Reply to: STN DBS as rescue therapy for LCIG associated biphasic-like dyskinesias

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We thank the authors for their interest in our case[1], and for sharing their experience of subthalamic nucleus (STN) deep brain stimulation (DBS) in the treatment of levodopa-carbidopa intestinal gel (LCIG) associated biphasic-like dyskinesia[2].

The benefits of STN DBS in treating biphasic dyskinesia were first unequivocally demonstrated by Krack et al. in 1999[3]. In this study, 27 Parkinson's disease (PD) patients with motor complications underwent levodopa challenge before and after 6 months of chronic high-frequency STN DBS - a 50% reduction in biphasic dyskinesia was observed. Most recently, Kim et al. reported outcomes from 66 patients with biphasic dyskinesia who had undergone STN DBS. In their cohort, biphasic events disappeared in 74% of patients, though in nearly half, this benefit took over 3 months to achieve[4].

The improvements in dyskinesia following STN DBS are generally thought to result from levodopa dose reduction following the procedure. This is certainly part of the explanation, particularly in relation to peak-dose dyskinesia, and there is a correlation between post-operative levodopa dose reduction and improvements in dyskinesia[4]. However, in some patients, such as the one presented here, benefit is obtained despite minimal changes in levodopa dose, suggesting an additional direct anti-dyskinetic effect of STN stimulation.

In contrast to the anti-akinetic effects of STN DBS, which are primarily mediated by suppression of beta-band oscillatory activity in the dorso-laterally located sensori-motor STN[5], stimulation above the STN is best for controlling dyskinesia. This effect is likely mediated through influences on pallidofugal fibres in the sub-thalamic region, interrupting pathological pallidal neuronal discharges from reaching the thalamus[6, 7].

These cases yield a number of important learning points. First, patients being considered for LCIG therapy should be counseled about the fact that though

motor OFF times are likely to improve, the effect of LCIG infusion on dyskinesia is more variable and indeed a significant minority may experience worsening or novel dyskinetic features[1, 8-10]. Second, both pallidal and STN DBS are effective treatments both for 'classic' biphasic dyskinesia and as rescue therapy in patients with LCIG-associated 'biphasic-like' dyskinesia. These interventions should be considered early for this debilitating condition, which is frequently refractory to medical management. Third, in those with pre-existing, or at high-risk of future biphasic phenomena (e.g. young-onset PD, advanced disease), DBS may be the preferred advanced therapy in appropriate surgical candidates. Finally, in those undergoing STN DBS for dyskinesia management, it may be worthwhile during electrode placement to ensure coverage of the sub-thalamic area[11].

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2 Statistical Analysis: A. Design, B. Execution, C. Review and Critique;

3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique

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The authors confirm that the approval of an institutional review board was not required for this work. Written informed consent was obtained from all patients for publication of this work. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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