Baroreceptor Sensitivity is Optimized by Deep Brain Stimulation in Humans

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1 OBJECTIVES

Dysautonomia can be debilitating and predominantly manifests as postural hypotension. Sympathetic myocardial denervation and deranged arterial baroreceptor reflex are among the abnormalities described in Parkinson's disease (PD) in which dysautonomia can affect up to 50% of patients. Deep brain stimulators placed within the brainstem or hypothalamus have been shown to modulate cardiorespiratory function and many of these stimulated sites are components of the central autonomic network and the baroreceptor circuit. Electrical stimulation is provided chronically through an implanted electrode, across the brain-machine interface. In humans, we have previously demonstrated a resistance to postural drop in blood pressure on standing and during head-up tilt with deep brain stimulation (DBS) of the periventricular grey matter of the midbrain and pedunculopontine nucleus at the junction of the midbrain and pons. This mirrors results found in animal studies. We investigated whether DBS could improve Valsalva response, an index of dysautonomia, using PD as the model of dysautonomia.

2 METHODS

Design: Prospective Controlled StudySubjects: Eight PD patients tested and stimulation On and Off in random order.

Valsalva manoeuvre to achieve a pressure of 30-40mmHg was sustained for 15 seconds. Portapress continuous non-invasive plethysmography to record blood pressure and electrocardiogram were recorded. Baroreceptor sensitivity (BRS) was calculated from the transfer function of systolic BP and R-R interval using autoregressive modelling. Valsalva ratio (VR) was calculated as the ratio between the quickest heart rate during Phase II against the slowest heart rate of Phase IV of the Valsalva manoeuvre (normal VR>1.21).

3 RESULTS

Six patients could be successfully tested. Valsalva ratio increased with stimulation from median 1.15 (SE +/- 0.06) Off to 1.20 (SE +/- 0.06) On ($p=0.028$). BRS increased significantly during Valsalva compared to rest with stimulation On versus Off ($p=0.028$). BRS increase had a major correlation with mean depth of PPN stimulating electrode contacts whereby it explained 89% of its variance (Spearman's $rho=0.943$, $n=6$, $p=0.005$).

4 DISCUSSION

Pathological cardiovascular response to Valsalva manoeuvre in PD, characteristic of dysautonomia, shifted towards normal. There was a direct effect on BRS itself suggesting central cardiovascular modulation by DBS. This adds to the body of human data supporting the beneficial cardiovascular modulation provided by DBS and this is the first study to show significant improvements in autonomic function in patients with existing dysautonomia.

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