Conscious Behaviors Following Bilateral Pallido-Thalamic Low Frequency Stimulation in Patients with Continuing Disorders of Consciousness

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To cite this version:

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Keywords: DBS, consciousness
Abstract:

**Introduction:** Chronic electric deep brain stimulation (DBS) has been proposed to enable consciousness recovery, targeting mainly the central thalamus. Our aim was to study clinical effects of bilateral pallido-thalamic low frequency stimulation intended to overdrive neuronal activity in continuing disorders of consciousness.

**Methods:** Five patients were included in a prospective, monocentric, 12-month clinical observational study, with blind crossover period (NCT01718249): P1 male, 32 y/o, 12 years after traumatic brain injury (TBI), vegetative status (VS); P2 female, 62 y/o, 14 months after intracerebral hemorrhage (ICH), minimally conscious state (MCS); P3 male, 24 y/o, 3 years after TBI, MCS; P4 female, 22 y/o, 4 years after TBI, MCS; P5 female, 47 y/o, 27 months after ICH, MCS. Four phases were individualized: (1) Baseline, at least 2 months; (2) DBS surgery and titration, 1 month; (3) blind, random, 3-month cross over (CO) period with 1.5-month ON (CO-ON) and OFF (CO-OFF) conditions; (4) unblinded, at least 5 months, DBS period (DBS-ON). Electrodes (DBS 3389, Medtronic, USA) were placed within the right and left targets accounting for the lesions of patients. Two neuropacemakers (ACTIVA, Medtronic, USA) were implanted. Primary outcome was the analysis of scores of the Coma Recovery Scale Revised (CRS-R; 0-23): assessments 2 times per week; for the 5 patients, n=419, scores ranging from 1 to 18. Statistical analyses were conducted for a two-sided Type I error of 5% using random-effects models accounting between and within patient variability due to repeated measurements.

**Results:** No mortality related to surgery and DBS. By individual we observed statistically significant improvement of CRS-R during DBS-ON versus baseline (P1, P3) and CO-On versus baseline (P3). For the 5 patients (group analysis) auditory, visual, motor, oromotor-verbal, communication subscores of CRS-R were significantly improved during DBS-ON versus baseline. Cross-over analysis did not show statistically significant improvement of CRS-R and subscores during CO-ON versus CO-OFF, except P2 and P3 motor sub scores.

**Conclusion:** Bilateral low frequency DBS in severe continuing disorders of consciousness improved patients on the short term without irreversible adverse effects. Individual analysis seems preferable facing the complexity of clinical features and pathophysiology. Given the current state of knowledge, expectations of relatives, caregivers and physicians should be weighted.