

Reply to Comment on: Successful Treatment of Levodopa/Carbidopa Intestinal Gel Associated “Biphasic-like” Dyskinesia with Pallidal Deep Brain Stimulation

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We thank the authors for their interest in our clinical vignette, and for highlighting potential difficulties in the diagnosis of 'biphasic-like' dyskinesia(1,2).

Of the three classically described variants of levodopa-induced dyskinesia, biphasic dyskinesia is arguably the least understood, most debilitating, and hardest to treat(3). Typical biphasic dyskinesia occurs early (10-20min) after levodopa intake, abates at peak serum concentrations, and recurs during the subsequent decay in plasma drug levels prior to administration of the next levodopa dose. Such temporal patterns facilitate diagnosis, though co-existence with peak-dose and end-of-dose dyskinesia within individual patients as well as bizarre phenomenology (an excellent example being the 'silly walks' of Parkinson's described by Růžička et al. in 2011)(4) means that mis-diagnoses remain common. Continuous dopaminergic stimulation approaches have added an extra layer of complexity. Indeed, while they are effective treatments for many motor complications (including dyskinesia), both levodopa-carbidopa intestinal gel and subcutaneous apomorphine have occasionally been associated with the emergence of 'biphasic-like' phenomena, likely due to continuous stimulation at a sub-therapeutic level(5,6).

The pathophysiologic basis of biphasic dyskinesia is complex and incompletely understood. Intuitively, increasing dopaminergic stimulation beyond the 'biphasic' level should ameliorate symptoms, and indeed this is the most commonly adopted strategy. However, it is not always effective and the benefits may be lost over time. In such cases, deep brain stimulation (DBS) should be considered. Both the subthalamic nucleus (STN) and internal portion of the globus pallidus (GPi) have proven efficacy as targets for treating levodopa-induced dyskinesia, including biphasic dyskinesia(7-9). Pallidal stimulation has superior efficacy, and exerts a direct anti-dyskinetic effect, while STN stimulation largely improves dyskinesia through permitting reductions in levodopa dosing⁷.

In our vignette, we illustrated the life-changing effects of successful GPi DBS for levodopa-carbidopa intestinal gel-associated biphasic-like dyskinesia. This management strategy should be considered for biphasic and 'biphasic-like' dyskinesia refractory to medical management, even in those with mild pre-existing cognitive symptoms or gait imbalance.

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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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