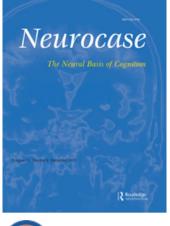
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Smile without euphoria induced by deep brain stimulation: a case report

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Poststroke central pain (PSCP) can be a debilitating medication-refractory disorder. We report a single case where right unilateral ventral capsule/ventral striatum (VC/VS) deep brain stimulation was used to treat PSCP and inadvertently induced a smile without euphoria. The patient was a 69 year-old woman who had a stroke with resultant dysesthesia and allodynia in her left hemibody and also a painful left hemibody dystonia. In her case, VC/VS stimulation induced a smile phenomenon, but without a euphoric sensation. This phenomenon was different from the typical smile responses we have observed in obsessive-compulsive disorder cases. This difference was considered to be possibly attributable to impairment in the emotional smile pathway.

Keywords: deep brain stimulation; chronic pain; smile; ventral capsule; ventral striatum

Poststroke central pain (PSCP) can be medication refractory and debilitating for the majority of sufferers. Pain has been described as having limbic and sensory components. There have been various surgical approaches aimed at specifically targeting each pain component (Sewards & Sewards, 2002). Motor cortex stimulation (MCS) is the only food and drug administration-approved surgical procedure for these types of pain patients. Deep brain stimulation (DBS) has been reported to have mixed outcomes for pain and also does not have a definitive randomized study supporting its use (Bittar et al., 2005).

In this article, we present a case of a unique DBS approach that aimed to modulate pain in a patient with PSCP. In this case, we stimulated the unilateral ventral striatum/ventral capsule (VS/VC) target. The choice of target was an intentional attempt to address the affective aspects of PSCP as has been reported in anterior cingulotomy. This target has been utilized for obsessive-compulsive disorder (OCD) (Goodman et al., 2010; Greenberg et al., 2006, 2010) and in medically refractory major depression cases (Malone et al., 2009), and in both disorders, there has been limited success. Several authors have reported that DBS in this region commonly results in intraoperative contralateral smile with euphoria (Haq et al., 2011; Nuttin et al., 2003; Okun et al., 2004) and occasionally hypomanic episodes (Haq et al., 2010; Tsai, Chen, Tsai, Hung, & Chang, 2010). In this case, we observed an unusual smile response that was not accompanied by euphoria.

Case report

The patient was a right-handed 69-year-old woman with history of cerebral infarction in the right middle cerebral artery region 9 years previous to her DBS surgery. The stroke lesion involved the cortical areas without directly involving the basal ganglia (Figure 1). She developed painful and burning dysesthesias and allodynia in her left hemibody. She was able to ambulate with a cane until three years ago and then developed left hemibody dystonia with severe left foot inward torsion and arm flexion at the elbow and the wrist. She ambulated only with the use of a wheelchair or a scooter. She had unsuccessfully tried intrathecal morphine and baclofen, a fentanyl pump, and oral gabapentin (1600 mg/day) as strategies for the pain. Sertraline (100 mg/ day) was also used, but despite all of these therapies, she reported only minimal nonmeaningful improvements in pain. She rated the pain as 8 to 9/10 on a standard visual analogue pain scale. She reported severe associated depression and a poor quality of life. On physical examination, the leg dystonia was nearly fixed and could not be manually reduced. There was severe allodynia of the left upper and lower limbs. Mild facial weakness on the left was also present. Her baseline modified Rankin scale score was 4.

The DBS procedure was based on our previously published protocol that utilized microelectrode recording (MER) and macrostimulation (Morishita, Foote, Haq, et al., 2010; Morishita, Foote, Wu, et al., 2010; Moscovich et al., 2013).

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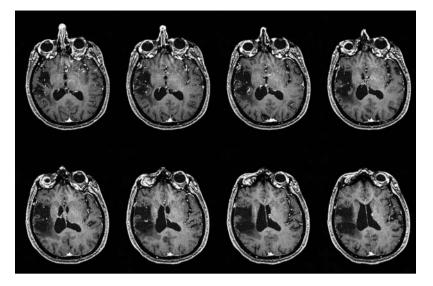


Figure 1. A T1 weighted image showing the stroke lesion in the middle cerebral artery area involving the cortical areas without directly involving the basal ganglia.

A high-resolution magnetic resonance imaging (MRI) scan was performed 1 day prior to surgery. On the morning of the DBS lead implantation, a Cosman– Roberts–Wells head ring was attached to the skull under local anesthesia, and then the patient was taken to a computed tomography (CT) scanner. The CT images were fused to the MRI. A safe DBS lead trajectory was determined for each target.

MERs were performed to map out the target structures, and macrostimulation was performed to document stimulation-induced side effects. First, a DBS electrode (Medtronic, model 3387, Minneapolis, MN, USA) was implanted in the VC/VS area based on our previously published procedure for OCD DBS (Figure 2) (Greenberg et al., 2010; Morishita et al., 2014). Macrostimulation was then performed. Stimulation of the most ventral contact (0) was accompanied by an increase in heart rate. Contralateral smile that rapidly spread to the ipsilateral face (5-7 volts) was observed without euphoria. The subject reported "something makes me smile." She denied any happy or euphoric feelings during the smile. This "smile" could be clearly differentiated from facial muscle movements induced by spread of stimulation to the internal capsule. The facial muscle movement induced by the spread of electric current to the internal capsule usually manifests as a pure unilateral motor response with and associated subjective uncomfortable feeling. In our case, the smile response quickly spreads from the contralateral face to the ipsilateral side. Also in our case, the higher voltage (8-10 volts) resulted in an aggravation of the burning pain in the left hemibody, but not worsening facial movements, or other motor (capsular) pulling phenomenon. No acute pain relief was reported with this DBS lead activation (Table 1).

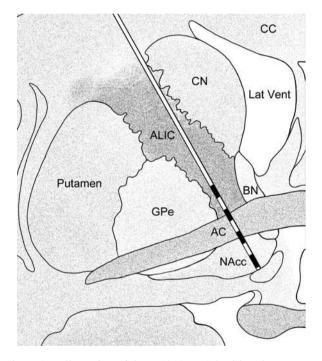


Figure 2. Illustration of the VC/VS DBS lead location.

Note: AC = anterior commissure, ALIC = anterior limb of internal capsule, BN = bed nucleus, CC = corpus callosum, CN = caudate nucleus, GPe = globus pallidus externa, NAcc = nucleus accumbens, Vim = ventralis intermedius nucleus, Vo = ventralis oralis.

A second DBS lead implantation was then performed in the same intraoperative session. A single MER pass was performed for the mapping of the border between the ventralis caudalis (Vc) and the ventralis intermedius nucleus (Vim) of the thalamus. We first implanted an electrode in the Vc region, because of

	VC/VS	Vo
DBS		
coordinates		
Х	5.5	10.5
Y	12	-1.7
Ζ	-6.2	-4.4
AC-PC angle	56	79
Center-line angle	38	35
	Anatomical lead locations	
Contact 0	Ventromedial NAcc	Posteromedial STN
Contact 1	Dorsolateral NAcc	Caudal Zi
Contact 2	Intersection of AC and ALIC	Vo-Vim thalamus
Contact 3	Ventral part of ALIC	Vo-Vim thalamus

Table 1. Postoperative DBS lead location.

Note: DBS coordinates are measured as the tip of the electrode relative to the mid-commissural point.

reports of effectiveness for chronic pain (Tsubokawa, Yamamoto, Katayama, Hirayama, & Sibuya, 1984). In our patient, macrostimulation of Vc induced intolerable pain even at low voltage and low frequency (Table 2). We intraoperatively removed this lead and implanted a DBS electrode in the ventralis oralis (Vo) thalamic area with the intention that this lead may better address dystonia (Morishita, Foote, Haq, et al., 2010). There was no acute side effect or benefit from the implantation of this lead. Approximately four weeks after the first surgery, the patient underwent implantation of a dual channel implantable pulse generator (Medtronic, Activa PC, Minneapolis, MN, USA).

The patient reported no pain relief from any programming setting during the initial clinic session. The initial session included a complete monopolar review of all DBS contacts. The threshold levels of stimulation-induced dysesthesia were unchanged when compared to the levels observed in the operative setting. There were seven programming sessions during her first post-operative year. At the 1-year follow-up, she stated that the pain was minimally improved as compared to preoperative levels. Objectively there was no change in either the pain scale scores, or dystonia. Interestingly, the patient reported aggravation of the pain when she turned off her stimulator with her remote device.

Discussion

Most neurosurgical techniques including MCS, spinal cord stimulation, and thalamic stimulation for chronic pain have aimed to modulate signal within the sensory pathways (Tsubokawa, Katayama, Yamamoto, Hirayama, & Koyama, 1993). MCS has in particular been reported to be a potentially favorable option especially when motor function is preserved (Katayama, Fukaya, & Yamamoto, 1998). The motor function in our case was not preserved. We felt that MCS would not be the best choice given the available literature, and we opted for DBS. Interestingly, Vc thalamic stimulation failed to address the burning pain sensation and also seemed to worsen pain. We therefore chose VC/VS and Vo as the final targets. Limbic circuit

Table 2. Intraoperative macrostimulation results and DBS settings at last visit.

	Response to macrostimulation		
	VC/VS	Vc	
90 μs/135 Hz	450 μs/120 Hz	90 μs/135 Hz	
No response	At 8 V increased burning pain and HR increased from 80 to 130	Dysesthesia in the left arm and leg at 1 V	
At 5 V smile, at 8–10 V more pain and anxiety	At 5 V smile; increased burning pain at 7 V	Dysesthesia in the left arm and leg at 2 V	
No response	At 10 V uncomfortable	Dysesthesia in the left arm and leg at 2–3 V	
At 5 V smile	At 5 V and 7 V smile; 10 V increase pain	Dysesthesia in the left arm and leg at 2–3 V	
	DBS setting at last visit		
	VC/VS	Vo	
(V)	2.5 (1.9–3.5) 180	9-, 10+ (equivalent to 1-, 2+) 2.5 (1.9-3.5) 150 60	
	No response At 5 V smile, at 8–10 V more pain and anxiety No response At 5 V smile	VC/VS 90 μ s/135 Hz 450 μ s/120 Hz No response At 8 V increased burning pain and HR increased from 80 to 130 At 5 V smile, at 8–10 V more pain and anxiety At 5 V smile; increased burning pain at 7 V No response At 10 V uncomfortable At 5 V smile At 5 V and 7 V smile; 10 V increase pain DBS setting at last v VC/VS tacts 2–3–, case+ (V) 2.5 (1.9–3.5) 1 (μ s) 180	

neuromodulation, using VC/VS DBS, is currently under investigation by another group, and the results remain unpublished but may be useful to later interpret our case (clinicalTrial.gov Identifier: NCT01072656) (Machado, Baker, Plow, & Malone, 2013).

A smile is considered to be both a motor and an emotional response. Additionally, both motor and emotional responses can be observed to increase with increasing voltages. Several authors have reported that unilateral smile can be intraoperatively induced by the VC/VS stimulation in OCD (Haq et al., 2011; Nuttin et al., 2003), and Haq et al. reported the intraoperative smile response was a predictive factor for a favorable outcome of OCD DBS (2011). In OCD cases, the smile response is typically accompanied by a positive mood.

In a recent paper, Lauterbach, Cummings, and Kuppuswamy described three smile pathways: volitional (motor), emotional, and composite (2013). The volitional pathway consists of corticopontine projections from premotor, supplementary motor, posterior cingulate, primary motor, and primary sensory cortices to the pons, as well as cortico-striato-pallido-thalamo-cortical and cortico-subthalamo-pallido-thalamo-cortical loops. The emotional pathway consists of limbic circuits involving the anterior cingulate cortex (ACC), orbitofrontal cortex, periaquedactal grey, amygdala, and hypothalamus. The volitional pathway is thought to inhibit the emotional pathway at multiple levels.

We speculate that the impairment of ACC function might be attributable to the phenomena described in our case. ACC is considered part of the emotional smile pathway (Lauterbach et al., 2013; Morecraft, Stilwell Morecraft, & Rossing, 2004), and several authors have reported the association of ACC function with smile and laughter and it is known that ACC lesions can be associated with gelastic seizure (Alkawadri, Mickey, Madden, & Van Ness, 2011; Alkawadri, So, Van Ness, & Alexopoulos, 2013; Arroyo et al., 1993; McConachie & King, 1997). Intraoperative stimulation of the ACC has been reported to induce laughter (Iwasa et al., 2002; Sperli, Spinelli, Pollo, & Seeck, 2006). In addition, the ACC has direct projections to the amygdala, and the overall network plays an important role in emotion (Buchanan, Thompson, Maxwell, & Powell, 1994; Müller-Preuss & Jürgens, 1976). Electrical stimulation to the amygdala has been previously reported to induce various responses such as fear, panic, and smile (King, 1961). Interestingly, increasing the voltage in our patient aggravated rather than alleviated the burning pain. This observation might be due to overactivation of the amygdala pain circuitry (Price, 2000); however, this issue will require further investigations. The impairment in ACC might also be secondary to ex vacuo changes following stroke; however, this would be difficult to prove in a single case.

In summary, we report a single unique case of smile without euphoria that was induced by DBS. The altered limbic function was considered to possibly contribute to the smile phenomenon. Further studies will be needed to refine our findings.

Disclosure statement

No potential conflict of interest was reported by the authors.

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References

- Alkawadri, R., Mickey, B. E., Madden, C. J., & Van Ness, P. C. (2011). Cingulate gyrus epilepsy: Clinical and behavioral aspects, with surgical outcomes. *Archives of Neurology*, 68, 381–385. doi:10.1001/archneurol.2011.21
- Alkawadri, R., So, N. K., Van Ness, P. C., & Alexopoulos, A. V. (2013). Cingulate epilepsy: Report of 3 electroclinical subtypes with surgical outcomes. *JAMA Neurology*, 70, 995– 1002. doi:10.1001/jamaneurol.2013.2940
- Arroyo, S., Lesser, R. P., Gordon, B., Uematsu, S., Hart, J., Schwerdt, P., ... Fisher, R. S. (1993). Mirth, laughter and gelastic seizures. *Brain*, 116, 757–780. doi:10.1093/brain/ 116.4.757
- Bittar, R. G., Kar-Purkayastha, I., Owen, S. L., Bear, R. E., Green, A., Wang, S., & Aziz, T. Z. (2005). Deep brain stimulation for pain relief: A meta-analysis. *Journal of Clinical Neuroscience*, 12, 515–519. doi:10.1016/j.jocn.2004.10.005
- Buchanan, S. L., Thompson, R. H., Maxwell, B. L., & Powell, D. A. (1994). Efferent connections of the medial prefrontal cortex in the rabbit. *Experimental Brain Research*, 100, 469–483. doi:10.1007/BF02738406
- Goodman, W. K., Foote, K. D., Greenberg, B. D., Ricciuti, N., Bauer, R., Ward, H., ... Okun, M. S. (2010). Deep brain stimulation for intractable obsessive compulsive disorder: Pilot study using a blinded, staggered-onset design. *Biological Psychiatry*, 67, 535–542. doi:10.1016/j. biopsych.2009.11.028
- Greenberg, B. D., Gabriels, L. A., Malone Jr., D. A., Rezai, A. R., Friehs, G. M., Okun, M. S., ... Nuttin, B. J. (2010). Deep brain stimulation of the ventral internal capsule/ventral striatum for obsessive-compulsive disorder: Worldwide experience. *Molecular Psychiatry*, 15, 64–79. doi:10.1038/ mp.2008.55
- Greenberg, B. D., Malone, D. A., Friehs, G. M., Rezai, A. R., Kubu, C. S., Malloy, P. F., ... Rasmussen, S. A. (2006). Three-year outcomes in deep brain stimulation for highly resistant obsessive-compulsive disorder. *Neuropsychopharmacology*, 31, 2384–2393. doi:10.1038/sj. npp.1301165
- Haq, I. U., Foote, K. D., Goodman, W. G., Wu, S. S., Sudhyadhom, A., Ricciuti, N., ... Okun, M. S. (2011). Smile and laughter induction and intraoperative predictors of response to deep brain stimulation for obsessive-

compulsive disorder. *Neuroimage*, 54, SS247–SS255. doi:10.1016/j.neuroimage.2010.03.009

- Haq, I. U., Foote, K. D., Goodman, W. K., Ricciuti, N., Ward, H., Sudhyadhom, A., ... Okun, M. S. (2010). A case of mania following deep brain stimulation for obsessive compulsive disorder. *Stereotactic and Functional Neurosurgery*, 88, 322– 328. doi:10.1159/000319960
- Iwasa, H., Shibata, T., Mine, S., Koseki, K., Yasuda, K., Kasagi, Y., ... Nakajima, Y. (2002). Different patterns of dipole source localization in gelastic seizure with or without a sense of mirth. *Neuroscience Research*, 43, 23–29. doi:10.1016/S0168-0102(02)00012-3
- Katayama, Y., Fukaya, C., & Yamamoto, T. (1998). Poststroke pain control by chronic motor cortex stimulation: Neurological characteristics predicting a favorable response. *Journal of Neurosurgery*, 89, 585–591. doi:10.3171/jns.1998.89.4.0585
- King, H. E. (Ed.). (1961). Psychological effects of excitation in the limbic system. Austin: University of Texas Press.
- Lauterbach, E. C., Cummings, J. L., & Kuppuswamy, P. S. (2013). Toward a more precise, clinically–informed pathophysiology of pathological laughing and crying. *Neuroscience & Biobehavioral Reviews*, 37, 1893–1916. doi:10.1016/j.neubiorev.2013.03.002
- Machado, A. G., Baker, K. B., Plow, E., & Malone, D. A. (2013). Cerebral stimulation for the affective component of neuropathic pain. *Neuromodulation: Technology at the Neural Interface*, 16, 514–518. doi:10.1111/j.1525-1403.2012.00517.x
- Malone Jr., D. A., Dougherty, D. D., Rezai, A. R., Carpenter, L. L., Friehs, G. M., Eskandar, E. N., ... Greenberg, B. D. (2009). Deep brain stimulation of the ventral capsule/ventral striatum for treatment-resistant depression. *Biological Psychiatry*, 65, 267–275. doi:10.1016/j.biopsych.2008.08.029
- McConachie, N. S., & King, M. D. (1997). Gelastic seizures in a child with focal cortical dysplasia of the cingulate gyrus. *Neuroradiology*, 39, 44–45. doi:10.1007/s002340050365
- Morecraft, R. J., Stilwell Morecraft, K. S., & Rossing, W. R. (2004). The motor cortex and facial expression: New insights from neuroscience. *The Neurologist*, 10, 235–249. doi:10.1097/01.nrl.0000138734.45742.8d
- Morishita, T., Fayad, S. M., Goodman, W. K., Foote, K. D., Chen, D., Peace, D. A., ... Okun, M. S. (2014). Surgical neuroanatomy and programming in deep brain stimulation for obsessive compulsive disorder. *Neuromodulation: Technology at the Neural Interface*, 17, 312–319. doi:10.1111/ner.12141
- Morishita, T., Foote, K. D., Haq, I. U., Zeilman, P., Jacobson, C. E., & Okun, M. S. (2010). Should we consider Vim thalamic deep brain stimulation for select cases of severe refractory dystonic tremor. *Stereotactic and Functional Neurosurgery*, 88, 98–104. doi:10.1159/000289354

- Morishita, T., Foote, K. D., Wu, S. S., Jacobson, C. E., Rodriguez, R. L., Haq, I. U., ... Okun, M. S. (2010). Brain penetration effects of microelectrodes and deep brain stimulation leads in ventral intermediate nucleus stimulation for essential tremor. *Journal of Neurosurgery*, *112*, 491–496. doi:10.3171/2009.7.JNS09150
- Moscovich, M., Morishita, T., Foote, K. D., Favilla, C. G., Chen, Z. P., & Okun, M. S. (2013). Effect of lead trajectory on the response of essential head tremor to deep brain stimulation. *Parkinsonism & Related Disorders*, 19, 789–794. doi:10.1016/j.parkreldis.2013.03.015
- Müller-Preuss, P., & Jürgens, U. (1976). Projections from the 'cingular' vocalization area in the squirrel monkey. *Brain Research*, 103, 29–43. doi:10.1016/0006-8993(76)90684-3
- Nuttin, B. J., Gabriëls, L. A., Cosyns, P. R., Meyerson, B. A., Andréewitch, S., Sunaert, S. G., ... Demeulemeester, H. G. (2003). Long-term electrical capsular stimulation in patients with obsessive-compulsive disorder. *Neurosurgery*, 52, 1263–1274. doi:10.1227/01.NEU.0000064565.49299.9A
- Okun, M. S., Bowers, D., Springer, U., Shapira, N. A., Malone, D., Rezai, A. R., ... Goodman, W. K. (2004). What's in a "smile?" Intra-operative observations of contralateral smiles induced by deep brain stimulation. *Neurocase*, 10, 271–279. doi:10.1080/13554790490507632
- Price, D. D. (2000). Psychological and neural mechanisms of the affective dimension of pain. *Science*, 288, 1769–1772. doi:10.1126/science.288.5472.1769
- Sewards, T. V., & Sewards, M. (2002). Separate, parallel sensory and hedonic pathways in the mammalian somatosensory system. *Brain Research Bulletin*, 58, 243–260. doi:10.1016/ S0361-9230(02)00783-9
- Sperli, F., Spinelli, L., Pollo, C., & Seeck, M. (2006). Contralateral smile and laughter, but no mirth, induced by electrical stimulation of the cingulate cortex. *Epilepsia*, 47, 440–443. doi:10.1111/j.1528-1167.2006.00442.x
- Tsai, H.-C., Chen, S.-Y., Tsai, S.-T., Hung, H.-Y., & Chang, C.-H. (2010). Hypomania following bilateral ventral capsule stimulation in a patient with refractory obsessive-compulsive disorder. *Biological Psychiatry*, 68, e7–e8. doi:10.1016/j. biopsych.2010.04.001
- Tsubokawa, T., Katayama, Y., Yamamoto, T., Hirayama, T., & Koyama, S. (1993). Chronic motor cortex stimulation in patients with thalamic pain. *Journal of Neurosurgery*, 78, 393–401. doi:10.3171/jns.1993.78.3.0393
- Tsubokawa, T., Yamamoto, T., Katayama, Y., Hirayama, T., & Sibuya, H. (1984). Thalamic relay nucleus stimulation for relief of intractable pain. Clinical results and β-endorphin immunoreactivity in the cerebrospinal fluid. *Pain*, 18, 115– 126. doi:10.1016/0304-3959(84)90879-0