DEFAULT MODE NETWORK AND WORKING MEMORY NETWORK DURING AN FMRI WORKING MEMORY TASK: DIFFERENCES AND CORRELATIONS WITH BEHAVIORAL PERFORMANCE

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INTRODUCTION

Previous neuroimaging studies have shown that working memory load has marked effects on regional neural activation[1-5]. However, the mechanism through which working memory load modulates brain connectivity is still unclear. During a working memory task, two of the most involved networks are the default mode network (DMN) and the working memory network (WMN)[6-7]: the selective focus on these networks can be useful in better understanding the load effects. Spatial independent component analysis (ICA)[8] has becomes a reliable technique to investigate the networks involved during an fMRI task, as it extracts spatiotemporal patterns of neural activity maximizing spatial independence. A specific study, conducted with ICA, investigating on how the load and phase of a working memory task are related with the activation and response time, is nowadays lacking. The aim of this work is to use the time course of DMN and WMN, selected by means of ICA, for studying: a) how these networks are involved with the complexity of the task and the phase; b) how, in these networks, complexity and phase are correlated with reaction times.

METHODS

MR Data Acquisition and preprocessing

Fifteen young adult healthy and right-handed were involved. The MR protocol consisted of one anatomical sequence 3D T1-weighted MP-RAGE (Voxel size: 1 x 1 x 1 mm) and three functional acquisitions of 15 minutes each performed with a T2*-weighted EPI sequence (TR/TE: 1500/30, In-plane resolution: 3.5x3.5 mm, Thickness: 3.5 mm, Nr of slices: 24, Field of view: 64 x 64 mm). All the images were collected with a Siemens Allegra 3T MR scanner (Siemens, Erlangen, Germany) and a standard head coil. During the fMRI acquisition the subjects performed a delayed spatial working memory paradigm presented with three levels of difficulty. The memory set consisted of one, three or five circles presented randomly in different locations and to the subjects were asked to judge whether or not a given target stimulus had been part of a previous memory stimulus set. Every experiment consisted of 90 working memory trials, 30 per load, divided in three runs. Data were analyzed with Brain Voyager QX. 2.4 (Brain Innovation, Maastricht, The Netherlands). FMRI preprocessing included: 3D head-motion correction, slice-scan time correction, spatial smoothing, temporal high pass filter and linear trend removal. Anatomic 3D data set was inhomogeneities corrected, filtered and transformed into Talairach coordinates and coregistered with the functional information.

Independent Component Analysis

This analysis was conducted using Brainvoyager QX 2.4. ICA analysis was performed on each subject's three functional acquisitions. A subsequent total ICA group analysis[9-10] was achieved by an *inter*-subject ICA group analysis of all the *intra*-subject ICA group analysis. From the obtained maps were selected two Independent Components (ICs) containing the WMN[1,2]: WMN1 defined by SPL and Precuneus, and WMN2 with DLPFC and IPS (Fig. 1b-c). Also one IC describing the DMN was considered, with PCC, IPL and MPFC (Fig.

Figure 1: Networks selected from ICA analysis (transversal view): (a) DMN, (b) WMN1 (c) WMN2.

1a)[11]. For each run of all the subjects the ICs time course was considered: three time windows of 3TR (4.5s) for each working memory task phase (encode, maintenance and retrieval) were selected taking into account the haemodynamic response by delaying the window of 5 volumes events from the start of every trial. The window time course was corrected for a baseline value. Mean values of the ICs where examined and a subsequent correlation between the mean values and the response time in every trial was estimated. A 3x3 two-way ANOVA on Fisher transformed correlation was conducted to test the variation of loads (load1=less complex, load3=more complex), phases and runs.

RESULTS

Figure 2 exhibits window mean activities and correlations divided for phase and load. DMN mean activity is negative while WMN1-2 mean activities have opposite behaviors regarding the phase, but similar concerning with the complexity (Fig. 2a-c). DMN shows a reduction of the correlation from encode to retrieval, instead of WM1-2 where it grows (Fig. 2d-f). The ANOVA showed significant variation for the phases over all the subjects in WMN1-2, an interaction of the variation of phases and runs in WMN2 and a interaction of phases, runs and loads in DMN.

Figure 2a-c: Mean values during encode, maintenance and retrieval. (a) DMN, (b) WMN1 and (c) WMN2.

Figure 2d-f: Correlation values during encode, maintenance and retrieval. (d) DMN, (e) WMN1 and (f) WMN2.

DISCUSSION

These findings suggest that working memory networks (WMNs), as isolated by means of ICA, display substantially opposed mean values related to a different areas specialization. WMN1 seems to be more involved in the first part of the mnemonic phase and the amount of this involvement is associated to the trial: the more complicated the task, the higher the activation with respect to baseline. On the other hand, WMN2 increases from the first to the last part of the trial and is probably more involved in the operation of retrieval. In Figure 2e-f it is also shown that in the retrieval there is a stronger correlation between WMN1-2 mean values and the response time probably because this phase is the more complex. DMN exhibits, over all the phases, smaller than zero mean values (due to the task inducted deactivation). In contrast, its correlation has a different trend and increases above zero during the maintenance, probably due to the free thought of this phase. The different behavior of load 3 is probably due to the fact that this type of complexity is totally different from the other two. In conclusion, this study shows that, by means of ICA, it is possible to isolate networks of connected regions and relate their time courses to task phases and behavioral performance. This is a promising approach to advance the understanding of connectivity modulations in several brain networks, including WMNs and DMN.

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[1] Rypma B. and D'Esposito M., Proc Natl Acad Sci USA (1999). [2] Rypma B. et al, Neuroimage (1999). [3] Veltman D.J. et al, Neuroimage (2003). [4] Tomasi D. et al, Brain Res (2007). [5] Jensen O. and Tesche C.D., Eur J Neurosci (2002). [6] Linden D.E.J., The Neuroscientist (2007). [7] Curtis C.E. et al, Trends Cog Sci (2003). [8] McKeown et al, Hum Brain Map (1998). [9] Esposito et al, Neuroimage (2005). [10] Van de Ven V., Neuroimage (2009). [11] B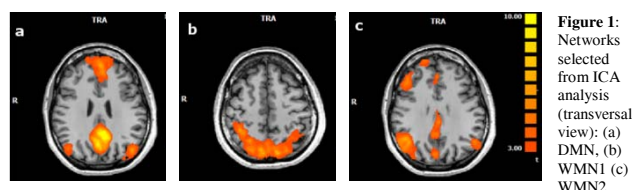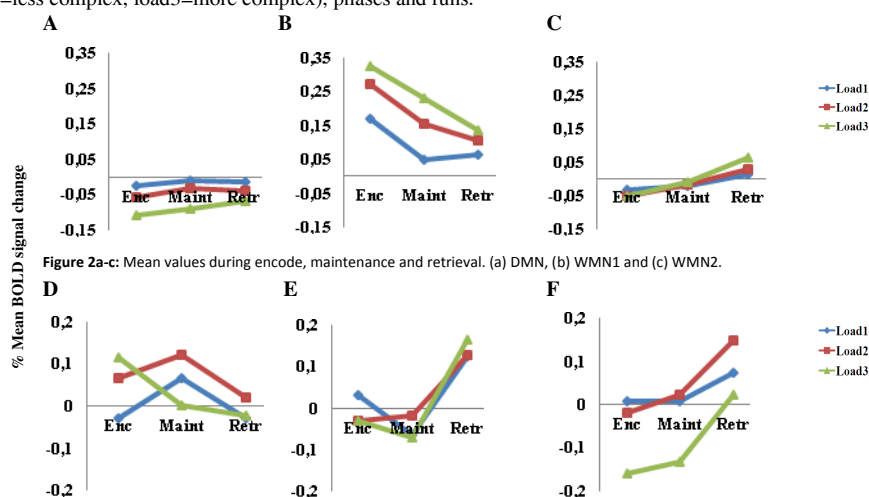uckner R.L. et al, Ann N Y Acad of Sci (2008).