

SUBJECTIVE VISUAL VERTICAL MAY BE ALTERED BY BILATERAL SUBTHALAMIC DEEP BRAIN STIMULATION

(Letter to the Editor)

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Abbreviations: CNS =central nervous system; STN = subthalamic nucleus; SVV = subjective visual vertical

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The direction of 'up' has traditionally been measured by setting a line to the apparent vertical, a direction known as the 'subjective visual vertical' (SVV)¹. Consequently, SVV is the angle between the physical vertical line and the position of a visual linear marker adjusted vertically by a subject. In normal persons, SVV has a mean error less than 2 degrees². The abnormal tilt of SVV is a sensitive sign for labyrinthine disorders, impairment of the vestibular nerve or the vestibular pathways within the brainstem or the dysfunction of the vestibular cortical areas represented in the non-dominant parietoinsular cortex³. Galvanic stimulation by surface electrodes over the mastoids might also alter SVV toward the anode side⁴; however, the electrical stimulation of CNS areas is not known to impair solely the SVV in humans.

In this paper, we describe how bilateral subthalamic deep brain stimulation (STN DBS) can alter the SVV as a stimulation-related adverse reaction, in a stimulus strength dependent manner.

Two of our Parkinson's disease patients (1 male and 1 female, age: 63 and 53 years, respectively) complained about discomfort of neck after changing the stimulation settings for their STN DBS. Retrospectively, both patients exposed that they noticed a neck discomfort few hours after the contact change, but it became more pronounced and subsequently painful with time.

Careful physical examination revealed abnormal head tilt toward the right side. We could not identify any cranial nerve or gaze problems and the parkinsonian symptoms were also unchanged. However, we suspected stimulation-related adverse reaction in the background, because lowering the stimulation voltage or turning off the stimulation or changing to bipolar stimulation mode or selecting a more proximal contact completely normalized the head posture and alleviated the neck discomfort.

To investigate the pathomechanism of this phenomenon, we examined our patients as approved by the Regional Ethical Committee. The occurrence of abnormal head tilt solely depended on the stimulation settings and not the antiparkinsonian medication. Only the unipolar

stimulation of the most distal contact of the electrode implanted into the dominant (left) hemisphere could produce altered head tilt. Routine brain MRI⁵ did not reveal any electrode dislocation. **(For electrode positions refer to Supplementary data).**

Surface and needle electromyography did not verify any dystonic or tetanic muscle activity on the affected side. Physically, the eye movements and cranial nerve functions were also normal. Subsequently, we analyzed the displacement of SVV compared to the amplitude of stimulation. At each voltage level, two independent investigators measured the angle of SVV tilt at least three times⁶. Because none of the variables followed the normal distribution, Mann-Whitney and Kruskal-Wallis tests were applied to test statistically significant changes compared to the baseline level (turned off stimulation). For correlations, the Kendall's tau was calculated (SPSS v16, SPSS Inc, MN).

As presented on **Figure 1**, the unipolar stimulation of contact 0 with voltage level above 1.0V produced abnormal SVV compared to the baseline. However, both patients complained about subjective discomfort and abnormal head tilt only whenever the amplitude was over 2.5V. Correlating the applied stimulation amplitude to the observed SVV tilt, a significant and strong correlation could be demonstrated (correlation coefficient 0.89, $p=0.01$).

Based on the clinical presentation, we assumed that in these two cases the abnormal head tilt accompanied by neck discomfort was a stimulation-related side-effect. Being a permanent and not habituating adverse reaction, only adjustments of the stimulating parameters could completely alleviate it. In the background, we could not identify other cause but the alteration of the SVV. This hypothesis was further strengthened by the observed correlation between the applied voltage and the SVV alterations.

In animal experiments, the stimulation of the medial longitudinal fasciculus or the Intersitial nucleus of Cajal could produce ipsilateral ocular torsion and head tilt; whereas, a lesion could cause contralateral deviation. In humans, tonic contraversive or paroxysmal ipsiversive ocular tilt reactions were described due to unilateral, paramedian, mesodiencephalic

lesions⁷. Since these structures are very close to the implanted DBS electrode, they might be involved in the observed SVV alteration. Further systematic examinations and neuroimaging studies would be required to determine the prevalence of the phenomenon and identify which structures are responsible for the SVV impairment.

Acknowledgements

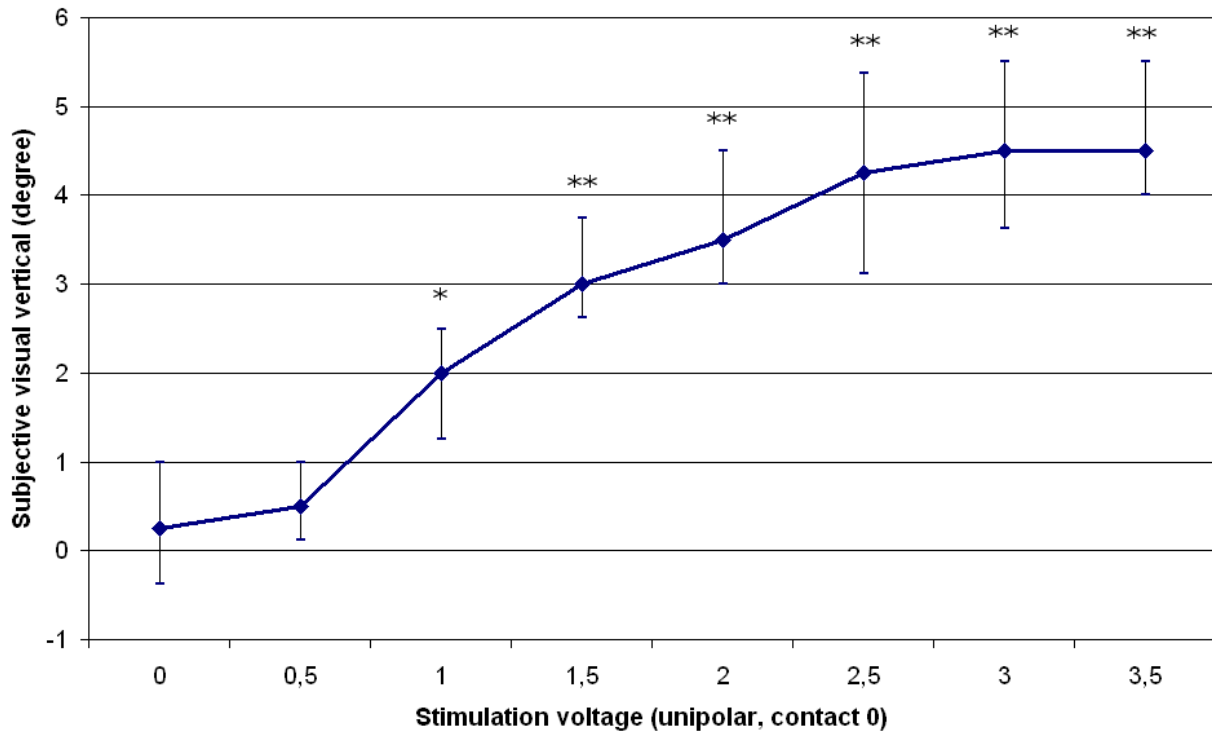
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Legends

Figure 1. Displacement of subjective visual vertical to the right side (in degrees) is plotted against the unipolar stimulation voltage of contact 0 on the dominant subthalamic electrode. Positive values reflect deviation to the right side. Because all values did not follow the normal distribution, median, 25th and 75th percentile are presented. Asterisk represent statistically significant change compared to the baseline (* p<0.05, ** p<0.01).



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