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Case Report

Microelectrode findings and topographic reorganisation of kinaesthetic cells after gamma knife thalamotomy

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Summary

A 64-year-old woman with Parkinson is disease had a severe resting tremor that was not completely relieved by right-sided gamma knife thalamotomy (GKT). We performed bilateral staged thalamic deep brain stimulation (DBS) and compared the right and left ventral intermediate nucleus (Vim) of the thalamus including the frequency of single units recorded with microelectrodes, and also the somatotopical distribution of kinaesthetic cells (Ki). The average frequency of units for the presumed left Vim exceeded that of the right (22.6 ± 19.2 Hz vs. 14.3 ± 8.8 Hz). Regarding the somatotopic distribution of Ki, the receptive field for the leg, which is usually situated in the dorsolateral Vim, was more widely scattered in the right Vim than the non-lesioned left side. Our findings raise the possibility that the specific properties of the neurons changed due to partial coagulation by GKT within both the coagulated and the surrounding thalamic lesions.

Keywords: Thalamic deep brain stimulation; gamma knife thalamotomy; kinaesthetic cell; Parkinson disease; plasticity.

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Introduction

We performed thalamic DBS for a patient with Parkinson's disease (PD) who had previously undergone GKT and revealed novel findings in the microelectrode recordings and topographic reorganisation of kinaesthetic cells (Ki). Hence, we hypothesise that this was in part due to partial coagulation by GKT.

Clinical details

The patient was a 64 year old woman with PD who had developed a resting tremor in the left arm from March 2000. After several days, a resting tremor appeared in the ipsilateral leg. Her symptoms gradually progressed thereafter, leading to the development of a tremor in the right arm a year later without other Parkinson symptoms such as rigidity, gait disturbance, or motor fluctuation. Unfortunately, increasing the dose of anti-parkinsonian medication induced visual hallucinations. GKT to the right thalamus was performed on September 29, 2004, with the aim of alleviating the severe left-sided tremor. GKT was delivered through a single 4 mm collimator with a maximum dose of 130 Gy. The left arm tremor improved by as much as 50% for the first post-operative year. However, it did not disappear completely, and GKT had no effect on the left leg tremor. Visual hallucinations developed and increased in proportion to the dose of

anti-Parkinsonian medication, which were increased during 17 months of conservative follow up. This complication led us to perform the bilateral thalamic-DBS surgery. On average unilateral thalamic DBS, at our facility, takes approximately 6 hours, since somatosensory stimulation (passive joint movement, light touch, skin tapping, skin pressure, or deep pressure to muscle mass or tendons) are considered. Therefore, we select the staged thalamic-DBS procedure for bilateral procedures in view of the stress on patients, preferring it not to prolong a procedure performed under local anaesthesia. In planning this procedure, we chose to perform the left thalamic DBS before the right thalamic DBS in order to see an early improvement of the right hand tremor which was the patient's dominant side.

Left thalamic DBS

Stereotactic left thalamic DBS was performed under local anaesthesia on March 15, 2006 using the MRI compatible, Leksell stereotactic frame (Elekta Instruments, Atlanta, GA). Tentative target coordinates were based on the anterior commissure (AC)-posterior commissure (PC) line on MRI. The tentative thalamic target was located in the ventral Vim, 4.4 mm (one fifth of the length of the AC-PC line) anterior from the PC. The lateral target was 17.4 mm lateral from the midsagittal plane, adjusted to a point 2 mm medial from the border between the internal capsule and thalamus, and the dorso-ventral target was at a depth corresponding to the AC-PC line. A detailed description of our stereotactic surgical procedure has been previously published [9]. A Ben's gun system (Medtronic, mm. Minneapolis, USA), an adjusted sheath (10 kΩ at 100 Hz) and needles (2 MΩ at 100 Hz) were used for microelectrode recording. Electrophysiological verification was performed using the Leadpoint (TM) system (Medtronic, mm. Minneapolis, USA) to determine the borders of the thalamic subnuclei (ventralis oralis posterior (Vop), Vim, and Vc). From +5.3 mm above the tentative target, the neural signal was recorded and the amplitude increased in comparison to when the microelectrode first entered the presumed Vim. Tremor-frequency activity (TFA) or single-unit recordings of bursting cell responses for passive joint movement were detected to determine the optimal implantation target [3, 4]. The area presumed to represent the Vim was estimated to be located +5.3 to −1.6 mm above the tentative target (length: 6.9 mm). In this zone, 26 single units were recorded and 11 units were Ki. The average frequency of these 26 units was 22.6 ± 19.2 Hz. After macrostimulation, we confirmed that at the site, 2 mm medial to and +0.5 mm above the tentative target, electrical stimulation effectively ceased the tremor with minimal side effects such as muscle contraction or paraesthesiae due to current spread to the IC or Vc. The DBS electrode lead (Medtronic model 3387; Medtronic, mm. Minneapolis, USA) was accordingly inserted into this position.

Right thalamic DBS

Right thalamic DBS was performed on April 12, 2006. MRI during right thalamic DBS (19 months post-GKT) revealed a discrete round shape indicating a GKT scar, which was hyperintense on T2-weighted images. The tentative target of the Y and Z coordinates was the same as the left site, but the X coordinate was 16.5 mm lateral to the midsagittal plane (a distance somewhat different from the left thalamic DBS target (17.4 mm lateral), due to the unavoidable result of GKT-induced distortion of the structures. During the first tracking, TFA and high background activity appeared from 5.7 mm above the tentative target (Fig. 1; upper right), indicating that the location was the upper border of the Vim. At +5.0 mm, neural signal amplitude fell (Fig. 1; upper left); this was considered to represent the transition to the necrotic area caused by the previous GKT. However, background neuronal activity in this presumed coagulated area was not completely silent, and TFA or low amplitude with a high frequency single unit was acquired. At +3.7 mm, the area considered to represent the ventral border of the previously coagulated area, the background signal increased again (Fig. 1; lower left) and many bursting cells with high amplitude were recorded. This showed that residual Vim tissue had been unaffected by GKT. Some clear TFA and high background activity, compared with that acquired in the coagulated area, were detected in a diffuse field, particularly at +2.7 to −1.0 mm. The location of the right Vim was estimated to be +5.7 to −1.5 mm (Fig. 1; lower right) above the tentative target (length: 7.2 mm); this included areas of coagulation and the residual Vim. In this recorded Vim, 23 single units were recorded and 11 units were Ki. The average frequency of these 23 units was 14.3 ± 8.8 Hz (Fig. 2). The somatotopographic localisation of Ki, receptive fields (RFs) of the leg were more widely scattered in the right Vim than the non-lesioned left side (Fig. 3). The tip of the DBS electrode (3387) lead was set at 0.5 mm inferior and 2 mm medial to the tentative target. Presently, 22 months after the right thalamic

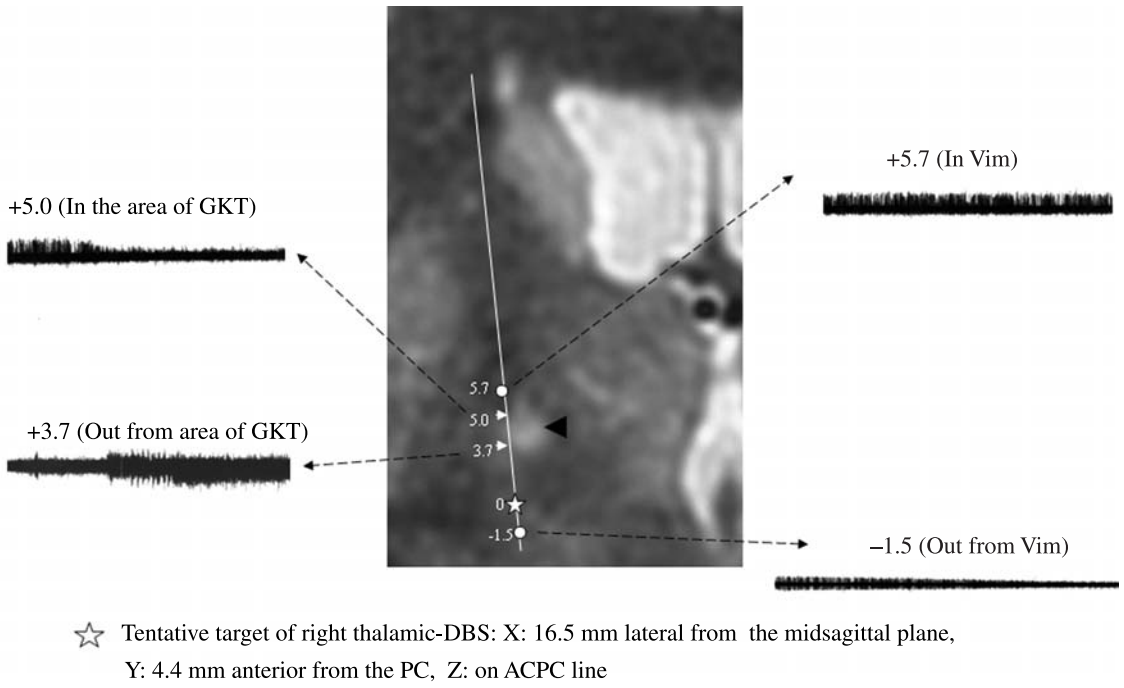

Fig. 1. Micro electrode recording during right thalamic DBS that were superimposed on coronal MRI. This coronal MRI on T2-weighted images was taken along a plane between the planned burr hole point and tentative target, revealing the trajectory view of our presumed microelectrode recording. Arrow head; a discrete round shape indicating a GKT scar +5.7 mm above the tentative target (dorsal border of the Vim area): Background noise increased and many bursting cells with high amplitude were recorded. +5.0 to 3.7 mm above the tentative target (*arrows*): coagulated area due to GKT. In this presumed coagulated area, neural noise amplitude fell but background neuronal activity was not completely silent, and TFA or low amplitude with high frequency single-units were acquired. +3.7 to −1.5 mm above tentative target: This area was considered to represent the ventral border of the previously coagulated area. Background noise increased and many bursting cells with high amplitude were recorded. These represented residual Vim tissue that had been unaffected by GKT. 0 mm (*asterion*): Our tentative thalamic target was located in the ventral Vim, at a site 4.4 mm anterior to the PC and 16.5 mm lateral to the midsagittal plane, with a depth corresponding to the ACPC line. Below −1.5: Background noise ceased, and evoked activities were recorded in the Vc in response to superficial stimulation (*light touch*)

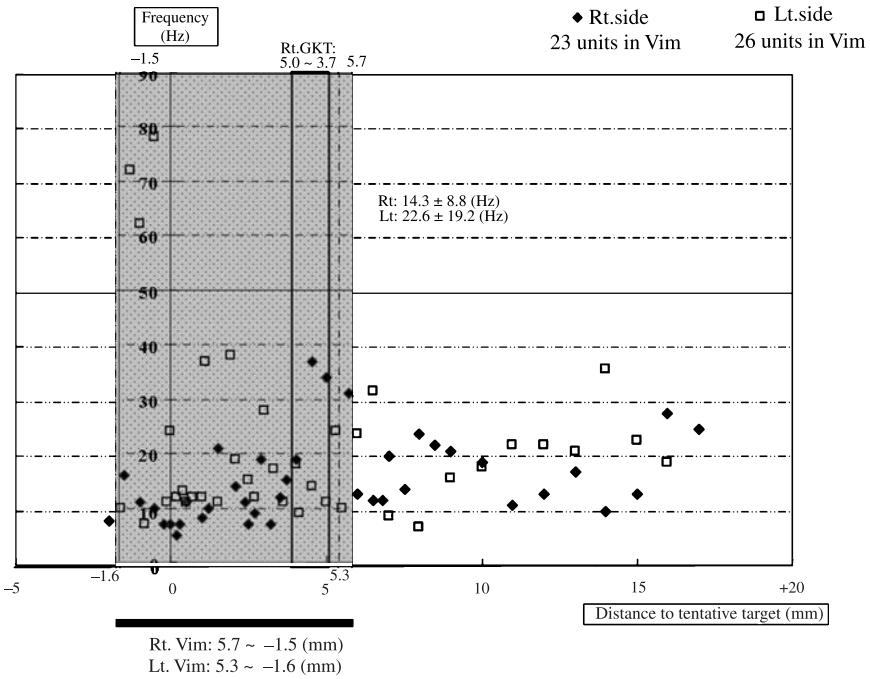

Fig. 2. Graph showing the average frequency of single units during microelectrode recorded on both sides. During microelectrode recording, the presumed Vim extended from +5.7 to −1.5 mm above the tentative target (GKT: from +5.0 to 3.7 mm) on the right and from +5.3 to −1.6 mm above the tentative target on the left. In this presumed Vim, 26 units were acquired on the left and 23 on the right. In particular, average frequency in the left Vim exceeded that on the right side (left, 22.6 ± 19.2 Hz; right, 14.3 ± 8.8 Hz)

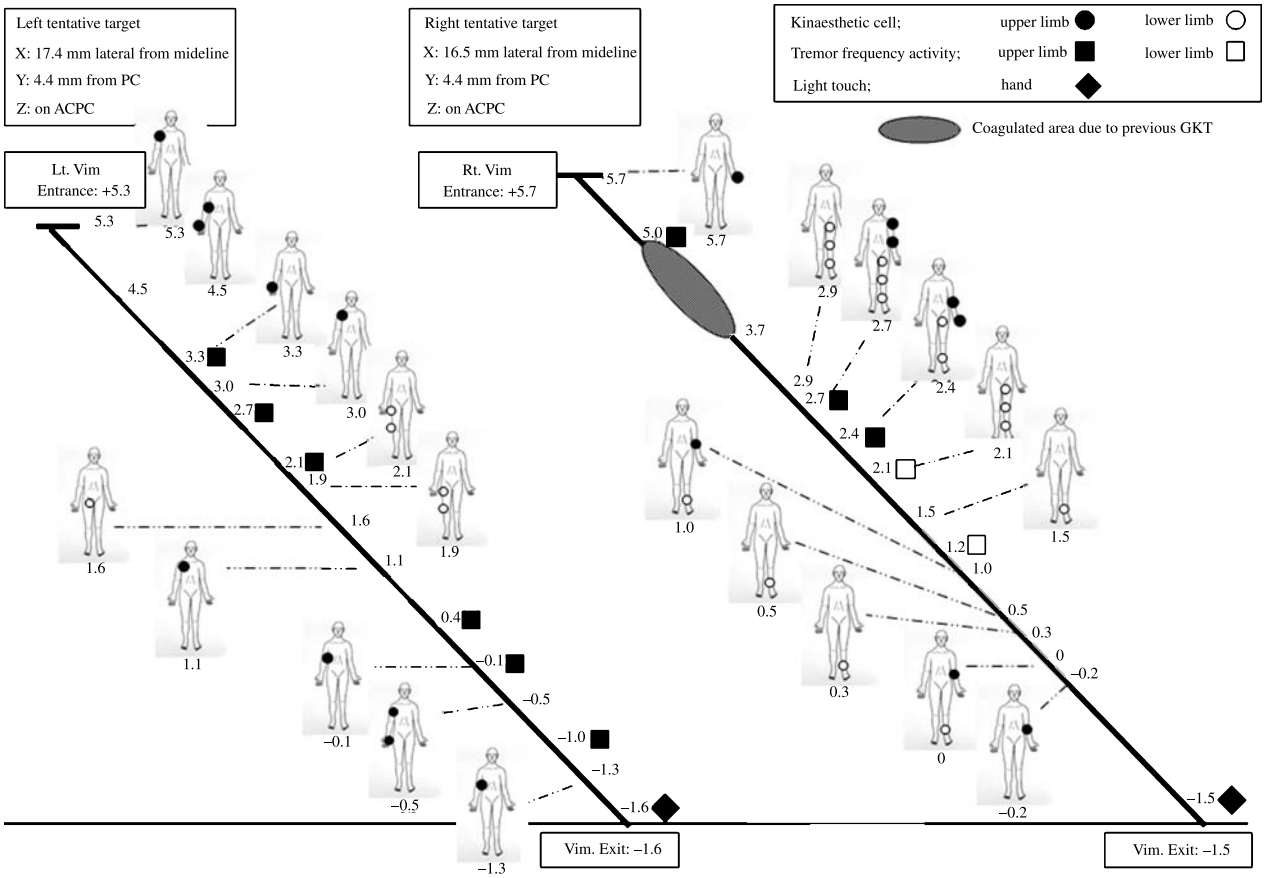

Fig. 3. Schema showing somatotopographic localisation of kinaesthetic neurons in the Vim (*right*: right Vim, *left*: left Vim). Receptive fields (*RFs*) for the leg were more scattered in the right Vim compared with the intact left side. Note that 4 of 11 Ki in the right Vim had many RFs over both the upper and the lower contralateral limb

DBS, bilateral optimal bipolar stimulation has suppressed the resting tremor without complication.

Discussion

As the resting tremor continued in the patient for 18 months after GKT, we suspected that tissue within the ventral Vim, which appeared intact on MRI, had escaped direct damage from GKT. When compared with the surrounding thalamic area that had not been coagulated, the GKT induced thalamic lesion demonstrated little background activity, with microelectrode recordings showing high frequency signals. These results disclosed the existence of surviving neurons in and adjacent to the GKT induced thalamic lesion [5]. Ohye *et al.* [6] has reported that normal, functionally almost intact neuronal activity remains within most of the high signal zone on proton image that surround the irradiated focus. Hence, our recording might have passed through the margin of the GKT induced thalamic lesion. Supporting this postulation, the captured length of the GKT zone during recording was only 1.3 mm, whereas the GKT scar that appeared hyperintense on both T2-weighted images on MRI was about 4.5 mm long.

Microelectrode recording revealed that the average frequency of recorded single units was higher in the left Vim than the right. Pessiglione *et al.* [7] demonstrated that a mean firing rate of 14.7 Hz in the pallidonigral territory mainly represents the Vop and that 19.7 Hz in the cerebellothalamic territory mainly represents the Vim, but stressed the high variability of frequency (from 0.2 to 75 Hz). This high variability was also observed in our patient, particularly on the coagulated right side.

In addition to the above mentioned interesting findings, the somatotopic distribution of Ki was unusual in our patient. In the right Vim, 36.4% (4 of 11) of Ki exhibited many RFs over both the upper and the lower contralateral limb. Furthermore, RFs of the leg, which are generally situated in the dorsolateral Vim [8, 10], the left Vim in our patient, were scattered broadly through

the recorded Vim on the right side. This might be because, prior to GKT, the left leg tremor (contralateral side to GKT) was more prominent than the right leg tremor and was barely diminished by GKT even though the left arm tremor improved by as much as 50% in appearance time. Accordingly, hyperafferentation from the left leg might have influenced the imbalanced expression of RFs on the right side. However, another reason might be that the kinaesthetic afferent input from the contralateral leg might have been interrupted after GKT, and this could have resulted in an altered representation of Ki in terms of the sequence of neuronal RFs[1,2]. Consequently, we hypothesised that plasticity led to somatotopographic reorganisation of Ki in the Vim during the post-operative repair process.

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Comments

This paper describes changes in the microelectrode frequency of neurons as well as an unexpected somatotopic organization of kinaesthetic cells in the ventral intermediate nucleus of the thalamus (Vim) follow a gamma knife thalamotomy (GKT) in a Parkinson patient. The authors speculate that neuronal plasticity following GKT led to somatotopographic reorganization of kinaesthetic cells in the Vim during the post-operative repair process. This interesting observation is supported by the discrepancy on lesion size that the lesion created by GKT to be smaller as identified by micro-electrode recordings than that seen on MRI. Although changes in neurophysiology following GKT seem intuitive, the publication of this observation and the described changes may prove to be useful to those groups who use micro-electrode targeting for deep brain stimulation placement.

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Terao *et al.* have submitted a manuscript for publication dealing with microelectrode recording investigations during a DBS procedure after unsuccessful gamma knife thalamotomy. The authors summarize their findings in a case of a 64 year old patient, they illustrate stepwise eletrophysiological recording results and discuss the underlying pathophysiology of somatotopographic reorganization processes.

Without a doubt, it is most interesting to see that there are recordable electrophysiological changes after gamma knife therapy of the thalamic nuclei and that some kind of plasticity (or somatotopographic reorganization) can be found, especially when clinical results of a thalamotomy are missing or vanishing after some time. However, since the captured length of the Gamma Knife treated zone during recording was only 1.3 mm, larger series have to prove now if we are facing a reproducible phenomenon or just unspecific electrophysiological changes secondary to radiation in a single case.

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