Oculomotor disorders in Huntington's chorea

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SUMMARY Electro-oculographic recordings were obtained from 11 patients with Huntington's disease. Significant reduction of saccadic velocity was constantly found. In all the patients vertical saccades were much more impaired than horizontal. When present, vertical saccades showed long latency, low amplitude, low velocity, and disturbances related to blinking. Following movements were jerky, and ability to perform repeated rhythmic movements was impaired. These results are in agreement with previous observations and underline the selective defect of rapid movements as a characteristic feature of Huntington's disease. Further, they suggest a possible correlation between the difficulty in performing repeated ocular movements and the impaired execution of gestural sequences involving a succession of different fundamental movements.

Impairment of eye movements has been reported in various diseases which involve the basal ganglia. Previous observations stressed the disturbance of saccadic eye movement as a particular aspect of a more general disorder of rapid movements which can be viewed as a basic motor defect of Huntington's disease (André-Thomas *et al.*, 1945; Dereux, 1945; Starr, 1967). Petit and Milbled (1973) suggest ocular saccade analysis as a sensitive detector of early impairment in relatives of patients affected with Huntington's disease.

A disorganisation of ocular movement (ocular cogwheel) is often noticeable in Parkinson's disease. This can be related to a selective impairment of the smooth pursuit system (Rodin, 1964) and the tendency to make erroneous small saccades as shown by Jones and Dejong (1971).

We present the results of electro-oculographic recordings obtained in 11 patients with Huntington's disease and discuss the findings.

Patients and methods

Electro-oculographic recordings (EOG) were obtained from 11 of 18 patients affected by Huntington's disease who were admitted to our institute during the past three years. The age of the 10 men and eight women patients ranged from 26 to 65

years. Duration from the first symptom was one to 10 years.

In the most affected patients EOG recordings were unobtainable because of the continuous hyperkinesia and lack of co-operation of these mentally impaired subjects. In these cases the evaluation of oculomotor alterations was based on cinematographic recordings.

Neuropsychological, biochemical, and pharmacological tests carried out on this same group of patients have been reported in detail in a previous paper (Caraceni *et al.*, 1977).

The EOG was recorded by using pairs of Beckman silver-silver chloride electrodes placed in the horizontal or vertical plane and coupled with a DC amplifier (Vescovin 549). The recordings were usually binocular for horizontal and monocular for vertical movements. The signals were monitored on a dual beam D13 Tektronix oscilloscope and simultaneously recorded on an Offner polygraph and Ampex SP300 FM tape recorder.

The subject was seated in a chair equipped with a head holder. In front of the subject spots of light of convenient size and shape were projected on a semicircular screen from a revolving mirror driven by a special control system (Avanzini *et al.*, 1978). The spot could be displaced across the screen at different angles and velocities ranging from 0 to 400°/s in both horizontal and vertical planes. Signals synchronous with the beginning and end of the spot track were generated by

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photoelectric cells and monitored with the EOG recordings.

Smooth pursuit movements were elicited by moving the light spot along the screen at velocities ranging from 10 to 30°/s; single and repeated to and fro movements were usually tested (Fig. 1).

Refixation saccades were elicited by displacing

the light spot up to 25° at maximum velocity along a track. Latency and amplitude were calculated and the values plotted on a duration/amplitude diagram (Fig. 2).

Voluntary saccades were elicited by asking the subject to look at an eccentric spot on verbal command.

Fig. 1 Normal subject. (A) Single and repeated smooth pursuit movements at two different tracking velocities. c-r=centre to right; r-c=right to centre. (B) Refixation saccadic movements. In each record the upper trace indicates the beginning and end of the spot track. Internal latency of stimulation system 60 ms.

Fig. 2 Three normal subjects. Duration/amplitude diagram. Each dot represents a single value, b =regression coefficient, r =correlation coefficient.

Fixation was evaluated by asking the subject to hold his gaze on a stationary spot of light.

Calibration was performed by asking the subject to look alternately at two spots placed at a fixed distance. Good linearity was found for saccades of less than 30° .

Results

FIXATION

The ability to maintain gaze on a central or eccentric target was consistently impaired in nine of the 11 patients (Fig. 3).

SMOOTH PURSUIT

Following was disorganised and irregular because of rapid movements of small amplitude which, considering their velocity, could be interpreted as saccadic movements. This feature was present in all but two of the patients and is more marked at higher target velocity ($30^\circ/\text{s}$) (Figs. 3A, 4A, B). In addition to these saccadic movements which could be regarded as compensatory, another rapid to and fro movement was observed (Fig. 3B). These movements were similar to those observed during fixation and did not perform any compen-

satory function. They could be the expression of a fixation disturbance which interferes with the activity of the tracking system.

Seven of the 11 patients were unable to execute a series of alternate rhythmical tracking movements. One patient who showed an irregularity of single pursuit movements was able to perform rhythmic tracking from centre to periphery (Fig. 3C). Two patients with only a slight irregularity of single pursuit movement had great difficulty with alternating rhythmical movement (Fig. 4A B).

SACCADIC MOVEMENT

There was a marked difference between horizontal and vertical saccadic movements.

Vertical saccades were seriously impaired or completely absent in all cases examined. When present they were characterised by long latency, low amplitude, and low velocity. Artefacts in the record were the result of blinking and head movement (Fig. 5). The difficulties in recording prevented a systematic study of the vertical saccades.

Horizontal refixation saccades frequently showed a second corrective saccade (Fig. 6). This is also present in 47% of normal subjects. The amplitude/

Fig. 3 Huntington's chorea. (A) Fixation, showing irregular oscillation. (B, C) Pursuit movement is disorganised (saccadic pursuit).

Fig. 4 Smooth pursuit movement from two affected siblings (A and B). Slight impairment of pursuit movement. Marked defect of rapid alternating pursuit.

Fig. 5 Huntington's chorea. Vertical saccades. U=upward; D=downward. Excursion is limited and velocity less than $200^\circ/\text{s}$.

duration curve for saccades shows that the regression lines for the patients are all in the upper part of the graph and indicates slowing of the saccades which is more evident when the movement is large (Fig. 7). Latency, percentage of double saccades, and metric error were also evaluated. The only significant feature was a slight increase in mean latency of the refixation saccades in choreic patients (17% more than in normal subjects). Voluntary saccades were also slower and similar to the refixation saccades (Fig 8). Study of

verbal command saccades shows an additional disturbance caused by head movement which precedes or accompanies the eye movement. In some cases this interfered with satisfactory recording.

OPTOKINETIC AND VESTIBULAR RESPONSES

Optokinetic and caloric nystagmus was examined in all cases (Dufour, 1978). The most important change was in the fast phase with a reduction of velocity, rhythm, and regularity.

Fig. 6 Huntington's chorea. Horizontal refixation saccades. Latency is increased (see Fig. 7). The second corrective saccade is often found in normal subjects.

Fig. 7 Duration/amplitude diagram. Each regression line refers to one patient; the continuous line is derived from the average of three normal subjects. Group 1 mild, group 2 severe clinical illness.

Fig. 8 Comparison between (A) reflexion saccade and (B) saccades on verbal command. Both types of saccade show slowing of movement.

CLINICAL CORRELATIONS

In an earlier study of the clinical and biochemical aspects of Huntington's disease the patients could be divided into two groups based on intellectual performance as determined by the Wechsler-Bellevue test, and motor ability tests. In fact, good agreement between intelligence quotient and the degree of motor impairment was evident. Those of higher intelligence performed better. The findings are summarised in the Table. The numbers were too small for statistical evaluation but some

aspects of the correlations can be specified. Fixation disturbance was associated with the hyperkinetic state but the two slightly hyperkinetic patients did not show gaze impersistence. The alteration of the single pursuit movements due to the interference of saccadic movements previously described shows a similar incidence in the two groups of patients. The loss of rhythm in the sequence of back and forth movements is revealed in all the patients in group 2 and in only one patient in group 1, showing a positive correlation

Table Summary of findings

Patient	Age (yr)	Illness duration (yr)	IQ performance*	Motor dexterity impairment†	Hyperkinesia‡	Ocular impersistence§	Smooth pursuit decomposition§	Rhythmic pursuit impairment§	Saccadic impairment
<i>Group 1</i>									
PA	65	1	96	0	9	—	+	—	+
CG	51	7	93	0.7	22	+	+	—	+
SA	50	4	92	1	20	+	+	—	—
ZG	60	8	92	1	9	—	+	—	—
PG	48	1	88	1	13	+	—	+	+
<i>Group 2</i>									
CE	32	2	65	2.5	16	+	—	+	++
SM	45	1	75	1.8	13	+	+	+	++
FI	46	1	72	1	22	+	+	+	+
GS	63	3	62	2.7	24	+	+	+	++
PP	41	9	73	1.5	26	+	+	+	++
PB	39	5	63	1.5	18	+	+	+	+

*=Wechsler-Bellevue performance scores; †=scores derived from drawing tests; ‡=rating values according to the severity of hyperkinesia; §= — absent; + present; ||= — absent; + mild; ++ severe.

with the severity of the disease. Reduction in average velocity of refixation saccades was more striking in the patients of group 2 (Fig. 7). In those patients in whom it was not possible to calculate the regression line (because of the insufficient number of saccades recorded) the distribution of single values showed significant velocity reduction in the more affected patients of group 2.

Discussion

Our results confirm the observations of Starr (1967) and Petit and Milbled (1973) who found a significant alteration in ocular motility in Huntington's disease. These authors have emphasised the serious impairment of vertical saccades as the most characteristic oculomotor disorder in this disease.

Abnormal vertical saccades were observed in all our patients. The few movements which could be recorded all showed prolonged latency and notably reduced velocity. They were almost always accompanied by blinking and head movement. Horizontal saccades were also impaired—the 11 patients examined all showed slowing of horizontal saccades which was much more marked in the advanced stages of the disease. In seven patients in whom EOG recordings were not possible the saccades appeared still more disturbed and were frequently replaced by unrelated movements of the head and by blinking. These findings are similar to those reported by Starr (1967) who noted in three out of nine of his patients that saccadic movements were completely absent.

The abolition of saccadic movements requires a comment. In Starr's three patients the movement which followed a stimulus designed to elicit a horizontal saccade did not exceed a velocity of 30°/s so that its velocity was still compatible with smooth pursuit movement. However, a movement evoked by the position of the target (and not by its speed) cannot be defined as a pursuit movement but rather as a slow saccade. The occurrence of ocular movement definable as slow saccades is seen in other pathological conditions such as the Steele-Richardson syndrome and in forms of hereditary ataxia characterised by an extreme slowing of ocular movement (Wadia and Swaami, 1971; Zee *et al.*, 1976a).

Taken together, the observations of Starr (1967), Petit and Milbled (1973), and our own confirm the existence of a serious alteration of rapid ocular movements in Huntington's disease but it is not possible to affirm that saccades could be totally abolished in this disease. Demonstration of the abolition of saccades requires an accurate EOG

study which is hindered in the more serious cases by lack of concentration on the part of the patients and the continuing interference of the hyperkinesia.

Taking into account what is known of the organisation of the saccadic system (Hoyt and Frisen, 1974) and of the pathology of Huntington's disease (Bruyn, 1968), various structures could be considered responsible for the saccadic alterations. The most likely sites are: the frontal oculomotor centre (Wagman and Mehler, 1972), the caudate nucleus in which contralateral stimulation elicits ocular movements (Laursen, 1963), the mesodiencephalic region, and, in particular, the superior colliculus and pre-tectal nuclei which control head co-ordination (Schneider, 1969; Wurtz and Goldberg, 1972), and the paramedian pontine reticular formation which carries out an essential role in the integration of saccadic movement (Cohen and Henn, 1972; Keller, 1974). The specific function of these structures is difficult to establish because of the lack of an experimental animal model of Huntington's disease. Other diseases affecting ocular motility mentioned above are of little help because of extensive involvement of the nervous system.

The more prominent defect of the voluntary saccades in comparison to those evoked by rapid displacement of the target could suggest a disorder of initiation of movement.

These findings and analogous observations reported by Corin *et al.* (1972) in Parkinsonism patients suggest a possible involvement of the frontal oculomotor centre (Petit and Milbled, 1973) or the caudate nucleus (Starr, 1967). In animals, a bilateral lesion of the caudate nuclei diminishes exploratory ocular movements (Mettler, 1964). On the other hand, the defect in the rapid phase of nystagmus present in some of our patients and the abolition of ocular movement during REM sleep pointed out by Starr call attention to the more elementary integrative structures such as the paramedian pontine reticular formation. At present we cannot exclude the possibility that the saccadic defects are a result of the sum of all these components.

The smooth pursuit movements have shown alteration which can be summarised as jerky decomposition, presence of non-compensatory movements, and impaired ability to perform repeated rhythmical movements. Decomposition of the movement constitutes a nonspecific finding that can be seen in many pathological situations. It has been described in Huntington's disease (Petit and Milbled, 1973), Parkinson's disease (Rodin, 1964; Corin *et al.*, 1972), degenerative cerebellar disease

(Baloh *et al.*, 1975; Zee *et al.*, 1976b) and with lesions of the cerebral hemispheres (Troost *et al.*, 1972).

However, it has also been demonstrated that irregularities of smooth pursuit movements can appear in normal subjects in relation to a lowered level of alertness or attention. It is noted that all of these conditions can interfere at various levels in the visual motor integration mechanisms which are responsible for smooth pursuit, resulting in a loss of the gain in the system (Zee *et al.*, 1976b).

The small saccades which interfere in the EOG tracings can be seen as compensatory movements tending to bring into the fovea the image of the object in motion.

The noncompensatory movements which avert and return the eyes from and to the target are not peculiar to Huntington's disease. Morphologically similar findings have been reported by Jung and Kornhuber (1964) who described square waves in cerebellar disease and related them to fixation instability.

The larger amplitude and irregularity of the movements present in our patients prompts us to consider the possibility that they represent hyperkinesia of the oculomotor system.

The disturbance of repetitive rhythmic movements was verified in some of our patients who presented particularly severe impairment of manual performance and intelligence. In these cases, the impairment of the rhythmic sequence of movements was more pronounced than one would expect from the analysis of the single pursuit movement. This might suggest a specific impairment of the rhythmicity of the movements in the context of the general impairment of motor functions characterising Huntington's disease.

Starr (1967), after a careful analysis of the characteristics of the eye and limb movements in choreic patients, found that a selective defect of rapid movement was the most characteristic abnormality in this illness.

Our observations suggest a possible correlation between the difficulty in performing repeated ocular movements and impaired execution of gestural sequences involving a succession of different fundamental movements. This difficulty, which is typical of frontal lesions (Luria, 1966; Lhermitte *et al.*, 1972), was also very marked in our choreic patients and, therefore, could be assumed to indicate the part played by the frontal cortex or its connections with the caudate nucleus.

The good correlation between the severity of disease, expressed by various clinical abnormalities and the impairment of ocular motility, particularly in relation to velocity and the disturbance of re-

petitive rhythmical movements, emphasises the value of the EOG as an objective method in a longitudinal study of the course of Huntington's disease.

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