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Case Report

Deep brain stimulation of the thalamus can influence penile erection

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Introduction

Penile erection is a complex neurovascular event.[1] It is controlled by a spinal generator network and a supraspinal controlling system and their reciprocal interactions.[2–6] The role of the spinal system has been extensively described.[7] On the other hand, little is known about the supraspinal control, specifically about the role of the thalamus.

Two patients underwent successful bilateral high-frequency stimulation (HFS) of the thalamus for Tourette's syndrome (TS). TS is a chronic neurological disorder characterized by vocal and motor tics.[8] The onset is generally in childhood and the disease is frequently self-limiting. A small number of patients, however, remain symptomatic and usually require pharmacological treatment. In 1999, Vandewalle *et al*[9] introduced chronic deep brain stimulation (DBS) of the thalamus as a treatment for intractable TS. There are no specific sexual disorders linked to TS. The two patients of this study experienced changes in penile erection in response to sexual stimuli, after the surgery. The first patient reported an increased frequency and amplitude of erection to erotic stimuli, whereas the second patient reported an inhibited erection during intercourse which forced him to turn off the stimulator. In the present study, penile erection in stimulation *on* and *off* conditions has been examined in a laboratory setting to investigate the role of the thalamus in erection.

Methods

Two patients (male, 42 and 45-y-old) with absent comorbidity underwent DBS of the thalamus for intractable TS. The patients gave written informed consent for the surgery and this study. Electrodes (Medtronic, model 3387) were implanted bilaterally in the thalamus at the level of the nucleus ventro-oralis internus (VOI), centromedian nucleus (Cm: as a part of the intralaminar thalamic nuclei), and substantia periventricularis (Spv: as a part of the midline thalamic nuclei) as described earlier.[9] The final position of the electrode was determined by the clinical response of the patients who were tested by the blinded neurologist. The coordinates were: left 5 mm and right 3 mm in patient 1, left 3 mm and right 5 mm in patient 2; lateral to the anterior–posterior commissure (AC-PC) line, 4 mm posterior to the midcommissural point, and at the AC–PC plane. Postoperative MR imaging confirmed the correct position of the electrodes. After 2 weeks, the pulsegenerators (Itrell III, Medtronic model 7425 for patient 1/Kinetra, Medtronic model 7428 for patient 2) were implanted subcutaneously beneath the clavicle. Extensive neuropsychological testing

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was performed pre- and postoperatively. The patients were followed for 5 y and 8 months, respectively. The stimulation parameters for patient 1 were: 1.6 V/130 Hz/90 μs, monopolar (electrode 1 and 5 negative) and for patient 2: 6.4 V/130 Hz/120 μs, monopolar (electrode 2 and 6 negative).

Penile erection in both the patients was evaluated at the same time of the day, during two sessions on subsequent days with the stimulation *on* and *off*. *Off* stimulation evaluations were performed 12 h after turning off the stimulation. An electromechanical strain gauge, developed by Barlow *et al*,[10] was used for penile circumference measurement. The gauge was connected to a BIO2-high-sensitivity bio-amplifier (Psylab) and an IBM-compatible computer. Calibration was performed after every session to translate millivolts into centimeter penile circumference. Participants received instructions on using the rotating dial of a potentiometer to indicate their subjectively experienced sexual arousal. Participants were shown five selected clips from erotic films, in color and with sound, each lasting 3 min. During another trial, they were asked to engage in a sexual fantasy for 3 min, either choosing a favorite fantasy of their own or repeating by imagery (portions of) the previously presented erotic video films.

As an internal validity check, film stimuli were accompanied by cognitive tasks of varying difficulty, producing increasing cognitive load, and competing for attention with the erotic stimuli. Previous work in this area demonstrated a robust inhibitory effect of increasing distraction on erectile response in sexually functional men.[11] After an adaptation period of 3 min, a 60-s penile circumference baseline was established. Between stimulus presentations, a rest period of a minimum of 3 min allowed the participant's arousal to return to baseline. The last 60 s of every interstimulus interval was used to measure prestimulus baseline penile circumference.

In addition, the International Index of Erectile Function (IIEF) was administered twice at the first day of testing to assess general sexual functioning. Patients were instructed to complete the first form according to their present level of functioning, and the second form as a retrospective measure, reflecting their function level during the last months before operation. The IIEF is a 15-item self-report questionnaire with five subscales, measuring erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall sexual satisfaction, and has been psychometrically evaluated.[12]

Results

Evaluation revealed a 90 and 92.1% reduction of tics at 5 y follow-up in patient 1 and at 8 months in patient 2. The general intelligence level for the patients was average to above average (IQ's 108 and 114 resp.). Preoperatively, the patients showed borderline to low results on verbal memory, and patient 2 performed below average for facial recognition. Postoperatively, patient 1 showed little or no change on the tests. Patient 2 had low scores on most timed tasks, including visual reaction time and word fluency. Verbal memory and facial recognition scores increased, with a possible retest effect.

The patients reported a normal preoperative sexual functioning, retrospectively. IIEF-scores, however, clearly demonstrated an increase in functioning on all aspects for patient 2 (Table 1). HFS of the thalamus was found to have a profound impact on the genital response to visual erotic stimulation and sexual fantasy under laboratory conditions, as shown in Figure 1. Patient 1 experienced almost no penile erection in the stimulation off condition, whereas patient 2 had a manifest erection. In the stimulation on condition, the speed of erection and amplitude of penile circumference was remarkably increased in patient 1. In patient 2, turning on the stimulation practically inhibited erection. These findings were consistent for all five erotic clips and one sexual fantasy within each session. On the whole, subjective sexual arousal (not shown) was found to follow the differential pattern of genital arousal during on and off conditions in both participants.

Discussion

Two patients suffering from intractable TS have undergone DBS of the thalamus. Both patients

Table 1 Sexual functioning of two patients with DBS for TS on IIEFa subscales

			Patient 1		*Patient 1*	
	No. of items	*Range*	*Preoperative*	*Postoperative*	*Preoperative*	*Postoperative*
Erectile function	6	0–30	30	30	13	30
Orgasmic function	2	0–10	10	10	0	10
Sexual desire	2	0–10	8	10	5	9
Satisfaction with intercourse	3	0–15	12	11	6	14
Overall sexual satisfaction	2	0–10	8	8	2	10

IIEFa = International Index of Erectile Functioning (Rosen *et al*[12]). High scores reflect better sexual functioning.

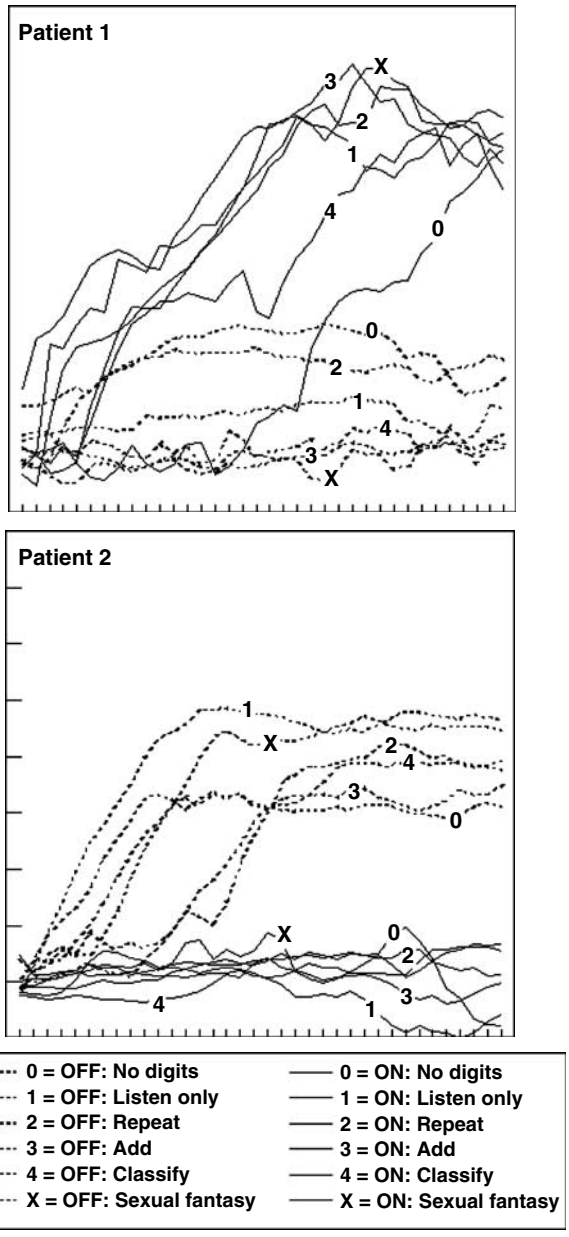

Figure 1 Time course of the speed of erection and amplitude of penile circumference during the five erotic clips and one sexual fantasy, while applying various methods of distraction. The test has been performed with stimulation on and 12 h *off*.

reported a normal preoperative sexual arousal, erection and ejaculation, retrospectively, which has also been confirmed by heteroanamnestic data from the partners. However, no specific examination of the sexual functioning was performed preoperatively, as no effect of DBS on these functions was expected. Postoperatively, both patients experienced changes in sexual responses. Interestingly, the patients reported opposite effects, for example, excitation versus inhibition. In the present study, these subjective changes have been confirmed. In laboratory conditions, thalamic stimulation increased erection in patient 1 and reduced it in patient 2. This confirms that opposite reactions can be seen in similar patients. These different penile reactions to visual erotic stimuli might be explained by differences in the stimulation settings. In patient 1, the location of the left electrode is 2 mm medial and the right electrode 2 mm lateral in relation to the position of the electrodes in patient 2. HFS of the thalamus is probably affecting the neural network, also comprising the amygdala and the orbitofrontal cortex, involved in sexual processing.[13] Different electrode positions could therefore give rise to these opposing effects, as a result of a possible differential organization of 'inhibitory' and 'excitatory' projections in this area. The difference in electrode localization has also been confirmed by postoperative MR imaging, which clearly demonstrated that the electrodes were placed in the medial part of the thalamus and showed approximately a 2 mm-asymmetric placement in the medio-lateral plane.

Another explanation (partly) for the difference could be the stimulation parameters for optimal motor effect. Patient 2 requires a relative high stimulus amplitude (6.4 V) to control the tics. It is well known that this leads to more diffusion of current to adjacent regions. Consequently, the inhibitory effect of HFS in patient 2 can result from an overall neural inhibition of the medial thalamus since the effect of HFS is equivalent to ablative surgery. For patient 2, the local application of a relative low amplitude (1.4 V) HFS might in turn activate parallel thalamic loops, which can result in excitation of the penile response. Finally, the interindividual variation could also explain the opposite effects, as patient 1 experienced a minor erection, whereas patient 2 had a manifest erection in the stimulation off condition. This difference in the off condition may, however, also be induced by long-term stimulation in patient 1 since this patient reported normal sexual function preoperatively.

Several studies hypothesize that a dysfunction of the cortico-basal ganglia-thalamocortical circuits underlies the pathophysiology of TS. The midline and intralaminar thalamic (Spv and Cm) nuclei play an important 'gating' role in the regulation of the basal ganglia-thalamocortical information flow.[9] DBS probably modulates the properties of this 'gate'. Data from preclinical studies suggest that the thalamic caudal and lateral intralaminar nuclei are possibly involved in processing the sexual outflow from the spinothalamic pathway towards the preoptic area, amygdala, temporal lobe, and the frontal cortex.[4] HFS of this region could interfere with the electrical activity of these 'gating' structures resulting in different erectile reactions to sexual stimuli. Furthermore, the possible involvement of the thalamus in human penile erection has also been demonstrated in recent studies using blood oxygenation level-dependent (BOLD) functional MRI.[14,15] Both the studies showed that the thalamus was

activated following visual erotic stimuli. Arnow *et al*[16] investigated, in a similar study, the relationship between sexual arousal and brain activation in heterosexual, young, and healthy subjects.[16] In contrast to the previous studies, no specific changes were noticed at the level of the thalamus in response to erotic clips. Arnow *et al*[17] concluded that future studies were required in order to study such discrepancies. Sewards *et al*[12] briefly mentioned in their review on the central representation of motivational drives, a study in which stimulation of the medial thalamus induced erection in primates. However, the exact stimulation sites were not reported in this review or in the original paper. Overall, there is a substantial amount of data suggesting that the thalamus might play a major role in sexual arousal and erection. However, the functional and spatial organization of the relay nuclei of the thalamus, in which the spinothalamic pathway is further processed upstream towards the preoptic area, amygdala, temporal lobe and orbitofrontal cortex and downstream back to the spinal network, remains unclear. Our data are suggestive of a parallel organization of inhibitory and excitatory projections within the intralaminar and midline nuclei of the thalamus.

Our findings confirm that the midline and intralaminar thalamic nuclei play an important role in penile erection and that erection can be modulated by HFS of this region.

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