Holmes tremor

Holmes' tremor (HT) is generally considered to be a symptomatic tremor associated with lesions of the cerebellum, midbrain, or thalamus.

Treatment

Pharmacotherapy is mostly not effective. Chronic deep brain stimulation (DBS) of ventralis intermedius nucleus (Vim) of thalamus has been described as being the best surgical approach in singular case series; various authors observe, however, cases with partial responses only; therefore, alternatives are still needed.

The use of 2 ipsilateral Deep brain stimulation (DBS) electrodes implanted in parallel within the thalamus for severe essential tremor has been reported. Since dual-lead stimulation within a single target can cover a wider area than single-lead stimulation, it produces greater effects. On the other hand, DBS of the subthalamic area (SA) was recently reported to be effective for refractory tremor.

Case series

Three right-handed patients diagnosed with Holmes tremor (HT), who suffered from pharmacotherapy-refractory tremor, were eligible for unilateral posterior subthalamic area deep brain stimulation (PSA-DBS). All patients were evaluated with the Fahn-Tolosa-Marin Tremor Rating Scale (FTMTRS) and Clinical Global Impression scale (CGI) before DBS, 6, and 12 months after the PSA-DBS as well as at the last follow-up. In all patients, we observed a significant improvement of tremor control as demonstrated by changes in the FTMTRS and the CGI scales. Mean improvement of tremor in all patients was 56% for the FTMRTS with a corresponding change in the CGI scale. Our study demonstrates that PSA-DBS is efficacious in the treatment of HT. Indeed, PSA is a promising target for DBS for intractable proximal and distal tremor, even in cases of previous, suboptimal functional neurosurgery. The beneficial effect lasts over a long-term follow-up. PSA-DBS may be considered as an alternative target of DBS in tremor treatment [1].

2015

ten patients with HT unresponsive to best medical therapy who underwent DBS in our center from March 2002 to June 2012. Based in our previous experience dealing with cases of unsatisfactory Vim intraoperative tremor control and in order to optimize surgical results, presurgical target planning included two Nuclei: Vim and posteroventral Globus pallidus internus (GPi) (Espinoza et al. 2010; Espinoza et al. Stereotact Funct Neurosurg 90(suppl 1):1-202, p 61, 2012). Definitive chosen target was decided after single-cell microelectrode recording, intraoperative test stimulation, thresholds for stimulation-induced adverse effects and best clinical response compared to baseline status. Fahn-Tolosa-Marin tremor rating scale (FTM-TRS) was used to evaluate outcome. The electrode was implanted in the nucleus with the best tremor suppression achievement; on the other hand, GPi DBS was initially decided if one of the following conditions was present: (a) If Vim nucleus anatomy was grossly altered; (b) when intraoperative tremor control was unsatisfactory despite Vim high-intensity stimulation; or © if unaffordable side effects or even tremor worsening occurred during intraoperative

macrostimulation. Seven patients received definitive Gpi DBS implantation, while three patients received Vim DBS. In all observed cases, we observed an improvement on the TRS. In two cases where Vim thalamic anatomy was altered by the pathological insult GPI was planned from the beginning, and same was true in two additional cases where the Gpi nucleus showed major alterations allowing only Vim planning. Over all cases, the average improvement in tremor was of 2.55 points on the TRS or a 64 % increase in measured results; with a minimum of 1 point (25 %) improvement in one case and a maximum of 4 points (100 % improvement) also in one case. All the results were sustained at 2 years follow-up. One case with predominant resting component, implanted in the GPi, achieved the maximum possible tremor reduction (from 4 to 0 points, meaning 100 % tremor reduction); in the nine resting cases, the average reduction was of 3 points (or 75 %). DBS demonstrated in this case series adequate tremor control in 10 patients unresponsive to medical therapy. Presurgical planning of two targets allowed choosing best optimal response. Gpi stimulation could be considered as an alternative target for cases in which thalamic anatomy is considerably altered or Vim intraoperative stimulation does not produce satisfactory results [2)].

2014

Kobayashi et al., implanted 2 DBS electrodes (one at the nucleus ventralis oralis/nucleus ventralis intermedius and the other at the SA) in 4 patients with HT. For more than 2 years after implantation, each patient's tremor was evaluated using a tremor rating scale under the following 4 conditions of stimulation: “on” for both thalamus and SA DBS; “off” for both thalamus and SA DBS; “on” for thalamus and “off” for SA DBS; and “on” for SA and “off” for thalamus DBS. Results The tremor in all patients was improved for more than 2 years (mean 25.8 ± 3.5 months). Stimulation with 2 electrodes exerted greater effect on the tremor than did 1-electrode stimulation. Interestingly, in all patients progressive effects were observed, and in one patient treated with DBS for 1 year, tremor did not appear even while stimulation was temporarily switched off, suggesting irreversible improvement effects. The presence of both resting and intentional/action tremor implies combined destruction of the pallidothalamic and cerebellothalamic pathways in HT. A larger stimulation area may thus be required for HT patients. Multitarget, dual-lead stimulation permits coverage of the wide area needed to suppress the tremor without adverse effects of stimulation. Some reorganization of the neural network may be involved in the development of HT because the tremor appears several months after the primary insult. The mechanism underlying the absence of tremor while stimulation was temporarily off remains unclear, but the DBS may have normalized the abnormal neural network.

The authors successfully treated patients with severe HT by using dual-electrode DBS over a long period. Such DBS may offer an effective and safe treatment modality for intractable HT [3)].

1)
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2)
Espinoza Martinez JA, Arango GJ, Fonoff ET, Reithmeier T, Escobar OA, Furlanetti L, Alvarez Berastegui GR, Fernandes da Silva FE, Contreras Lopez WO. Deep brain stimulation of the globus pallidus internus or ventralis intermedius nucleus of thalamus for Holmes tremor. Neurosurg Rev. 2015 Oct;38(4):753-63. doi: 10.1007/s10143-015-0636-0. Epub 2015 May 20. PubMed PMID: 25990341.
3)
Kobayashi K, Katayama Y, Oshima H, Watanabe M, Sumi K, Obuchi T, Fukaya C, Yamamoto T. Multitarget, dual-electrode deep brain stimulation of the thalamus and subthalamic area for treatment

of Holmes' tremor. J Neurosurg. 2014 May;120(5):1025-32. doi: 10.3171/2014.1.JNS12392. Epub 2014 Mar 7. PubMed PMID: 24605838.