Autonomic failure following deep brain stimulation for Parkinson's disease

Introduction

Deep brain stimulation of the subthalamic nucleus may be used to treat the symptoms of Parkinson's disease in selected patients. This article reports a case of significant worsening of orthostatic hypotension following deep brain stimulation for the treatment of Parkinsonian tremor and discusses the potential mechanisms involved.

Discussion

There is autonomic nervous system involvement even in the early stages of Parkinson's disease and the prevalence of orthostatic hypotension may be as high as 20% (Stemper et al, 2006). Owing to disease progression and the hypotensive effect of levodopa treatment, orthostatic hypotension often becomes more severe and disabling over time.

Epidemiological studies have shown that orthostatic dysfunction significantly impacts the activities of daily life in Parkinson's disease, independently of motor deficits (Magerkurth et al, 2005). Deep brain stimulation of the subthalamic nucleus may be used to treat the symptoms of Parkinson's disease in selected patients and although the exact mechanism of action is incompletely understood, subthalamic nucleus stimulation has been shown to increase regional cerebral blood flow in the anterior cingulate cortex that plays a role in central autonomic control, and also affect basal ganglia output involved in heart rate and blood pressure control (Stemper et al, 2006).

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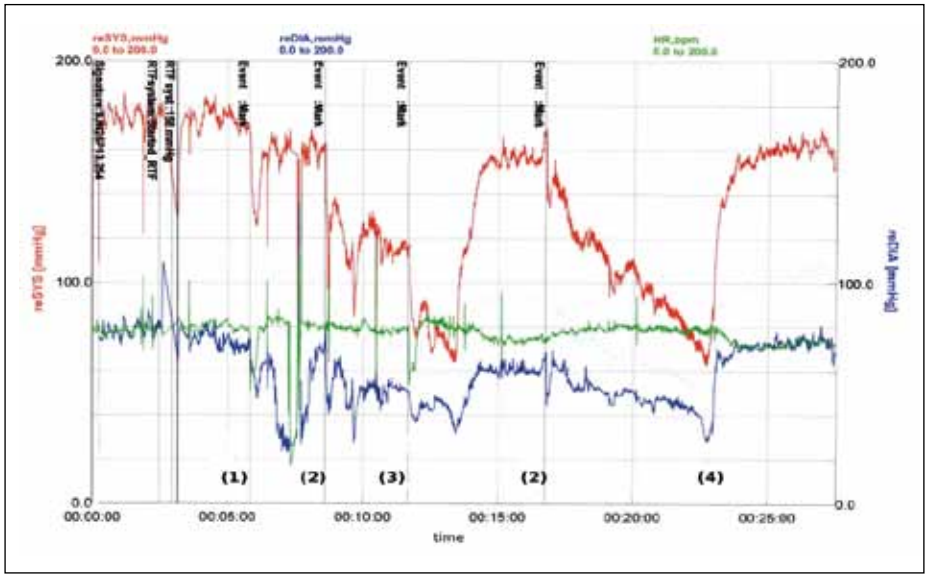
Some studies have shown deep brain stimulation to improve orthostatic hypotension acutely by increasing sympathetic stimulation and peripheral vasoconstriction and baroreflex sensitivity, and by reducing pharmacotherapy with levodopa (Stemper et al, 2006; Ludwig et al, 2007). While prospective, follow-up studies have shown deep brain stimulation to have no demonstrable effect on autonomic dysfunction (Holmberg et al, 2005; Zibetti et al, 2007), this patient developed significant worsening of orthostatic hypotension 2 years after deep brain stimulation insertion.

Peripheral adrenoreceptors autoregulate in response to sympathetic stimulation, both via receptor down-regulation and inactivation by phosphorylation, and chronic low-level sympathetic stimulation

Figure 1. Tilt table test showing significant orthostatic fall in systolic (red) and diastolic (blue) blood pressure without compensatory increases in heart rate (green). Event marks: (1) = carotid sinus massage supine; (2) = lying to standing; (3) = carotid sinus massage erect; (4) = standing to lying. HR = heart rate; reDIA = diastolic blood pressure; reSYS = systolic blood pressure.



Case Report

An 81-year-old man presented with recurrent blackouts. He was diagnosed with idiopathic Parkinson's disease in 2001 when asymptomatic orthostatic hypotension was noted (blood pressure 139/71 mmHg supine, 100/55 mmHg standing). The disease was tremor-predominant with truncal rigidity but minimal bradykinesia and normal eye movements. Despite increasing medical treatments, his tremor became more disabling and in 2004 a deep brain stimulator was implanted which caused almost complete resolution of the tremor.

The patient remained well until 2006 when he reported recurrent blackouts when sitting from lying or standing from sitting. Investigations revealed significant hypotension during episodes of unresponsiveness (e.g. blood pressure 63/47 mmHg) and Holter monitoring demonstrated first degree heart block and pauses of up to 4 seconds. A dual chamber permanent pacemaker was inserted which relieved the electrocardiographic abnormalities but not the symptoms of syncope. Formal tilt-table assessment identified significant orthostatic hypotension (*Figure 1*). Despite increased fluid intake, compression stockings and midodrine therapy, the patient remained wheelchair-bound and declined further investigations of autonomic function.

has been shown to reduce responsiveness of the peripheral autonomic nervous system (Senard et al, 1991; Zhao et al, 1996; El-Armouche et al, 2007). Through such a mechanism, deep brain stimulation over a prolonged period may contribute to autonomic failure as occurred in this patient. A potential solution may therefore be to reduce deep brain stimulation at nighttime to allow re-sensitization to occur but this approach was not possible in this case because of disabling tremor.

Studies of deep brain stimulation in Parkinson's disease patients are limited by the small numbers of patients included and short duration of follow up. No study has provided prolonged follow up for more than 2 years and this may contribute to the conflicting effects seen in this patient and those described in the literature. Indeed, autonomic failure following deep brain stimulation for Parkinson's disease has not been previously described and the authors suggest a need for studies examining the long-term autonomic effects of deep brain stimulation as a treatment for Parkinson's disease. BJHM

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LEARNING POINTS

- Autonomic nervous system involvement is common in Parkinson's disease.
- Orthostatic dysfunction significantly impacts the activities of daily life in Parkinson's disease.
- Deep brain stimulation may be used to treat the symptoms of Parkinson's disease in selected patients.
- In the short term, deep brain stimulation may improve orthostatic hypotension in Parkinson's disease.
- Over a prolonged period, deep brain stimulation may contribute to autonomic failure.