Clinical Saccadometry: Establishing Evaluative Standards Using a Simplified Video Oculography Protocol in the Adult Population

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Abstract

Background Saccadometry is an advanced ocular motor test battery that allows for the functional evaluation of the varied brain regions and circuits involved in the generation of fast, purposeful, and accurate saccadic eye movements. The test battery is composed of prosaccade (PS) and antisaccade (AS) tests that progressively increase cognitive demand. Existing saccadometry protocols qualitatively describe trends across the lifespan, but have not been widely adopted by clinicians.

Purpose The aims of this study are to design an efficient and simplified clinical saccadometry protocol using video oculography (VOG) equipment and establish associated evaluative standards across the lifespan.

Study Sample Data were reported on 273 adults ages 18 to 69 years.

Results Evaluative data on four measures: directional error rate (DE), latency (Lat), peak velocity (Vel), and accuracy (Acc) during PS and AS measurements were provided. Age-group differences were found in Lat (p < 0.01) and Vel (p = 0.04) during PS and age-group differences were found in DE (p = 0.04), Lat (p < 0.01) and Vel (p < 0.01) during AS. Gender differences were found in DE (p = 0.01) and Lat (p < 0.01) during AS.

Conclusions This study established a standardized and time-efficient protocol with evaluative standards for individuals ages 18 to 69 years old to enable the use of saccadometry as an objective measure in the clinic. Saccadometry allows clinicians to look beyond the traditional saccade test and evaluate complex oculomotor and cognitive functions that will better help clinicians differentiate between peripheral and central diagnoses.

Saccades are fast eye movements that orient the visual fovea toward a target of interest. A prosaccade (PS) is a movement that is directed toward a presented target. An antisaccade (AS) is a movement generated away from a presented target (Hallett1). A growing body of research has investigated foundational executive functions using saccadic eye movements.
as biomarkers of these processes (Leigh and Zee,2 Leigh and Kennard,3 Everling and Fischer4).

Saccadic eye movements are easy to measure in the laboratory and the underlying neural networks have been studied. Munoz and Everling5 and Coe and Munoz6 described a saccade oculomotor circuit including both excitatory and inhibitory pathways elucidated through lesion studies, human behavioral testing, functional neuroimaging, and animal studies. These studies have suggested the following areas to be involved in pro- and antisaccadic generation: frontal cortex (supplementary eye fields, dorsolateral prefrontal cortex, frontal eye fields), parietal cortex (lateral intraparietal area, parietal eye fields), visual cortex, thalamus, basal ganglia (caudate nucleus external segment of globus pallidus, subthalamic nucleus, substantia nigra pars reticulate), lateral geniculate nucleus, superior colliculus (superficial and intermediate layers of superior colliculus), premotor circuits in the reticular formation of the brainstem and cerebellum. Because these networks span almost the entire brain, there is considerable likelihood that neurological degeneration or malfunction may influence saccade performance.

AS have been widely studied as biomarkers of executive function because of the complexity of the task. Successful AS require suppression of the reflexive saccade and the generation of a voluntary saccade to an abstract location. In addition, AS increase the demand on bihemispheric integration. Research demonstrates degraded AS performance in neuropsychiatric conditions including depression (Hoffman et al7), obsessive-compulsive disorder (Hu et al8), schizophrenia (Obyedkov et al9, Reilly et al10), Tourette's disorder (LeVasqueur et al,11 Tajik-Parvichi and Sandor12), and attention-deficit hyperactivity disorder (Sanchez et al13 Fernandez-Ruiz et al14). The AS test has shown utility in the assessment of neurodegenerative disorders (MacAskill and Anderson15), including Parkinson's and Alzheimer's disease (Pretegian and Optican,16 Moloiotor et al,17 Levy et al18), as well as in the assessment of traumatic brain injury (Stuart et al,19 Webb et al20).

There are existing saccadometry protocols that qualitatively describe trends in saccade performance in neurodevelopmental, aging, and pathological populations (Yep et al,21 Coe and Munoz,6 Munoz et al22), but these have not been widely adopted in the clinical setting. To our knowledge, there has not been a simplified, time-efficient saccadometry protocol with evaluative benchmarks across the adult lifespan available to clinicians. Saccadometry can be assessed in several ways with variation in equipment and technique (block vs. interleaving). A block trial refers to the same test type and parameters (PS or AS) performed within a trial. An interleaved trial refers to randomly switching between test types and/or parameters (PS and AS) within a trial. Antoniades et al proposed an international standardized protocol for saccades that alternated PS and AS in 60 and 40 trials, respectively, for a total of 5 blocks with a 1-minute rest between blocks (Antoniades et al23). Their testing procedure required 13 to 16 minutes. Newer protocols have required up to 20 minutes, an amount of time that might not be feasible in some clinical settings.

In this study, we aimed to examine a time-efficient saccadometry protocol that could be easily adopted and interpreted by clinicians using equipment they already have, namely video oculography (VOG). Second, we aimed to establish evaluative standards for later saccadometry protocol testing in different pathological groups. Our protocol was designed to overcome barriers in the adoption of saccadometry within clinical test batteries. A standardized and practical clinical test with supporting evaluative data using equipment readily available to clinicians has not been available to this point.

**Methods**

**Subjects**

A saccadometry protocol was explored for feasibility and data were collected at each clinical research site. A collective 296 healthy subjects (38.9% male, 61.6% female) ages 18 to 69 years were reviewed with approval under the Banner University Medical Center/University of Arizona Institutional Review Board (00000291). The participants were screened for a history of recent concussion (defined as within 6 months of testing), persisting symptoms after concussion, brain injury, neurodegenerative disorders, disorders of hearing and balance, and known attention-deficit disorders. A participant would be excluded if they did not perform as expected on a horizontal random saccade (RS) test.

The subjects were grouped into five age-dependent subgroups to provide distribution by decade (Table 1). The youngest age group spans more than one decade to include the youngest adults ages 18 and 19 years old. Each subgroup was composed of a minimum of 45 subjects.

**Table 1** Cohort stratified by age-dependent subgroups

<table>
<thead>
<tr>
<th>Group</th>
<th>Age</th>
<th>Subject</th>
<th>Subject included in the analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Years</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Group 1</td>
<td>18–29</td>
<td>68</td>
<td>61</td>
</tr>
<tr>
<td>Group 2</td>
<td>30–39</td>
<td>55</td>
<td>47</td>
</tr>
<tr>
<td>Group 3</td>
<td>40–49</td>
<td>63</td>
<td>61</td>
</tr>
<tr>
<td>Group 4</td>
<td>50–59</td>
<td>63</td>
<td>59</td>
</tr>
<tr>
<td>Group 5</td>
<td>60–69</td>
<td>47</td>
<td>45</td>
</tr>
</tbody>
</table>
**Equipment**

The equipment used for this study included head-mounted VOG eye recording goggles with eye-tracking technology and VisualEyes proprietary software from Interacoustics (Middelart, Denmark) on a laptop computer, with a TV screen to display the stimulus target and a stable chair. Stimulus target is calculated based on screen size and is 1% of the total width of the screen. The video image was sampled at a standard rate of 100 Hz. Evaluative data for the RS test are documented and validated in this software. As the latencies for the PS and AS are prolonged compared with the original saccade data, a 100 Hz sampling rate is sufficient for this study (Shepard and Jacobson^24^). This is also supported by the American National Standard (ANSI/ASA S.45-2009). The distance between the subject and the TV screen and the size of the TV screen are recorded in the software at the initiation of the study to achieve a consistent 10-degree angle away from midline for presentation of stimuli targets for PS and AS tests. The chair was centered in front of the TV screen and the screen adjusted to the height of the subject to center the midline stimulus target. The VOG was calibrated at the start of the test battery: RS, PS, AS.

**Protocol**

The test sequence was the same for each subject: RS followed by PS and then AS. The TV screen background for each test was black and the stimuli targets were red to minimize overstimulation. For both PS and AS tests, the subjects were instructed to complete both fast and accurate eye movements. Both PS and AS tests had a fixed center target that was the same size and color as the stimuli targets. The center target remained on during the entire test. Each stimulus target was presented on the screen at a consistent distance of 10 degrees randomized either to the left or right of the fixed center target after a random delay (1–2 seconds; mean interval time was 1.5 second. PS and AS tests were 151 seconds (2.5 minutes) long to generate a total of 60 trials, 30 toward each side. For the PS test, subjects moved their eyes quickly to the stimulus target and returned quickly to the center target. For the AS test, subjects looked equal and opposite to the direction from the stimulus target and then quickly returned to the center target (Munoz and Everling^5^).

Exact test instructions are outlined in **Table 2**.

The threshold for detection of a saccade was 100 d/s. For all tests, the artifact rejection was on. Artifact rejection filters out saccades with values that are outside the common acceptable range. If the latency is below 100 d/s or above 1000 d/s, if the latency is below the threshold value of 100 milliseconds or above 700 milliseconds, or if the accuracy in PS is below 20% or above 350%, the saccade is filtered out. The software calculated the mean peak velocity (Vel), latency (Lat), accuracy (Acc), and directional error rate (DE) for each test. Mean Vel was measured in degrees per second. Lat was measured in milliseconds. Acc was measured in a percentage (actual eye movement vs. target eye movement). DE were displayed in a bar graph format for both DE and overall errors. Overall error rate includes DE and rejected saccades. In the PS test, a DE occurs when the subject looks away from the newly presented stimulus target. Conversely, in the AS test, a DE occurs when the subject looks toward the newly presented stimulus target. For this study, the mean values across both eyes in both target directions were analyzed statistically and are presented here.

**Statistical Methods**

A total of 296 records were reviewed for this study. For each age group, the overall directional errors in PS and AS were used to determine poor performance data using the method

**Table 2** Saccadometry procedure

<table>
<thead>
<tr>
<th>Test</th>
<th>Duration, direction</th>
<th>Instructions to subject</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random saccades</td>
<td>46 s horizontal</td>
<td>Relax and look straight ahead. Don’t move your head; only move your eyes while tracking the targets on the screen in front of you. You will see a red dot. Keep your eyes moving wherever the dot goes.</td>
</tr>
<tr>
<td>Prosaccades</td>
<td>151 s horizontal</td>
<td>Relax and look straight ahead. Don’t move your head; only move your eyes while tracking the targets on the screen in front of you. You will start by looking at the middle dot. Another dot will appear to either the right or the left. Move your eyes to the new dot and quickly back to the middle dot. Accuracy and speed are both important so, please, do your best to follow the target and move your eyes as soon as the target on the side appears and then back to the center dot.</td>
</tr>
<tr>
<td>Antisaccades</td>
<td>151 s horizontal</td>
<td>Relax and look straight ahead. Don’t move your head; only move your eyes. You will start by looking at the middle dot. Another dot will appear to either the right or the left. THIS TIME move your eyes to the equal and opposite side of the new dot and quickly back to the middle dot. Accuracy and speed are both important so, please, do your best to move your eyes to the position the dot would be in if it were on the opposite side.</td>
</tr>
</tbody>
</table>
of Dixon (Dixon25). In this way, data that were 1.5 interquartile range greater than the 75th percentile were identified as poor performance data. Any subject with poor performance was not included in further analysis. Reference ranges for each parameter were determined as follows: because almost all the parameters in each age group were distributed as expected, the means and standard deviations of each age-group data point were used to construct a reference range (Table 3). This reference range was defined as the mean ± 2.0 standard deviations. This parametric analysis was performed to maintain consistency within the current software (Interacoustics, VisualEyes 3.1). Separated Factorial analysis of variances (ANOVA) were performed to compare the age-group, gender differences, and age-group × gender interaction in DE, Lat, Vel, and Acc values for PS and AS. Post hoc tests with Bonferroni correction were performed if the between-subjects effects were significant. The significant level was set as p < 0.05. Statistical analyses were performed using SPSS version 28 (SPSS, Inc., Armonk, NY).

Results

Twenty-three subjects were determined to have poor performance, leaving 273 subjects for analysis. Table 1 summarized the total subjects in each age group and the number of subjects included in the final analysis. Data from a 62-year-old patient are shown in Fig. 1A to illustrate the raw data that were collected for each subject. The RS test, according to our inclusion criteria, needed to have expected Lat, Vel, and Acc values for that subject’s age. The evaluative standard ranges are shown in the white area and the abnormal results would be plotted in the gray area. – Fig. 1B shows the left-eye results of the PS test. Each saccade eye movement is plotted as a single dot on the graph. The numerical means are also shown. In the summary plot, mean values for both eyes and both target directions are displayed, which were used in the statistical summaries to report the thresholds per decade. – Fig. 1D shows the AS summary plot. The AS DE is much higher at 27%, compared with 0% in the PS test. There were also longer latencies, faster velocities, and poorer accuracy in the AS test.

### Table 3 Summary of evaluative thresholds for prosaccades and antisaccades by age group

<table>
<thead>
<tr>
<th>Prosaccades</th>
<th>Directional error rate (%)</th>
<th>Latency (ms)</th>
<th>Velocity (degrees/s)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group</td>
<td>Mean</td>
<td>Reference range</td>
<td>Mean</td>
<td>Reference range</td>
</tr>
<tr>
<td>18–29</td>
<td>0.36</td>
<td>0–1.86</td>
<td>208.13</td>
<td>150.89–265.37</td>
</tr>
<tr>
<td>30–39</td>
<td>0.21</td>
<td>0–1.65</td>
<td>209.19</td>
<td>148.61–269.77</td>
</tr>
<tr>
<td>40–49</td>
<td>0.75</td>
<td>0–3.43</td>
<td>207.70</td>
<td>139.28–276.12</td>
</tr>
<tr>
<td>50–59</td>
<td>0.63</td>
<td>0–3.25</td>
<td>221.29</td>
<td>151.17–291.41</td>
</tr>
<tr>
<td>60–69</td>
<td>0.60</td>
<td>0–3.28</td>
<td>228.13</td>
<td>165.63–290.63</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antisaccades</th>
<th>Directional error rate (%)</th>
<th>Latency (ms)</th>
<th>Velocity (degrees/s)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group</td>
<td>Mean</td>
<td>Reference range</td>
<td>Mean</td>
<td>Reference range</td>
</tr>
<tr>
<td>18–29</td>
<td>7.08</td>
<td>0–20</td>
<td>278.97</td>
<td>195.85–362.09</td>
</tr>
<tr>
<td>30–39</td>
<td>8.74</td>
<td>0–23.58</td>
<td>292.49</td>
<td>199.27–385.71</td>
</tr>
<tr>
<td>60–69</td>
<td>12.2</td>
<td>0–26.76</td>
<td>304.39</td>
<td>174.73–434.05</td>
</tr>
</tbody>
</table>
approximately 44.9 milliseconds slower than Group 1, 31.38 milliseconds slower than Group 2, 27.85 milliseconds slower than Group 3, and 28.56 milliseconds slower than Group 4 during AS. Group 5 also had faster velocities compared with Group 1 ($p < 0.01$) and Group 2 ($p < 0.01$). Group 5 had faster velocities, approximately 31.93 degrees/s faster than Group 1 and 32.90 degrees/s faster than Group 2 during AS. No significant differences were found in DE ($F(4, 263) = 1.11$, $p = 0.26$; – Fig. 2A) and Acc ($F(4, 263) = 2.00$, $p = 0.10$; – Fig. 2G) during PS. There was also no significant difference noted in Acc ($F(4, 263) = 2.33$, $p = 0.06$; – Fig. 2H) during AS.

**Gender Difference**

Gender differences were found in DE ($F(4, 263) = 6.89$, $p = 0.01$) and Lat ($F(4, 263) = 8.65$, $p < 0.01$) during AS. Overall, females had 3.03% higher DE ($p = 0.01$) and 16.39 milliseconds longer Lat compared with males ($p < 0.01$) during AS.

No gender differences were found in DE ($F(4, 263) = 0.22$, $p = 0.64$), Lat ($F(4, 263) = 0.13$, $p = 0.72$), Vel ($F(4, 263) = 0.15$, $p = 0.70$), and Acc ($F(4, 263) = 1.59$, $p = 0.21$) during PS, and Vel ($F(4, 263) = 0.39$, $p = 0.53$) and Acc ($F(4, 263) = 0.39$, $p = 0.53$) during AS.

**Age-Group and Gender Interaction**

Age-group and gender interactions were found in DE during AS ($F(4, 236) = 3.39$, $p = 0.01$; – Fig. 3). During AS, DE gradually increased from 6.95% in Group 1 to 13.78% in Group 4 and slightly decreased to 11.81% in Group 5 for female participants, whereas DE decreased from 8.62% in Group 2 to 5.65% in Group 4 and increased to 12.20% in Group 5 for male participants.

No age-group and gender interaction was found in Lat ($F(4, 236) = 0.13$, $p = 0.97$), Vel ($F(4, 236) = 0.54$, $p = 0.71$), and Acc ($F(4, 236) = 0.65$, $p = 0.63$) during PS, and Lat ($F(4, 236) = 1.87$, $p = 0.12$), Vel ($F(4, 263) = 0.34$, $p = 0.85$), and Acc ($F(4, 263) = 0.34$, $p = 0.85$) during AS.
Prosaccade and Antisaccade Evaluative Thresholds

The results showed that AS values were higher than PS values in DE ($F(1, 544) = 306.94$, $p < 0.01$), Lat ($F(1, 544) = 479.03$, $p < 0.01$) and Vel ($F(1, 544) = 134.5$, $p < 0.01$). No difference was found in Acc ($F(1, 544) = 0.30$, $p = 0.58$) when performing AS or PS.

Mean threshold values and reference ranges for PS and AS test are shown in Table 3.

Discussion

This study describes a practical, time-efficient saccadometry protocol using widely available VOG equipment and evaluative thresholds per decade for young to older adults. Our study provided PS and AS data on four measures of this protocol: DE, Lat, Vel, and Acc. PS testing demonstrated significant age-group differences of Lat and Vel. AS testing...
demonstrated significant age-group differences of DE, Lat, and Vel. There were also significant differences in PS compared with AS measures of DE, Lat, and Vel. Our PS and AS data results follow previously reported age-related trends, where results change with increasing age (22, 27–29).

Consistent with previously reported PS evaluative data, our velocity data (measured for a 10-degree stimulus) lies within the values reported by Hopf et al.\(^{13}\) (stimulus measurements between 5 and 15 degrees resulting in velocity approximately 206 ± 29 degrees/s (mean ± SD) in 5 degrees and 339 ± 48 degrees/s, respectively). Our PS latency data were also consistent with the Hopf et al data, which noted 160 ± 30 milliseconds for 5 degrees and 190 ± 50 milliseconds for 15 degrees. Our PS and AS data for latency were consistent with previous studies by Cee et al and Klein et al.\(^{27}\) Evdokimidis et al.\(^{28}\) studied the value for the AS task in younger adults and reported a latency of 270 ± 39 milliseconds, which is similar to our younger group, which averaged 278.97 milliseconds. Slight differences in reported values between studies may be due to the number of repetitions in the saccadic movement, sampling difference, moving degrees for saccadic movement, and given instruction during the test. Our data indicated a gender difference where females had higher DE and longer Lat than males in AS testing. Longer Lat has been reported in previous studies and is consistent with Mack et al.\(^{33}\)

When analyzing trends in our dataset across the PS and AS tests, the AS test has greater directional errors for all age groups compared with the PS test. In addition, the AS latency is longer than PS and velocity is slower than the PS. It is well known that PS and AS reflect the operation of different cognitive components. According to Liu et al, "over the last decade, researchers have shown that the saccadic eye-movement system can be influenced by a wide range of cognitive factors, including attention, learning, working memory, and decision-making processes. Such differences between PS and AS latencies highlight the flexible control of the oculomotor system" (Liu et al.\(^{13}\)). The AS test requires greater recruitment of cerebral resources and interhemi- spheric coordination compared with the simpler PS task (Ting et al.\(^{10}\)). The comparison of PS and AS tasks may provide additional clinical value. The potential importance of anticost is an example of the importance of both tests. Anticost is the difference in latency between the more cognitively demanding AS and automated PS thought to reflect integrity of executive function. Previous research suggests that the AS time-cost lies in the response inhibition of an incorrect PS and the triangulation of a mirror-symmetrical position (Connolly et al.\(^{21}\)). An AS involves at least three separate operations: covert orienting, response suppression, and coordinate transformation (Wilcockson et al.\(^{22}\)).

The value of the anticost is evident in a blocked protocol compared with an interleaved protocol demonstrated by Liu and colleagues. That study also showed that differences in AS latency could be reduced by removing the attentional reorientation processes (like in an interleaved protocol) or increasing stimulus location probability (implicit learning). To eliminate both these effects, we chose a blocked trial with 10-degree peripheral stimulus location. Several studies have well described age-related trends in randomly interleaved PS/AS protocols (Yep et al.\(^{21}\) Coe and Munoz,\(^{22}\) Mack et al.\(^{13}\)). Although these seem quite valuable in research settings, they have yet to be widely adopted by clinicians. This could be due to the complexity and time required by these protocols. In the laboratory, behavioral paradigms have been developed to study the ability of the brain to respond flexibly to our environment. AS have been an ideal task because they contain a manipulation of stimulus–response compatibility that decouples stimulus encoding and response preparation.

In this study, we reported on evaluative standards for a time-efficient blocked saccadometry protocol using equipment commonly found in the clinic (VOG). Our protocol focused on mimicking the neurological bedside exam, minimizing variables in test procedure, and using equipment commonly found in audiological clinical settings.

The blocked protocol, which separates the PS from the AS task closely mimics a neurological bedside exam. We used a consistent degree of our stimulus (10 degrees in the horizontal plane) to remove variability in measurement parameters, such as latency. Lastly, the use of VOG equipment for saccadometry evaluation is unique to the literature and our protocol offers a time-efficient alternative to existing research protocols.

**Limitations**

Even with the blocked trials, the total length of the test protocol was just under 6 minutes over the three tests (RS, PS, AS). We did not vary the sequence of the subtests. Fatigue, even in otherwise healthy individuals, could have played a role in performance. The sequence and duration of the individual subtests are potential areas of future research to determine if our choices in testing are optimal for analyzing results. As far as we are aware, all previous studies use interleaved protocols or position the PS task before the AS task. Future research should explore the significance of this effect as well.

We chose an adult population, presuming to study the mature brain. That choice limits application in younger and older populations. Future research should investigate evaluative data using this simplified protocol for populations outside of our dataset.
We know saccadometry is likely to be used as a part of a battery of tests to help determine a patient’s diagnosis and should not be considered a standalone diagnostic test at this time. It is possible that, in the future, we will be able to better correlate measurement parameter patterns with certain central diagnoses.

**Conclusion**

This study standardized a time-efficient protocol that all subjects could complete using VOG equipment commonly found in the clinic. We established evaluative data for patients ages 18 to 69 years. Future studies will focus on older age groups (70 years of age and above) and different neurological disorders, such as mild traumatic brain injury, Parkinson’s disease, and Alzheimer’s disease. Saccadometry allows clinicians to look beyond the traditional saccade test and evaluate complex oculomotor and cognitive functions that will better help clinicians differentiate between peripheral and central diagnoses.

**Acknowledgment**

We would like to acknowledge Kamran Barin, PhD, for his insight and expertise in contributing to, and reviewing, our manuscript.

**Conflict of Interest**

All authors were engaged in developing the protocol and data collection. M.P. is a part-time employee in private practice and an employee of Interacoustics. At the time of the study and initial write-up, L.F. was in private practice. After the study was completed, she became an employee of Interacoustics. A.A., S.M., D.D., and G.Z. are consultants to Interacoustics providing clinical knowledge for the development of products.

**Data Availability Statement**

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

**Author Contributions**

Daniel Demian, Michelle Petrak, Glen Zielinski, Shelly Massingale, Liz Fuemmeler, and Amy Alexander collected and charted data. Chia-Cheng Lin provided the statistical analysis. All authors reviewed the text and approved the final paper for submission.

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