SHORT COMMUNICATION

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Visual disturbances in patients with Parkinson's Disease treated with oral medications or deep brain stimulation

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ABSTRACT

Aim of the study. Ophthalmological symptoms are common in patients with Parkinson's Disease (PD) and can be evaluated by the Visual Impairment in Parkinson's Disease Questionnaire (VIPD-Q). This study aimed to assess the prevalence of ophthalmological symptoms in PD depending on the type of treatment used i.e. pharmacological or subthalamic nucleus deep brain stimulation (STN-DBS).

Material and methods. We performed a cross-sectional study. The data was gathered from a VIPD-Q and from medical records. Patients with PD were divided into two groups based on the type of treatment – pharmacological (control group, CG) (39 patients) or STN-DBS (40 patients).

Results. The great majority of patients — 72 (91.1%) — experienced an ophthalmological symptom. The prevalence of three symptoms differed significantly between the groups. A burning sensation or a gritty feeling in the eyes occurred more often in patients in the STN-DBS group (40.0% *vs.* 15.4%; p = 0.015). On the other hand, the inability to read plain text on a coloured or grey background and problems with rapid changes of light intensity were more common in the CG group (38.5% *vs.* 15.0%, p = 0.018 and 28.2% *vs.* 10.0%, p = 0.039, respectively).

Conclusions and clinical implications. The prevalence of ophthalmological symptoms in PD is high. Despite significant differences in the three symptoms, the overall prevalence of ophthalmological clinical features was similar in the evaluated groups.

Key words: Parkinson's Disease, deep brain stimulation, ophthalmological symptoms, levodopa

Introduction

Parkinson's Disease (PD) is the second most frequent neurodegenerative disorder, and, at the same time, the most frequent movement disorder [1]. Non-motor symptoms in PD are common and can contribute to reduced quality of life [2, 3]. Among non-motor symptoms, ophthalmological symptoms are of significant importance [4, 5]. The most common of these symptoms include defects in visual acuity, eye movements, pupil abnormalities, lens opacity, and diplopia [6, 7]. Visual impairment, together with postural and gait impairment, increases the risk of falls and fall-related injuries [8].

Recently, a new PD-specific questionnaire, the Visual Impairment in Parkinson's Disease Questionnaire (VIPD-Q), has been developed to assess ophthalmological symptoms [8]. This instrument facilitates the assessment of both the prevalence of specific symptoms and the domains in which those symptoms manifest themselves. There is a paucity of

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data on the impact on ophthalmological symptoms of treatment modalities used to treat PD. The aim of this study was to assess the prevalence of visual impairment in patients with PD treated only pharmacologically, i.e. with l-dopa, or by a combination of oral treatment with subthalamic nucleus deep brain stimulation (STN-DBS).

Material and methods

Study design

This cross-sectional study was conducted in one academic centre between June 2020 and June 2021. Ethical approval was granted by the institutional review board (opinion number: 1072.6120.104.2020). Participants provided written informed consent.

Consecutive patients meeting the following inclusion criteria were recruited: a PD diagnosis based on the UK Brain Bank Criteria [9]; first symptoms of the disease having occurred after the age of 30; stable doses of PD medications (for at least four weeks); age at least 60; and ability to give informed consent for participation in the study. Exclusion criteria were as follows: a score of ≥ 4 on the Hoehn and Yahr scale [10]; secondary parkinsonism (drug-induced, vascular, tumour, infectious, immunological); dementia according to DSM-IV (not allowing questions to be understood); a major depressive disorder according to DSM-IV; a psychotic disorder according to DSM-IV; previous brain surgery (except for DBS); previous ophthalmological surgery (except for cataract surgery); blindness in one eye; medication that influences normal visual function other than PD medication (detailed information see ref. [8]); systemic diseases which may influence visual function; a history of lesions near the optic chiasm or occipital cortex; and migraine.

Additional data was obtained from medical records. Patients were divided into two groups based on their type of PD treatment. Patients in the control group (CG) were treated with oral medications, while patients in the other group were treated with STN-DBS in combination with oral treatment. The Polish version of the VIPD-Q was administered to patients during a visit to the outpatient clinic. Detailed information on the VIPD-Q was presented in a previous study [8].

The main outcome of our study was the prevalence of ophthalmological symptoms in the two groups depending on the type of PD treatment.

Questionnaire and analysis

VIPD-Q consists of 17 questions divided into four domains: ocular surface, intraocular, oculomotor, and optic nerve [8]. The answers "every week" or "every day" were defined as the presence of all symptoms except for hallucinations, the presence of which was defined as the answer "every month" or higher [8]. The total score of the VIPD-Q and the score in each domain were calculated.

Statistical analysis

The analysis was conducted with IBM SPSS Statistics 28. Descriptive variables were presented as mean and standard deviations (SD) or median and first and third quartiles (Q1–Q3) depending on the distribution. The distribution was explored with Shapiro-Wilk's test. The differences between non-normally distributed variables were assessed with the Mann-Whitney *U* test and Spearman's rho was used for correlation analysis. Categorical variables were presented as number (n) and percentage (%). The differences between qualitative data were analysed with the Chi-square test. P-value < 0.05 was considered significant.

Results

Seventy-nine patients were included in the study. The demographic and clinical features of patients are set out in Table 1.

Almost all of the patients (72; 91.1%) experienced at least one ophthalmological symptom that occurred at least once a week; 37 (94.9%) patients in the CG group and 35 (87.5%) in the STN-DBS group (p = 0.432). The median total VIPD-Q score (Q1–Q3) in both groups was 9.0 (5.0–14.0); 9.0 (6.0–16.0) in the CG group and 9.0 (4.0–14.0) in STN-DBS group (p = 0.312). The median score in the ocular surface was 4.0 (2.0–5.0); in CG it was 3.0 (2.0–5.0), and in STN-DBS it was 4.0 (2.0–6.0) (p = 0.933). In the intraocular domain, median score overall and in both groups separately was 2.0 (0.0–4.0) (p = 0.536). The median score in the oculomotor domain was 1.0 (0.0–3.0); in CG it was 1.0 (0.0–3.0) and in STN-DBS it was 1.0 (0.0–2.0) (p = 0.551). In the optic nerve domain, the median score was 1.0 (0.0–4.0); in CG it was 2.0 (0.0–4.0) and in STN-DBS it was 1.0 (0.0–3.0) (p = 0.096) (Tab. 2). The prevalence of the three symptoms differed significantly between the groups. Burning sensation or gritty feelings in the eyes occurred in six (15.4%) patients in the CG group and in 16 (40.0%) patients in the STN-DBS group (p = 0.015; 95% confidence interval (CI) for proportions difference: 5.7%–43.5%). The inability to read plain text on a coloured or grey background was present in 15 (38.5%) patients in the CG group and in six (15.0%) in the STN-DBS group (p = 0.018; 95%CI for proportions difference: –42.4% to –4.6%). Problems with rapid changes of light intensity occurred in 11 (28.2%) patients in the CG group and in four (10.0%) patients in the STN-DBS group (p = 0.039; 95%CI for proportions difference: –35.1% to –1.3%) (Fig. 1).

Considering both groups together, there was a significant positive correlation between VIPD-Q total score and UPDRS III (rho = 0.278, p = 0.013). In a separate analysis, a moderate correlation between VIPD-Q total score and UPDRS III was found only in the STN-DBS group (rho = 0.392, p = 0.012). Time from STN-DBS implantation moderately correlated with 'intra-ocular' and 'oculomotor' domains (rho = 0.327, p = 0.040, rho = 0.331, p = 0.037; respectively).

Table 1. Characteristics of study group

Parameter		All patients (n = 79)	CG (n = 39)	STN-DBS (n = 40)	P-value
Male, n (%)		46 (58.2%)	26 (66.7%)	20 (50.0%)	0.203
Age (years), median (Q1-Q3)		69.0 (60.0–73.0)	70.0 (60.0–73.0)	65.5 (60.0–71.8)	0.211
Disease duration (years), median (Q1-Q3)*		11.0 (7.0–16.0)	7.0 (5.0–11.0)	14.0 (11.5–19.5)	< 0.001
Subtype of PD**	Tremor dominant, n (%)	11 (14.7%)	7 (18.4%)	4 (10.8%)	0.703
	PIGD, n (%)	34 (45.3%)	16 (42.1%)	18 (48.6%)	
	Mixed, n (%)	30 (40.0%)	15 (39.5%)	15 (40.5%)	
LEDD (mg), median (Q1–Q3)		580.0 (410.0–760.0)	705.0 (535.0–1,360.0)	480.0 (380.0–618.8)	< 0.001
UPDRS part III, median (Q1-Q3)		16.0 (8.0–26.0)	18.0 (8.0–28.0)	14.0 (7.0–22.8)	0.247
Comorbidity, n (%)		70 (88.6%)	37 (94.9%)	33 (82.5%)	0.154
Dementia, n (%)		21 (26.6%)	15 (38.5%)	6 (15.0%)	0.023
Diabetes mellitus type 2, n (%)		11 (13.9%)	9 (23.1%)	2 (5.0%)	0.025
Coronary artery disease, n (%)		11 (13.9%)	6 (15.4%)	5 (12.5%)	0.711
Hypertension, n (%)		36 (45.6%)	22 (56.4%)	14 (35.0%)	0.056
Atrial fibrillation, n (%)		11 (13.9%)	5 (12.8%)	6 (15.0%)	0.780
Any medication for disease other than PD, n (%)		68 (86.1%)	36 (92.3%)	32 (80.0%)	0.210
Time from STN-DBS implantation (years), median (Q1-Q3)		–	–	3.5 (2.0-6.8)	–

*data available for 37 patients in CG group and 37 patients in DBS group;
**data available for 38 patients in CG group and 37 patients in DBS group
CG — control group; STN-DBS — subthalamic nucleus deep brain stimulation; PIGD — postural instability and gait disturbance; LEDD — levodopa equivalent daily dose; UPDRS III — Unified Parkinson's Disease Rating Scale III

Table. 2. Overall and 4-domains VIPD-Q results

Domain	All patients (n = 79)	Controls (n = 39)	STN-DBS (n = 40)	P-value
Ocular surface, median (Q1–Q3) (95% CI)	4.0 (2.0–5.0) (4.0–5.0)	3.0 (2.0–5.0) (3.0–5.0)	4.0 (2.0–6.0) (3.0–5.0)	0.933
Intra-ocular, median (Q1–Q3) (95% CI)	2.0 (0.0–4.0) (2.0–3.0)	2.0 (0.0–4.0) (2.0–3.0)	2.0 (0.0–4.0) (2.0–5.0)	0.536
Oculomotor, median (Q1–Q3) (95% CI)	(0.0–3.0) (0.0–2.0)	1.0 (0.0–3.0) (0.0–2.0)	1.0 (0.0–2.0) (0.0–2.0)	0.551
Optic nerve, median (Q1–Q3) (95% CI)	(0.0–4.0) (1.0–2.0)	2.0 (0.0–4.0) (2.0–4.0)	1.0 (0.0–3.0) (1.0–3.0)	0.096
Total VIPD-Q score, median (Q1–Q3) (95% CI)	9.0 (5.0–14.0) (7.0–12.0)	9.0 (6.0–16.0) (7.0–13.0)	9.0 (4.0–14.0) (7.0–12.0)	0.312

Discussion

Our study is one of the first to compare ophthalmological symptoms in patients with PD treated with medications and STN-DBS. Patients treated with oral medication more often complained about two symptoms from the optic nerve domain, while one symptom from the ocular surface domain was more frequent in patients with STN-DBS.

Ophthalmological symptoms are common in patients with PD as has been shown by previous studies [5]. In our study, their prevalence reached over 91% without significant differences in the treatment type groups. This is higher than in the existing literature where the prevalence has ranged between 10% and 78% [6]. However, it is in line with the previously published studies using the VIPD-Q, which took into consideration a greater number of ophthalmological symptoms — there the prevalence reached 82% and 92% [8, 11].

There is only our previous study comparing ophthalmological symptoms in patients treated with DBS or with l-dopa [12]. However, only saccadic eye movements were analysed, showing better results in patients with DBS. The current study took into consideration a broad spectrum of ophthalmological symptoms.

Patients with STN-DBS experienced a burning sensation in the eyes more often than those in CG. Nevertheless, those

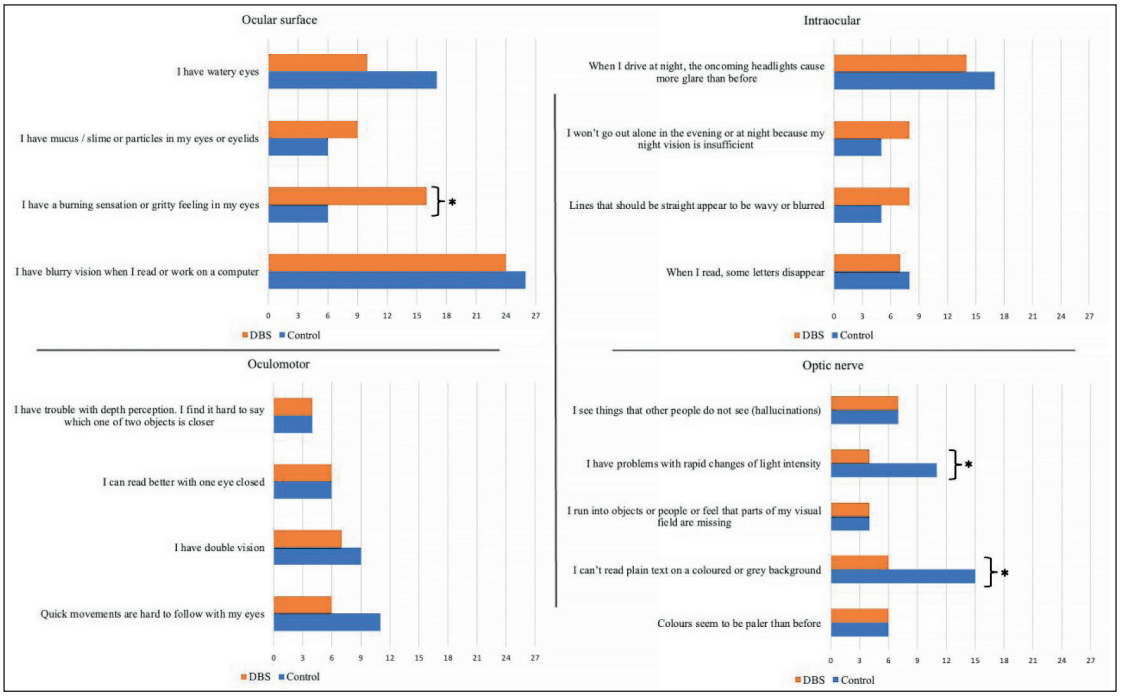

Figure 1. Prevalence of symptoms with division into domains. DBS — deep brain stimulation; *p < 0.05

results did not influence the median score of VIPD-Q domains, which showed no significant differences between groups. Dry eyes in PD are thought to result from a decreased blink rate, but they may also result from decreased tear production caused by autonomic dysfunction, based on the partial parasympathetic innervation of the lacrimal gland [5]. Bologna et al. revealed that the spontaneous blink rate increases after either STN-DBS or l-dopa [13]. Thus, we speculate that autonomic dysfunction and STN-DBS may have a pivotal role in decreased tears production in such patients. Moreover, a "burning sensation in the eye" may be considered, among others, an ocular adverse effect after STN-DBS in PD patients [14, 15].

Reduced contrast sensitivity, which is a common symptom in PD, is not yet fully understood [6]. A deficiency of retinal dopamine and impaired primary visual cortex function is thought to be involved [8]. Treating retinal and optic nerve pathology involves the optimisation of the l-dopa therapy [16]. The results of our study are contradictory. CG patients experienced an inability to read plain text on a coloured or grey background and difficulties with adaptation to rapid light changes significantly more often than STN-DBS patients. We suggest that this might be due to the impact of l-dopa or other antiparkinsonian medication (e.g. amantadine), especially since the CG group had a significantly higher LEDD. According to the literature, PD medications cause several adverse effects concerning the vision, such as mydriasis, miosis, and reduced accommodation [5]. Thus, antiparkinsonian medication may lead to adaptation difficulties [5]. In addition, the inability to read plain text on a coloured or grey background and difficulties with adaptation to rapid light changes had a lower prevalence in the STN-DBS group. That led us to speculate that STN-DBS positively impacted upon their prevalence. Moreover, this would be in line with the existing literature that shows that STN-DBS improves saccades as well as other more complex eye movements such as gaze holding or fixation [17].

Moreover, CG patients experienced fluctuations in ON and OFF states, commonly unpredictable in advanced condition. The evaluation of VIPD-Q was performed regardless of the ON or OFF condition, introducing a bias toward a more severe outcome. Symptoms may also result from PD itself, as has been shown in a previous study [18].

We demonstrated that the severity of ophthalmological symptoms weakly correlated with motor disability. Visual impairment in PD may be caused by the neurodegenerative process underlying PD itself [19, 20]. Considering the groups separately, a positive correlation between motor disability and VIPD-Q score was found in the STN-DBS group. Although patients suffered from motor symptoms of a similar severity (there was no significant difference in UPDRS part III between the groups), patients in the STN-DBS group had a significantly longer disease duration. This leads us to speculate that the degenerative changes in the brain were more severe in those patients. The literature shows that brain volume decreases with the duration of PD, and that the visual tract — especially the occipital lobe — is also affected [21].

We acknowledge that this study has several limitations, such as a small sample size. Patients completed the questionnaires on their own. Thus, even though they were given precise instructions, they could have made some mistakes.

Furthermore, patients might have overinterpreted their symptoms while reading them in the questionnaire.

Conclusions

We have confirmed that the prevalence of ophthalmological symptoms in PD is high. Although we found some significant differences regarding single symptoms between the methods, there were no significant differences in the overall prevalence of symptoms between the group treated pharmacologically and the group treated with STN-DBS. However, there was a significant correlation between UPDRS III and VIPD-Q total score, showing that motor severity is positively correlated with ophthalmological symptoms prevalence.

Clinical implications/future directions

Patients with PD should be regularly assessed ophthalmologically, especially in the advanced state as the symptoms might progress with disease duration. The detailed influence of STN-DBS on the optic tract should be further studied in order to establish the precise interaction.

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