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Clinical Section

Compulsive Thalamic Self-Stimulation: a Case with Metabolic, Electrophysiologic and Behavioral Correlates [1]

Russell K. Portenoy [2], Jens O. Jarden, John J. Sidtis, Richard B. Lipton, Kathleen M. Foley and David A. Rottenberg

Unified Pain Service and Department of Neurology, Albert Einstein College of Medicine, Bronx, NY 10461, and Pain Service and Department of Neurology, Memorial Sloan-Kettering Cancer Center and Cornell University Medical College, New York, NY (U.S.A.)

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Summary

A 48-year-old woman with a stimulating electrode implanted in the right thalamic nucleus ventralis posterolateralis developed compulsive self-stimulation associated with erotic sensations and changes in autonomic and neurologic function. Stimulation effects were evaluated by neuropsychologic testing, endocrine studies, positron emission tomographic measurements of regional cerebral metabolic rate for glucose, EEG and evoked potentials. During stimulation, vital signs and pupillary diameter increased and a left hemiparesis and left hemisensory loss developed. Verbal functions deteriorated and visuospatial processing improved. Plasma growth hormone concentrations decreased, and adrenocorticotrophic hormone and cortisol levels rose. With stimulation, glucose metabolism increased in both thalami and both hemispheres, reversing baseline right-sided hypometabolism and right–left asymmetries. EEG and both somatosensory and brain-stem auditory evoked potentials remained unchanged during stimulation, while visual evoked potentials revealed evidence of anterior visual pathway dysfunction in the left eye. This case establishes the potential for addiction to deep brain stimulation and demonstrates that widespread behavioral and physiological changes, with concomitant alteration in the regional cerebral metabolic rate for glucose, may accompany unilateral thalamic stimulation.

Key words: thalamus; self-stimulation; deep brain stimulation

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[2] Address correspondence and reprint requests to: Dr. R.K. Portenoy, Department of Neurology, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461, U.S.A.

Introduction

Therapeutic deep brain stimulation (DBS) was first described more than 30 years ago [32]. The use of DBS for the management of pain was spurred by the discovery of stimulation-induced analgesia in animals [36] and the elucidation of the multiple endogenous pain-modulating systems [1]. In recent years, numerous series of patients undergoing chronic stimulation for pain have been reported, varying widely in site and technique of stimulation, clinical indications, extent of evaluation, and results [6,9,14,15,19,20,22,31,34,37,38,40,43,52].

The low incidence of adverse or associated reactions to analgesic DBS suggests that it functions through activation of discrete neural pathways [13,14,37,38,51]. With stimulation in sensory thalamus, reactions other than analgesia have been limited almost exclusively to paresthesias and occasional minor motor effects [13,19,46,48,51,52]. Two patients have been reported who exhibited excessive self-stimulation of implanted electrodes; one was described as 'addicted' to the device [6]. In these cases, however, the site of stimulation was not precisely defined and clinical details were lacking.

We describe a patient with an electrode implanted in nucleus ventralis posterolateralis (nVPL) for pain management who developed compulsive stimulation associated with erotic sensations and a variety of abnormal motor, sensory and autonomic responses. Behavioral and physiologic measures, including positron emission tomographic (PET) measurements of regional cerebral metabolic rate for glucose (rCMRGlu), were evaluated in the unstimulated and stimulated states.

Case report

A 48-year-old, right-handed alcoholic woman developed a chronic pain syndrome following an L5–S1 herniated nucleus pulposus 10 years prior to presentation. Conservative treatments during the ensuing years included a variety of antidepressant and analgesic drugs, acupuncture, transcutaneous nerve stimulation, and cognitive behavioral therapies; all consistently failed to provide lasting benefit despite numerous trials. Opioid drugs were prescribed throughout her course, despite occasional problems with unsanctioned dose escalation. Surgical therapies also provided only transient relief of pain. These included 4 laminectomies during the 2 years after pain onset: unilateral, then bilateral, facet denervations; 2 trials of spinal epidural stimulation; multi-level hemilaminectomy; and L5 and S1 dorsal rhizotomies. Five years prior to presentation, a right posterior medial thalamic electrode was inserted, with the tip lateral to the posterior aspect of the third ventricle. Stimulation elicited a flush and a warm sensation in the left hemibody which was associated with analgesia for less than 6 months. The ineffective electrode was left in situ and a low cervical percutaneous right anterolateral cordotomy was performed, which relieved pain for only 6 weeks. Approximately 4 years prior to presentation, a second electrode was implanted in the right nVPL. Stimulation here elicited tingling paresthesias in the left side of the body associated with several

months of adequate analgesia. Pain then recurred, and though slight improvement with stimulation was thereafter reported by the patient, pain remained generally intractable from that time on.

Soon after insertion of the nVPL electrode, the patient noted that stimulation also produced erotic sensations. This pleasurable response was heightened by continuous stimulation at 75% maximal amplitude, frequently augmented by short bursts at maximal amplitude. Though sexual arousal was prominent, no orgasm occurred with these brief increases in stimulation intensity. Despite several episodes of paroxysmal atrial tachycardia and the development of adverse behavioral and neurological symptoms during maximal stimulation, compulsive use of the stimulator developed. At its most frequent, the patient self-stimulated throughout the day, neglecting personal hygiene and family commitments. A chronic ulceration developed at the tip of the finger used to adjust the amplitude dial and she frequently tampered with the device in an effort to increase the stimulation amplitude. At times, she implored her family to limit her access to the stimulator, each time demanding its return after a short hiatus. During the past 2 years, compulsive use has become associated with frequent attacks of anxiety, depersonalization, periods of psychogenic polydipsia, and virtually complete inactivity.

Methods

The patient reported that medication intake during all study periods was constant, including methadone 30 mg 4 times daily and the tricyclic antidepressant, doxepin, 250 mg nightly. A computerized tomographic scan prior to the neurophysiologic studies confirmed the presence of two electrodes in the right thalamus, one abutting the wall of the third ventricle and the other, currently active electrode situated in the lateral thalamus.

Study 1

Day 1. The patient had not stimulated for 2 months. A baseline neurological examination was obtained and supine and standing pulse and blood pressure, temperature, respiratory rate and pupillary diameter were determined 3 times at 4 h intervals. Blood was taken at 8 a.m. for determination of plasma levels of thyroid-stimulating hormone (TSH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), growth hormone (GH), adrenocorticotrophic hormone (ACTH), prolactin and cortisol. A plasma concentration of methadone was measured concurrently. Neuropsychological testing was performed during the morning and comprised alternate items from the Revised Wechsler Adult Intelligence Scale (WAIS-R), form II of the Wechsler Memory Scale, Temporal Orientation and alternate items of the Visual Form Discrimination Test [2], alternate items of the Hooper Visual Organization Test, Benton Visual Retention Test (form C), the Rey Auditory Verbal Learning Test, and several subtests of the Boston Diagnostic Aphasia Exam (left/right discrimination, commands, recitation, and repetition). An 8-channel EEG was obtained at noon.

Day 2. The patient began stimulating nVPL at 6 a.m. using a Medtronic Model 3522 stimulator, which produced a 120 Hz signal at 1 msec pulse width, 0–10 V amplitude. Stimulation simulated home use, with continuous middle-range amplitude stimulation punctuated by bursts at maximum amplitude lasting several seconds and occurring approximately every 5 min. This pattern of stimulation continued throughout the day and was altered only during EEG and PET studies, when high amplitude bursts were omitted.

Neurological examinations were repeated with the stimulator set at mid-range amplitudes and again at near-maximal values. Pulse, blood pressure, temperature, respiratory rate and pupillary diameter were determined as before. Blood was taken for determination of plasma concentrations of TSH, LH, FSH, GH, ACTH, prolactin, and cortisol at 8 a.m. (2 h after stimulation began) and 4 p.m. and a plasma methadone level was repeated. As on day 1, neuropsychologic testing occurred in the morning and consisted of a repetition of the previous examination. To avoid a practice effect on specific test items, the remaining alternate items were used for the WAIS-R, Hooper Visual Organization Test, and Visual Form Discrimination Tests. Similarly, form I of the Wechsler Memory Scale, form D of the Benton Visual Retention Test, and a different word list for the Rey Auditory Verbal Learning Test were used. A repeat 8-channel EEG was obtained after 6 h of stimulation.

PET studies. rCMRGlu was determined using the 'autoradiographic' 2-deoxy-D-[^{18}F]glucose (FDG)/PET method of Phelps et al. [30]. FDG, produced by a modification of Tewson's synthesis [45], was > 97% radiochemically pure (specific activity 15 mCi/mmole). Approximately 8 mCi FDG was injected as an intravenous bolus, and a 10 min PET scan was acquired 45–55 min later using the PC 4600 Positron Camera [17]. Accurate patient repositioning was facilitated by a custom-molded poly-urethane head holder–immobilizer [18] and crossed Gammex lasers. The patient lay quietly in the scanner gantry, blindfolded and listening to light music through acoustically isolated earphones. A transmission scan, obtained before each emission study, served to confirm the anatomical level of section and to correct for tissue attenuation.

Region-of-interest (ROI) analysis was performed on 128 × 128 PET reconstructions, which were appropriately corrected for random coincidence, tissue attenuation and electronic dead time. A thresholding strategy was used to obtain regional estimates of ^{18}F concentration from reconstructed images: frontal, temporal, parietal and occipital cortex, hippocampus, thalamus, lentiform nucleus and cerebellum were outlined by irregular ROIs, the upper 10% of ROI pixel values were highlighted and the mean of these pixel values calculated. This characteristic mean value was then used to calculate rCMRGlu according to Huang et al. [16] using a lumped constant of 0.418. Hemispheral glucose metabolic rates were calculated as the weighted means of frontal, temporal, parietal and occipital rCMRGlu values [7].

After PET scans were obtained in the unstimulated and stimulated states, the effect on metabolic rate was assessed by calculating ratios A and B:

$$\text{Ratio A} = \left[(R_j2 - R_j1)/R_j1/(H_2 - H_1)/H_1\right]$$

where R_j1 and R_j2 are rCMRGlu values for ROI_j in the unstimulated and stimulated states, respectively, and H_1 and H_2 are the corresponding hemisphere means; and

Ratio B = Rr/Rl,

where Rr and Rl refer to rCMRGlu values from right- and left-sided ROIs, respectively.

Day 3. Stimulation ceased at 5 p.m. on day 2; the patient was not stimulated on day 3. As on prior days, a neurological examination, vital signs and pupillary diameter were repeated. A blood sample was taken at 8 a.m. for cortisol, and a trough plasma methadone level was repeated. Neuropsychological testing consisted of Temporal Orientation, Benton Visual Retention (form E), and a third version of the Rey Auditory Verbal Learning Test. An 8-channel EEG was repeated and rCMRGlu was determined by PET scan, as described above.

Study 2

The patient did not stimulate during a 6 week interim. On day 1, visual evoked potentials (VEPs), brain-stem auditory EPs (BAEPs), and somatosensory EPs (SEPs) were performed using standard clinical protocols and a 20-channel EEG was obtained in the unstimulated state. SEPs were recorded to unilateral stimulation of the median nerve at the wrist from electrodes at Erb's point, the cervical spine (C7), the mid-inion, and contralateral sensorimotor cortex. BAEPs were recorded monaurally to 11/sec clicks at 85 dB SPL and 65 dB HL. Pattern reversal VEPs were recorded monocularly to full-field stimulation with 28 min checks. On day 2, stimulation was initiated and continued throughout the day as described for study 1. Repeat studies were done in the same order as before beginning 2 h after the start of stimulation. During each study, the stimulator was maintained at middle-range intensities; between studies, the patient returned to intermittent bursts of high intensity stimulation.

Results

Clinical status

In the unstimulated site, neurological examination revealed saccadic visual pursuit (more apparent on gaze to the right), evidence of a left hemiparesis (flattening of the left nasolabial fold and minimal pronator drift), and a mild postural tremor. After 2 h of stimulation, examination with the stimulator set at mid-range amplitude revealed persistence of saccadic visual pursuit and postural tremor; worsening of the left hemiparesis, with a mild supranuclear facial palsy, moderate pronator drift and left-sided reflex preponderance; and mild loss of proprioception in the left toes. Sensory examination was otherwise normal. At high amplitude stimulation, a mild flexion dystonia was superimposed upon an obvious hemiparesis, with left hemibody hypertonus, an unequivocal left facial palsy and marked reflex asymmetry. Pro-

proprioceptive loss in the toes worsened, though this remained the only sensory deficit, and both abnormal visual pursuit movements and postural tremor were unchanged. Maximal stimulation was described as 'pleasurable discomfort' and could be maintained for several seconds. During this period, severe left-sided posturing occurred, with blepharospasm and contraction of left lower facial muscles, head turning to the left, flexion at the elbow and wrist, extension at all joints of the left leg, and less severe torsion of the upper body to the left.

During the stimulation session, the patient expressed an irresistible urge to momentarily maximize stimulation every 5–10 min. She described erotic sensations often intermixed with an undercurrent of anxiety. She also noted extreme thirst, drinking copiously during the session, and alternating generalized hot and cold sensations.

In the unstimulated state, mean pulse and blood pressure were respectively 89 beats/min (bpm) and 119/76 mm Hg while supine and 103 bpm and 121/81 mm Hg while standing. After several hours of stimulation, mean pulse rate increased to 106 bpm supine and 116 standing, while blood pressure rose to 144/90 mm Hg supine and 126/90 mm Hg standing. From the unstimulated to the stimulated state, mean temperature increased 1°C (36.4–37.4°C), respiratory rate rose 4 breaths/min (11–15), and pupillary size with ambient light controlled increased 1.9 mm (5.1–7 mm).

Endocrine studies

ACTH concentration increased 20-fold (< 10–199 pg/ml) and cortisol rose more than 3-fold (15.4–49.8 μg/dl) with stimulation. These levels were lower the day following stimulation (70 pg/ml and 39.4 μg/dl respectively), while those obtained during the afternoon on the day of stimulation were similar to baseline values. Other endocrine changes associated with stimulation included a 90% decrease in GH level (7.8–0.8 ng/ml) and a consistent decline in prolactin levels (30.7, 15.1 and 5.5 ng/ml on days 1 through 3 of study 1, respectively). Neither TSH, LH or FSH were altered by stimulation.

Though the patient reported that plasma methadone concentration was determined at the same interval after an equal dose on each day, this was considered to be unreliable. Levels were 419, 146 and 983 ng/ml on the morning of each day of study 1, respectively.

Neuropsychological evaluation

Verbal and performance IQ and memory function were decreased when compared to prior testing in 1980 and 1982. With stimulation during study 1, verbal IQ decreased further, while performance IQ and memory quotient improved, the latter due largely to faster performance on the mental control subtest and improved visual reproduction. The results are summarized in Table I.

Differences between stimulated and unstimulated states were less significant on other tests. Visual reproduction memory was poor on day 1, but within normal limits on day 2 (both unstimulated days), and intermediate on day 2 (during stimulation). Performance on the visual organization test was uniformly poor, but

TABLE I

PSYCHOMETRIC EVALUATIONS CARRIED OUT PRIOR TO AND DURING THE PRESENT STUDY

All scores incorporate age corrections. The Wechsler Adult Intelligence Scale (WAIS) and the Wechsler Memory are scaled so that the normal average is in the range of 90–109.

	1980	1982	1985	
			Unstimulated	Stimulated
WAIS-IQ				
Full scale	99	99	88	83
Verbal	110	108	101	82
Performance	86	89	75	85
Wechsler Memory Scale				
Memory quotient	96	97	64	73

was worse during stimulation and temporal orientation was normal on each day. There was no aphasia, and speech was never dysarthric or dysprodic. Five-step commands could be carried out in either state, and there was no left/right confusion.

PET studies

The effect of stimulation on rCMRGlu in 8 cortical and subcortical regions is described in Table II and illustrated in Fig. 1. In the unstimulated state, right–left asymmetries in metabolic rate were apparent (ratio B), with relatively lower rCMRGlu in both right cortex and subcortical structures. With stimulation, mean right and left hemispheral cortical rCMRGlu increased by 71% and 60%, respec-

TABLE II

EFFECT OF RIGHT THALAMIC STIMULATION ON rCMRGlu (mg/100 g/min) IN 8 CORTICAL AND SUBCORTICAL REGIONS

Hemisphere values represent or, in the case of ratio B, are derived from the weighted means of frontal, temporal, parietal and occipital cortical rCMRGlu. Ratios A and B are defined in the text.

Region	Unstimulated		Stimulated		Ratio A		Ratio B	
	Left	Right	Left	Right	Left	Right	Unstim.	Stim.
Frontal cortex	2.46	2.11	4.08	3.88	1.10	1.17	0.86	0.95
Temporal cortex	2.19	2.30	3.56	3.80	1.04	0.91	1.05	1.07
Parietal cortex	3.09	2.59	5.04	4.62	1.05	1.10	0.84	0.92
Occipital cortex	3.39	3.17	4.94	4.00	0.76	0.37	0.94	0.81
Hippocampus	1.75	1.83	2.61	2.92	0.82	0.83	1.05	1.12
Thalamus	2.93	2.28	4.06	4.08	0.64	1.11	0.78	1.00
Lentiform nucleus	3.46	3.20	5.20	4.98	0.84	0.78	0.92	0.96
Cerebellum	2.98	3.12	4.87	4.56	1.05	0.65	1.05	0.94
Hemisphere mean	2.75	2.52	4.40	4.32	–	–	0.93	0.99

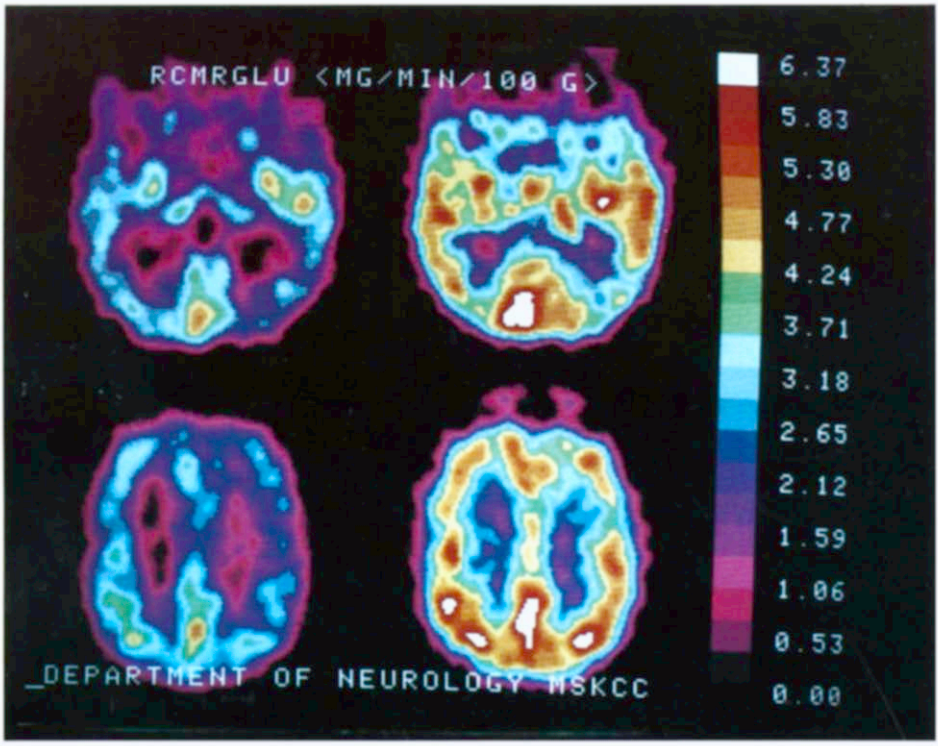

Fig. 1. FDG/PET images of regional cerebral metabolic rate for glucose (rCMRGlu) in the unstimulated (left tier) and stimulated (right tier) states. Images in the upper and lower rows correspond to PET brain slices at the level of the thalami and the semioval centers, respectively. The global increase in cerebral metabolic rate for glucose associated with right thalamic stimulation becomes apparent when the left tier images are compared with the co-planar images to the right. The right side of the scan is the patient's right.

tively. Relative changes in metabolic rate with stimulation were evaluated by indexing the change in rCMRGlu of specific structures to that of the ipsilateral hemisphere (ratio A). These changes were most marked in left thalamus, right occipital cortex and right cerebellum. Ratio B values increased with stimulation, with the greatest change in thalamus, where stimulation reversed the relative hypometabolism of the right thalamus. Overall, ratio B values for mean hemisphere cortex increased from 0.93 to 0.99, indicating that stimulation nearly equalized the metabolic rates of the 2 hemispheres.

Electrophysiological evaluation

Neither routine EEG obtained on consecutive days of study 1 nor the 20-channel EEG of study 2 changed with stimulation. All records were abnormal, with mild background slowing (posterior background 7.5–8 Hz) and increased frontal fast activity. SEPs were well formed, symmetric and all components were of normal

latency before and during DBS. BAEPs prior to stimulation were well formed from each ear and the peripheral and central transmission times were normal. There were no significant changes during stimulation. Prior to DBS, the VEPs were well formed and the major positivities had normal latency to full-field monocular stimulation. During DBS, the responses elicited to right eye stimulation were unchanged, while the major positivity of the left eye response broadened and increased in latency (from 109 to 117 msec) and the latency of the subsequent negativity increased as well.

Discussion

The studies of DBS in this patient must be interpreted in light of abnormal baseline neurological function and a long history of substance and DBS abuse. Though the patient's experience provides an opportunity to correlate clinical and neurophysiological responses and raises several issues relevant to the management of chronic pain with DBS, it may not be representative of routine DBS in an otherwise intact brain. Further study of the long-term effects of stimulation is needed to clarify the relationship between this extreme response and the usual pattern. It must also be noted that the precise localization of the electrode at the time of the studies is uncertain. Though initial placement in nVPL is likely given the contralateral paresthesias experienced by the patient after implantation, shifting of the electrode may have occurred; CT imaging at the time of the study suggested localization in the lateral thalamus, but could not confirm placement in nVPL. Even if the electrode was situated in nVPL, direct stimulation of outside structures is likely due to the high stimulation intensities used by the patient. This uncertainty emphasizes again the tentative relationship between our case and the usual results of DSB in nVPL. Finally, though fluctuations in plasma methadone level may also confound extrapolation of the current findings to other cases of DBS, these more likely represent unreported changes in the dose and interval before blood sampling rather than sustained differences in daily concentration and are therefore of limited importance. The patient was highly tolerant to opioid medications and the independence of stimulation effects and drug concentration is suggested by the stability of some neuropsychological measures with both increases and decreases in others, the hemispheric asymmetries on PET scanning, and the constant background EEGs during periods of differing plasma drug concentration.

The clinical features of this case illustrate common pitfalls in the therapy of chronic non-malignant pain. During 10 years of treatment, virtually every intervention, whether surgical or non-surgical, yielded only a brief respite from pain. Such aggressively help-seeking individuals whose prominent placebo response or complaisance results in transient benefit with every trial are often encountered and may come to multiple ineffective procedures undertaken by a number of well-meaning physicians. The difficult clinical task is to identify this pattern after it has begun and intercede to alter it. This can often be assisted by referral to a multidisciplinary pain center, where decisions about additional invasive measures for pain are

evaluated from varying perspectives. Though this course may not provide pain relief, as demonstrated by this patient, it may prevent division of care, interfere in the cycle of useless procedures and change the focus of therapy from analgesia at all costs to improvement of function.

Of equal clinical import is the demonstration by this case of the potential for addiction to DBS. Though some degree of analgesia occurred, the patient developed aberrant, stimulation-seeking behaviors associated with compromise in function, a pattern which defines addiction to drugs. The factors responsible for these behaviors remain speculative and most likely comprise some combination of an idiosyncratic physiological response to stimulation and a personality prone to addiction, as suggested by the history of alcoholism and inappropriate use of analgesic medications. The development of addiction to DBS must be viewed as a rare additional risk of the procedure with important therapeutic implications for the management of chronic pain. Treatment with non-pharmacologic, often invasive, measures is often undertaken with the desired goal of preventing drug addiction by eliminating the need for medication. This case, as well as others [6], suggests that addictive behaviors do not develop solely from properties inherent in the treatment, such as the capacity to produce physical dependence, but also from characteristics unique to the patient. DBS, therefore, should not be undertaken merely to avoid the risk of addiction.

Pleasurable sensations during stimulation provided the probable substrate for addiction in this patient. Reinforcing stimulation in subcortical structures has been extensively evaluated in animals [3,8,29,33,42]. In man, pleasurable sensations have been noted after stimulation in a wide variety of subcortical sites, though never in nVPL specifically [9,11,39,41,46], and the potential for compulsive self-stimulation has been suggested both by requests for additional stimulation during electrode placement and by the rare reports of excessive stimulation after implantation [6,11,41]. Other stimulation sites have produced anxiety and related negative emotions, often in regions within 1 cm of sites eliciting pleasure [39,41]. These responses also have not been reported with nVPL stimulation. The mix of emotions reported by this patient may be due to activation outside of this region, as demonstrated by PET.

Thalamic damage or stimulation has been reported to produce a variety of neurobehavioral syndromes. Both bilateral and unilateral dominant thalamic lesions can cause amnesia [4,10,12,50]. Stimulation of the dominant pulvinar can disrupt short-term memory [26], while activation of dominant and non-dominant ventrolateral nucleus has been shown to influence short-term recall of verbal and visuospatial information respectively [23–25]. Similarly, an aphasic syndrome can follow damage or stimulation in the dominant thalamus [28,35], while injury to the non-dominant thalamus can produce a unilateral neglect or hemispatial disorder [21,49]. In the present case, the long-standing non-verbal deficits may have resulted from either electrode implantation in right thalamus or chronic nVPL stimulation with secondary involvement of nearby thalamic structures. Acute stimulation affected memory, language and visuospatial function, with deterioration of verbal skills and improvement in visuospatial processing. This probably reflects reorganiza-

tion of activity in both thalami as well as the cortical regions with which they interact, a process that is suggested by the observed bilateral changes in rCMRGlu.

There has been no previous attempt to evaluate the effect of thalamic stimulation on rCMRGlu in man. As demonstrated in Table II, cortical and subcortical rCMRGlu were profoundly reduced in both hemispheres, especially the right, in the absence of self-stimulation. It is unlikely that methadone treatment per se could explain this degree of hypometabolism. The asymmetric thalamic hypometabolism is clearly abnormal [7] and suggests that electrode placement and/or chronic thalamic stimulation may have altered normal metabolic function. Global hypometabolism has been reported in patients with dementia [5] and in this patient may correlate with the deterioration in intellect revealed found by psychometric testing.

Animal studies, which utilized 2-deoxy-[^{14}C]glucose and quantitative autoradiography, suggest that brain-stem stimulation produces discrete activation of specific brain regions and their projections [8,33]. The diffuse increases in rCMRGlu observed in the present study during thalamic stimulation, as well as the observed asymmetries, may relate to different electrode placement, higher relative amplitudes of stimulation, or species differences. Though an explanation for these patterns is lacking, they do suggest that correlation of stimulation site and clinical effects in man must be made cautiously, since metabolic activation of a distant brain region may in fact be responsible.

Such electrophysiological measures as EPs and EEG were, for the most part, unresponsive to the changes produced by nVPL stimulation. Though surprising in light of the dramatic clinical and metabolic effects of stimulation in this patient, the EEG has been reported to lack utility for electrode localization during DBS [44,46]. The dysfunction in the left anterior visual pathway demonstrated by VEPs during stimulation was clinically inapparent and, though difficult to explain on physiologic grounds, supports the impression that DBS may produce widespread unanticipated changes. The normal SEPs indicate that the portions of the somatosensory pathway essential to their generation were intact and that transmission through the nVPL of the large fiber volley elicited by median nerve stimulation was not substantially disrupted by DBS in this patient.

Though changes in blood pressure and respiratory rate, as well as other autonomic effects, have been observed after stimulation in a variety of cortical and subcortical sites [11,27,37,38,46], none has been reported with stimulation in nVPL specifically. The changes noted in this patient were consistent with enhanced sympathetic activity and could therefore be related either to generalized arousal or direct spread of stimulation to hypothalamic structures. Either explanation would account for the impressive increases in ACTH and cortisol accompanying stimulation. The decrements in GH and prolactin, however, more likely reflect a direct effect on hypothalamus. Hormonal levels, other than beta-endorphin [14,51], have not previously been evaluated in patients undergoing DBS. Stimulation of brain regions outside of nVPL accounts also for the motor effects observed during stimulation. Perhaps these responses were related to asymmetric activation of anterior thalamic structures, which both receive afferents from globus pallidus and project to motor cortex.

After multiple neuroablative and stimulatory procedures and a period of inappropriate analgesic use, this patient developed aberrant behaviors consistent with addiction to DBS. A clinical and neurophysiological evaluation revealed both widespread and selective effects of stimulation. The mode of action of DBS requires further elucidation and its clinical indications need to be refined. Longitudinal studies using sensitive neuropsychological measures, PET technology and electrophysiologic techniques would be a fruitful undertaking in patients receiving DBS for pain.

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