Combining microelectrode recordings from human peripheral nerves with functional magnetic resonance imaging of the brain

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Blood pressure is controlled on a beat-to-beat basis through fluctuations in heart rate and the degree of sympathetically-mediated vasoconstriction in skeletal muscles. By recording muscle sympathetic nerve activity (MSNA) at the same time as performing functional magnetic resonance imaging (fMRI) of the brain, we recently showed that it is possible to use the nerve signal to identify structures within the human brainstem responsible for the beat-to-beat fluctuations in MSNA *via* the baroreflex, specifically the serial pathway comprising the nucleus tractus solitarius, caudal ventrolateral medulla and rostral ventrolateral medulla (Macefield & Henderson, 2010). We have now extended this approach to identify cortical structures involved in the control of blood pressure. Spontaneous bursts of MSNA were recorded *via* a tungsten microelectrode inserted percutaneously into the peroneal nerve of 14 healthy subjects in a 3T MRI scanner. Blood Oxygen Level Dependent (BOLD) contrast - gradient echo, echo-planar - images were continuously collected in a 4s ON, 4s OFF sampling protocol. MSNA burst amplitudes were measured during the OFF periods and BOLD signal intensity was measured during the subsequent 4s period to allow for neurovascular coupling and nerve conduction delays. Group analysis demonstrated regions showing fluctuations in BOLD signal intensity that covaried with the intensity of the concurrently recorded bursts of MSNA. Signal intensity and MSNA were positively correlated in the left insula, bilateral dorsolateral prefrontal cortex, bilateral posterior cingulate cortex and bilateral precuneus. In addition, MSNA covaried with signal intensity in the left dorsomedial hypothalamus and bilateral ventromedial hypothalamus (VMH). Construction of a functional connectivity map revealed coupling between activity in VMH and the insula, dorsolateral prefrontal cortex, precuneus, and the left and right rostroventrolateral medulla (RVLM). This suggests that activity within suprabulbar regions may regulate resting MSNA by projections to the premotor sympathetic neurones in the rostroventrolateral medulla. We conclude that concurrent microelectrode recordings of sympathetic nerve acitivity and fMRI allows 'real-time' imaging of the cortical and subcortical sites involved in cardiovascular control. We are currently extending this approach to understanding the functional changes in the brain in patients with obstructive sleep apnoea or congestive heart failure, two pathophysiological states associated with greatly elevated MSNA.

Macefield VG & Henderson LA. (2010) Real-time imaging of the medullary circuitry involved in the generation of spontaneous muscle sympathetic nerve activity in awake subjects. *Human Brain Mapping* **31**: 539-549