Accounting for vascular reactivity to clarify the role of subcortical regions in attention

2791

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Introduction

Extensive research has identified distinct neural networks underpinning attention[1]. Recent studies have highlighted that certain regions, such as the subcortical regions, may serve as critical hubs in attentional processes[2].

Such findings are often based on blood oxygenation level-dependent (BOLD) functional MRI data. However, regional variations in BOLD response due to differences in cerebral blood flow and neurovascular coupling are well-known[3]. Cerebrovascular reactivity (CVR) mapping, used to quantify the ability of blood vessels to react to vasoactive stimuli, can be used to correct for regional physiological heterogeneities affecting BOLD signal patterns[4]. More accurate activation maps and increased sensitivity to less-vascularized brain regions may help resolve the roles of the subcortical regions in attention.

The aim of the present research was to evaluate the utility of combining task-based fMRI with CVR mapping to investigate the attention networks. It was hypothesized that CVR-corrected activation maps to an attention task would show increased signal in the subcortical regions using whole-brain analyses.

Methods

Participants
15 healthy volunteers (age = 38.5 ±13.6y, 8 F) participated in this study, which was approved by the local ethics committee.

Behavioural Task
The Attention Network Test-Revised (ANT-R) was implemented[5]. This task disentangles three distinct attention networks: alerting, orienting and executive control. Orienting is separated by three contrasts: moving and engaging, disengaging and validity effects. Further information about these attention networks can be found in Xuan et al. (2016).

Gas challenge
A 6-minute hypercapnia challenge was performed by all participants to calculate CVR. A gas mixture containing medical air and 5% carbon dioxide (CO_2) was delivered for 2-minutes, interleaved by 2 x 2-minute blocks of medical air only. Gas mixtures were administered to participants inside the scanner via a dedicated breathing circuit[6].

CVR maps were calculated by dividing %ΔBOLD by the change in end-tidal CO_2 ($ETCO_2$).

Data acquisition
All images were acquired on a 3T MR scanner (GE Healthcare) using a 32-channel head coil (Nova Medical Inc., MA, USA). BOLD images were collected using multiband fMRI (multi-slice acceleration factor = 3, TR/TE/ flip angle = 1800ms/30ms/80º, 2 mm^3 voxels, 128 x 128, 63 slices). A 3D T_1-weighted anatomical scan was collected.

4 x 8-minute runs of the ANT-R task (265 volumes) and a 6-minute run of the hypercapnia challenge (210 volumes) were collected per participant.

Data analysis
Images were processed in SPM12. Spatial smoothing was limited to 4mm FWHM. First-level analyses were performed as per prior work[5]. Group-level ANOVAs for each of the 5 contrasts of interest were calculated to evaluate BOLD fMRI without CVR-correction. ANCOVAs, with CVR maps as covariates, were used to evaluate BOLD fMRI activation corrected by CVR. This was achieved using the Robust Biological Parametric Mapping Toolbox in MATLAB[7].

Results

Behavioural data
The overall mean reaction time, averaged across all conditions, was 757ms (±161ms). The overall error rate was 4.23%.

CVR fMRI
All subjects demonstrated robust BOLD activations to the CO_2 stimulus. The mean change in $ETCO_2$ to the hypercapnia gas challenge was 9.5 (±2.9) mmHg. Example CVR maps from 3 representative participants are shown in Figure 1, where it can be seen that reduced CVR is found in the subcortical regions.

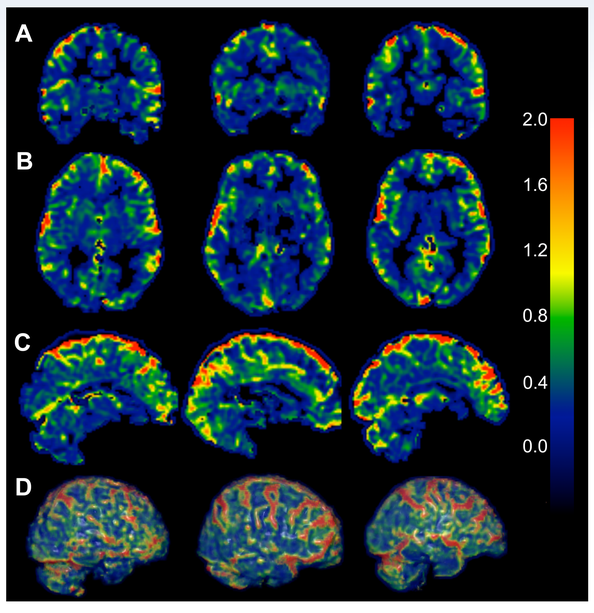

Figure 1. Representative CVR maps from 3 different subjects. Coronal (A), axial (B), sagittal (C) and surface renderings (D) shown. Each column represents a single subject.
Colour bar = %ΔBOLD/Δ$ETCO_2$(mmHg).

BOLD fMRI (without CVR correction)
Brain regions corresponding to the three attention networks were identified for the alerting, orienting and executive control networks. Most contrasts showed some similar activated regions to those reported previously[5], with exceptions for the orienting networks, which were the most difficult to replicate. Significant clusters are shown in Table 1 under "Before CVR correction".

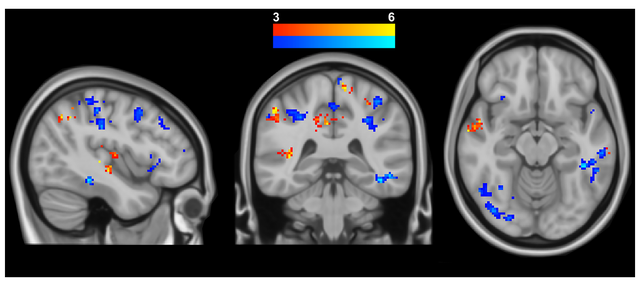

Figure 2. Activation maps for the BOLD fMRI (without CVR correction) in blue and CVR-corrected fMRI in red for the Executive Control contrast. Peak clusters found in the inferior temporal gyrus, superior parietal lobe before CVR correction. Peak clusters after CVR correction were in the precuneus, inferior parietal lobule, supramarginal gyrus.
Cluster-level $P < 0.05$, colour bar = t values.

Table 1. MNI coordinates and anatomical location of activations (cluster-level $P < 0.05$). Only top 5 according to peak t value shown.

Contrast	X Y Z (MNI)	Location
Alerting		
Before CVR correction	-58 -44 12	Superior temporal gyrus
	48 26 2	Inferior frontal gyrus
	-52 8 -22	Temporal pole
	-28 52 30	Middle frontal gyrus
	-2 44 40	Superior medial gyrus
After CVR correction	30 12 60	Middle frontal gyrus
Moving and Engaging		
Before CVR correction	48 -46 32	Angular gyrus
	14 -68 8	Calcarine gyrus
	46 -32 50	Postcentral gyrus
	-36 -74 -8	Inferior occipital lobe
After CVR correction	28 -52 64	Superior parietal lobule
	-40 -4 32	Precentral gyrus
	-8 -70 20	Calcarine gyrus
	10 60 34	Superior medial gyrus
	-38 -52 48	Inferior parietal lobule
Disengaging		
Before CVR correction	-56 -46 8	Middle temporal gyrus
	-52 -8 -10	Superior temporal gyrus
	-42 -56 32	Angular gyrus
After CVR correction	48 -36 52	Angular gyrus
	48 16 34	Inferior frontal gyrus
Validity		
Before CVR correction	34 14 2	Insula
	-36 -14 -10	Superior temporal gyrus
	-30 2 6	Putamen
After CVR correction	-32 4 34	Middle frontal gyrus
	-12 -100 0	Middle occipital gyrus
	52 16 8	Inferior frontal gyrus
	-22 20 -4	Putamen
	50 -26 52	Postcentral gyrus
Executive control		
Before CVR correction	-42 -38 -14	Inferior temporal gyrus
	-26 48 10	Middle frontal gyrus
	34 -62 8	Calcarine gyrus
	-22 -52 64	Superior parietal lobule
	6 -50 68	Precuneus
After CVR correction	38 -22 46	Postcentral gyrus
	-8 -74 40	Precuneus
	52 -42 24	Supramarginal gyrus
	18 18 48	Superior frontal gyrus
	-48 -42 38	Inferior parietal lobule

CVR-corrected BOLD fMRI
The executive control contrast demonstrated the most differences between CVR-corrected and uncorrected fMRI activation maps. Activation maps for this contrast are shown in Figure 2.

CVR correction increased activation most for the orienting network. The validity effect (a combination of the other effects of orienting[5]) increased activation in visual/motor regions after CVR correction. This is shown in Figure 3.

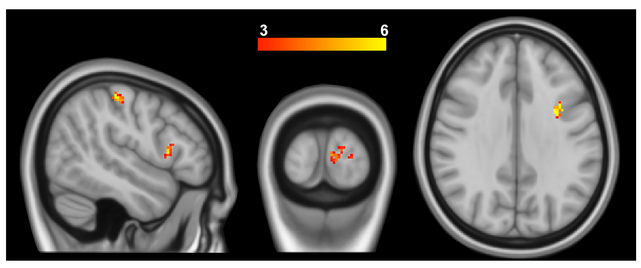

Figure 3. Activation maps for CVR-corrected fMRI for the Validity contrast. Small but significant clusters were found in visual and motor regions, as well as the putamen. Before CVR correction, minor activations for this contrast were found in the temporal lobe and putamen.
Cluster-level $P < 0.05$, colour bar = t values.

Conclusion

CVR-corrected fMRI shifted the location of the peak clusters for all three attention networks. However, BOLD activations in the subcortical regions were consistently low both before and after CVR correction. The present BOLD activation patterns differ slightly from prior work using the same task[5], which may be attributed to differences in image acquisition and preprocessing.

Common regions before and after CVR correction were found, such as the angular gyrus. Some regions showed only activation in CVR-corrected fMRI, such as the inferior parietal lobule. Further work is required to determine the significance of these regions. Overall, these results demonstrate that including CVR covariates can have a dramatic effect on BOLD activation patterns.

References

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