Letter to the Editor

Subthalamic Nuclei Deep Brain Stimulation Improves Color Vision in Patients with Parkinson’s Disease

Dear Editor:

Visual deficits in people with Parkinson’s disease (PD) cover a broad spectrum of signs and symptoms and contribute to the overall disability of individuals with PD [1,2]. However, there is currently no unifying mechanism explaining ocular motor deficits [1], pupillary abnormalities [2] and color vision (CV) deficits [3] in PD.

Subthalamic nucleus (STN) deep brain stimulation (DBS) improves PD motor symptoms, reduces the need for dopaminergic medications and may ameliorate non-motor symptoms in PD [4]. Particularly, STN-DBS has been reported to improve smooth pursuit and ocular saccades performance in patients with PD [2]. As little is known about how DBS influences other frequent ophthalmologic features of PD, we investigated the effect of STN-DBS on pupillary reactivity and CV.

Ten consecutive subjects with PD and bilateral STN-DBS were tested on their current medication regimen. We analyzed pupil diameter as a function of time after onset of bright visual stimuli to estimate the speeds of pupillary constriction as well as the absolute constriction size (the difference between pupillary area before visual stimulation and its nadir). Pupillary reactivity was measured by presenting visual stimuli of different luminance on an LCD screen. We presented 24 trials, each consisting of a 7s baseline (blank screen) followed by a 2s long presentation of bright squares. Pupil size was measured with an eye tracker (EyeLink 1000), CV ability was assessed using standard Ishihara Color Vision plates in ambient light.

CV values and pupillary reactivity parameters (changes in pupillary size, pupillary constriction and re-dilation speed) with visual stimulation, demographic data, age at the time of PD diagnosis and DBS implant, amount of dopaminergic medication, UPDRS and NMSS were recorded and analyzed. We chose a pairwise design where we first established baseline parameters with DBS turned ON, reflective of a stable state, because in these patients DBS was ON continuously for at least the previous six months with unchanged parameters. We then turn DBS OFF and waited 30 minutes, to measure the acute effect of withdrawing electrical stimulation. Each parameter of interest was compared between the DBS OFF and DBS ON conditions for the same patient in order to identify whether DBS has an effect on the study parameters.

The mean CV was 13.4 ± 0.62 (range 9–15) when tested with the DBS ON and deteriorated to a mean value of 12.5 ± 0.86 (p = 0.01, Fig. 1A, one-tailed, paired t-test) 30 minutes after DBS was turned OFF. Interestingly, the 4 patients with unaffected CV at baseline (CV = 15) did not show any deterioration after DBS was switched OFF. In contrast, the six subjects with CV deficits at baseline (mean 12.3 ± 0.76) showed a significant impairment after turning OFF DBS, with 5 out of 6 subjects showing a CV decline of 1.8 points on average, from 12.2 ± 0.91 to 10.4 ± 0.97 (p = 0.004, one-tailed, paired t-test), while one remained unchanged. Compared to PD patients with normal CV at baseline, patients with CV impairment were older (age 65 versus 52), were diagnosed with PD at a later age (51 versus 41), had worse average UPDRS scores (OFF 19 versus 17, ON 13 versus 9), were taking higher levodopa total daily dosages (716 versus 562 mg), had DBS for longer time (4.8 versus 3.7 years), and had lower NMSS scores (46.5 versus 76).

When bilateral STN-DBS was turned ON, the mean pupillary constriction size was reduced by 7.1% (p = 0.03), as compared to DBS OFF (Fig. 1B). There was a trend toward increased pupillary constriction speed (increase of 32.2 %, p = 0.09) and no significant difference in the pupillary re-dilation speed (increase of 1%, p = 0.4), relative to the DBS OFF state. Notably, in the subgroup of patients with CV impairment, the differences in constriction size between the DBS ON and OFF state were more pronounced (10.2% reduced, p = 0.009), but constriction speed was not affected (p = 0.3).

We conclude that bilateral STN-DBS ON significantly improved CV and pupillary constriction size compared to DBS OFF condition. This is the first time these ocular functions were studied in subjects with PD and bilateral STN-DBS. Our results concur with STN-DBS effects on other ocular features [1] and non-motor functions [4].

Impairment of CV and contrast discrimination are common early signs of PD [3,5], with complex pathophysiology. In addition to retinal dopamine loss and dysfunctional cortical areas [2,5], sympathetic system dysfunction is implicated in CV deficit in PD [6,7]. While a few of our patients had normal CV, the majority presented a CV deficit at baseline, which further deteriorated when stimulation was turned OFF. Notably, in this subgroup of patients, also the effect of DBS on the pupillary size was more pronounced.

Longer light reflex latencies and pupillary constriction times, as well as reduced pupillary constriction amplitudes were also classically observed in patients with PD, suggesting autonomic imbalance in pupillary control systems [2]. Greater spontaneous changes of pupil diameter in darkness were reported in association with autonomic cardiovascular dysfunction in patients with PD [2,8]. We found that STN-DBS significantly lowered the pupillary constriction size, while pupillary constriction speed variation changes reached only borderline statistical significance.

Autonomic nervous system dysfunction is a well-recognized and therapeutically challenging feature of PD. In addition to sympathetic cardiovascular and urinary bladder changes [9], amelioration in postural hypotension was recently reported in PD patients treated with STN-DBS [10]. We found that STN-DBS improves ocular functions that are under autonomic control [2,7]. The mechanisms by
which DBS modulates autonomic ocular function is unknown, one hypothesis being that DBS may positively affect autonomic pathways.

Given the limited number of patients tested and the use of Ishihara plates, future work on a larger patient population is needed to confirm our findings with the more specific Farnsworth-Munsell 100-hue test. The impact of STN-DBS on vision-related quality of life also remains to be investigated.

These ocular effects suggest that PD subjects with visual system dysfunction might benefit from DBS therapies. Additionally, our observations endorse that larger studies on the effects of DBS on autonomic dysfunction and PD non-motor symptoms are warranted.

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References


