Resting-state Functional Connectivity of Specialized Occipitotemporal Cortical Regions

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Introduction: A number of areas in the human occipitotemporal cortex (OTC) are specialized for processing particular types of sensory stimuli [1-4]. These include the lateral occipital complex (LOC), an object-selective area; the fusiform face area (FFA), a face-selective area; the parahippocampal place area (PPA), a scene-selective area; and the extrastriate body area (EBA), a body part-selective area. We reported earlier that, when these areas were defined using coordinates from the literature, the EBA and LOC exhibited differential resting-state connectivity patterns [5]. In this study, resting state functional connectivity of functionally localized EBA, LOC, FFA and PPA was examined with seed-based cross-correlation analysis followed by graph theory based network analysis [6].

Methods: Twenty right-handed normal subjects (10 male; median age ~22 yrs) were scanned in a Siemens 3T Tim Trio scanner using a 12-channel array receive-only head coil. Informed consent was obtained from all participants and the protocol was approved by the Emory Institutional Review Board. Participants underwent an 11-minute functional connectivity MRI (fcMRI) scan during which they lay quietly in the scanner with their eyes open while scans were acquired with an axial whole-brain gradient echo EPI (TR/TE = 3000/24 ms, FA = 90°, in-plane resolution = 3 mm x 3 mm; 48 slices with thickness 3 mm). The fcMRI time-series were motion-corrected, spatially normalized to the MNI template and low-pass filtered (cutoff frequency = 0.1 Hz), followed by spatial smoothing with a FWHM = 5 mm isotropic gaussian kernel. ROI-averaged time-series were obtained from 5mm spherical seeds placed at centers of activation in EBA, LOC, FFA and PPA seen in body, object, face and scene localizer fMRI scans, which served as reference vectors in cross-correlation analyses (CCA). Mixed-effects ANOVA was performed to assess the functional connectivity networks of EBA, LOC, FFA and PPA, as well as differences in functional connectivity between the 4 regions. The resultant statistical parametric maps were clustered and significance of activation was assessed using Monte Carlo modeling to correct for multiple comparisons [7]. Graph theory measures were employed to further probe the network structure of each OTC sub-region's functional connectivity maps. Graphs for OTC ROIs were formed by considering areas significantly connected (average $CC_{ROI} > 0.3$; cluster $p < 0.0001$) to respective ROIs, restricted to grey matter and resampled to 6 mm^3 voxels. For each ROI, a binary distance matrix was constructed by averaging the individual correlation matrices for all subjects and setting all connections below the threshold average CC to 0. The threshold was adjusted so that the modularity, M [6,8], of the graph was > 0.3 [8]. Modularities of equivalent random graphs [6], M_{random} were also obtained for comparison. Data analysis was performed with AFNI, FSL and Brain Connectivity toolboxes [6].

Results & Discussion: EBA exhibited strong functional connectivity (CC > 0.3, cluster-level $p < 0.0001$) with a number of different brain regions, which segregated into three modules (Modularity (M) > 0.3; Mrandom = 0.02) upon graph analysis (Table 1): a default mode network (DMN) module; a second module consisting of primary (S1) and secondary (S2) somatosensory and primary motor (M1) cortical areas, Brodmann area (BA) 5 and superior temporal gyrus (STG); and a third module comprising visual cortical areas. When modularity analysis was applied to regions strongly connected to LOC, three modules were obtained (Table 1): a module comprising visual cortical areas and cerebellum; a second module consisting of precuneus, inferior and superior parietal lobules (IPL, SPL); and a third module covering S1, S2, M1, BA5 and STG. The FFA connectivity network graph segregated into a similar set of modules as LOC. The PPA functional connectivity network graph segregated into 3 modules (Table 1); a module comprising inferior and middle occipital gyrus, lateral OTC; a parietal module consisting of superior aspects of IPL, SPL, superior occipital gyrus; and a third module covering cuneus, medial occipital lobe and OTC, and cerebellum.

Examining differential functional connectivity between OTC regions, the right EBA (REBA) exhibited significantly (cluster-level $p < 0.05$) higher functional connectivity with DMN regions compared to both right LOC (Figure 1A) and right FFA (RFFA). The left FFA exhibited stronger connectivity with the frontoparietal attention network compared to both left LOC (LLOC) (Figure 1B) and left EBA (LEBA). The left FFA exhibited weaker functional connectivity with sensorimotor regions compared to LLOC (Figure 1B) and LEBA.

These findings, which confirm and extend our previously reported findings obtained using seeds based on the literature, indicate that regions of OTC exhibit both common and differential connectivity patterns with other neocortical regions. The stronger functional connectivity of EBA with DMN is consistent with studies that report a role for self-referential processing [9] in visual representation of bodies. The stronger functional connectivity of FFA to frontoparietal attention networks indicate enhanced involvement of attention in face-processing compared to visual processing of body-parts and objects [10]. On the other hand the increased functional connectivity of LOC and EBA, compared to FFA, may indicate a greater role of sensorimotor connections in visual processing of objects and body parts [11,12].

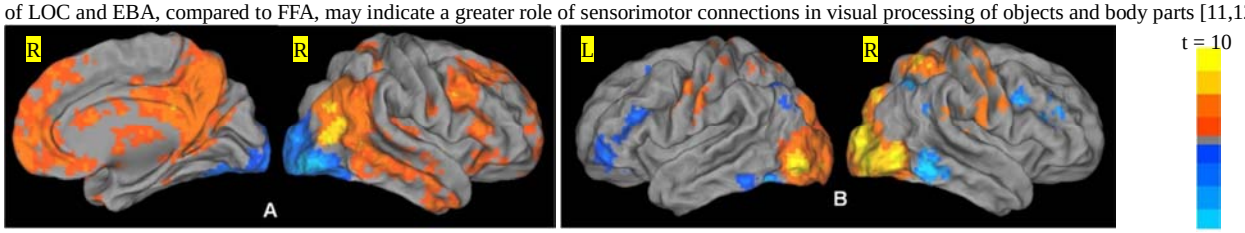

Figure 1: Surface renderings of t-contrast maps (corrected $p < 0.05$): (A) REBA – RLOC; (B) LLOC – LFFA

EBA Module 1 414 nodes	posterior cingulate, lateral parietal cortex, posterior IPL, SPL, BA 40, precuneus, medial prefrontal cortex, and whole of middle temporal gyrus.	**LOC** Module 1 933 nodes	Occipital lobe and OTC	**PPA** Module 1 117 nodes	Superior aspects of BA7, IPL, SPL, BA 40
EBA Module 2 839 nodes	M1, premotor, S1, S2, cingulate, SMA, BA5, anterior IPL and the whole of STG.	**LOC** Module 2 650 nodes	M1, premotor, S1, S2, cingulate, BA5, anterior IPL, and the whole of STG.	**PPA** Module 2 343 nodes	Medial occipital lobe, cuneus, precuneus, PPA
EBA Module 3 996 nodes	Occipital lobe and OTC	**LOC** Module 3 225 nodes	Precuneus, BA 7, posterior IPL, SPL, BA 40, IFG	**PPA** Module 3 264 nodes	Inferior and middle occipital gyrus, lateral OTC

Table 1: Modules from graphs of areas functionally connected to bilateral EBA, LOC and PPA seeds

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