CASE STUDY

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Reduction of thalamic tremor with deep brain stimulation performed for post stroke chronic central pain

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Abstract

Deep brain stimulation (DBS) of the sensory thalamus and the periventricular/ peri-aqueductal grey area complex may be applied for the treatment of intractable neuropathic pain syndrome. The presented study concerns a patient who experienced ischemic stroke within the posterolateral part of the left hypothalamus, with subsequent severe burning pain localized in the right upper limb, predominantly within the hand, and thalamic tremor which occurred 4 months after the stroke. After 2 years of ineffective pain treatment, the patient was offered implantation of electrodes to the periventricular grey matter (PVG)/periaqueductal grey matter (PAG), as well as implantation of an electrode to the ventroposterolateral thalamic nucleus (VPL). Soon after starting simultaneous PAG/PVG and PVL stimulation, significant alleviation of the patient's thalamic tremor in the hand was observed, which persisted over subsequent months. The presented study discusses possible mechanism underlying tremor suppression in the patient concerned, probably at the level of the cerebellar outflow pathways. The study highlights the fact that DBS provide more insight into the functional anatomy of the thalamus, which used to be available only from animal studies.

Key words

thalamic stroke, thalamic tremor, deep brain stimulation, periaqueductal grey matter, periventricular grey matter, neuropathic pain

INTRODUCTION

Deep brain stimulation (DBS) for the treatment of medically intractable pain has been in use for nearly 60 years. In 1980, Mazars et al. [1] reported that in patients with chronic central pain and associated dyskinesia or thalamic pain syndromes after cerebrovascular accident, chronic thalamic stimulation could not only relieve pain, but also in certain cases improve the associated movement disorder. This experience was supported by later observations that electrical stimulation of the thalamus in the course of thalamotomy could alleviate or arrest limb tremor. Presently, DBS of the sensory thalamus and the periventricular/ peri-aqueductal grey area (PVG/ PAG) complex may be applied for intractable neuropathic pain syndrome [2].

CASE DESCRIPTION

The case is presented of a patient who experienced ischemic stroke within the posterolateral part of left thalamus, with subsequent severe burning pain localized in the right upper limb, predominantly in the hand, and postural and rest thalamic tremor which occurred 4 months after the stroke. On neurological examination, the patient presented sensi-motor right hemi-syndrome and thalamic tremor. Brain MRI revealed a cerebral infarction in the left posterolateral thalamic area, medial left temporal lobe and inferomedial temporal area, extending to left occipital lobe (Fig. 1). No abnormalities were found in the basal ganglia or brainstem. The dentate nucleus, superior cerebellar peduncle, red nucleus, and ventrolateral nucleus were all intact (Fig. 1). Surface EMG (recorded from the muscles of the upper right limb) showed rhythmic grouping discharges of 3.5 Hz that

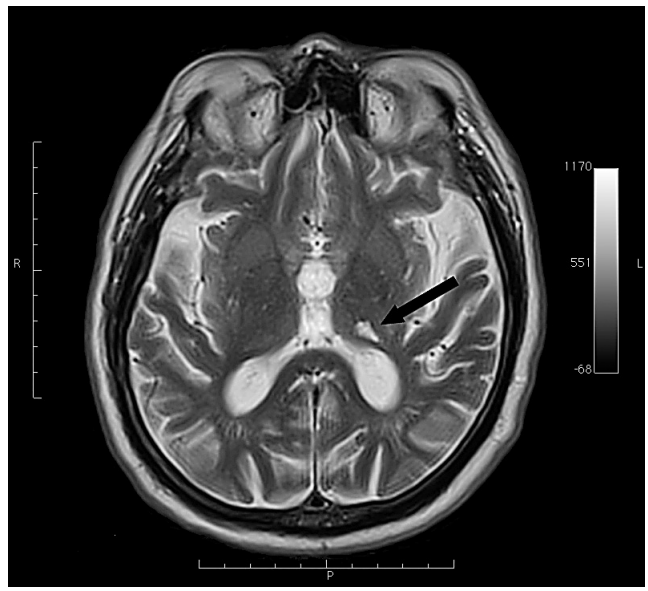

Figure 1. Brain MRI of the patient with post-stroke thalamic pain (thalamic infarct indicated by arrow)

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appeared synchronously between the wrist extensor and flexor muscles.

In the preoperative period, the patient was treated with tricyclic and heterocyclic antidepressants, opioid analgesics, including morphine, benzodiazepines, non-narcotic analgesics, carbamazepine and gabapentine, without major effect. The patient also underwent a series of transcranial magnetic stimulation, without satisfactory results. Before surgery, the patient received buprenorphine 1.6 mg/day and gabapentine 2,400 mg/day. After 2 years of ineffective pain treatment, he was referred for DBS surgery. The patient was offered implantation of electrodes to the periventricular grey matter (PVG)/periaqueductal grey matter (PAG), as well as the implantation of an electrode to the ventroposterolateral thalamic nucleus (VPL). Microelectrode recording, microstimulation, and macrostimulation were all used in the process of target localization, apart from defining the exact target for stimulation by the stereotactic MRI. Correct target localization in the VPL was confirmed when a 50Hz stimulation elicited paresthesia in the contralateral limb. Once the physiologic targets had been defined with stimulation, permanent electrodes were introduced (electrode type 3389), and the leads were externalized through a separate stab wound in the scalp for trial stimulation. Each electrode was externalized for 2 days to test the stimulation effects, and to internalize one or both of these electrodes, based upon the results of trial stimulation. Different possible stimulation combinations were explored during the trial stimulation with frequencies ranging from 5 – 100 Hz, intensity ranged from 1.5 – 2.5 V, the pulse width was kept constant at 210 ms.

Eventually, after trial stimulation and assessment of pain intensity on the visual analogue scale (VAS), PVG/ PAG was chosen as the target for permanent stimulation, and the patient was implanted with a subcutaneous pulse generator (Soletra, Medtronic Inc.). Results of VPL stimulation for pain reduction were comparable with PVG/PAG, but both electrodes were internalized.

After a few months, the patient reported an increase of pain intensity, difficult to alleviate only with PVG/PAG stimulation. Therefore, it was decided to administer additional VPL stimulation. Baseline pain intensity was assessed using the McGill-Melzack visual analogue scale – 7.9 points with PVG/PAG stimulation and 4.9 points with PVG/PAG and VPL stimulation (score was averaged over 10 trials). The parameters of permanent stimulation were selected as follows: amplitude 1.6 V, pulse width 210 μs, frequency 50 Hz, on the contact number 2 (assuming contact 0-the deepest, contact 3-the most superficial).

Interestingly, soon after starting simultaneous PAG/PVG and VPL stimulation, significant alleviation of the patient's thalamic tremor in the hand was observed, which persisted over subsequent months.

DISCUSSION

Tremor rarely occurs as a consequence of thalamic lesion. The posterolateral thalamic region is usually responsible for delayed tremor [3], although the reason why lesions in the posterolateral thalamus induce tremor is unknown. It is still uncertain at present which mechanism contribute to the genesis of thalamic tremor: interruption of ascending inputs to the posterolateral thalamus from the brainstem or cerebellum, or destruction of the posterolateral thalamic neurons themselves [4]. Interestingly, at the same time, the thalamic ventral intermedius nucleus (Vim) is a target site for stereotaxic surgery to alleviate the tremor.

In the patient in the presented study, stimulation was administered to the ventral posterolateral nucleus of the thalamus, which receives major ascending projections from spinothalamic tract neurons and project to several cortical areas, including the primary somatosensory cortex. While the exact mechanisms of DBS are unclear, one widely accepted mechanism seems to be the functional lesioning of the stimulated structure produced by high stimulation frequency. However, there is some evidence that Vim DBS facilitates the cerebellothalamocortical pathway [5], which contradicts the popular hypothesis that DBS inactivates the target area. There is also evidence that DBS of the VPL, which is a somatosensory nucleus of the thalamus, increases blood flow and oxygen metabolism in the ipsilateral postcentral cortex in patients with chronic pain [6]. Some findings suggest that activation of the DBS target area prevents the tremor-inducing signals from reaching the cortex [5]. Data from experimental studies also suggest that DBS may change the firing pattern of neurons in the stimulated area, thereby preventing the passage of an abnormal signal to the cortex [7]. Recent data suggest that the optimal target for tremor suppression is defined by its remote connections going from thalamus and cerebellum to the primary motor cortex through the ventrolateral thalamus, which is the key integrative structure and main input station to the motor system [8]. Since VPL and Vim are located in close proximity, stimulation in the VPL could spread to the Vim. It can be hypothesized that a higher amount of current during VPL stimulation might be sufficient to achieve a similar tremor suppressing effect as during direct Vim stimulation. Thus, tremor suppression in the patient presented here was achieved by interruption of the cerebellothalamocortical pathway, probably at the level of Vim. But it cannot be excluded that inhibition of the cerebellothalamocortical circuit was achieved only by direct VPL stimulation, as evidence exists that neurons from the ventrolateral thalamus project into the motor cortex [9].

The presented study highlights the fact that patients undergoing DBS provide more insight into the functional anatomy of the thalamus, which used to be available only in animal studies. Additionally, patients who undergo VPL stimulation for chronic central pain after thalamic stroke may benefit also from alleviation of thalamic tremor.

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