Is Motor Cortex Stimulation Suitable for Elderly PD Patients?

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Opinion

To date bilateral deep brain stimulation of subthalamic nucleus (STN) and globus pallidum internum (GPi) are accepted options for treatment of selected patients with advanced Parkinson's disease (PD) resistant to medical therapy [1-4]. Despite continuous improvements in imaging techniques, neurophysiological recording possibilities and hardware and software technology, these procedures are not free from complications related to surgery and neurostimulation [5,6]. Furthermore they are less effective on axial symptoms, such as posture instability and freezing of gait, and on non-motor and non-dopaminergic symptoms, has been associated with psychiatric side effects, cognitive sequelae and cannot be offered in elderly PD patients (aged over 70 years) who can also have health conditions that would make surgery with deep electrode placement too risky [2,3].

Many efforts have been directed in order to find minimally invasive neuromodulation procedures which can be used for PD cases excluded from DBS or unresponsive to DBS.

Implantable motor cortex stimulation (MCS), introduced in clinical practice in the year 2000 by Canavero [7], may be a possibility not only for PD but also for other movement disorders [8-22] especially in elderly patients [23]. Early results of MCS were confirmed by results obtained with another technique of stimulation of the motor cortex, the repetitive Transcranial Magnetic Stimulation (rTMS). MCS procedure is less tough than DBS procedure for both patient and for neurosurgeon [24]. Indeed the implant of MCS device does not require frame-based stereotactic equipment and it is performed generally under local anaesthesia with conscious sedation [21]. Primary motor cortex (M1) is identified with high resolution CT scan, MRI with fiducial markers and neuronavigation [25]. Single burr hole or two burr holes are performed on central sulcus controlaterally to the most affected side and quadripolar paddle lead is placed over the long axis of the motor cortex at the hand knob in epidural space [26]. In uncommon case of lead implant in subdural space a small craniotomy is used. Correct position is verified neurophysiologically using somatosensory evoked potentials (SSEPs) to identify the central sulcus and motor evoked potential (MEP) to identify the primary motor cortex (M1) [12].

Paddle lead is externalized with percutaneous extension in parietal region and stimulation period of 2–3 weeks is performed for detection of most beneficial stimulation parameters and adverse effects. To achieve this all contacts are checked in bipolar setting using low frequencies (20–40 Hz) and high pulse widths (180–210 microsec): the amplitude is raised until the subthreshold voltage (2.5–4.0 V) for appearance of adverse motor and/or sensory response. On basis of improvement of symptoms above 50% and patient's satisfaction, the epidural lead is connected to the pulse generator implanted in subclavicular subcutaneous pocket and chronic stimulation began with the most efficacious setting obtained during test period (2.5–4.0 V, 40 Hz, 180 microsec.) continuously delivered night and day [27].

In PD patients moderate improvement of motor symptoms (rigidity, bradykinesia and tremor) assessed with total UPDRS and UPDRS III total in off-medication condition is bilaterally observed, a little more marked in the hemibody opposite to the stimulated side. The improvement is less than obtained with STN DBS and GPi DBS.

Largest and sustained improvement is obtained on axial symptoms, especially on walking and “freezing” of gait, as measured by the UPDRS III items [27,31]. OFF-med and on verbal fluency, mostly in elderly patients; clinical benefits of those items have important impact on patient quality of life and on assistance of care-givers [16,24,28]. MCS allows significant attenuation of L-dopa-induced dyskinesias and dystonia with reduction of UPDRS IV score and reduction of L-dopa and dopamine agonists usage documented with L-Dopa Equivalent Daily Dose [8,12,14].

The clinical changes induced by MCS are usually delayed and persisting for some days after IPG switching off: this phenomenon is likely be due to plastic modifications of the central neural circuits [13,21,29].

Complication rate and adverse events are low [26,28]. Epidural hemotoma is serious complication but it is very rare making the risk of perioperative hemorrhage much lower compared to DBS. Sporadic epileptic seizures may occur during test stimulation but not during chronic stimulation. Pain on site of paddle lead implant is reported mostly during stimulation: superficial denervation of the dura performed around the lead with bipolar coagulation allows to control this adverse event.

The motor cortex region is the final common link between deeper circuitry coordinating movement and the spinal cord itself and it is connected to the basal ganglia via direct cortico-subthalamic circuit and indirect cortico-striatal pathway [27]. Therefore MCS may induce effects at cortical level and/or at subcortical level. At cortical level MCS may modulate the “suppressor cortical system” or the activity of supplementary motor area (SMA) interfering with inhibitory axons in the cortex or with axons of afferents and afferents running parallel to the lead [11,22,30–34]. MCS may exert its effect on basal ganglia activity modulating the subthalamic nucleus (STN) directly or through the loop cortex-striatum-lateral globus pallidus-STN [27]. Chronic MCS may operate altering the firing patterns in the basal ganglia or disrupting the abnormal synchronized rhythms (antikinetic beta band) between cortex and basal ganglia that are found in PD [16].

The bilateral effects on motor symptoms and the improvement of axial symptoms for unilateral paddle lead implant over the motor strip at the hand knob can be explained with the progressive enlargement and displacement of somatotopic representations of hand motor map that occurs in advanced PD patients and with the bi-directional
interconnectivity through trans-callosal interconnections of the hand areas and of body parts outside hand areas [12,13,16,22].

In conclusion, although till today there are no large clinical studies, minimally invasive MCS may be more suitable in elderly advanced PD patients excluded from DBS as it allows to control moderately all major symptoms and to a greater degree axial symptoms and L-Dopa induced dyskinesias/dystonia with reduction of daily intake of antiparkinsonian drugs. Also verbal fluency is improved. Compared to DBS invasive MCS is easier and safer option because it can be performed without use of stereotactic apparatus and deep electrodes but it is globally less effective. Bilateral efficacy with single lead implant make it convenient in terms of costs for the healthcare system.

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