Blood Pressure Changes Affect the Detection of Cerebral Activation to Stimulation of Forepaw Using Functional Magnetic Resonance Imaging

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Introduction

Functional MR imaging (fMRI), which detects blood oxygen level dependent (BOLD) signal changes in T2* weighted images, is an indirect measure of neural activity since such changes in BOLD signal predominately arise from alterations in cerebral hemodynamics that accompany a local change in brain function. However, when autoregulation is impaired or not entirely effective, increases or decreases in arterial blood pressure (BP) can directly affect cerebral hemodynamics and thereby the BOLD signal. We hypothesized that a transient increase in BP would produce an increase in the number of active voxels within T2* images that would be dependent on BP and result in an enhanced detection of the cerebral activation response to simultaneous stimulation of the sensory-motor cortex whereas a transient decrease in BP would produce a decrease in the number of active voxels resulting in a loss of detection of this cerebral activation.

Material and Methods

Functional MR experiments were performed in 28 rats using a 9.4T Bruker Avance MR system. Rats were anesthetized with alpha-chloralose while body temperature, respiration and blood gases were controlled. For each scan a set of 32 gradient echo T2* images were acquired during either electrical stimulation of the forepaw (off/on/off/on/off paradigm), arterial BP increases (norepinephrine, 0.15-1.2 ug/kg, I.V.), arterial BP decreases (trimethyl camsylate, 0.5-3.25 mg/kg, I.V.), or electrical stimulation with simultaneous BP changes. Fuzzy clustering (EvIdent) and cross-correlation ($p<0.001$) analysis were used to identify voxels of apparent activation in 5 different regions of interest (ROIs) - sensory-motor cortex (Cortex), insular cortex (Insula), region around the third ventricle (Ventricle), the rest of the brain areas (Other) and muscle overlying the scalp (Muscle). In each ROI, the regional 'activation' response was represented by the number of voxels with a change in intensity over time course (TC) that correlated to either the stimulation TC or the BP change TC normalized by the total number of voxels in that ROI. All the normalized 'activation' responses were then placed into their BP range (1-30, 31-45, 46-60 and > 60 mmHg) according to the maximum BP change occurring during that scan.

Results

BP increases without electrical stimulation. When the BP increases were small (0 or 1-30 mm Hg), relatively few voxels were detected as an 'activation' response whereas with moderate (31-45 mmHg) or more extreme BP increases (46-60 and >60 mmHg), a correspondingly greater 'activation' was detected throughout the brain. Regionally, the 'activation' response in the 'Other' region was already significantly greater than that of the control group (0 mmg) when BP changes were greater than 15 mmHg ($P<0.05$). Similarly, with the higher BP ranges, blood pressure dependent increases in the 'activation response were detected in 'cortex', 'ventricle' and 'insula' but not in 'muscle' (Fig 1A). When correlated to the stimulation TC, despite no stimulation there was significant 'activation' responses in the 'Other' region when BP increases were more than 30 mmHg ($P<0.05$) and within 'cortex', 'ventricle' and 'insula' when BP increases were higher than 46 or 60 mmHg (Fig 1B). ***BP increases with electrical stimulation.*** As with BP increases alone, there was a cerebral 'activation' response detected as a correlation to the change in BP TC that increased as the change in BP increased (Fig 2A). However, the correlation analysis to the stimulation TC detected an increased activation in the sensory-motor cortex and this extended to other brain regions, particularly when stimulation was accompanied by a large increase in BP (e.g. > 46 mmHg)($P<0.05$) (Fig 2B). ***BP decreases without electrical stimulation.*** With either no or small decreases in BP (1-30 mmHg), relatively few voxels were detected as a 'deactivation' in response to the change in BP TC whereas with moderate (31-45 mmHg) or more extreme BP decreases (46-60 and >60 mmHg), there was a correspondingly greater 'deactivation' response throughout the brain. The increases in this 'deactivation' response were significant in all the ROIs when BP decreases were greater than 30 mmHg ($P<0.05$). On the other hand, when analyzed by correlating to the stimulation TC, no significant 'activation' response was detected in any ROI within any decreased BP range. ***BP decreases with electrical stimulation.*** As with the BP decreases alone, correlation to changes in BP TCs demonstrated significant increases in a cerebral 'deactivation' response in all the ROIs for all ranges of BP decreases. Correlation analysis to the stimulation TC showed no significant effect of BP decreases on the brain's normal 'activation' response to electrical stimulation.

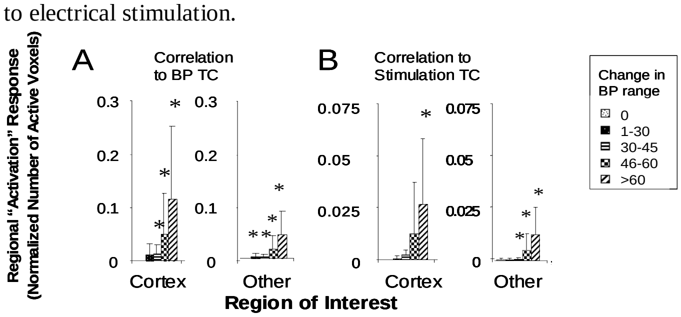

Fig 1. BP increases without electrical stimulation. Regional 'activation' response of the brain correlated to **A.** BP changes or **B.** electrical stimulation time course (TC) shown in two ROIs ('Cortex' and 'Other').*$P<0.05$, different from 0mmHg BP change group.

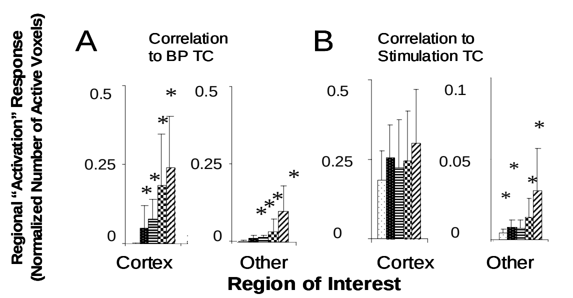

Fig 2. BP increases with electrical stimulation. Regional 'activation' response of the brain correlated to **A.** BP changes or **B.** electrical stimulation time course (TC) shown in two ROIs ('Cortex' and 'Other'). *$P<0.05$, different from 0mmHg BP change group.

Conclusions.

Whether or not there is simultaneous electrical stimulation of the forepaw, BP increases (>15 mmHg) produce an apparent 'activation' response in various brain regions. This results in an enhanced detection of cerebral activation to simultaneous electrical stimulation of the sensory-motor cortex. In contrast, BP decreases (>30 mmHg) produce an apparent 'deactivation' response in various brain regions and this has no significant effect on the detection of this cerebral activation. *Supported by Canadian Institutes for Health Research.*