The effects of task context and brain injury on default mode network brain functional connectivity

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INRODUCTION

The default mode network (DMN) has been a major area of research in recent years. Studies have sought to determine the exact nature of its activity and how these profiles of neural activity respond to cognitive demands or are abnormal in pathological conditions [e.g. 1-3]. Activity within the network has been correlated with rest and anti-correlated with task performance [4]. As such, it is important to better determine how task performance affects activity within this network compared with rest. A major question about overall network performance is whether the DMN is discrete, or whether additional brain regions are co-engaged with non-"classical" DMN during difference active cognitive contexts. Following the work done by Calhoun et al. (2008) [5], we present a comparison of functional connectivity within the default mode network during both rest and performance of a simple attentional orienting/working memory cognitive task in both healthy adults and a comparison group of patients with mild TBI to determine the effects that both task performance and brain injury have on this network. Mild TBI has been associated with poor performance on a variety of cognitive tasks, particularly those involving working memory and attention [e.g. 6-7], making it a useful comparison group to initially address whether or not possible differences in the DMN or extended DMN engagement might be markers of a brain-injured or abnormal state.

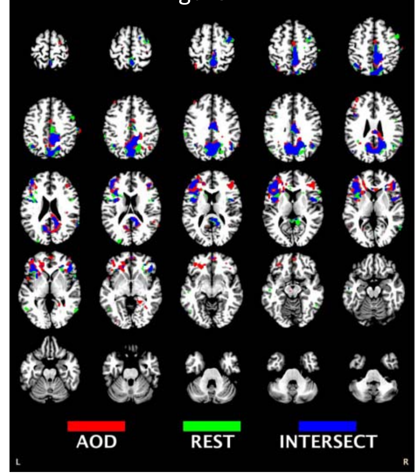
METHODS

Functional MRI data were acquired on thirty mild TBI subjects, as defined by the American Congress of Rehabilitation Medicine Guidelines [8], and thirty age/sex matched healthy controls on a 3T Siemens Allegra scanner (Siemens Medical Solutions, Erlangen, Germany) during the performance of a three-stimulus auditory oddball discrimination task (AOD) [e.g. 9-10] and during rest with eyes open using a 29 slice gradient echo EPI sequence with the following parameters (TR = 1.5s; TE = 27ms; FOV = 24cm; matrix = 64x64; flip angle = 70°; slice thickness (gap) = 4(1) mm) yielding whole brain coverage. Data corrected for slice timing, motion using INRIAlign [11], and smoothed with a 9 mm FWHM Gaussian kernel in SPM5 (Wellcome Department of Cognitive Neurology, London, UK). The data were then concurrently processed in GIFT [12] within a single ICA model to determine a common default mode network across both tasks and both subject groups. Analyses were conducted in SPM5 to determine the modulatory effects of task performance and brain injury state on the functional connectivity among the DMN components. The individual back-projected subject data were compared across tasks via SPM5 conjunction analysis to determine network brain regions within the DMN common to both tasks and those exclusive to the AOD or 'resting' task. The individual back-projected subject data were also compared across subject groups using a mixed factorial ANOVA (between groups; within tasks) to determine the effect of brain injury on functional connectivity of both those DMN regions common to both tasks as well as those specific to the oddball task.

RESULTS

Figure 1 shows the combined map of the default mode network associated uniquely with the AOD task (RED), the resting state task (GREEN), and the regions engaged by both fMRI task contexts (BLUE). All conjunction maps have been threshold at $p<0.05$, corrected for multiple comparisons via family-wise error (FWE). While the brain regions commonly associated with the DMN [13] are readily observed in all three maps, the AOD task recruits additional regions not usually associated with this network, particularly in the bilateral ventrolateral and mid-dorsolateral frontal regions. The 'resting' task does not appear to show any significant areas of additional recruitment beyond what is common to both tasks. Figure 2 shows the results from the mixed factorial ANOVA masked with the intersection of the DMN for both tasks (Figure 1 BLUE). This figure shows brain regions significant positive interaction between Group and the AOD task (RED) and those showing negative interaction between Group and the AOD task (BLUE). Because we had a priori knowledge of which regions to investigate from the primary conjunction analysis, these results are presented at $p<0.05$ uncorrected for multiple comparisons. From Figure 2, one can see a significant Task x Group interaction with the TBI group showing diminished functional connectivity during the AOD task compared to rest in the negative-going BOLD signal in the posterior aspects of the commonly-engaged DMN (particularly the precuneus). There also was diminished connectivity of the positive-going BOLD signal in the ventrolateral frontal regions in the TBI group.

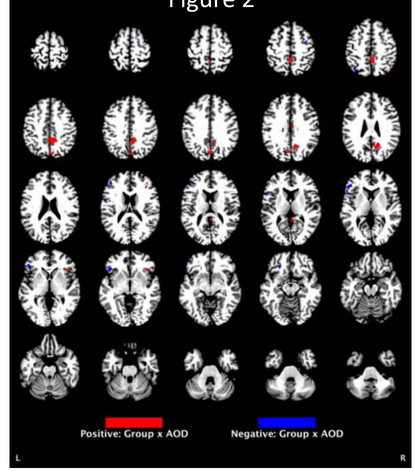
Figure 1



DISCUSSION

We have shown that the default mode network, whose activity is traditionally associated with rest, is spatially modulated by performance of a simple cognitive task. Performance of the auditory oddball task resulted in recruitment of additional brain regions, most notably several foci in bilateral ventrolateral and mid-dorsolateral frontal lobes, consistent with cognitive models of the attention and working memory demands of the AOD task. In comparing the two subject groups, we also showed that subjects with the mild TBI had different profiles of how strongly the attention task engaged key DMN network regions. Further study is merited in how other tasks, cognitive or otherwise, may spatially modulate regional functional connectivity of the default mode network. The current results also suggest that dysfunction within the default mode network may be a marker of brain injury or dysfunction, and additional investigation is warranted to further elucidate the nature of this dysfunction.

Figure 2



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