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Eye movements in essential tremor patients with parkinsonian and cerebellar signs

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ABSTRACT

Apart from intention tremor essential tremor (ET) patients may display other cerebellar signs, like dysmetria or tandem gait disturbances as well as parkinsonian signs like resting tremor, cogwheel sign, subtle bradykinesia. Previous reports claimed the occurrence of the eye movement abnormalities characteristic for dysfunction of cerebellar dorsal vermis in ET patients with concomitant cerebellar signs. There are no previous reports evaluating the eye movement abnormalities in ET patients with concomitant parkinsonian signs.

The objective of this study was to determine the relationship between the occurrence of parkinsonian and cerebellar signs and the oculomotor abnormalities in ET patients.

Method: Fifty ET patients including 6 (12.0%) patients with concomitant parkinsonian signs (ET-P), 20 (40.0%) patients with cerebellar signs (ET-C), 7 (14.0%) with mixed parkinsonian and cerebellar signs (ET-M), 17 (34.0%) patients with the only tremor (ET-T) together with 42 healthy controls were included to the study. Reflexive, pace-induced and cued saccades were recorded using Saccadometer Advanced. Smooth pursuit and fixation were tested using EOG.

Results: Latency of pace-induced saccades was significantly longer in ET-C and ET-M patients compared to ET-T and ET-P patients. Latency of cued saccades was significantly longer in ET-M patients compared to ET-T. There were no significant differences of the eye movement parameters between ET-P patients compared to ET-T patients.

Conclusion: In ET patient with concomitant cerebellar signs prolonged volitional saccades latency was detected. There are no particular differences in the eye movements in ET patients with concomitant parkinsonian signs compared to ET patients without concomitant signs.

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1. Introduction

Until very recently, essential tremor (ET) has been regarded as a monosymptomatic entity characterized by action tremor involving mainly hands and forearms, less commonly head, voice, jaw, trunk and lower extremities. However, clinical observations of recent years showed that ET patients may display the other motor (parkinsonian, cerebellar, oculomotor) as well as non-motor (personality disturbances, depression, fear, fatigue, sleep disturbances, cognitive deficits, pain, hearing and olfaction loss) symptoms and signs [1]. Parkinsonian signs including resting tremor [2–5], subtle bradykinesia [6], slight arm rigidity in the form of cogwheel sign [7], decreased arm swing or hypomimia [8] occur in elderly patients. Likewise, cerebellar signs, so as intention tremor [9], dysdiadochokinesia and impaired tandem gait [10–14] usually appear in advanced stage of ET. The presence of parkinsonian or cerebellar signs might cause misdiagnosis of even 20–50% of ET cases mainly as parkinsonism or cerebellar syndrome [15–17].

Deuschl et al. [18] distinguished the cerebellar dysfunction in ET patients from that of patients with other cerebellar degeneration by the absence of the eye movement disturbances. However, Helmchen et al. [19] founded eye movement changes originated from cerebellar dorsal vermis dysfunction like impaired smooth pursuit initiation and pathological suppression of vestibulo-ocular reflex by heat tilt in ET patients with dominant intention tremor. Gitchel et al. [20] assessed eye movements in 60 ET patients regardless of the co-occurrence of concomitant signs and found abnormalities of dynamic parameters in reflexive saccades including prolonged latency and decrease velocity and fixation break by increase number of square wave jerks intrusions. Our previous study of 50 ET patients indicated the presence of the cerebellar oculomotor abnormalities including reflexive saccades dysmetria and deficit of smooth pursuit and no abnormalities of pace-induced saccades, cued saccades and fixation [21]. To the best of our knowledge there are no previous reports evaluating the eye movement abnormalities in ET patients with concomitant parkinsonian signs.

The aim of this study was to assess the relation between the occurrence of parkinsonian and cerebellar signs and the oculomotor abnormalities in ET patients.

2. Methods

The participation in the study was proposed to all patients diagnosed as ET visited the Movement Disorders Clinic, Department of Neurology, University Hospital in Cracow, Poland between January 2008 and June 2010. The diagnosis of ET was made according to the National Institute of Health Collaborative Genetic Criteria (1996) [22]. Exclusion criteria were: 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, taking drugs which influence the eye movements except levodopa, propranolol and prymidon, alcohol or drugs abuse, past intoxication by drugs, carbon monoxide or other chemical agent, schizophrenia or other sever psychiatric disease, symptomatic hypo- or hyperthyroidism, autoimmune disease, malignancy, severe cardiac, renal, hepatic or pulmonary insufficiency, and contraindication for MRI. The presence of exclusion criteria was verified based on interview and neurological examination, laboratory tests including TSH and ceruloplasmine blood level, ophthalmic examination, brain MRI and other examinations as needed. In order to exclude Parkinson disease each patient underwent levodopa challenge.

The control group, matched by age (±3 years) and gender, was recruited from patients' spouses and acquaintances. All control subjects fulfilled qualification criteria to the study.

Before the beginning of the research procedures each participant signed written consent for participation in the study. The study was approved by the Jagiellonian University Bioethics Committee. All research procedures were performed in compliance with the principles in the Declaration of Helsinki.

Patients with ET were interviewed about the age of disease onset, character of symptoms and disease course. Patients and controls were asked about concomitant medical history, current medication, stimulants, contact with toxic substances and family history. Each participant underwent neurological examination extended by the Mini Mental State Examination and evaluation of depression symptoms in the Beck Depression Inventory (BDI). The severity of tremor was assessed using the Clinical Rating Scale for Tremor (CRST) [23].

For each subject we assessed reflexive saccades, two types of volitional saccades including pace-induced saccades and cued saccades, smooth pursuit and fixation. The methodology of assessment of the eye movements was described in our previous publication [21].

2.1. *Statistic methods*

The statistical analysis was performed using STATISTICA software (version 9.0 for Windows 7.0, StatSoft. Inc., PL). Numeric variables were present as mean ± standard deviation (SD). Normal population distribution was verified by the Kolmogorov–Smirnov test. Differences between categorical variables were analyzed by Pearson χ^2 test or, in case of small sample size, by Fisher's test and between parametric variables by Kruskal–Wallis one-way analysis of variance for more then two groups. In the post hoc analysis Dunn's test was applied. A p value < 0.05 was considered significant.

3. Results

Fifty eligible ET patients (mean age: 59.2 ± 21.7 years, 26 men and 24 women) and 42 healthy volunteers (mean age: 60.6 ± 19.0 years, 17 men and 25 women) agreed for participation in the study. There were no significant differences in age and gender between patients with ET and controls.

The group of ET patient was divided into four subgroups according to the presence of parkinsonian and cerebellar signs. There were 17 (34%) patients with the only tremor (ET-T), 6 (12%) with parkinsonian signs (ET-P), 20 (40%) with cerebellar signs (ET-C) and 7 (14%) with mixed parkinsonian and

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