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Saccadic eye movements in juvenile variant of Huntington disease

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ABSTRACT

Background and purpose: Huntington disease (HD) is a neurodegenerative disease leading to involuntary movements, cognitive and behavior decline. The juvenile variant of HD (JHD) manifests in people younger than 21 and is characterized by a different clinical presentation, i.e. rigidity and bradykinesia. Rapid eye movements were not extensively studied in patients with JHD. Aims of our study were to describe the saccadic eye movements in JHD patients and to find a correlation between the saccade abnormalities, severity of the disease and cognitive and behavior deterioration.

Materials and methods: We studied 10 patients with JHD and 10 healthy subjects. Reflexive and volitional saccades were assessed with the Saccadometer Advanced. The battery of cognitive and behavior tests was performed as well.

Results: We found a prolonged latency, slowness and decreased velocity of reflexive and voluntary saccades and reduced amplitude of voluntary saccades. Moreover, patients with JHD executed a significantly lower number of volitional saccades and made more incorrect cued saccades than controls. We noted a significant correlation between prolonged latency of reflexive saccades with gap task and disease severity and significant inverse correlation between prolonged latency of reflexive saccades with overlap task, an increased number of incorrect saccades made on a cue and impairment in working memory.

Conclusion: Abnormalities of saccade eye movements in patients with JHD were similar to those reported in patients with HD. Our findings did not confirm abnormalities previously reported in patients with early onset HD. Abnormal saccade parameters correlated also with a disease severity and cognitive deterioration.

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1. Introduction

Huntington disease (HD) is a progressive, neurodegenerative disease, caused by the expanded number of CAG repeats in huntingtin gene on the chromosome 4. Mean age of disease onset is 40 years [1]. In almost 5% of cases [2], disease begins before the age of 21 and is called as juvenile HD (JHD) [3]. JHD is commonly characterized by similar clinical symptoms as HD but rigidity, bradykinesia and dystonia are more prominent than chorea. However, in some cases, early – onset HD, known as Westphal variant, manifests with rigidity and hypokinesia without choreatic movements [4].

Saccades are fast movements of eyes, generated in regard to a fast shift of an animated signal. Saccades could be triggered automatically, in response to suddenly appearing visual stimulus (reflexive saccades), or internally initiated, either on a command or to remembered location of a target (voluntary saccades). Impairment of saccadic eye movements reflects pathological changes in brain and therefore is a useful tool for assessing and tracking various neurological disorders, especially neurodegenerative diseases [5].

Saccade impairments have long been described in HD. At the beginning of disease, patients show deficits of volitional saccades, especially increased latency and hypometric amplitude of saccades. Additionally, they are unable to suppress reflexive saccades to a suddenly appearing visual target. With a disease progression, slowness of volitional saccades and abnormalities of reflexive saccades such as prolonged latency, slowness and hypometria, are detected [5–9]. Saccade impairments in JHD patients were described roughly and only in case reports [10]. Lasker et al. [11] compared patients who developed HD before and after the age of 30 and noted some differences between these two groups. In patients with early onset of symptoms we frequently observed problems with saccades' amplitude and saccades with smaller amplitude. In contrast, patients who developed symptoms later, presented difficulties with saccades' initiation and made saccades with increased latency.

The aim of the study was to assess the saccadic eye movement abnormalities in patients with JHD, as compared to the healthy controls, and to determine the relation between saccade impairments and disease severity and the cognitive and behavioral findings.

2. Materials and methods

The involvement to the study was proposed to all patients with genetically confirmed JHD who participated in the study 'REGISTRY' conducted by the European Huntington Disease Network in Krakow and Gdansk between 2008 and 2010. Eight patients remained under the care of Krakow Center and 2 were recruited from patients from Gdansk. Controls were recruited from medical students and their relatives. They were matched to the patients with the age (±5 years) and sex. The control subjects were interviewed paying special attention to the neurological disorders, as well as their family history; the number of CAG repeats was not determined. All participants provided informed consent to participate in the study.

Exclusion criteria were as follows: restriction of the eyes motility, scotomy, severe refraction abnormalities, red or green color blindness, other diseases of nervous system or muscles which cause oculomotor abnormalities, use of medications which influence the eye movements except for propranolol and primidone, alcohol or drug abuse, endured intoxication by drugs, carbon monoxide or other chemical agent, symptomatic hypo- or hyperthyroidism, autoimmune disease, malignancy, severe cardiac, renal, hepatic or pulmonary insufficiency.

The interview concerning demographic and clinical data was obtained from each patient and family member who took care of the patient. During the interview we also collected information about ophthalmological diseases Neurological examination and laboratory tests (including thyroid stimulating hormone and ceruloplasmine) were performed in all patients. Severity of disease was assessed by the Clinical Global Impression (CGI) 7-point scale (1 – without symptoms, 2 – slight symptoms, 3 – mildly ill, 4 – moderately ill, 5 – markedly ill, 6 – severely ill, 7 – extremely ill).

Severity of motor signs was assessed using the motor part of the United Huntington's Disease Rating Scale (UHDRS) [12]. Severity of depression symptoms was assessed by the Beck Depression Inventory (BDI) [13] and the Hamilton scale [14]. Behavioral characteristics of patients were assessed using the Problem Behaviors Assessment for Huntington's Disease – short version (PBA-s) [15]. Patients were also checked by a cognitive battery, consisted of three domains which are part of UHDRS scale and assessing prefrontal functions: the Symbol Digit Modality Test (SDMT) [16], the Stroop Color Word Test (SCWT) [17] and the Verbal Fluency Test (VFT, one category and three letters) [18].

The eye movements were recorded using Saccadometer Advanced (Ober Consulting, Poland). It comprises four light-emitting diodes: two (one green and one red) located in central position and two others 10 degrees bilaterally, which enable to examine visually-guided saccades [19]. The examinations were made in a soundproof and darkened room. The apparatus was mounted on the subject's head, which prevented the influence of head movements on the saccade recording. Each participant was asked to sit at a fixed distance of 100 cm from a screen, on which the light targets were projected and to follow with their eyes the red laser dots according to the instruction given by the investigator. We investigated 10- and 20-degree reflexive saccades, 20-degree pace-induced saccades, where subject was asked to look alternately at continuously illuminated two light dots as quickly as possible within 30 s and 10-degree cued saccades, where task instruction ('look at right or left visual stimulus') was indicated by the color of the central light cue. Additionally, latencies of reflexive saccades were assessed with gap and overlap paradigm. In the gap paradigm, there was 200-ms pause between disappearance of central fixation target and appearance of the peripheral one. For each task, except pace-induced saccades, sixty experimental trials were performed. All tasks were preceded by 20 calibration trials. Ten-degree reflexive saccades were assessed for latency. Twenty-degree reflexive saccades were used for evaluation of amplitude, duration and velocity. In the gap and overlap paradigm, only the latency were assessed. The comparison between the mean