To the Editor:

Bahramisharif et al. (1) reported that deep brain stimulation (DBS) delivered to the ventral capsule/ventral striatum (VC/VS) target for obsessive-compulsive disorder (OCD) decreased beta-gamma cross-frequency coupling (CFC) in electroencephalographic (EEG) recordings from the occipital cortex. They suggested that this may represent changes in bottom-up visual processing that may make disorder-related stimuli exceptionally salient. They further noted a recent report of DBS-induced changes in motor cortex beta-gamma coupling during DBS for Parkinson’s disease (PD) (2) as potentially supporting that hypothesis.

OCD, however, is different from PD in several respects. First, although there is no basal-ganglia-linked hypothesis of OCD (3), there is no clear degenerative lesion as there is in PD. Second, multiple groups have identified abnormal cortical and subcortical beta rhythms in PD (4), whereas there is no robust visually driven, resting-state EEG from the occipital cortex. They suggested that this may represent changes in bottom-up visual processing that may make disorder-related stimuli exceptionally salient. They further noted a recent report of DBS-induced changes in motor cortex beta-gamma coupling during DBS for Parkinson’s disease (PD) (2) as potentially supporting that hypothesis.

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In this independent sample, we were unable to replicate the results of Bahramisharif et al. (1) (Figure 1). Within the zone of significant change identified by the original article (white box in Figure 1), VC/VS slightly increased CFC, opposite to the authors’ original findings. This increase was not statistically significant (p = .209, two-sample Kolmogorov-Smirnov test). It was, however, strongest at Oz, with smaller mean differences and higher p values at other midline electrodes (Cz, Fz, Pz). We further tested for specific coupling between alpha (8–12 Hz), beta (13–30 Hz), and theta (5–8 Hz) bands and found no significant effects even before multiple-comparisons correction (all p > .1). Overall, our results are most consistent with a lack of VC/VS DBS effect on CFC of midline electrodes.

This conflicting result could be explained by diagnoses, since most of our sample patients did not have OCD. The single OCD subject in our analysis, however, showed a stronger on > off CFC pattern than the group as a whole. It might also be that the results of Bahramisharif et al. (1) are specific to high-frequency DBS. Excluding the subject

Figure 1. (A) Cross-frequency coupling (CFC), averaged across subjects, normalized to maximum of the analysis window (white box). Preprocessing and analysis parameters are identical to Bahramisharif et al. (1). We observed a moderate but nonsignificant increase in CFC with deep brain stimulation (DBS) on, opposite to the original authors’ effect. (B) Average CFC values over the window highlighted in (A), with error bars representing the standard error of the mean over all analyzed patients (n = 5). The two conditions are not significantly different (p = .209) by a two-sample Kolmogorov-Smirnov test. a.u., arbitrary unit; freq, frequency; Norm., normalized.
with 40 Hz to 50 Hz DBS, however, drove the difference between DBS-on and DBS-off closer to 0 (to .003 normalized units) in our cohort. Next, since our study involved only a brief DBS discontinuation, the original authors’ findings might only be visible after their week-long withdrawal. While we cannot rule this out, animal studies of DBS-like stimulation suggest that immediately after stimulation withdrawal, brain electric potentials rebound in a direction opposite to the DBS effect (9). Our short time window should have revealed an even stronger CFC effect than Bahramisharif et al. (1) observed.

We suggest that these opposing CFC findings more likely depend on unmodeled characteristics of the two samples. This could include preoperative clinical or electrophysiologic phenotypes, slight surgical variation in electrode placement, choice of active DBS contacts, or even subtle features of the testing environment. To the latter point, individual peak frequencies and phase locking of occipital rhythms have been shown to change quickly in response to attentional processing and expectancy (9). Subjects’ internal state, such as the negative ruminations of major depressive disorder or obsessions of OCD, may have driven the findings in either sample. More importantly, while DBS likely does have strong cortical effects, we believe our data suggest that the specific finding of altered CFC cannot be considered a general mechanism of action. Further study, including presurgical baseline observations, will be needed to identify the origins and clinical significance of DBS-induced CFC changes. Multicenter coordination on study protocols would help to mitigate the small sample size issues inherent to the Bahramisharif et al. (1) study and our replication.

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Article Information

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References