for SPEMITEM2=2:(temp2-8) %This loop determines rate at each observation
      rat=abs((posy(SPEMITEM2)-posy(SPEMITEM2-1)));
      if rat <= maxrat
```

```
            raty(j,1)=rat;
            asreset=0;
            cupreset=0;
            j=j+1;
        else %This counts anticipatory and catchup saccade events
            if rat >= (2*maxrat);
                for fl=1:8
                    f(fl)=abs((posy(SPEMITEM2+1)-posy(SPEMITEM2)));
                          f(fl)=abs((posy(SPEMITEM2+2)-posy(SPEMITEM2+1)));
                   f(fl)=abs((posy(SPEMITEM2+3)-posy(SPEMITEM2+2)));
                    f(fl)=abs((posy(SPEMITEM2+4)-posy(SPEMITEM2+3)));
                    f(fl)=abs((posy(SPEMITEM2+5)-posy(SPEMITEM2+4)));
                    f(fl)=abs((posy(SPEMITEM2+6)-posy(SPEMITEM2+5)));
                    f(fl)=abs((posy(SPEMITEM2+7)-posy(SPEMITEM2+6)));
                    f(fl)=abs((posy(SPEMITEM2+8)-posy(SPEMITEM2+7)));
                    favg=mean(f);
                    fmax=max(f);
                end
                if fmax <= (2*maxrat)
                    if favg <= (meanrat/2);
                        if asreset==0
                            as=as+1;
                            asreset=1;
                        else
                        end
                    else
                        if favg <=maxrat
                            if cupreset==0
                            cupdist=cupdist+abs(rat);
                                                                    cup=cup+1;
                            cupreset=1;
                            else
                            end
                        else
                        end
                    end
                else
                end
            else
            end
        end
    end
    cupamp=(cupdist/cup);
    gain=(mean(raty)/mean(actraty));
    SPEMCOUNT=j;
    i=i+2;
    SPEMMAT(VERLOOP,7)=gain;
    SPEMMAT(VERLOOP,8)=as;
    SPEMMAT(VERLOOP,9)=cup;
    SPEMMAT(VERLOOP,10)=cupamp;
    SPEMMAT(VERLOOP,11)=SPEMCOUNT;
    SPEMMAT(VERLOOP,12)=numblinks;
end
```

```
%This section processes the horizontal component of movement from the
%orbital task
i=2; %This accounts for twice the distance traveled in a cycle
for HORLOOP=11:15
   start=eventfile(HORLOOP,4);
   posx=zeros(5000,1);
   numblinks=0;
   for SPEMITEM=1:5000
      if positionfile(start+SPEMITEM-1,x+2) > 0
         posx(SPEMITEM,1)=positionfile(start+SPEMITEM-1,x);
      else
         numblinks=numblinks+1;
      end
   end
   posx=nonzeros(posx);
   %posy=nonzeros(posy);
   temp=sort(posx);
   temp2=size(temp);
   temp2=temp2(1);
   tempmax=temp(round(temp2*.99));
   tempmin=temp(round(temp2*.01));
   obsdistance=(tempmax-tempmin);
   ratx=zeros(1,1);
   raty=zeros(1,1);
   actposx=zeros(temp2,1);
   actratx=zeros((temp2-1),1);
   actposx=zeros(temp2,1);
   actratx=zeros((temp2-1),1);
   anticipatory=0;
   catchup=0;
   for actualloop=1:temp2 %This loop calculates the actual target rate and position at each
measurement
      change=1+cos(-pi+(i*pi*2*actualloop)/5000);
      change=(change/pi)*(obsdistance)*(pi/2);
      actposx(actualloop)=(tempmax-change);
   end
   for actratloop=2:(temp2-1)
      actratx(actratloop,1)=abs((actposx(actratloop)-actposx(actratloop-1)));
   end
   maxrat=max(actratx)*2;
   meanrat=mean(actratx);
   j=1;
   hcup=0;
   has=0;
   asreset=0;
   cupreset=0;
   hcupdist=0;
   for SPEMITEM2=2:(temp2-8) %This loop determines rate at each observation
      rat=abs((posx(SPEMITEM2)-posx(SPEMITEM2-1)));
      if rat <= maxrat
         ratx(j,1)=rat;
         asreset=0;
```

```
            cupreset=0;
            j=j+1;
        else %This counts anticipatory and catchup saccade events
            if rat >= (2*maxrat);
                for fl=1:8
                    f(fl)=abs((posx(SPEMITEM2+1)-posx(SPEMITEM2)));
                        f(fl)=abs((posx(SPEMITEM2+2)-posx(SPEMITEM2+1)));
                    f(fl)=abs((posx(SPEMITEM2+3)-posx(SPEMITEM2+2)));
                    f(fl)=abs((posx(SPEMITEM2+4)-posx(SPEMITEM2+3)));
                    f(fl)=abs((posx(SPEMITEM2+5)-posx(SPEMITEM2+4)));
                    f(fl)=abs((posx(SPEMITEM2+6)-posx(SPEMITEM2+5)));
                    f(fl)=abs((posx(SPEMITEM2+7)-posx(SPEMITEM2+6)));
                    f(fl)=abs((posx(SPEMITEM2+8)-posx(SPEMITEM2+7)));
                    favg=mean(f);
                    fmax=max(f);
                end
                if fmax <= (2*maxrat)
                    if favg <= (meanrat/2);
                        if asreset==0
                            has=has+1;
                            asreset=1;
                        else
                        end
                    else
                        if favg <= maxrat
                            if cupreset==0
                            hcupdist=hcupdist+abs(rat);
                            hcup=hcup+1;
                            cupreset=1;
                            else
                            end
                        else
                        end
                    end
                else
                end
            else
            end
        end
    end
    hcupamp=(hcupdist/hcup);
    hgain=(mean(ratx)/mean(actratx));
    hSPEMCOUNT=j;
    i=i+2;
    SPEMMAT(HORLOOP,1)=hgain;
    SPEMMAT(HORLOOP,2)=has;
    SPEMMAT(HORLOOP,3)=hcup;
    SPEMMAT(HORLOOP,4)=hcupamp;
    SPEMMAT(HORLOOP,5)=hSPEMCOUNT;
    SPEMMAT(HORLOOP,6)=numblinks;
end

%This section processes the vertical component of movement
```

```
i=2; %This accounts for twice the distance traveled in a cycle
for VERLOOP=11:15
   start=eventfile(VERLOOP,4);
   posx=zeros(5000,1);
   posy=zeros(5000,1);
   numblinks=0;
   for SPEMITEM=1:5000
      if positionfile(start+SPEMITEM-1,y+1) > 0
         posy(SPEMITEM,1)=positionfile(start+SPEMITEM-1,y);
     else
         numblnks=numblinks+1;
      end
   end
   posx=nonzeros(posx);
   posy=nonzeros(posy);
   temp=sort(posy);
   temp2=size(temp);
   temp2=temp2(1);
   tempmax=temp(round(temp2*.99));
   tempmin=temp(round(temp2*.01));
   tempmean=temp(round(temp2/2));
   obsdistance=(tempmax-tempmin);
   ratx=zeros(1,1);
   raty=zeros(1,1);
   actposy=zeros(temp2,1);
   actraty=zeros((temp2-1),1);
   actposy=zeros(temp2,1);
   actraty=zeros((temp2-1),1);
   anticipatory=0;
   catchup=0;
   for actualloop=1:(temp2) %This loop calculates the actual target rate and position at each
measurement
      change=sin(-pi+(i*pi*2*actualloop)/5000);
      change=(change/pi)*(obsdistance)*(pi/2);
      actposy(actualloop)=(tempmean-change);
   end
   for actratloop=2:(temp2-1)
      actraty(actratloop,1)=abs((actposy(actratloop)-actposy(actratloop-1)));
   end
   maxrat=max(actraty)*2;
   meanrat=mean(actraty);
   j=1;
   vcup=0;
   vas=0;
   asreset=0;
   cupreset=0;
   vcupdist=0;
   for SPEMITEM2=2:(temp2-8) %This loop determines rate at each observation
      rat=abs((posy(SPEMITEM2)-posy(SPEMITEM2-1)));
      if rat <= maxrat
         raty(j,1)=rat;
         asreset=0;
         cupreset=0;
```

```
        j=j+1;
      else %This counts anticipatory and catchup saccade events
        if rat >= (2*maxrat);
          for fl=1:8
            f(fl)=abs((posy(SPEMITEM2+1)-posy(SPEMITEM2)));
                f(fl)=abs((posy(SPEMITEM2+2)-posy(SPEMITEM2+1)));
            f(fl)=abs((posy(SPEMITEM2+3)-posy(SPEMITEM2+2)));
            f(fl)=abs((posy(SPEMITEM2+4)-posy(SPEMITEM2+3)));
            f(fl)=abs((posy(SPEMITEM2+5)-posy(SPEMITEM2+4)));
            f(fl)=abs((posy(SPEMITEM2+6)-posy(SPEMITEM2+5)));
            f(fl)=abs((posy(SPEMITEM2+7)-posy(SPEMITEM2+6)));
            f(fl)=abs((posy(SPEMITEM2+8)-posy(SPEMITEM2+7)));
            favg=mean(f);
            fmax=max(f);
          end
          if fmax <= (2*maxrat)
            if favg <= (meanrat/2);
              if asreset==0
                vas=vas+1;
                asreset=1;
              else
              end
            else
              if favg <=maxrat
                if cupreset==0
                vcupdist=vcupdist+abs(rat);
                vcup=vcup+1;
                cupreset=1;
                else
                end
              else
              end
            end
          else
          end
        else
        end
      end
    end
    vcupamp=(vcupdist/vcup);
    vgain=(mean(raty)/mean(actraty));
    i=i+2;
    vSPEMCOUNT=j;
    SPEMMAT(VERLOOP,7)=vgain;
    SPEMMAT(VERLOOP,8)=vas;
    SPEMMAT(VERLOOP,9)=vcup;
    SPEMMAT(VERLOOP,10)=vcupamp;
    SPEMMAT(VERLOOP,11)=vSPEMCOUNT;
    SPEMMAT(VERLOOP,12)=numblinks;
  end
```

Appendix I: Fixation Test Analysis Script

```
%This function is called by MOVEPROCESS and analyzes data from the Fixation Task.
%Data returned to file '<subj>.txt_new.txt' beginning at row 501 reflect the following:
%(1)=item
%(2)=number of saccade observations
%(3)=mean difference of observations from center
%(4)=median difference of observations from center
%(5)=standard deviation of differences of observations from center
%(6)=percent of observations identified as fixation
%(7)=percent of fixation observations w/in (1.5 interquartile distance) radius from center

function [FIXMAT]=FIXPROCESS(positionfile,eventfile,eye);
global eventfilename
global FIXMAT
if eye==1;
   x=3;
   y=4;
   pup=5;
else
   x=6;
   y=7;
   pup=8;
end
brkout=1;
for finddata=16:250
   if brkout>=1
      check=eventfile(finddata,1);
      if check==6
         start=finddata;
         brkout=0;
      else
      end
   else
   end
end
FIXMAT=zeros(36,7);
i=1;
for fixloop=start:(start+35)
   firstobs=eventfile(fixloop,4);
   lastobs=eventfile(fixloop,5);
   ssize=lastobs-firstobs;
   tempmat=zeros((ssize-1),1);
   a=1;
   for fixitemloop=(firstobs):(lastobs-1)
      xdif=((positionfile(fixitemloop,x))-(positionfile(fixitemloop+1,x)))^2;
      ydif=((positionfile(fixitemloop,y))-(positionfile(fixitemloop+1,y)))^2;
      tempmat(a,1)=(xdif+ydif)^.5;
      a=a+1;
   end
   tempmat2=sort(tempmat);
   q1=round(ssize*.25);
   q3=round(ssize*.75);
```

```
    q1=tempmat2(q1);
    q3=tempmat2(q3);
   mdn=median(tempmat2);
    cut=mdn+(1.5*(q3-q1));
    sac=0;
    a=1;
    tempmatx=zeros(1,1); tempmaty=zeros(1,1); centmat=zeros(1,1);
    if cut > 8
        cut=7.99
    else
    end
    for fixsacloop=1:(ssize-1);
        check=tempmat(fixsacloop);
        if check>cut;
            sac=sac+1;
        else
            tempmatx(a,1)=(positionfile(fixsacloop+firstobs-1,x));
            tempmaty(a,1)=(positionfile(fixsacloop+firstobs-1,y));
            a=a+1;
        end
    end
    centx=mean(tempmatx);
    centy=mean(tempmaty);
    for fixitemloop=1:(a-1)
        xdif=(tempmatx(fixitemloop,1)-centx)^2;ydif=(tempmaty(fixitemloop,1)-centy)^2;
        centmat(fixitemloop,1)=(xdif+ydif)^.5;
    end
    centmat2=sort(centmat);
    q1=round(a*.25);
    q3=round(a*.75);
    q1=centmat2(q1);
    q3=centmat2(q3);
    mdn=median(centmat2);
    radlim=mdn+(1.5*(q3-q1));
    cent=0;
    offcent=0;
    for offcentloop=1:(a-1);
        check=centmat2(offcentloop);
        if check>radlim;
            offcent=offcent+1;
        else
            cent=cent+1;
        end
    end
    FIXMAT(i,1)=i;
    FIXMAT(i,2)=sac;
    FIXMAT(i,3)=mean(centmat2);
    FIXMAT(i,4)=median(centmat2);
    FIXMAT(i,5)=std(centmat2);
    FIXMAT(i,6)=((a-sac)/(a-1));
    FIXMAT(i,7)=((cent)/(a));
    i=i+1;
end
```

Appendix J: Reflexive Test Analysis Script

```
%This function is called by MOVEPROCESS and analyzes data from the Reflexive Saccade
Task.
%Data returned to file '<subj>.txt_new.txt' beginning at row 301 reflect the following:
%(1)=latency of eyes to reach target
%(2)=latency of eyes to begin moving to target
%(3)=rate of primary saccade towards target (if present)
%(4)=average rate of saccade towards target
%(5)=number of saccade observations not towards target
%(6)=response accuracy;

function [REFLEXMAT]=REFLEXPROCESS(positionfile,eventfile,eye);
global eventfilename
global REFLEXMAT
if eye==1;
   x=3;
   y=4;
   pup=5;
else
   x=6;
   y=7;
   pup=8;
end
brkout=1;
for finddata=16:5000
   if brkout>=1
      check=eventfile(finddata,1);
      if check==7
         start=finddata;
         brkout=0;
      else
      end
   else
   end
end
REFLEXMAT=zeros(114,5);
i=1;
for fixloop=start:(start+113)
   firstobs=(eventfile(fixloop,4));
   lastobs=(eventfile(fixloop,5)+10);
   ssize=lastobs-firstobs;
   tempmat=zeros((ssize-1),1);
   vectormat=zeros((ssize-1),2);
   a=1;
   %This loop identifies the start of the first saccade towards the target
   for fixitemloop=(firstobs):(lastobs-1)
      xdif=((positionfile(fixitemloop,x))-(positionfile(fixitemloop+1,x)));
      ydif=((positionfile(fixitemloop,y))-(positionfile(fixitemloop+1,y)));
      tempmat(a,1)=((xdif)^2 + (ydif)^2)^.5;
      vectormat(a,1)=xdif;
      vectormat(a,2)=ydif;
      a=a+1;
```

```
end
a=1;
tempmat2=sort(tempmat);
q1=round(ssize*.25);
q3=round(ssize*.75);
q1=tempmat2(q1);
q3=tempmat2(q3);
mdn=median(tempmat2);
cut=mdn+(5*(q3-q1));
saccut=(cut)/(2^.5);
fixobs=0;
initfix=1;
missac=0;
sacnum=0;
sacveloc=0;
targfix=0;
cont=1;
deltaxy=0;
targlat=0;
latency=0;
prisac=0;
%This loop formats the vector matrix to compare with target location
for vectorloop=1:(ssize)
   if vectormat(a,1)>saccut
          vectormat(a,1)= -1;
   else
          if vectormat(a,1)<(0-saccut)
               vectormat(a,1) = 1;
          else
               vectormat(a,1) = 0;
          end
   end
   if vectormat(a,2)>saccut
      vectormat(a,2)=-1;
   else
      if vectormat(a,2)<(0-saccut)
          vectormat(a,2) = 1;
      else
          vectormat(a,2) = 0;
      end
   end
   a=a+1;
end
%This loop extracts latency and saccade velocity
%This loop smooths saccade activity vectors
for smoothloop=1:(ssize-5)
   xchange=vectormat(smoothloop,1);
   ychange=vectormat(smoothloop,2);
   if xchange == 0
      if ychange ==0
      else
          yc(1)=vectormat(smoothloop+1,2);
          yc(2)=vectormat(smoothloop+2,2);
```

```
            yc(3)=vectormat(smoothloop+3,2);
            yc(4)=vectormat(smoothloop+4,2);
            yc(5)=vectormat(smoothloop+5,2);
            if abs(mean(yc)) >= 4
                xc(1)=vectormat(smoothloop+1,1);
                xc(2)=vectormat(smoothloop+2,1);
                xc(3)=vectormat(smoothloop+3,1);
                xc(4)=vectormat(smoothloop+4,1);
                xc(5)=vectormat(smoothloop+5,1);
                rep=round(mean(xc));
                for sactrack=smoothloop:smoothloop+5
                    vectormat(sactrack,1)=rep;
                end
            else
            end
        end
    else
        xc(1)=vectormat(smoothloop+1,1);
        xc(2)=vectormat(smoothloop+2,1);
        xc(3)=vectormat(smoothloop+3,1);
        xc(4)=vectormat(smoothloop+4,1);
        xc(5)=vectormat(smoothloop+5,1);
        if abs(sum(xc)) >= 4
            yc(1)=vectormat(smoothloop+1,2);
            yc(2)=vectormat(smoothloop+2,2);
            yc(3)=vectormat(smoothloop+3,2);
            yc(4)=vectormat(smoothloop+4,2);
            yc(5)=vectormat(smoothloop+5,2);
            rep=round(mean(yc));
            for sactrack=smoothloop:smoothloop+5
                vectormat(sactrack,2)=rep;
            end
        else
        end
    end
end
for expsacloop=1:(ssize)
    if initfix==1
        if tempmat(expsacloop,1)<cut
            fixobs=fixobs+1;
        else
            if expsacloop <= (ssize-1)
                if vectormat(expsacloop,1)==eventfile(start+i-1,6)
                    if vectormat(expsacloop,2)==eventfile(start+i-1,7)
                        if vectormat(expsacloop+1,1)==eventfile(start+i-1,6)
                            if vectormat(expsacloop+1,2)==eventfile(start+i-1,7)
                                initfix=0;
                                latency=fixobs+missac;
                                pos1x=positionfile(firstobs+expsacloop-1,x);
                                pos1y=positionfile(firstobs+expsacloop-1,y);
                                pos2x=positionfile(firstobs+expsacloop,x);
                                pos2y=positionfile(firstobs+expsacloop,y);
                                deltaxy=(((pos2x-pos1x)^2)+(pos2y-pos1y)^2)^.5;
```

```
                    prisac=deltaxy/500;
                    sacnum=2;
                  else
                  initfix=1;
                  end
                else
                  initfix=1;
                end
              else
              missac=1+missac;
              initfix=1;
              end
            else
              missac=missac+1;
              initfix=1;
            end
          else
          end
        end
      else
        if cont==1;
          if expsacloop+1 <= ssize
            if tempmat(expsacloop+1,1)>(cut/2)
              sacnum=sacnum+1;
            else
              if sacnum >= 3;
                targlat=fixobs+missac+sacnum+unksac;
                pos2x=positionfile(firstobs+expsacloop,x);
                pos2y=positionfile(firstobs+expsacloop,y);
                deltaxy=(((pos2x-pos1x)^2)+(pos2y-pos1y)^2)^.5;
                sacveloc=(deltaxy/sacnum)/250;
                cont=0;
              else
                initfix=1;
                cont=1;
              end
            end
          else
            sacnum=sacnum+1;
            targlat=0;
            pos2x=positionfile(firstobs+expsacloop,x);
            pos2y=positionfile(firstobs+expsacloop,y);
            deltaxy=(((pos2x-pos1x)^2)+(pos2y-pos1y)^2)^.5;
            sacveloc=(deltaxy/sacnum)/250;
          end
        else
          end
        end
    end
      if targlat==0
        targlat=9999;
      else
      end
```

```
        if latency==0
            latency=9999;
        else
        end
        REFLEXMAT(i,1)=targlat;
        REFLEXMAT(i,2)=latency;
        REFLEXMAT(i,3)=prisac;
        REFLEXMAT(i,4)=sacveloc;
        REFLEXMAT(i,5)=missac;
        REFLEXMAT(i,6)=eventfile((start+i-1),3);
        i=i+1;
end
```

Appendix K: Express Test Analysis Script

```
%This function is called by MOVEPROCESS and analyzes data from the Express Saccade
Task.
%Data returned to file '<subj>.txt_new.txt' beginning at row 501 reflect the following:
%(1)=latency of eyes to reach target
%(2)=latency of eyes to begin moving to target
%(3)=rate of primary saccade towards target (if present)
%(4)=average rate of saccade towards target
%(5)=number of saccade observations not towards target
%(6)=response accuracy;

function [EXPRESSMAT]=EXPRESSPROCESS(positionfile,eventfile,eye);
global eventfilename
global EXPRESSMAT
if eye==1;
   x=3;
   y=4;
   pup=5;
else
   x=6;
   y=7;
   pup=8;
end
brkout=1;
for finddata=16:5000
   if brkout>=1
      check=eventfile(finddata,1);
      if check==8
         start=finddata;
         brkout=0;
      else
      end
   else
   end
end
EXPRESSMAT=zeros(114,5);
i=1;
for fixloop=start:(start+113)
   firstobs=(eventfile(fixloop,4));
   lastobs=(eventfile(fixloop,5)+10);
   ssize=lastobs-firstobs;
   tempmat=zeros((ssize-1),1);
   vectormat=zeros((ssize-1),2);
   a=1;
   %This loop identifies the start of the first saccade towards the target
   for fixitemloop=(firstobs):(lastobs-1)
      xdif=((positionfile(fixitemloop,x))-(positionfile(fixitemloop+1,x)));
      ydif=((positionfile(fixitemloop,y))-(positionfile(fixitemloop+1,y)));
      tempmat(a,1)=((xdif)^2 + (ydif)^2)^.5;
      vectormat(a,1)=xdif;
      vectormat(a,2)=ydif;
      a=a+1;
```

```
end
a=1;
tempmat2=sort(tempmat);
q1=round(ssize*.25);
q3=round(ssize*.75);
q1=tempmat2(q1);
q3=tempmat2(q3);
mdn=median(tempmat2);
cut=mdn+(5*(q3-q1));
saccut=(cut)/(2^.5);
fixobs=0;
initfix=1;
missac=0;
sacnum=0;
sacveloc=0;
targfix=0;
cont=1;
deltaxy=0;
targlat=0;
latency=0;
prisac=0;
%This loop formats the vector matrix to compare with target location
for vectorloop=1:(ssize)
   if vectormat(a,1)>saccut
         vectormat(a,1)= -1;
   else
         if vectormat(a,1)<(0-saccut)
              vectormat(a,1) = 1;
         else
              vectormat(a,1) = 0;
         end
   end
   if vectormat(a,2)>saccut
      vectormat(a,2)=-1;
   else
      if vectormat(a,2)<(0-saccut)
          vectormat(a,2) = 1;
      else
          vectormat(a,2) = 0;
      end
   end
   a=a+1;
end
   %This loop smooths saccade activity vectors
for smoothloop=1:(ssize-5)
   xchange=vectormat(smoothloop,1);
   ychange=vectormat(smoothloop,2);
   if xchange == 0
      if ychange ==0
      else
          yc(1)=vectormat(smoothloop,2);
          yc(2)=vectormat(smoothloop+1,2);
          yc(3)=vectormat(smoothloop+2,2);
```

```
            yc(4)=vectormat(smoothloop+3,2);
            yc(5)=vectormat(smoothloop+4,2);
            if abs(mean(yc)) >= 4
                xc(1)=vectormat(smoothloop,1);
                xc(2)=vectormat(smoothloop+1,1);
                xc(3)=vectormat(smoothloop+2,1);
                xc(4)=vectormat(smoothloop+3,1);
                xc(5)=vectormat(smoothloop+4,1);
                rep=round(mean(xc));
                for sactrack=smoothloop:smoothloop+5
                    vectormat(sactrack,1)=rep;
                end
            else
            end
        end
    else
        xc(1)=vectormat(smoothloop,1);
        xc(2)=vectormat(smoothloop+1,1);
        xc(3)=vectormat(smoothloop+2,1);
        xc(4)=vectormat(smoothloop+3,1);
        xc(5)=vectormat(smoothloop+4,1);
        if abs(sum(xc)) >= 4
            yc(1)=vectormat(smoothloop,2);
            yc(2)=vectormat(smoothloop+1,2);
            yc(3)=vectormat(smoothloop+2,2);
            yc(4)=vectormat(smoothloop+3,2);
            yc(5)=vectormat(smoothloop+4,2);
            rep=round(mean(yc));
            for sactrack=smoothloop:smoothloop+5
                vectormat(sactrack,2)=rep;
            end
        else
        end
    end
end
%This loop extracts latency and saccade velocity
for expsacloop=1:(ssize)
    if initfix==1
        if tempmat(expsacloop,1)<cut
            fixobs=fixobs+1;
        else
            if expsacloop <= (ssize-1)
                if vectormat(expsacloop,1)==eventfile(start+i-1,6)
                    if vectormat(expsacloop,2)==eventfile(start+i-1,7)
                        if vectormat(expsacloop+1,1)==eventfile(start+i-1,6)
                            if vectormat(expsacloop+1,2)==eventfile(start+i-1,7)
                                initfix=0;
                                latency=fixobs+missac;
                                pos1x=positionfile(firstobs+expsacloop-1,x);
                                pos1y=positionfile(firstobs+expsacloop-1,y);
                                pos2x=positionfile(firstobs+expsacloop,x);
                                pos2y=positionfile(firstobs+expsacloop,y);
                                deltaxy=(((pos2x-pos1x)^2)+(pos2y-pos1y)^2)^.5;
```

```
                        prisac=deltaxy/500;
                        sacnum=2;
                    else
                    initfix=1;
                    end
                else
                    initfix=1;
                end
            else
            missac=1+missac;
            initfix=1;
            end
        else
            missac=missac+1;
            initfix=1;
        end
    else
    end
  end
else
  if cont==1;
    if expsacloop+1 <= ssize
      if tempmat(expsacloop+1,1)>(cut/2)
        sacnum=sacnum+1;
      else
        if sacnum >= 3;
          targlat=fixobs+missac+sacnum+unksac+unkobs;
          pos2x=positionfile(firstobs+expsacloop,x);
          pos2y=positionfile(firstobs+expsacloop,y);
          deltaxy=(((pos2x-pos1x)^2)+(pos2y-pos1y)^2)^.5;
          sacveloc=(deltaxy/sacnum)/250;
          cont=0;
        else
          initfix=1;
          cont=1;
        end
      end
    else
      sacnum=sacnum+1;
      targlat=0;
      pos2x=positionfile(firstobs+expsacloop,x);
      pos2y=positionfile(firstobs+expsacloop,y);
      deltaxy=(((pos2x-pos1x)^2)+(pos2y-pos1y)^2)^.5;
      sacveloc=(deltaxy/sacnum)/250;
    end
  else
    end
  end
end
 if targlat==0
   targlat=9999;
 else
 end
```

```
        if latency==0
           latency=9999;
        else
        end
        EXPRESSMAT(i,1)=targlat;
        EXPRESSMAT(i,2)=latency;
        EXPRESSMAT(i,3)=prisac;
        EXPRESSMAT(i,4)=sacveloc;
        EXPRESSMAT(i,5)=missac;
        EXPRESSMAT(i,6)=eventfile((start+i-1),3);
        i=i+1;
end
```

Appendix L: AntiSaccade Test Analysis Script

```
%This function is called by MOVEPROCESS and analyzes data from the AntiSaccade Task.
%Data returned to file '<subj>.txt_new.txt' beginning at row 701 reflect the following:
%(1)=latency of eyes to reach target
%(2)=latency of eyes to begin moving to target
%(3)=rate of primary saccade towards target (if present)
%(4)=average rate of saccade towards target
%(5)=number of saccade observations not towards target or distractor
%(6)=response accuracy;
%(7)=presence of antisaccade;
%(8)=rate of primary saccade towards distractor;

function [ANTIMAT]=ANTIPROCESS(positionfile,eventfile,eye);
global eventfilename
global ANTIMAT

if eye==1;
   x=3;
   y=4;
   pup=5;
else
   x=6;
   y=7;
   pup=8;
end
brkout=1;
for finddata=16:5000
   if brkout>=1
      check=eventfile(finddata,1);
      if check==9
         start=finddata;
         brkout=0;
      else
      end
   else
   end
end
ANTIMAT=zeros(114,8);
i=1;
for fixloop=start:(start+113)
   firstobs=(eventfile(fixloop,4));
   lastobs=(eventfile(fixloop,5)+10);
   ssize=lastobs-firstobs;
   tempmat=zeros((ssize-1),1);
   vectormat=zeros((ssize-1),2);
   a=1;
   %This loop identifies the start of the first saccade
   for fixitemloop=(firstobs):(lastobs-1)
      xdif=((positionfile(fixitemloop,x))-(positionfile(fixitemloop+1,x)));
      ydif=((positionfile(fixitemloop,y))-(positionfile(fixitemloop+1,y)));
      tempmat(a,1)=((xdif)^2 + (ydif)^2)^.5;
      vectormat(a,1)=xdif;
```

```
    vectormat(a,2)=ydif;
    a=a+1;
 end
 a=1;
 tempmat2=sort(tempmat);
 q1=round(ssize*.25);
 q3=round(ssize*.75);
 q1=tempmat2(q1);
 q3=tempmat2(q3);
 mdn=median(tempmat2);
 cut=mdn+(5*(q3-q1));
 saccut=(cut)/(2^.5);
 fixobs=0;
 initfix=1;
 missac=0;
 sacnum=0;
 sacveloc=0;
 targfix=0;
 cont=1;
 deltaxy=0;
 targlat=0;
 latency=0;
 antisac=0;
 correctsac=0;
 wrongsac=0;
 prisac=0;
 %This loop formats the vector matrix to compare with target location
 for vectorloop=1:(ssize)
    if vectormat(a,1)>saccut
          vectormat2(a,1)= -1;
    else
          if vectormat(a,1)<(-saccut)
              vectormat2(a,1) = 1;
          else
              vectormat2(a,1) = 0;
          end
    end
    if vectormat(a,2)>saccut
       vectormat2(a,2)=-1;
    else
       if vectormat(a,2)<(-saccut)
           vectormat2(a,2) = 1;
       else
           vectormat2(a,2) = 0;
       end
    end
    a=a+1;
 end
for smoothloop=1:(ssize-5)
    xchange=vectormat(smoothloop,1);
    ychange=vectormat(smoothloop,2);
    if xchange == 0
       if ychange ==0
```

```
        else
            yc(1)=vectormat(smoothloop,2);
            yc(2)=vectormat(smoothloop+1,2);
            yc(3)=vectormat(smoothloop+2,2);
            yc(4)=vectormat(smoothloop+3,2);
            yc(5)=vectormat(smoothloop+4,2);
            if abs(mean(yc)) >= 4
                xc(1)=vectormat(smoothloop,1);
                xc(2)=vectormat(smoothloop+1,1);
                xc(3)=vectormat(smoothloop+2,1);
                xc(4)=vectormat(smoothloop+3,1);
                xc(5)=vectormat(smoothloop+4,1);
                rep=round(mean(xc));
                for sactrack=smoothloop:smoothloop+5
                    vectormat(sactrack,1)=rep;
                end
            else
            end
        end
    else
        xc(1)=vectormat(smoothloop,1);
        xc(2)=vectormat(smoothloop+1,1);
        xc(3)=vectormat(smoothloop+2,1);
        xc(4)=vectormat(smoothloop+3,1);
        xc(5)=vectormat(smoothloop+4,1);
        if abs(sum(xc)) >= 4
            yc(1)=vectormat(smoothloop,2);
            yc(2)=vectormat(smoothloop+1,2);
            yc(3)=vectormat(smoothloop+2,2);
            yc(4)=vectormat(smoothloop+3,2);
            yc(5)=vectormat(smoothloop+4,2);
            rep=round(mean(yc));
            for sactrack=smoothloop:smoothloop+5
                vectormat(sactrack,2)=rep;
            end
        else
        end
    end
end
%This loop extracts latency and saccade velocity
for expsacloop=1:(ssize)
    if initfix==1
        if tempmat(expsacloop,1)<cut
            fixobs=fixobs+1;
        else
            if expsacloop <= (ssize-1)
                if vectormat2(expsacloop,1)==eventfile(start+i-1,6)
                    if vectormat2(expsacloop,2)==eventfile(start+i-1,7)
                        if vectormat2(expsacloop+1,1)==eventfile(start+i-1,6)
                            if vectormat2(expsacloop+1,2)==eventfile(start+i-1,7)
                                initfix=0;
                                if antisac==0;
                                    latency=fixobs+missac;
```

```
                    else
                    end
                    pos1x=positionfile(firstobs+expsacloop-1,x);
                    pos1y=positionfile(firstobs+expsacloop-1,y);
                    pos2x=positionfile(firstobs+expsacloop,x);
                    pos2y=positionfile(firstobs+expsacloop,y);
                    deltaxy=(((pos2x-pos1x)^2)+(pos2y-pos1y)^2)^.5;
                    correctsac=deltaxy/500;
                else
                initfix=1;
                end
            else
                initfix=1;
            end
        else
            if vectormat2(expsacloop,2)==(-eventfile(start+i-1,7))
                if vectormat2(expsacloop+1,1)==(-eventfile(start+i-1,6))
                    if vectormat2(expsacloop+1,2)==(-eventfile(start+i-1,7))
                        antisac=antisac+1;
                        latency=fixobs+missac;
                        pos1x=positionfile(firstobs+expsacloop-1,x);
                        pos1y=positionfile(firstobs+expsacloop-1,y);
                        pos2x=positionfile(firstobs+expsacloop,x);
                        pos2y=positionfile(firstobs+expsacloop,y);
                        deltaxy=(((pos2x-pos1x)^2)+(pos2y-pos1y)^2)^.5;
                        wrongsac=deltaxy/500;
                    else
                    end
                else
                end
            else
                missac=1+missac;
            end
        end
    else
        if vectormat2(expsacloop,1)==(-eventfile(start+i-1,6))
            if vectormat2(expsacloop,2)==(-eventfile(start+i-1,7))
                if vectormat2(expsacloop+1,1)==(-eventfile(start+i-1,6))
                    if vectormat2(expsacloop+1,2)==(-eventfile(start+i-1,7))
                        latency=fixobs+missac;
                        antisac=antisac+1;
                        pos1x=positionfile(firstobs+expsacloop-1,x);
                        pos1y=positionfile(firstobs+expsacloop-1,y);
                        pos2x=positionfile(firstobs+expsacloop,x);
                        pos2y=positionfile(firstobs+expsacloop,y);
                        deltaxy=(((pos2x-pos1x)^2)+(pos2y-pos1y)^2)^.5;
                        wrongsac=deltaxy/500;
                    else
                    end
                else
                end
            else
                missac=1+missac;
```

```
                    end
                else
                end
            end
        else
        end
    end
else
    if cont==1;
        if expsacloop+1 <= ssize
            if tempmat(expsacloop+1,1)>(cut/2)
                sacnum=sacnum+1;
            else
                if sacnum==0
                    sacnum=1;
                else
                end
                targlat=fixobs+missac+sacnum+unksac;
                pos2x=positionfile(firstobs+expsacloop,x);
                pos2y=positionfile(firstobs+expsacloop,y);
                deltaxy=(((pos2x-pos1x)^2)+(pos2y-pos1y)^2)^.5;
                sacveloc=(deltaxy/sacnum)/250;
                cont=0;
            end
        else
            sacnum=sacnum+1;
            targlat=0;
            pos2x=positionfile(firstobs+expsacloop,x);
            pos2y=positionfile(firstobs+expsacloop,y);
            deltaxy=(((pos2x-pos1x)^2)+(pos2y-pos1y)^2)^.5;
            sacveloc=(deltaxy/sacnum)/250;
        end
    else
        end
    end
end
  if targlat==0
     targlat=9999;
  else
  end
  if latency==0
     latency=9999;
  else
  end
  if antisac >= 1
     antisac = antisac+1;
  else
  end
  ANTIMAT(i,1)=targlat;
  ANTIMAT(i,2)=latency;
  ANTIMAT(i,3)=correctsac;
  ANTIMAT(i,4)=sacveloc;
  ANTIMAT(i,5)=missac;
```

```
    ANTIMAT(i,6)=eventfile((start+i-1),3);
    ANTIMAT(i,7)=antisac;
    ANTIMAT(i,8)=wrongsac;
    i=i+1;
end
```

Appendix M: Eye Movement Analysis Script

```
%This script is called by MOVEPARSE.m and quantifies the types of eye movement activity
observed during completion of all movement tests - most notably, the Velocity Discrimination
%test which has no other processing scripts. The purpose of the script is to determine
whether smooth pursuit movement has been elicited by the Velocity Discrimination test (as
hypothesized) or any of the tests (which should not elicit smooth pursuit).
%Data returned to file '<subj>.txt_new.txt' beginning at row 1001 reflect the following:
%Column 1= item
%Column 2= accuracy
%Column 3= # blinks
%Column 4= #fixation observations
%Column 5= #fixation periods
%Column 6= #major saccades observations
%Column 7= #major saccades
%Column 8= #likely microsaccades
%Column 9= conservative estimate of # of SPEM observations
%Column 10= mean velocity of SPEM
%Column 11= median velocity of SPEM
%Column 12= std of SPEM velocity
%The output is

function [NOSPEMMAT]=MOVEPARSE(positionfile,eventfile,eye);
global NOSPEMMAT

if eye==1;
   x=3;
   y=4;
   pup=5;
else
   x=6;
   y=7;
   pup=8;
end
number_of_events=size(eventfile);
number_of_events=number_of_events(1);
%This Loop separates eye position data by trial, & removes blinks from analyses of eye
movements.
spemcut=2;
last=1;
NOSPEMMAT=zeros(number_of_events,12); %This is the output matrix
for VELOCLOOP=1:number_of_events;
   VELOCITYLOOP = (VELOCLOOP);
   start=eventfile(VELOCLOOP,4);
   endobs=eventfile(VELOCLOOP,5);
   trialmove4=zeros(1,1); %This is the most important matrix, which contains the observations
of SPEM
   trialmove3=zeros(1,1);
   trialmove2=zeros(1,1);
   trialmove1=zeros(1,1);
   trialmove=zeros(1,1);
   trialmove5=zeros(1,1);
   trialmove6=zeros(1,1);
```

```
    medmatrix=zeros(1,1);
    trialpos=zeros(1,1);
    i=1;
    j=1;
    k=1;
    l=1;
    m=1;
    n=1;
            series=0;
    blink=0;
            majsac=0;
    SPEMCOUNT=0;
            microsac=0;
            fixation=0;
    maxseries=3;
    fixnum=0;
    majsacnum=0;
    fixcount=0;
    saccount=0;
    for Loop1c=0:(endobs-start)
        if positionfile((start+Loop1c),y+1)==0
            blink=blink+1;
        else
            trialpos(i,1)=positionfile((start+Loop1c),x);
            trialpos(i,2)=positionfile((start+Loop1c),y);
            i=i+1;
        end
    end
%This Loop creates eye movement file from trial position file & removes major saccades &
fixations
            if i>4; % occassionally very very bad or missing data will prevent any analysis
    for Loop2a=2:(i-1)
        xmove=((trialpos(Loop2a,1))-(trialpos(Loop2a-1,1)));
        ymove=((trialpos(Loop2a,2))-(trialpos(Loop2a-1,2)));
        move=((xmove^2)+(ymove^2))^.5;
        trialmove(Loop2a,1)=trialpos(Loop2a,1);
        trialmove(Loop2a,2)=trialpos(Loop2a,2);
        trialmove(Loop2a,3)=move;
    end
    trialmove2=trialmove;
    medsize=size(trialmove2,1);
    medmatrix=trialmove2(:,3);
    median1=median(medmatrix);
    medmatrix=sort(medmatrix);
            quart1=round(medsize*.25);
            quart3=round(medsize*.75);
            quart1=medmatrix(quart1);
            quart3=medmatrix(quart3);
            quartdist=quart3-quart1;
    cut=median1+(1.5 * quartdist);
    if cut >= 8.0 %This number is an upper limit to ensure that SPEM is included in the
distribution
        cut = 8.0;
```

```
   else
   end
   if cut < 1
      cut = 1;
   else
   end
   for Loop2c=1:(medsize-1)
      trialmove4=zeros(1,3);
      if trialmove2(Loop2c,3)<=cut
         endsac=0;
         saccount=0;
         trialmove3(k,1)=trialmove2(Loop2c,1);
         trialmove3(k,2)=trialmove2(Loop2c,2);
         trialmove3(k,3)=trialmove2(Loop2c,3);
         k=k+1;
         eventremain=1;
      else
         majsac=majsac+1;
         fixcount=1;
         if saccount==0
              %This section determines whether a series of non-saccades represent fixation or
smooth pursuit
            seriessize=size(trialmove3,1);
            z=0;
            eventremain=0;
            if seriessize < 8; %only potential runs of 32ms or more of smooth pursuit are
analyzed
               fixation=seriessize+fixation;
               if fixcount==1;
               fixnum=fixnum+1;
               fixcount=0;
               else
               end
            else
               xdist=0;
               ydist=0;
               for series=5:(seriessize-5) %This section removes fixation periods from smooth
pursuit data
                  xdist=0;
                  ydist=0;
                  for secondseries = -4:4
                     xdist=xdist + (trialmove3(series+secondseries+1,1)-
trialmove3(series+secondseries,1));
                     ydist=ydist + (trialmove3(series+secondseries+1,2)-
trialmove3(series+secondseries,2));
                  end
                  if (abs(xdist))+(abs(ydist)) < spemcut;
                     fixation=fixation+1;
                     if fixcount==1;
                        fixnum=fixnum+1;
                        fixcount=0;
                     else
                     end
```

```
                else
                    z=z+1;
                    trialmove4(z,1)=trialmove3(series,1);
                    trialmove4(z,2)=trialmove3(series,2);
                    trialmove4(z,3)=trialmove3(series,2);
                    fixcount=0;
                end
            end
            %This Loop removes microsacades from eyemovement matrix via predictive
vectors (linear extrapolation)
            SPEMCOUNT=SPEMCOUNT+2; %Allows first two observations to qualify as
SPEM
            for Loop3=3:(z);
            xchange=((trialmove4((Loop3-1),1))-(trialmove4((Loop3-2),1)));
            ychange=((trialmove4((Loop3-1),2))-(trialmove4((Loop3-2),2)));
            dist=((xchange^2)+(ychange^2))^.5;
            predx=((trialmove4((Loop3-1),1))+(xchange*dist));
            predy=((trialmove4((Loop3-1),2))+(ychange*dist));
            xerror = (trialmove4(Loop3,1)-predx)^2;
            yerror = (trialmove4(Loop3,2)-predy)^2;
            error = (xerror+yerror)^.5;
            radius = cut;
                    if error <= radius;
                        trialmove5(m,1)=trialmove4(Loop3,1);
                        trialmove5(m,2)=trialmove4(Loop3,2);
                        trialmove6(m,1)=trialmove3(Loop3,3);
                        SPEMCOUNT=SPEMCOUNT+1;
                        m=m+1;
                    else
                        microsac=microsac+1;
                    end
            end
        end
        majsacnum=majsacnum+1;
        saccount=1;
        k=1;
        trialmove3=zeros(1,3);
      else
      end
    end
  end
  if eventremain==1; %Runs through in cases where event does not end w/ a saccade
    trialmove4=zeros(1,3);
    seriessize=size(trialmove3,1);
    z=0;
    eventremain=0;
    if seriessize < 8; %only potential runs of 32ms or more of smooth pursuit are analyzed
      fixation=fixation+seriessize;
      if fixcount==1;
        fixnum=fixnum+1;
        fixcount=0;
      else
      end
```

```
        else
            xdist=0;
            ydist=0;
            for series=5:(seriessize-5) %This section removes fixation periods from smooth pursuit
data
                xdist=0;
                ydist=0;
                for secondseries = -4:4
                    xdist=xdist + (trialmove3(series+secondseries+1,1)-
trialmove3(series+secondseries,1));
                    ydist=ydist + (trialmove3(series+secondseries+1,2)-
trialmove3(series+secondseries,2));
                end
                if (abs(xdist))+(abs(ydist)) < spemcut;
                    if fixcount==1;
                        fixnum=fixnum+1;
                        fixcount=0;
                    else
                    end
                    fixation=fixation+1;
                else
                    fixcount=1;
                    z=z+1;
                    trialmove4(z,1)=trialmove3(series,1);
                    trialmove4(z,2)=trialmove3(series,2);
                    trialmove4(z,3)=trialmove3(series,2);
                end
            end
%This Loop removes microsacades from eyemovement matrix via predictive vectors (linear
extrapolation)
            SPEMCOUNT=SPEMCOUNT+2; %Allows first two observations to qualify as SPEM
            for Loop3=3:(z);
                xchange=((trialmove4((Loop3-1),1))-(trialmove4((Loop3-2),1)));
                ychange=((trialmove4((Loop3-1),2))-(trialmove4((Loop3-2),2)));
                dist=((xchange^2)+(ychange^2))^.5;
                predx=((trialmove4((Loop3-1),1))+(xchange*dist));
                predy=((trialmove4((Loop3-1),2))+(ychange*dist));
                xerror = (trialmove4(Loop3,1)-predx)^2;
                yerror = (trialmove4(Loop3,2)-predy)^2;
                error = (xerror+yerror)^.5;
                radius = cut;
                if error <= radius;
                    trialmove5(m,1)=trialmove4(Loop3,1);
                    trialmove5(m,2)=trialmove4(Loop3,2);
                    trialmove6(m,1)=trialmove3(Loop3,3);
                    SPEMCOUNT=SPEMCOUNT+1;
                else
                    microsac=microsac+1;
                end
            end
        end
        else
        end
```

```
        NOSPEMMAT(VELOCITYLOOP,1)=eventfile(VELOCLOOP,2);
        NOSPEMMAT(VELOCITYLOOP,2)=eventfile(VELOCLOOP,3);
        NOSPEMMAT(VELOCITYLOOP,3)=blink;
        NOSPEMMAT(VELOCITYLOOP,4)=fixation;
        NOSPEMMAT(VELOCITYLOOP,5)=fixnum;
        NOSPEMMAT(VELOCITYLOOP,6)=majsac;
        NOSPEMMAT(VELOCITYLOOP,7)=majsacnum;
        NOSPEMMAT(VELOCITYLOOP,8)=microsac;
        NOSPEMMAT(VELOCITYLOOP,9)=SPEMCOUNT;
        NOSPEMMAT(VELOCITYLOOP,10)=mean(trialmove6);
        NOSPEMMAT(VELOCITYLOOP,11)=median(trialmove6);
        NOSPEMMAT(VELOCITYLOOP,12)=std(trialmove6);
    else
    end

end
```

Appendix N: Eye-tracking Outcome Measures

VARIABLE	DESCRIPTION
SPEM_GAIN	**Mean gain for all SPEM stimuli**
SPEM_SAC	**Mean # of saccades (catch-up & anticipatory) for all SPEM stimuli per second**
SPEM_CAMP	**Mean amplitude of catch-up saccades for all SPEM stimuli**
SPEM_HOR_GAIN	Mean SPEM gain from horizontal stimuli
SPEM_HOR_AS	Mean # of anticipatory saccades from horizontal stimuli
SPEM_HOR_CUP	Mean # of catch-up saccades from horizontal stimuli
SPEM_HOR_CAMP	Mean amplitude of horizontal catch-up saccades
SPEM_HOR_COUNT	Mean # of SPEM obs. from horizontal stimuli (max=5000)
SPEM_HOR_BLINKS	Mean # of blinks during Horizontal task
SPEM_VER_GAIN	Mean SPEM gain from vertical stimuli
SPEM_VER_AS	Mean # of anticipatory saccades from vertical stimuli
SPEM_VER_CUP	Mean # of catch-up saccades from vertical stimuli
SPEM_VER_CAMP	Mean amplitude of vertical catch-up saccades
SPEM_VER_COUNT	Mean # of SPEM obs. from vertical stimuli (max=5000)
SPEM_VER_BLINKS	Mean # of blinks during Vertical task
SPEM_ORB_GAIN	Mean gain from hor and ver components of orbital stimuli
SPEM_OH_GAIN	Mean gain from horizontal component of orbital stimuli
SPEM_OV_GAIN	Mean # gain from vertical component of orbital stimuli
SPEM_OH_AS	Mean # of horizontal anticipatory saccades from orbital stimuli
SPEM_OH_CUP	Mean # of vertical anticipatory saccades from orbital stimuli
SPEM_ORB_CAMP	Mean amplitude of catch-up saccades
SPEM_ORB_COUNT	Mean # of SPEM obs. from orbital stimuli, lesser of ver or hor (max=5000)
SPEM_ORB_BLINKS	Mean # of blinks during Orbital task
VEL_NUMTRIALS	# of Velocity Discrimination trials
VEL_BLINKS	Mean # of blinks during Velocity Discrimination trials
VEL_FIXOBS	Mean # of fixations during Velocity Discrimination trials
VEL_FIXPER	Mean # of fixation periods during Velocity Discrimination trials
VEL_MAJSAC_OBS	Mean # of major saccade obs. during during Velocity Discrimination trials
VEL_MAJSAC	Mean # of major saccades during Velocity Discrimination trials
VEL_MICSAC_OBS	Mean # of micro saccades during Velocity Discrimination trials
VEL_SP_OBS	**Percentage of obs identified as SPEM during Velocity Discrimination trials**
VEL_MN_SP	Mean rate of SPEM during Velocity Discrimination trials
VEL_MD_SP	Median rate of SPEM during Velocity Discrimination trials
VEL_SD_SP	Standard deviation of SPEM during Velocity Discrimination trials

FIX_SAC	# **of saccade obs. during Fixation test**
FIX_MEAN	Mean distance from center during Fixation test
FIX_MED	Median distance from center during Fixation test
FIX_SD	Standard deviation of distance from center during Fixation test
FIX_OBS	**Mean percentage of fixation time during Fixation test**
FIX_CENTOBS	Mean # of fixation obs. w/in 1.5 interquartile distances from median of center
REF_TARGLAT	**Mean latency for eyes to reach target during Reflexive test**
REF_LAT	Mean latency for first saccade towards target during Reflexive test
REF_PRISAC	Mean amplitude of first saccade towards target during Reflexive test
REF_SACVEL	Mean of average saccade velocity towards target during Reflexive test
REF_MISSAC	Mean # of off-target saccades during Reflexive test
EXP_TARGLAT	**Mean latency for eyes to reach target during Express test**
EXP_LAT	Mean latency for first saccade towards target during Express test
EXP_PRISAC	Mean amplitude of first saccade towards target during Express test
EXP_SACVEL	Mean of average saccade velocity towards target during Express test
EXP_MISSAC	Mean # of off-target saccades during Express test
ANTI_TARGLAT	**Mean latency for eyes to reach target during AntiSaccade test**
ANTI_LAT	Mean latency for first saccade towards target during AntiSaccade test
ANTI_PRISAC	Mean amplitude of first saccade towards target during AntiSaccade test
ANTI_SACVEL	Mean of average saccade velocity towards target during Antisaccade test
ANTI_MISSAC	Mean # of off-target & off-distractor saccades during AntiSaccade test
ANTI_ANTISAC	# **of trials WITH saccades towards target AND saccades towards distractor**
REF_EARLY	# of trials excluded in the Reflexive test b/c saccade before target
EXP_EARLY	# of trials excluded in the Express test b/c saccade before target
ANTI_EARLY	# of trials excluded in the AntiSaccade test b/c saccade before target
REF_NO	# of trials excluded in the Reflexive test b/c no saccade
EXP_NO	# of trials excluded in the Express test b/c no saccade
ANTI_NO	# of trials excluded in the AntiSaccade test b/c no saccade

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