Deep Brain Stimulation of the Periaqueductal Grey Induces Vasodilation in Humans


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To the Editor:

Surgical implantation of electrodes into deep brain structures for the management of conditions such as chronic pain provides an opportunity for assessment of the physiological impact of stimulation of focal brain nuclei in humans. Recent studies in humans have suggested that stimulation of the periventricular (PVG)/periaqueductal grey (PAG) regions can result in changes in systemic blood pressure (BP). In the present case, we examined the physiological impact of such stimulation in humans by obtaining continuous measures of limb blood flow, peripheral resistance, stroke volume, and heart rate (HR) during deep brain stimulation (DBS) of the PVG/PAG. The patient, a 55-year-old woman, was referred for management of recalcitrant chronic neuropathic, phantom limb pain (affecting both lower limbs) in 2004, subsequently leading to PVG/PAG DBS surgery in 2005 at the Radcliffe Infirmary in Oxford.

Assessments and procedures were approved by the Oxford Ethics Committee and performed in a quiet thermostatically controlled room (26°C). The patient was placed in a semirecumbent position, at which point the stimulator was turned off for an initial 20-minute rest period. After a baseline BP assessment using a Finometer PRO (Finapres Medical Systems, Amsterdam, Netherlands), the stimulator was turned on, and BP, stroke volume, total peripheral resistance, and brachial artery diameter and blood flow velocity (Terason T3000, Teratech Corporation, Burlington, MA) were recorded for 5 minutes of this "on" period. Activation of the 2 proximal contacts in single bipolar arrangement on the model 3389 quadripolar lead (Medtronic, Minneapolis, MN) was set to a frequency of 40 Hz with a pulse width of 450 μs and amplitude of 3.1 V.

The patient’s mean brachial BP increased transiently when the stimulator was turned on but then persistently decreased below

![Graphs showing changes in blood pressure, flow, resistance, output, and heart rate](image_url)

**Figure.** Mean brachial blood pressure, brachial blood flow, total peripheral resistance, cardiac output, stroke volume, and RR interval (heart rate) before and during stimulation.

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resting values (103±2 to 96±2 mm Hg; see Figure). This decrease in BP was associated with a contemporaneous increase in brachial artery blood flow (72±11 to 148±12 mL/min) and decrease in total peripheral resistance (15.2±0.6 to 12.9±0.5 mm Hg • mL⁻¹ • min⁻¹). Stroke volume increased (79±2 to 89±3 mL) along with cardiac output (6.7±0.2 to 7.5±0.3 L/min), whereas RR intervals (and HR) remained relatively stable throughout the rest and stimulation periods (0.70±0.02 versus 0.71±0.02 seconds).

Although this report is consistent with previous studies describing changes in BP in awake humans during PVG/PAG stimulation,² it is the first to our knowledge to report changes in vascular tone and peripheral resistance in response to DBS in humans. We observed an initial brief spike in BP, possibly relating to transient facial pain lasting 5 seconds when the stimulator was activated. Once the pain resolved, BP dropped rapidly and consistently, accompanied by a decrease in total peripheral resistance. Blood flow increased through the brachial artery, whereas brachial diameter remained relatively constant, suggesting that changes in the vasomotor tone of resistance vessels downstream were responsible for the changes in flow and pressure.

We interpret the data from this subject as being consistent with a primary impact of DBS on vascular tone, as both BP and blood flow data rapidly and simultaneously changed after stimulation. Blood pressure is, of course, a highly regulated variable, and any decrease would be expected to induce reflex homeostatic responses. In this context, we might have expected some compensatory increase in cardiac output and/or peripheral resistance as stimulation continued, with emphasis on the cardiac change if the vasomotor increase in cardiac output and/or peripheral resistance as response to DBS in humans. We observed an initial brief spike in BP, possibly relating to transient facial pain lasting 5 seconds when the stimulator was activated. Once the pain resolved, BP dropped rapidly and consistently, accompanied by a decrease in total peripheral resistance. Blood flow increased through the brachial artery, whereas brachial diameter remained relatively constant, suggesting that changes in the vasomotor tone of resistance vessels downstream were responsible for the changes in flow and pressure.

An important limitation of case presentations lies in their limited generalizability. We cannot assume, from this report, that all patients undergoing this procedure will exhibit similar hemodynamic changes on stimulation. It is likely, as with other physiological responses, that “responders” and “nonresponders” will exist, and such variability in hemodynamic responses is accentuated by small inconsistencies in electrode positioning. Indeed, the original report describing the BP effects of PAG DBS in humans observed responses in some, but not all, subjects.²,³

In summary, these combined blood flow and pressure data suggest that stimulation of the PVG/PAG can impact vasomotor control. This finding compliments previous reports pertaining to the impact of DBS on BP and extends findings to the vasculature in humans.²,³

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Howard H. Carter
School of Sport Science, Exercise and Health
University of Western Australia
Crawley, Western Australia, Australia

Ellen A. Dawson
N. Timothy Cable
Research Institute for Sport and Exercise Science
Liverpool John Moores’ University
Liverpool, United Kingdom

Shanika Basnayake
Tipu Z. Aziz
Alexander L. Green
David J. Paterson
Nuffield Department of Surgery and
Department of Physiology, Anatomy, and Genetics
University of Oxford
Oxford, United Kingdom

Christopher R.P. Lind
Department of Neurosurgery
Sir Charles Gairdner Hospital
Perth, Western Australia, Australia
School of Surgery
University of Western Australia
Crawley, Western Australia, Australia

Dick H.J. Thijssen
Research Institute for Sport and Exercise Science
Liverpool John Moores’ University
Liverpool, United Kingdom
Department of Physiology
Radboud University Nijmegen Medical Centre
Nijmegen, The Netherlands

Daniel J. Green
School of Sport Science, Exercise and Health
University of Western Australia
Crawley, Western Australia, Australia
Research Institute for Sport and Exercise Science
Liverpool John Moores’ University
Liverpool, United Kingdom

