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Oculomotor control in asymptomatic and recently diagnosed individuals with the genetic marker for Huntington's disease

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Abstract

We compared oculomotor control among individuals in the early stages of Huntington's disease (HD), with that of individuals who are presymptomatic HD gene carriers (PSGC) and nongene carriers (NGC). The oculomotor testing paradigm included both traditional tests and a novel experimental procedure to assess visual scanning. Traditional tests elicited saccades, pursuit and optokinetic nystagmus (OKN). HD patients demonstrated marked delay in the initiation of volitional saccades (anti-saccade and memory-guided saccades), a reduced number of correct volitional saccades, reduced velocity of saccades, and a decreased OKN gain. We also studied visual scanning while the participants completed the Digit Symbol Subscale of the Wechsler Adult Intelligence Survey-Revised (WAIS-R). The HD participants demonstrated an abnormal gaze strategy, which may be associated with attention and/or planning deficits.

Differences between the PSGC and NGC groups were only observed for two measures: PSGC had a decreased number of memory-guided saccades and a subtle delay in the initiation of volitional saccades. Our results suggest that oculomotor measures are a sensitive biomarker in the early stage of HD and demonstrate that the combination of more traditional oculomotor tests with visual scanning tests is useful in the evaluation of visual performance.

Keywords: Saccade; Pursuit; Optokinetic; Visual scanning; Huntington disease

1. Introduction

Human eye movements are necessary for adequate visual perception of the surrounding world. Depending on the visual requirements, physiological properties, and anatomical substrates, eye movements are classified into distinct functional classes (saccades, smooth pursuit, optokinetic and others; Leigh & Zee, 1999). In every day life, saccades are used to inspect visual scenes, bringing an object of interest to the fovea for better visual acuity. Smooth pursuit holds the small moving object on the fovea. Optokinetic stimulation occurs naturally during sustained self-rotation. The pattern of eye movements is controlled by the demand of the visual, motor or cognitive tasks and, in its turn, the pattern influences the visual and cognitive processes. The studies of eye movement in patients with specific brain lesion (or neurodegenerative disease) are essential to gain an understanding of the processes underlying visual and cognitive performance.

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Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder, which results from an increased number of triplet (CAG) repeats in the huntingtin gene (Huntington's Disease Collaborative Research Group, 1993). HD is characterized clinically by progressive motor, cognitive and emotional symptoms (Folstein, 1989). Patients with advanced disease demonstrate a broad range of eye movement abnormalities including impairment of saccades, pursuit, optokinetic response, and fixation (Leigh et al., 1983; Petit & Milbled, 1973; Starr, 1967). The most prominent symptoms in mildly affected HD patients are deficits of volitional saccades (saccades made as a part of purposeful behavior, such as anti-saccades and memory-guided saccades) and impairment of steady fixation (Lasker, Zee, Hain, Folstein, & Singer, 1987; Tian, Zee, Lasker, & Folstein, 1991). Siemers et al. (1996) and Kirkwood et al. (1999, 2000) documented eye movement deficits in presymptomatic HD gene carriers. Zangemeister and Mueller-Jensen (1985) also showed a high incidence of abnormalities in at-risk subjects using quantitative recordings of eye movements. However, Collewijn, Went, Tamminga, and Vegter-Van der Vlis (1988) and Rothlind, Brandt, Zee, Codori, and Folstein (1993) did not find deficits in at-risk subjects. Although the eye movements of HD patients have been extensively studied using traditional, laboratory based oculomotor experiments, little is known about a patient's performance when experimental condition are more similar to the natural state. It is also not known if the detection of eye movement abnormalities in an individual at-risk for HD correlates with the presence of a defective gene or if it could be a valuable diagnostic marker to identify onset of the disease.

HD is characterized neuropathologically by atrophy of the frontal lobe and certain structures within the basal ganglia, particularly the caudate nucleus (CN) and the substantia nigra pars reticulata (SNpr) (Oyanagi, Takeda, Takahashi, Ohama, & Ikuta, 1989). According to a current model of the neural mechanisms, the projection from the frontal lobe areas to the superior colliculus via CN and SNpr is associated with the control of volitional saccades (Leigh & Zee, 1999). This model and the results of clinical studies led to the hypothesis that this projection is affected at an early stage of disease (Lasker & Zee, 1997).

The goal of our project was to assess the range of potential eye movement deficits in a sample of mildly affected HD patients and presymptomatic HD gene carriers (PSGC). We hypothesized that visual scanning, which put a higher demand on the oculomotor control system, would be a sensitive test to assess the deficits in PSGC and patients in the early stages of HD. The testing paradigm included both traditional oculomotor tests and a novel experimental procedure designed to assess visual scanning while participants completed the Digit Symbol Subscale of the Wechsler Adult Intelligence Survey-Revised (WAIS-R) (Wechsler, 1981).

2. Methods

2.1. Subjects

Participants were recruited from a sample of at-risk individuals previously studied (Kirkwood et al., 2000) as well as through the National Research Roster for HD Patients and Families. DNA samples were tested with a polymerase chain reaction-based diagnostic screen to determine the number of CAG repeats in the huntingtin gene (Goldberg, Andrew, Clarke, & Hayden, 1993; Bond & Hodes, 1996). An experienced neurologist conducted clinical neurological examination of all subjects. The neurologist knew that all subjects were at-risk for HD but was not aware of the results of molecular testing. Based on the results of the molecular testing and the neurological examination, individuals were assigned to one of three groups: (1) nongene carriers (NGC, the number of NGC participants, $n = 19$), defined as those individuals with two unexpanded HD alleles (<32 CAG repeats); (2) presymptomatic gene carriers (PSGC, $n = 9$), defined as those individuals with an expanded HD gene ($\geqslant 38$ CAG repeats) but who were not diagnosed with manifest HD by the neurologist; and (3) manifest HD ($n = 8$), defined as those individuals with an expanded HD gene ($\geqslant 38$ CAG repeats) who had been recently (within 1–2 years) diagnosed with HD.

Our study was approved by the local institutional review board (IUPUI IRB Study No. 0002-44). Written informed consent was obtained from participants after the risks and benefits were explained to them.

2.2. Eye movement tracker

The vertical and horizontal positions of the participant's eye pupils were recorded binocularly with two ultra-miniature high-speed (250 HZ) video cameras and then digitized at 250 HZ for later analysis (Eyelink, SR Inc, spatial resolution <0.1°). The cameras were attached to the headband; therefore, the technique used recorded eye positions in orbit while participants completed the tests. During blinks, the video system did not identify the participant's pupil and a large, negative constant value was recorded to mark missing data. An example of eye position and blink records are presented in Fig. 1.

2.3. Testing procedure

The testing paradigm included both traditional oculomotor tests and a visual scanning test. A calibration

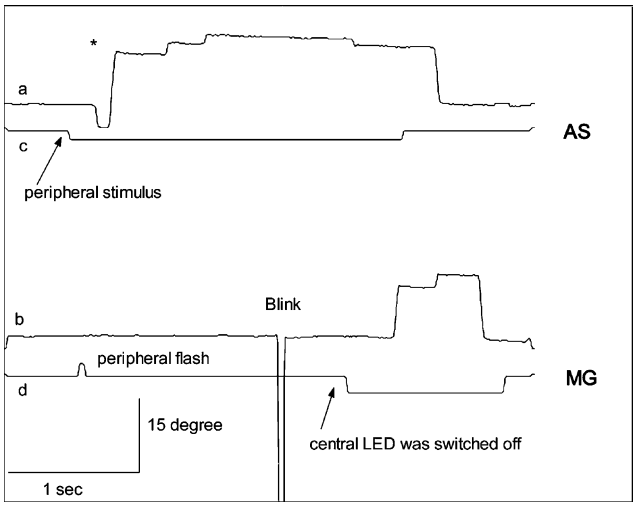

Fig. 1. Horizontal position of right eye ((a) shows AS trial, (b) shows MG trial) and timing and directions of peripheral LED ((c) and (d)) for PSGC participant. In the AS trial, the participant was instructed to look in the opposite direction to the peripheral LED. In this trial, participant made a reflexive glance toward the peripheral LED. The asterisk indicates an incorrect response. In the MG trial, the participant was instructed to look toward the remembered position of the flash. Participant performed this trial correctly.

trial preceded each test. The traditional oculomotor tests elicited saccades, pursuit, and optokinetic nystagmus (OKN). The participants were seated in a special chair in a darkened room, one meter from a large white screen. Before each test, the participants were given a complete explanation and instruction for all procedures; however, no practice trials were performed. The participants' position and head movements were restricted by a neck support, head restraint, and chair belt. During the visual scanning test, participants completed the Digit Symbol Subscale of the WAIS-R. Participants were seated in front of a table (1/3 m from testing material). The participants' position and head were not restrained, although participants were instructed to remain in their initial position until the test was completed and a neck support collar was employed to discourage head movements.

After completion of the tests, we carried out an analysis of the eye position records using an interactive program (Blekher, Siemers, Abel, & Yee, 2000) written in Matlab (Mathworks, Inc., Natick, MA).

The program identified blinks in accordance with the missing data criteria. To minimize an artifact noise, the program removed blinks, applied linear spline and Gaussian smoothening to the blink's areas, and created an array to store the coordinates of the blink's areas. Then, the program differentiated the eye position signal with respect to time and detected the beginning and the end of the saccades by using an algorithm suggested by Sauter, Martin, Renzo, and Vomscheid (1991). The algorithm constructed a predicted eye velocity by using an innovation sequence generated by a Kalman filter, and compared the predicted eye velocity with the actual one. A significant event (a significant difference between the predicted and actual eye velocities) corresponded to a saccade. When applied to the records of the saccadic tests, this algorithm was compatible with the velocity algorithm of 35°/s at the beginning and 20°/s at the end of saccades. The program presented the eye movements records with the marked saccades on a computer screen, allowing us to verify manually that all saccades were detected. To avoid any possible bias, the analysis of all records was done by only one individual, who was not aware of the participant's medical condition or the results of neurological and molecular testing. By using this procedure, the right eye records were processed. Finally, the program quantified the primary measures, as described for each test.

2.3.1. Saccades

A horizontal target array of green light-emitting diodes (LED) was located on the screen. Three separate test conditions (visually guided, anti-saccade, and memory guided) were assessed. Each test condition consisted of 30 trials. During a trial, participants were instructed to fixate on a central illuminated LED (0° deflection) and to redirect their gaze in response to a peripheral LED illumination (±5°, ±10°, and ±15°). The timing and position of the peripheral LED were chosen pseudo-randomly.

2.3.1.1. Visually guided (VG) trial. The central LED was extinguished simultaneously with the illumination of a peripheral LED. Participants were instructed to follow the target light as rapidly as possible.

2.3.1.2. Anti-saccade (AS) trial. This trial was visually identical to the VG trial except that participants were instructed to look in the opposite direction of the peripheral LED at an equal distance from the center.

2.3.1.3. Memory-guided (MG) trial. Participants were instructed to fixate on the central LED while an eccentric flash (50 ms duration) occurred on the peripheral LED. Participants were asked to continue to fixate on the central LED until it was switched off after an additional delay (1–2 s). They were then instructed to look at the remembered position of the flash.

The AS and MG trials tested the ability to both suppress a saccade toward a suddenly appearing visual target and to make a volitional saccade elicited by an internal trigger. Fig. 1 shows an AS and an MG trial for PSGC participant.

The program marked each saccade, which met the following four criteria: (1) it was the first saccade after the central LED offset; (2) the saccade was initiated between 100 and 600 ms after the central LED offset; (3)

the direction of the saccade was consistent with instruction for the test condition; and (4) the saccade did not overlap with the blink's area. Most subjects made more than 10 marked saccades in MG and AS test conditions and more that 20 qualified (marked) saccades in VG test condition. The results from two HD and two PSGC individuals in MG condition, and one HD individual in AS condition were excluded from group analysis because the individuals made less then six qualified saccades. For each condition, latency, amplitude, and peak velocity of the marked saccades were quantified and three averaged measures were derived for each participant: (1) the mean latency; (2) the mean accuracy of saccades, i.e. the mean ratio of saccade amplitude to the LED amplitude; and (3) average peak velocity of 15° saccades. To evaluate average peak velocity of 15° saccades, the amplitude (A, degree) and peak velocity (V, deg/s) data were fitted, using a least-square-regression algorithm, to a main sequence equation, $V = B*(1 - \exp(-CA))$ where B and C are constants (Bahill, Clark, & Stark, 1975). The equation was used to calculate the peak velocity for an idealized 15° saccade (the procedure slightly modified from that of Bittencourt, Wade, Smith, & Richens, 1981). The advantage of this method is that all qualified saccades contribute to this calculated velocity. Additionally, we counted the fraction of reflexive (error) saccades in AS task and the fraction of correct saccades in MG task, i.e. the ratio of number of reflexive (or number of correct saccades for MG test condition) to the number of trials.

2.3.2. Pursuit

Pursuit was assessed using a red, helium-neon laser spot (0.25° in diameter) that was rear-projected on the screen by a computer-controlled mirror galvanometer. Pursuit tests consisted of 10 cycles of horizontal and vertical sinusoidal tracking at 0.25 and 0.5 HZ. Pursuit gains were calculated as the mean ratio of the eye velocity to target velocity for all points of smooth pursuit (saccades and blinks were excluded) except where the target velocity was near 0.

2.3.3. Optokinetic nystagmus (OKN)

OKN was assessed by rotating a large drum (radius 1 meter) with vertical stripes at sine wave velocities of 0.2 Hz (23°/s maximum drum velocity) and 0.05 HZ (60°/s maximum drum velocity). Participants were instructed to look at each new stripe that came in front of his/her view. OKN gains were calculated as the ratio of eye velocity to drum velocity (slow phase eye velocity was averaged near the maximum drum velocity).

2.3.4. Visual scanning

During the Digit Symbol test, the participants were presented with a series of digits, 0–9, in boxes along with a key at the top of the page matching these digits to particular symbols (for example, 1 to –, 2 to ⊥, etc.), see Fig. 2a. The participants were given 90 s to write the corresponding symbol from the key in the box below each digit as quickly and accurately as possible.

We computed two measures from the Digit Symbol test: the number of correctly written symbols and the number of shifts of the line of sight (i.e. shifts of eye position) during the test. The shift consisted of one, two or three saccades made in the same direction and separated by short time interval (<250 ms). The same direction was interpreted in a broad sense, namely (right, up), (left, up), (right, down), and (left, down). The total amplitude of shift should be greater than 2.5°. The number of shifts made by the participant during the Digit Symbol test was a robust measure which did not change significantly with variation in the time interval between saccades (<150–300 ms), or in the total amplitude (2°–2.5°). The shifts were detected by a computer program. The program detected all saccades with an amplitude greater then 1.5°; united saccades made in the same directions and separated by short interval, and identified all saccades with total amplitude greater then 2.5°. The program presented the eye movement records with the marked shifts on a computer screen so that they could be verified manually to ensure that all shifts were detected correctly.

2.4. Statistical analysis.

The HD, PSGC, and NGC groups were compared for each of the eye movement measures using Kruskal–Wallis nonparametric tests. Additionally, post hoc multiple comparison tests (Kruskal–Wallis Rank Sum) were performed to identify pair-wise differences between the groups.

3. Results

In our sample, the HD individuals were only mildly affected, with a mean Independence Scale score (Huntington Study Group, 1996) of 82.5 ± 8.9. For this test, higher scores correspond to better functioning and the maximum possible score is 100. All PSGC subjects had an Independence Scale score of 100 and considered themselves unaffected.

Demographic characteristics for the study participants, shown in Table 1, indicated that the three groups were of comparable ages and education.

3.1. Saccades

The difference in saccades between the three groups was significant across latencies, velocities and the number of correct/error responses in MG and AS test conditions (see Table 2). There were no significant group

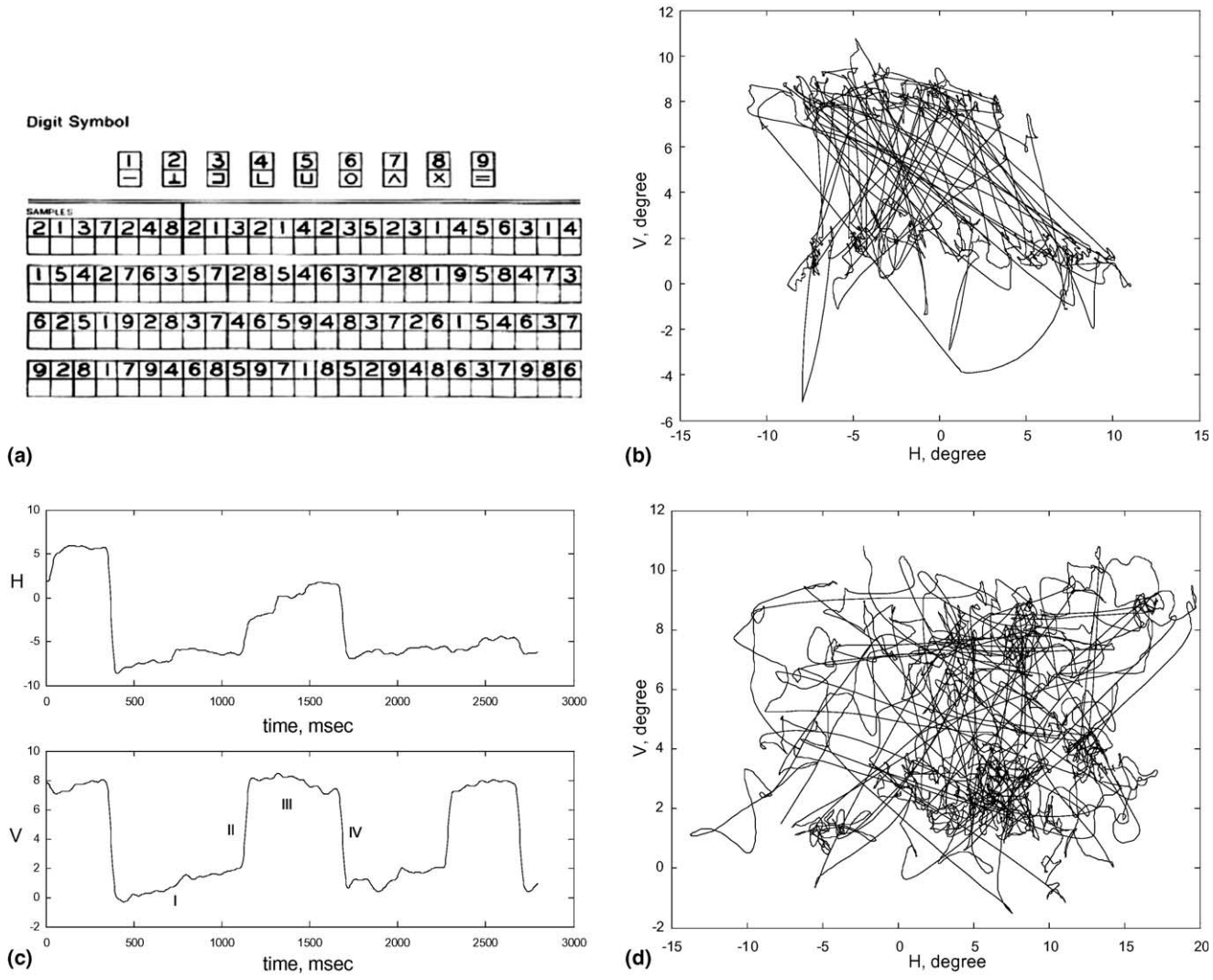

Fig. 2. (a) The Digit Symbol template. During the experiment, the template was located on the table, 1/3 m from the subject's eyes. A linear calibration test preceded the Digit Symbol test. The key area is located on the top of the template. (b) Eye path (*H*—horizontal and *V*—vertical coordinates of eye position) during a 30 s time interval, while NGC performed the Digit Symbol test. For graphical presentation of the eye path, blinks were removed from the records, linear spline and Gaussian smoothening (six steps window) were applied to the raw eye path data. Zero degree corresponded to the middle of the second row of samples of the Digit Symbol template. The key area is located at ~8° vertically up. The NGC participant performed regular back and forth movements from the second row of the samples to the key area on the top. (c) Horizontal (top) and vertical (bottom) coordinates of eye position in degrees near the beginning of the eye path on Fig. 2b. The typical component consisted of a four step pattern: (I) fixation accompanied with small eye movements at a box in the second row; (II) shift to the key area located ~8° vertically up; (III) fixation at the key area, and (IV) shift back. (d) 50 s time interval of the eye path (*H*—horizontal and *V*—vertical components of eye positions in degrees) while an HD patient performed the Digit Symbol test.

Table 1
Demographic data (mean ± standard deviation) for the 36 study participants

Demographic	HD ($n=8$)	PSGC ($n=9$)	NGC ($n=19$)	*P*-value
Age (years)	50.4 ± 9.1	49.7 ± 8.9	50.4 ± 9.9	0.99
Education (years)	15.9 ± 2.9	14.0 ± 2.9	15.1 ± 3.3	0.39
Male–female ratio[a]	5/3	4/5	7/12	0.55

[a] Ratio evaluated by Fisher's exact test statistic. All other comparisons performed by nonparametric Kruskal–Wallis test.

effects on the accuracy of VG and MG saccades. Table 2 presents data for those measures with significant group effects.

Multiple-comparison tests showed that the HD participants demonstrated prolonged latency, reduced velocity, an increased fraction of errors in the AS task,

Table 2
Primary measures of saccades (mean ± SD) for the HD, PSGC, and NGC groups

	HD ($n=8$)	PSGC ($n=9$)	NGC ($n=19$)	P-value[a]
Visually guided				
Latency (ms)	275 ± 23	259 ± 32	246 ± 23	0.02
Velocity (deg/s)	274 ± 69	365 ± 59	387 ± 44	0.0006
Anti-saccade				
Fraction of errors[b]	0.5± 0.2	0.3 ± 0.2	0.25 ± 0.2	0.004
Latency (ms)	384 ± 102	348 ± 75	296 ± 41	0.02
Velocity (deg/s)	246 ± 60	319 ± 41	336 ± 41	0.004
Memory guided				
Fraction of correct saccades[c]	0.3 ± 0.2	0.3 ± 0.2	0.6 ± 0.2	0.0001
Latency (ms)	375 ± 115	319 ± 38	281 ± 37	0.04
Velocity (deg/s)	235 ± 72	328 ± 62	326 ± 48	0.008

[a] p-Value corresponds to a Kruskal–Wallis nonparametric test for the three groups.
[b] Ratio of the number of reflexive (error) saccades to the number of trials (30).
[c] Ratio of the number of correct saccades to the number of trials (30).

Table 3
Digit Symbol test for the three study groups: mean and SD for the HD, PSGC, and NGC groups

	HD	PSGC	NGC	P-value[a]
Number of correctly written symbols	32 ± 10	52 ± 10	57 ± 11	0.0003
Number of shifts of the line of sight	57 ± 19	111 ± 26	108± 26	0.0005

[a] p-value corresponds to a Kruskal–Wallis nonparametric test for the three groups.

and a decreased fraction of correct saccades in the MG task as compared with the NGC participants (VG, AS, and MG tasks, $p<0.05$). In contrast, the PSGC group differed significantly from the NGC group only in the fraction of correct saccades in the MG task ($p<0.05$). Although the latency of the AS and MG saccades (Table 2) were prolonged in the PSGC group as compared with the NGC group, the difference did not reach statistical significance (the difference was significant at the level of 0.13 and 0.18, respectively). There were no differences in the velocity of the saccades between the PSGC and NGC subjects.

For the HD individuals, there were significant correlations (Spearman correlation coefficient) between the velocity of the saccade and the number of CAG repeats in huntingtin gene (visually guided saccades, $r=-0.88$, $p=0.02$; anti-saccades, $r=-0.82$, $p=0.08$; memory guided saccades, $r=-0.82$, $p=0.08$). In contrast with the results from the HD participants, the correlation was not significant for the PSGC and NGC individuals.

There were no significant correlations between the latency of saccades and the number of CAG repeats for the HD, PSGC, and NGC individuals.

3.2. Pursuit

The pursuit gain of vertical and horizontal tracking was preserved in all groups (range 0.87–0.93) and there were no significant differences between the HD, PSGC, and NGC participants.

3.3. OKN

There was a significant group effect on OKN gain at 60°/s maximum drum velocity ($p=0.03$). A multiple-comparison test revealed that the HD subjects demonstrated reduced OKN gain compared to the NGC subjects ($p<0.05$), but the PSGC did not differ from the NGC. No group difference in OKN gain was observed at 23°/s maximum drum velocity.

3.4. Visual scanning

During the Digit Symbol test, a typical component of the participant's eye movements consisted of a four step pattern: (I) fixation accompanied with small eye movements at a box in a current work area, (II) shift of the line of sight to keys at the top of the page (key area), (III) fixation at the key area, and (IV) shift back to the box in the current work area (see Fig. 2c). Occasionally, the participants shifted the line of sight (step II) to the completed boxes in the work areas instead of the keys at the top of the page, fixated at the completed boxes, and shifted back to the box in the current work area. Fig. 2b and d depicts the eye path of an NGC and HD participant and Table 3 presents the mean and SD of the number of correctly written symbols and the number of shifts of the line of sight for the HD, PSGC, and NGC groups.

The effect of group on the number of correctly written symbols was statistically significant (Table 3,

$p = 0.0003$) and post-hoc multiple comparison tests showed a significant difference between HD and PSGC ($p < 0.05$) individuals and HD and NGC ($p < 0.05$) individuals but no difference between PSGC and NGC individuals. Similarly, there were significant group effects on the number of shifts of the line of sight (Table 3, $p = 0.0005$). Also, similar to the number of correctly written letters, multiple comparison tests indicated that the HD subjects made significantly fewer shifts compared with the NGC and PSGC ($p < 0.05$).

The NGC and PSGC participants repeated more consistently the typical four-step pattern of eye movements than the HD patients (Fig. 2b and d). For the NGC and PSGC groups, there were significant correlations between the number of correctly written symbols and the number of shifts (NGC: Spearman's correlation coefficient, $r = 0.84$, $p = 0.0001$; PSGC: $r = 0.89$, $p = 0.01$). In contrast, for the HD group, the correlation was not significant ($r = 0.42$, $p = 0.3$).

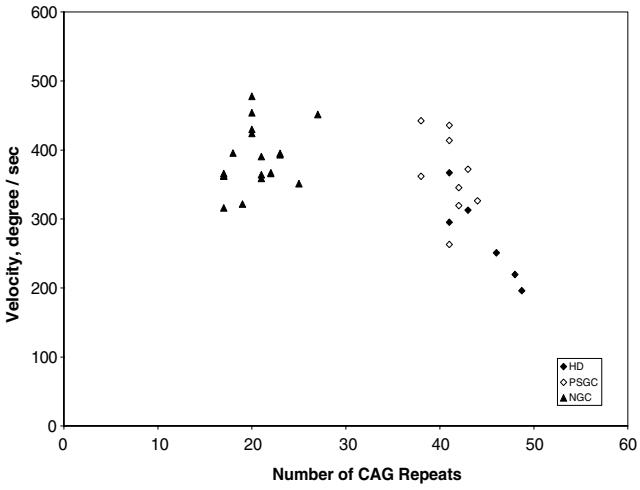

Fig. 3. Relationship between the velocity of visually guided saccade and the number of CAG repeats for the HD ($n = 6$), PSGC ($n = 9$), and NGC (16) individuals. For technical reason, we do not have an explicit number of CAG repeats for 2 HD and 3 NGC individuals. Relationship between velocity and the number of CAG repeats was similar for anti-saccade and memory-guided saccades. Three HD individuals with large number of CAG repeats demonstrated significant slowing of velocity. A mean Independence Scale score for those individuals was 76.7 slightly less then average.

4. Discussion

The hypothesis of an early involvement of the frontal—basal ganglia projection postulates that the patients in the early stage of HD would show marked deficits in volitional saccades elicited by an internal trigger (this category includes AS and MG saccades) (Lasker & Zee, 1997). Indeed, we found that the HD subjects demonstrated delays in initiation of saccades (~30% increase in latency of AS and MG saccades and 12% increase in latency of VG saccades) and a reduced fraction of correct AS and MG saccades due to their inability to suppress reflexive glances to suddenly appearing peripheral stimuli. On the other hand, we also found that the HD group demonstrated significant slowing of all saccades and a decreased OKN gain. The saccade velocity of HD individuals was significantly correlated with the number of CAG repeats in the huntingtin gene (Fig. 3). This result is consistent with the results of Garcia Ruiz et al. (2001).

Our rather conservative statistical analysis demonstrated that there were no differences between the PSGC and NGC groups for most measures except a decreased number of correct saccades in MG task and a subtle delay in initiation of volitional saccades.

While completing the Digit Symbol test the PSGC and NGC participants wrote a significantly greater number of correct symbols and made a significantly greater number of shifts of the line of sight than the HD participants. The number of shifts of the line of sight was the robust measure of eye movements, which we do not believe was significantly affected by small head movements. To simplify the presentation of the results we will refer in the future to the typical repeated pattern, i.e. shifts between work and key areas only (Fig. 2c; the results are the same for all shifts). The number of shifts is inversely related to the mean time of fixation accompanied with small eye movements at the work and key areas (the mean time of step I and step III in the typical component, Fig. 2c). In accordance with the lower number of shifts, the HD participants demonstrated prolonged mean time of fixation compared to the NGC participants. The observed slowing of the HD group during the Digit Symbol test was in good agreement with observed slowing of the HD group during traditional oculomotor saccadic tests, particularly with prolonged time of initiation of saccades and decreased velocity of saccades. Nevertheless, the overall slowing was not the only deficit that the HD patients demonstrated. The NGC and PSGC repeated a four step pattern more consistently then the HD patients (Fig. 2b and d). The correlation between the numbers of correctly written symbols and the number of shifts between the working and key areas for the NGC and PSGC subjects as well as the lack of such correlation for the HD subjects, pointed to an abnormal strategy during problem solving. The observed abnormal strategy of the HD patients may be associated with attention and/or planning deficits. In turn, the deficits of attention would increase the latency of anti-saccades and memory guided saccades, increase the number of errors, and decrease OKN gain observed in the traditional tests. Our results are consistent with recent results (Hodgson, Tiesman, Owen, & Kennard, 2002) that demonstrated an abnormal gaze strategy during problem solving in patients with Parkinson's disease, another disorder of the basal ganglia.

Although only a modest sample of HD and PSGC participants were studied in this project, our results demonstrate significant group effect and suggest that oculomotor control measures are a sensitive biomarker in the early stage of HD. Our results also demonstrated that the combination of more traditional oculomotor tests with visual scanning tests is very useful in the evaluation of visual performance of patients with brain lesions or neurodegenerative disorders. Longitudinal studies are necessary to characterize the oculomotor control and attention deficits in the early stages of HD progression.

Acknowledgments

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