Pathological Crying Caused by High-Frequency Stimulation in the Region of the Caudal Internal Capsule

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Background: Pathological crying has been rarely reported after deep brain stimulation. The exact neural substrate is unknown, but it is often assumed that pathological crying and the pseudobulbar syndrome result from disturbances of a common neural pathway.

Results: Stimulation in the region of the caudal internal capsule resulted in pathological crying but no other features of pseudobulbar palsy.

Conclusions: At least 1 of the pathways controlling crying passes through the region of the caudal internal capsule, and this pathway is distinct from those involved with laughter and nonemotional facial movements. Moreover, different stimulation frequencies may elicit either crying or anxiety but not both.

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**Pathological Crying** (PC) is a disorder of emotional expression characterized by involuntary, recurrent bouts of crying that are incongruent with the prevailing emotional, cognitive, and social context and is not associated with a sensation of sadness. This condition may be accompanied by laughter (pathological laughter and crying [PLC]), which is assumed to share a common mechanism. Pathological laughing and crying are often included as part of a wider pseudobulbar syndrome that may include disturbances of swallowing, speech, bulbar function, and exaggeration of facial, palatal, and jaw reflexes.

Although PLC is frequently encountered in a variety of neurological disorders, reports of crying or laughing following stimulation of the thalamus, globus pallidus interna, subthalamic nucleus (STN), and substantia nigra are rare and have all been associated with an emotional component. Prior to this article, there has only been 1 other case of PC following deep brain stimulation (DBS) to our knowledge. In that article, PC, slurring of speech, and exaggeration of facial and gag reflexes were observed with monopolar stimulation through contacts extending from the subthalamus to the thalamus. We report a case where high-frequency stimulation via a single contact in the region of the caudal internal capsule (CIC) resulted only in PC. This very localized effect argues for a distinct neural pathway for PC, separate from the larger constellation of symptoms that occur in PLC or the pseudobulbar syndrome.

**Report of a Case**

A 48-year-old, left-handed woman with a 9-year history of Parkinson disease presented with severe motor fluctuations and disabling dyskinesias despite receiving 1150 mg of levodopa, 1200 mg of entacapone, 5 mg of selegiline hydrochloride, and 6 mg of pramipexole dihydrochloride daily. Structured preoperative neuropsychiatric evaluation and brain imaging revealed no cognitive, mood, or psychiatric disturbances or structural lesions. Preoperative Unified Parkinson Disease Rating Scale motor subscale scores while receiving and not receiving medication were 52 and 13, respectively. She underwent bilateral insertion of STN electrodes (Medtronic 3389; Medtronic, Inc, Minneapolis, Minnesota). The targets were selected from axial fast...
short time inversion recovery magnetic resonance images and adjusted intraoperatively following microelectrode recordings and macroelectrode stimulation. Approaching the left target \((x, y, z = -13.7 \text{ mm}, -1.3 \text{ mm}, -6.1 \text{ mm})\), microelectrode recordings characteristic of the STN were encountered from 2 mm above the target \((t = -2)\) to 3 mm below it \((t = +3)\) and the substantia nigra from \(t = +4.5\). There was significant clinical improvement during macrostimulation. The most distal contact was placed at \(t = +3\). The right STN electrode was implanted in a similar manner. Electrode contacts were numbered 0 to 3 from deep to superficial on the right and 4 to 7 from deep to superficial on the left.

Stimulation titration began 6 weeks postoperatively with the patient not receiving medication for at least 12 hours. The patient began to cry uncontrollably within seconds of monopolar stimulation \((0.5 \text{ V}, 60 \text{ microseconds}, 130 \text{ Hz})\) involving contact 6 \((x, y, z = -11.5 \text{ mm}, -3.8 \text{ mm}, -12.2 \text{ mm})\). This occurred even when parameter changes were visibly concealed from the patient. Sham testing did not elicit a similar response. The patient did not know why she was crying and could not stop herself from crying. There was no sensation of sadness, pain, or persecution. Crying stopped within 5 seconds of stimulation cessation. Similar responses were observed with bipolar stimulation through contacts 6 (cathodal) and 7 (anodal) at amplitudes of 1.0 V or greater. The Beck Depression Inventory score before and during monopolar stimulation of contact 6 was 10 (0-10 being normal, with scores >10 indicative of increasing mood disturbance). Stimulation through other contacts did not elicit a similar response. Interestingly, the patient became anxious but did not cry when monopolar stimulation at a frequency of 50 Hz via contact 6 or 7 \((0.5 \text{ V}, 60 \text{ microseconds})\) was applied. As the frequency increased, anxiety was replaced by an urge to cry; however, crying only occurred when the frequency equaled or exceeded 130 Hz. The patient did not experience anxiety when she cried unless the episode was prolonged. She had no pseudobulbar symptoms during or immediately after episodes of stimulation-induced crying. Postoperative magnetic resonance imaging showed that contacts 6 and 7 were in the region of the CIC on the left. Similar responses were observed with bipolar stimulation through contacts 6 (cathodal) and 7 (anodal) at amplitudes of 1.0 V or greater.

The patient’s parkinsonian symptoms improved with monopolar stimulation through contact 4 \((x, y, z = -11.5 \text{ mm}, -2.7 \text{ mm}, -9.6 \text{ mm})\) on the left \((2.0 \text{ V}, 60 \text{ microseconds}, 130 \text{ Hz})\) and contact 3 on the right \((1.6 \text{ V}, 60 \text{ microseconds}, 130 \text{ Hz})\). Two years after surgery, her Unified Parkinson Disease Rating Scale motor subscale score was 4, the dyskinesias had completely resolved, and the levodopa dose had been reduced by 80%. The postoperative magnetic resonance imaging scan showed that the chronic stimulating electrodes were within the dorsolateral STN (not shown).

**Comment**

Wilson\(^2\) hypothesized that a brainstem fasceorespiratory center coordinates the action of several systems involved in emotional expression. Descending pathways from undefined cortical centers to the fasciorespiratory center\(^2\) and modulatory input from the cerebellum\(^2\) are believed to be important in the control of voluntary and involuntary expression of emotion. In this case, the patient’s response to stimulation of contact 6 was similar to the response to stimulation of the CIC in patients with pseudobulbar palsy. This suggests that stimulation of the CIC may be a viable treatment for patients with pseudobulbar palsy. However, further studies are needed to determine the fate of patients treated with CIC stimulation.
bulbar symptoms. To date, the actual neural pathway involved in PLC is unknown but the internal capsule is almost always involved.

Our case confirms that PC can exist in the absence of other pseudobulbar symptoms, suggesting that separate neural pathways exist for the control of crying, laughing, and bulbar movements at least in the region of the CIC. Further subdivision of this pathway may also be present because negative emotional responses (anxiety or crying) but not positive ones (laughing) could be produced by altering the stimulation frequency. Frequency-dependent neural modulation has been shown to be responsible for alterations in verbal fluency and motor symptoms due to the activation of different neural pathways in patients with STN-DBS.12 Our case suggests that it may also affect the expression of different aspects of negative emotional responses.

A weakness of our study is our inability to determine the actual neural substrate that caused PC. Structures in the region of the CIC include the subcortical gray matter (basal ganglia, hypothalamus, thalamus, STN, substantia nigra) and fibers connecting the cortex, subcortical gray matter, and brainstem structures such as the corticobulbar and spinal tracts, zona incerta, and medial forebrain bundle. The magnetic resonance imaging scan shows that contact 6 lies within the posterior limb of the CIC without touching the surrounding deep gray matter (Figure). Experimentally, the current spread around a monopolar electrode at 1.0 V is approximately 2.5 mm.12 The degree of current spread around the monopolar electrode causing PC at 0.5 V would be expected to be less than 2 mm. A current density sphere with a radius of 2 mm would be largely confined to the white matter in the region of the CIC. This, together with the fact that large myelinated axons have a lower firing threshold than local cells13 and are more likely to be stimulated at 0.5 V, suggests that the effects of stimulation in our case must be mediated through fiber tracts. In the other reported case of PC after DBS, higher stimulation amplitudes (1.5 V) and pulse widths (90 microseconds) through all of the contacts extending from the subthalamus to the thalamus were used, and the patient had slurred speech and hyperactive facial and gag reflexes.6 This was absent in our patient and suggests that the PC seen in the study by Okun et al8 resulted from stimulation of surrounding white matter tracts (which includes the CIC) due to the greater current spread.

There is no strong evidence to suggest that the placement of the contralateral electrode predisposes to the development of PC. Most STN-DBS electrodes are implanted bilaterally, yet PC after DBS is extremely rare. In the only other reported case of PC after STN-DBS, only 1 electrode was implanted, and this was on the same side as a previous pallidotomy.6 In addition, PLC has been reported after unilateral strokes.14,15

Finally, it has been suggested that the optimal electrode position for subthalamic DBS is in the zona incerta and upper STN region,16 and there has been a recommendation to insert electrodes more dorsally to avoid STN-induced mood disorders.17 However, clinicians should be aware that more dorsally located stimulation may potentially result in PC.