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Reply to: "Spinal Cord Stimulation for Parkinson's Disease: Dynamic Habituation as a Mechanism of Failure?"

We kindly thank Cury and colleagues for their comments on our study and for sharing some of our concerns on spinal cord stimulation (SCS) for Parkinson's disease (PD). It is established that the current literature on this topic is extremely fragmented and heterogenous to make conclusions. Cury and colleagues are now proposing "habituation" as a mechanism explaining the decay of benefit seen in some of our and their patients. They illustrate the example of a single patient with PD who was evaluated for 4 weeks under an arbitrary cycling paradigm (SCS on and off for 15 minutes each epoch) and hypothesize that the delivery of a variable stimulation paradigm could minimize habituation by avoiding the phase coupling of pathological oscillation and SCS.

Although the concept of cycling stimulation is interesting, to our knowledge there has been no published experience with this type of stimulation in SCS patients with PD, or any other type of condition susceptible to SCS. A slightly different type of stimulation is intermittent dosing SCS (using several seconds SCS ON/OFF intervals with unchanged frequency and pulse width) in pain patients, overall showing that this approach is superior to continuous tonic stimulation only in terms of battery life.[1]

Furthermore, in Feng et al.'s[2] paper, cited by Cury and colleagues, the hippocampal cells of healthy rats were stimulated with a variable interpulse interval, causing synchronization of neuronal activity at a local level. How this can be extrapolated to patients with PD is difficult to say. Interestingly, there are reports in patients with PD and essential tremor (the latter also susceptible to habituation), as well as computer simulations and animal studies, showing that random deep brain stimulation is less effective than continuous stimulation.[3-5]

Importantly, one component highly susceptible of habituation is placebo effect, which is how we interpreted the transient 50% improvement of freezing seen in one of our patients 1 month after SCS. In contrast with most SCS studies published so far, we used subthreshold stimulation to lessen the placebo effect, although we changed to suprathreshold stimulation (ie, causing lower limbs paresthesias) during the last month of trial.

Finally, we agree with Cury and colleagues[1] that there might be a role for noninvasive stimulation to predict SCS response in patients with PD, although the issue of placebo will still need to be addressed.

In conclusion, a decade after the first cases of SCS for PD were published, the role of this therapy is still unclear beyond what has been claimed by enthusiastic review papers. Double-blinded prospective studies in humans and using paresthesia-free suprathreshold stimulation (eg, burst stimulation) or, in keeping with what is proposed here, cycling stimulation might help elucidate this issue.

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