Deep Brain Stimulation of the Subthalamic Nucleus in Parkinson's Disease Induces Impulsivity through Modulation of the Value of Sensory Information

Dennis London M.D.; Michael Pourfar MD; Alon Y. Mogilner MD

Introduction

In addition to its motor functions, the subthalamic nucleus (STN) has a cognitive role in inhibiting impulsivity. Previous studies have suggested that the STN raises the evidence threshold for making decisions.

Methods

We tested this theory in 8 patients receiving bilateral DBS of the STN using an auditory task (n=5085 trials) in which subjects listen to bilaterally presented "clicks" and decide which side has more. Subjects' decision-making could be interrupted prior to reaching their evidence threshold, resulting in non-reaction time (non-RT) trials. Non-interrupted trials are RT trials. The statistics of stimulus presentation and trial ending were designed so that subjects could not predict when these events would occur, resulting in evidence accumulation to a bound.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) understand that DBS of the STN can cause impulsivity, 2) understand what decision-making parameters can be altered by DBS, and 3) understand how DBS can affect how patients react to errors.

Results

We expected performance to decline in the DBS ON compared to the OFF condition on trials where subjects hit their decision bound (RT trials). However, DBS caused a performance decrease in only leftward RT trials (p=1.82 * 10-4, Fisher's exact test). Drift-diffusion modeling showed that DBS caused 6/8 subjects to increase the value of clicks that occur temporally close to other clicks. There was no clear effect on decision bound. Using model-free analysis, we found that subjects responded impulsively to bursts of evidence that were associated with high levels of conflicting evidence. In addition, DBS caused subjects to paradoxically become more likely to hit their decision threshold after an error; there was an increased likelihood that an RT trial followed an incorrect RT trial when DBS was ON (p=0.0050, Fisher's exact test), but errors did not cause a difference when DBS was OFF (0.58, Fisher's exact test).

Conclusions

While DBS of the STN may lower the decision bound, our data suggests that it may also prevent premature responses to bursts of evidence that portend conflict. It likely also has a role in preventing post-error impulsivity.

References

1. Benabid AL, Chabardes S, Mitrofanis J, et al. Deep brain stimulation of the subthalamic nucleus for the treatment of Parkinson's disease. Lancet Neurol. 2009;8(1):67-81. doi:10.1016/S1474-4422(08)70291-6.
2. Castrioto A, Lhommée E, Moro E, Krack P. Mood and behavioural effects of subthalamic stimulation in Parkinson's disease. Lancet Neurol. 2014;13(3):287-305. doi:10.1016/S1474-4422(13)70294-1.
3. Hälbig TD, Tse W, Frisina PG, et al. Subthalamic deep brain stimulation and impulse control in Parkinson's disease. Eur J Neurol. 2009;16(4):493-497. doi:10.1111/j.1468-1331.2008.02509.x.
4. Zavala B, Zaghloul K, Brown P. The subthalamic nucleus, oscillations, and conflict. Mov Disord. 2015;30(3):328-338. doi:10.1002/mds.26072.
5. Ratcliff R, McKoon G. The diffusion decision model: theory and data for two-choice decision tasks. Neural Comput. 2008;20(4):873-922. doi:10.1162/neco.2008.12-06-420.
6. Baunez C, Nieoullon A, Amalric M. In a rat model of parkinsonism, lesions of the subthalamic nucleus reverse increases of reaction time but induce a dramatic premature responding deficit. J Neurosci. 1995;15(10):6531-6541.
7. Eagle DM, Baunez C, Hutcheson DM, Lehmann O, Shah AP, Robbins TW. Stop-signal reaction-time task performance: role of prefrontal cortex and subthalamic nucleus. Cereb Cortex. 2008;18(1):178-188. doi:10.1093/cercor/bhm044.
8. Obeso I, Wilkinson L, Casabona E, et al. The subthalamic nucleus and inhibitory control: impact of subthalamotomy in Parkinson's disease. Brain. 2014;137(5):1470-1480. doi:10.1093/brain/awu058.
9. Frank MJ, Samanta J, Moustafa AA, Sherman SJ. Hold your horses: impulsivity, deep brain stimulation, and medication in parkinsonism. Science. 2007;318(5854):1309-1312. doi:10.1126/science.1146157.
10. Frank MJ. Hold your horses: A dynamic computational role for the subthalamic nucleus in decision making. Neural Networks. 2006;19(8):1120-1136. doi:10.1016/j.neunet.2006.03.006.
11. Brunton BW, Botvinick MM, Brody CD. Rats and humans can optimally accumulate evidence for decision-making. Science. 2013;340(6128):95-98. doi:10.1126/science.1233912.
12. Cavanagh JF, Wiecki T V, Cohen MX, et al. Subthalamic nucleus stimulation reverses mediofrontal influence over decision threshold. Nat Neurosci. 2011;14(11):1462-1467. doi:10.1038/nn.2925.
13. Cavanagh JF, Sanguinetti JL, Allen JJB, Sherman SJ, Frank MJ. The Subthalamic Nucleus Contributes to Post-error Slowing. J Cogn Neurosci. 2014;26(11):2637-2644. doi:10.1162/jocn_a_00659.
14. Siegert S, Herrojo Ruiz M, Brücke C, et al. Error signals in the subthalamic nucleus are related to post-error slowing in patients with Parkinson's disease. Cortex. 2014;60:103-120. doi:10.1016/j.cortex.2013.12.008.
15. Zavala B, Tan H, Ashkan K, et al. Human subthalamic nucleus–medial frontal cortex theta phase coherence is involved in conflict and error related cortical monitoring. Neuroimage. 2016;137:178-187. doi:10.1016/j.neuroimage.2016.05.031.

[DEFAULT POSTER]