Heart-Brain Interaction: An fMRI Study of the Human Brain Response to the Cold Pressor Test

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Introduction

The neurogenic component of the cardiovascular response to stress is well described, but the central regulation of the physiological changes in heart rate, blood pressure and vascular tone is not fully understood. The cold pressor test (CPT) is a valuable model of a neurogenic cardiovascular stress response. Using functional MRI (fMRI) it is now possible to characterize the components of this pressor mechanism and thereby establish the extent and nature of heart-brain interaction. Neurogenic control is mediated by the sympatheric and parasympathetic components of the autonomic nervous system. Cardiovascular baroreceptor and chemoreceptor afferents are carried in cranial nerves IX and X (vagus nerve) which terminate in the nucleus tractus solitarius (NTS) of the brainstem. The fibers involved in cardiovascular control then project to areas in the hypothalamus (H), amygdale (A), and insular cortex (IC) which have integrating function for the control of blood pressure, heart rate and vascular tone. Descending pathways pass through the CVLM and RVLM in the Medulla then back to the cardiovascular system. The goal of this study is to establish the extent and characteristics of the heart-brain interaction through the neurogenic response to the CPT using fMRI.

Methods

This study was approved by the institutional review board of St Francis Hospital. Six healthy volunteers (5 male, 5 right handed) provided informed consent for CPT and fMRI. Initial tests were performed using a hydrostatic phantom to establish magnet stability and finger tapping experiments to calibrate the signal characteristics of the Siemens 1.5T MRI scanner (Siemens, Malvern, PA). Subjects were briefed before CPT and instructed to place the right hand in an ice-water bath when a light, visible from inside the scanner, was switched on. The baseline condition was rest for the first 60 seconds of the scan. CPT blocks were alternated with rest blocks for six repeated measurements. The experimental design for two subjects required the hand to be dipped in ice-water for 60 seconds, followed by a rest period where the subject's hand was removed from the ice-water for 120 seconds. The duration of the fMRI scan was 18 minutes for these subjects. For the remaining four subjects, the CPT lasted 45 seconds with rest periods of 105 seconds for total scan time of 15 minutes. The head coil and foam cushions along with head phones were used to minimize head motion which was limited to 1 mm or less. The images acquired were: scout, field map, high resolution T1-wighted, and EPI sensitive to BOLD contrast for fMRI analysis. EPI image parameters were: TR 2.5s, 30 slices, 4 mm slice thickness, 1 mm gap, 64x64 matrix, and 430 or 380 images of each slice. Functional analysis was done using Statistical Parametric Mapping (SPM) software. The activity threshold for the t-test was set to $t = 1$ based on results form the finger tapping experiment, with threshold $p < 0.01$ within each subject. The location of activation in each subject was recorded from the brain activation maps (Table 1 and Figure 1).

Results

The magnet stability tests show a drift of less than 2% over a 10 minute fMRI scan while the finger tapping tests revealed that six blocks are required to produce a significant response in the motor cortex ($p < 0.01$) using the statistical t-test threshold of $t = 1$.

Activity in the insular cortex was observed in all subjects during CPT while the hypothalamus was seen to be active in 4 out of 6 subjects as shown in Table 1. The region of the brainstem with definitive connection to cardiovascular function is the NTS, but NTS activity was recorded in only two subject during 60s CPT. The first three CPTs showed different activity levels and locations from the second three CPTs suggesting a progressive response to the CPT.

Conclusions

The neurogenic response to the CPT involves the insular cortex as seen by the activity in this location in all subjects. However, activity in the NTS, hypothalamus and amygdala is detectable in some but not all subjects, suggesting individual differences in the brain response to cold stress. Early observations suggest that the response may be progressive becoming stronger if the stimulus is persistent.

Subjects	A	H	IC	NTS
1	X	X	X	X
2	X	X	X	X
3			X	
4		X	X	
5	X		X	
6		X	X	

Table 1: showing the activity in the four brain centers connected with the cardiovascular response to CPT: A – amygdale, H – hypothalamus, IC – insular cortex, NTS – nucleus tractus solatarius.

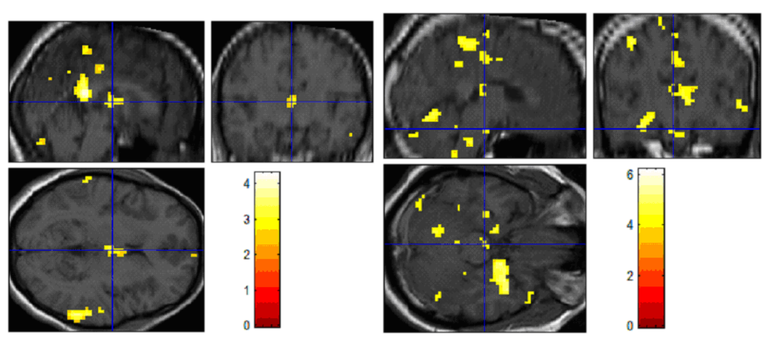

Figure 2: (above left) activity map from two subjects showing activity in the hypothalamus (cross hairs); and (above right) activity in the brainstem (cross hairs) as a result of the CPT.