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Reversible Increase in Smoking after Withdrawal of Ventral Capsule/Ventral Striatum Deep Brain Stimulation in a Depressed Smoker

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Introduction

How smoking affects reward systems in mood disorders remains unclear. Functional neuroimaging suggests more dysfunction among depressed than nondepressed smokers (Brody, 2009). Abnormal reward mechanisms could increase smoking's hedonic value, thus sustaining dependence (Koob & LaMoal, 1997). Deep brain stimulation (DBS) of the ventral striatum and adjacent ventral capsule (VC/VS) enhances positive affect in OCD or major depression (Greenberg et al., 2008; Malone et al, 2009). DBS might compensate for reward deficits and reduce smoking. Conversely, smoking might increase if DBS stops.

Case Report

A 43-year-old woman enrolled in an FDA- and IRB-approved trial of DBS for otherwise intractable depression (Malone et al, 2009). Before surgery, lifetime cigarette consumption (average <10/day) and tobacco dependence was low (Fagerstrom Test for Nicotine Dependence=3). Bilateral DBS leads (Model 3391, Medtronic Inc.) were implanted following the trajectory of the anterior limb of the internal capsule at the level of the anterior commissure, extending into VS (on right: 0.2mm anterior to the anterior commissure, 7.5mm lateral, and -1.8mm below the AC-PC plane; on left: 0.1, 8.9, and -1.9mm, respectively). Before DBS, depression remained severe despite aggressive conventional treatments (Montgomery-Åsberg Depression Rating Scale (MADRS=33). After left unilateral VC/VS DBS she sustained remission (MADRS 7) for four years, except when stimulator batteries were depleted. Stimulation parameters: contacts 0+1-2-3+, 130Hz, pw 120 µSec, 6.0V. Concomitant medications including Valproate 1500 mg; Clonazepam 3 mg; Eszopiclone 3 mg; Oxcarbazepine 600 mg.

Smoking before and after DBS interruption

During chronic DBS, smoking remained stable. However, on three separate occasions when DBS was interrupted (e.g. battery depletion), smoking increased dramatically (50–200%). Figure 1 displays her reported smoking during two recent DBS interruption episodes recalled with confidence, including when stimulation restarted. Off DBS, she noticed mood

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changes and markedly increased urges to smoke, simultaneously experiencing smoking as ‘intensely’ unpleasant. Depressive symptoms increased to near a MADRS remission threshold (<10) on both occasions (MADRS=7 and 10 during episodes 1 and 2, respectively). When DBS resumed, smoking rate and pattern returned to baseline, and depressive symptoms declined (MADRS=5 and 2 during episodes 1 and 2, respectively). No increases in appetite were observed with DBS off; her substance use remained limited to tobacco.

Comment

DBS to the same network modulated reportedly affected reward in depressed patients (Schlapfer et al., 2008) and was associated with smoking cessation in an OCD patient (Mantione et al., 2010). Nicotine and cues for nicotine delivery activate the VS and regions functionally connected to the VC/VS (Brody, et al. 2009; David et al. 2007). Withdrawal of chronic smoking may raise reward thresholds by compromising dopaminergic inputs to the VS (Koob & Lamoal, 1997; Balfour, 2004; Epping-Jordan, et al., 1998). Though reliant upon retrospection, like acute smoking cessation, DBS withdrawal in this case led to reproducible acute increases in craving and increased smoking and mild increases in depressive symptoms. These findings suggest significant potential for exploring the neurobiology of tobacco dependence, which may involve MAO-inhibitors as well as nicotine, in DBS patients. Such patients include those with intractable OCD, depression, and chronic pain.

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Figure 1.

Changes in smoking rate during two episodes of DBS disruption. Therapeutic effects routinely decrease during the final 2 weeks of battery life, when DBS currents diminish markedly. Changes in smoking thus were associated temporally with DBS withdrawal.