Probing Neural Networks Involved in Upregulation of Heart Rate and Blood Pressure During Handgrip

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Introduction Central command is considered to play an important role in up-regulation of heart rate (HR) and blood pressure (BP) during exercise. Studies have investigated the possible network using PET, SPECT, and MRI [1-4]. The typical paradigm uses visual feedback to maintain maximum voluntary contraction (MVC) handgrip and use block correlation analysis to map brain activation. Those studies found activations in the thalamus, insular cortex, anterior cingulate gyrus, ventral medial prefrontal cortex and others to be involved in the central commands that drive BP increases. However, problems remain with the designs. PET and SPECT have limited temporal resolution, and while fMRI has high temporal resolution, BP cannot be measured continuously in the scanner. Moreover, the visual feedback handgrip tasks and block paradigm correlation both have confounding effects in identifying the central command that BP increases, because the brain activations come from task performing or the activation related with driving HR or BP increase are hardly separated.

We constructed a MRI-compatible handgrip device with visual feedback to maintain a target MVC in the MR scanner. We then correlated BP with HR at every heartbeat on individual subjects outside the magnet such that continuous HR recording in the magnet could provide continuous BP data indirectly to allow temporal correlation analysis of fMRI data. Two fMRI analyses (block correlation and correlation with HR) were performed. The purpose of this study is trying to separate the brain activations come from task performing or the activation related with driving HR or BP increase.

Anatomical Area (BA)	Block 20% & 30%	Block 5%	Linear 20% & 30%
Insular (BA 13)	+++	+	-
Thalamus	+++	-	-
Anterior Cingulate	+	++	-
Posterior Cingulate	++	+	-
Cerebellum	+++	+	++
Cingulate Gyrus	+++	-	-
Visual Cortex	++	+	+++
Motor Cortex	++	-	-
Brodmann Area 40	+++	-	++
Brodmann Area 7	-	-	++
Brodmann Area 6	+++	-	++
Brodmann Area 9	++	++	++
Brodmann Area 39	-	-	+++

Table 1. Major Brain Activations Areas in Different Analysis
*Strong +++, Middle ++, Mild +, None -

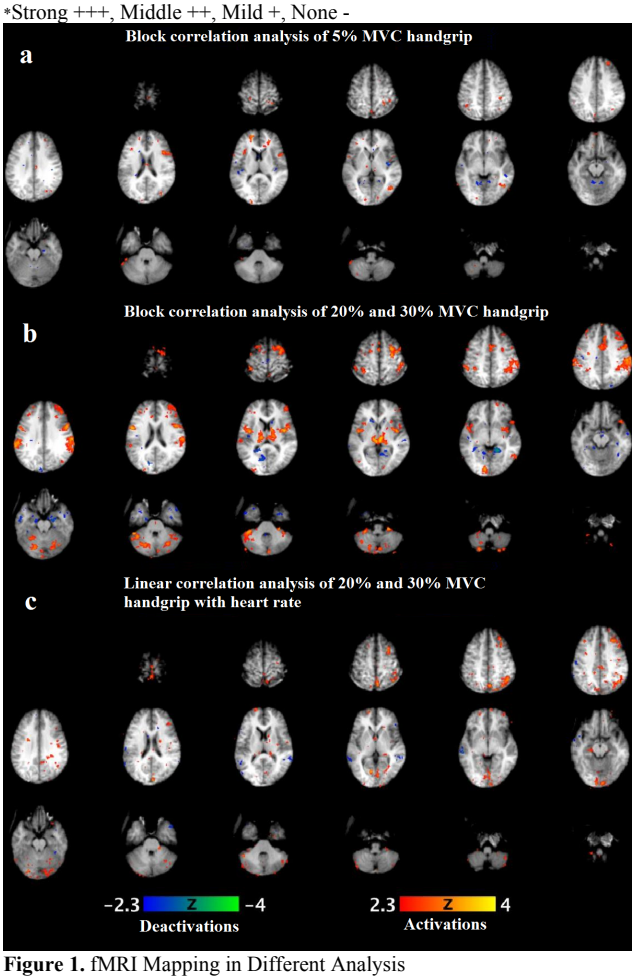

Figure 1. fMRI Mapping in Different Analysis

Methods Four healthy right handed volunteers were studied (average age 24.5 years old). Outside the magnet, subjects performed 3 epochs of [3-min rest, 3-min unilateral handgrip exercise and 3-min rest] at 5%, 20% and 30% of MVC using a custom-made device that provided visual feedback to target each individual's % MVC. Multiple trials were done, alternating between left and right hand. Simultaneous systolic and diastolic BP and HR were measured continuously at the opposite middle finger every 10 seconds using a non- MRI compatible Finapres BP monitor. Mean arterial pressure (MAP) then was caculated. The HR increase shows a very high correlation with MAP increase ($r=0.88$, $p<0.001$).

The same handgrip paradigm was used for fMRI study with continuous HR recording. fMRI was performed on a Siemens 3T TIM Trio using single shot gradient echo EPI with TR=3000ms, TE=30ms, 1.72x1.72mm, slice thickness=3.5mm. Two fMRI analyses were performed using FSL: 1) block-correlation of rest versus handgrip, and 2) linear-correlation with HR.

Results and Discussion While the 5% MVC trials did not show an increase in HR ($P>0.05$), the 20% and 30% MVC trials linearly increased HR from 0-2 mins and plateaued at 2 mins after handgrip onset. Trials without linear HR increases were excluded from further analysis. There were no major differences in activation patterns between 20% and 30% MVC, and they were grouped together to contrast with the 5% MVC data.

Locations of activations have been grouped according to analysis categorized as strong, medium, mild and none base on the activation cluster size (Table 1). With the block correlation, 20% and 30% MVC fMRI data showed stronger positive activations in cingulate gyrus, insula, thalamus and cerebellum, and negative activations in the posterior cingulate gyrus when compared with the 5% MVC handgrip (Figure1.a, b). These activation areas are well accepted as the central command areas that drive the BP increase in previous publications. When linear correlation with heart rate was applied, activations mentioned above largely disappeared (Figure1.c). Except motor planning, the activations that remained in cerebral hemisphere are mainly related with visual cortex and areas associated with spatial orientation from visual feedback (i.e., Brodmann area 7, 39 and 40).

Previous publications have addressed the brain activation areas associated with BP/HR increase. However, most of the studies either measured the BP/HR periodically with low temporal resolution and compared with the brain activation size or magnitude in MRI or observed BP/HR continuously but only gave one radiotracer injection in PET or SPECT. The limitation is that HR/BP increase is always associated with sustained effort, no matter physically or psychologically. From simple block correlation, it is very hard to distinguish whether those activations or blood flow increase are from increased sensing of effort or from regulation of BP or HR. In contrast, use individual increase HR to correlate brain activations will largely remove the task related activations.

Conclusions The handgrip task to maintain a target MVC via visual feedback is highly demanding. With block correlation, the activated structures are likely associated with engagement of the demanding task (i.e., sustained effort to maintain the target MVC). By correlation analysis with linear increased HR, we concluded that the commonly identified activation of thalamus and insular cortex, anterior cingulated are likely to be involved in performing the visual feedback tasks, but unlikely to be the predominant central command network that drive HR or BP increases during exercise.

References: (1) Williamson et al., J Appl Physiol (2002). (2) Wang et al., NeuroImage (2007). (3) Gianaros et al., Psychosomatic Medicine (2005). (4) Williamson et al., J Appl Physiol (2003)