Impaired Default-Mode Network Activity in Schizophrenia: A Resting-State fMRI Study

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Introduction:

Over a decade ago Biswal detected low frequency signal fluctuations in functionally connected bilateral motor cortices [1]. Since then the same method and variations on it using independent component analysis (ICA) have proven robust in detecting several other resting-state neuronal networks [2]. Brain pathology alters the spatial characteristics and temporal coherence of the detected network components [3]. Functional task related connectivity has been shown to been altered in schizophrenics [4]. To our knowledge there are no studies on resting-state ICA signal sources of schizophrenic subjects compared to the birth cohort controls. The current study focuses on detecting schizophrenia-induced changes in default-mode network activity [3]. The results demonstrate clear defects in functional network connectivity in schizophrenia and also support recent studies suggesting that inverse correlations in these resting-state networks may also be informative [5,6,7].

Methods:

Subjects were selected from the Northern Finland 1966 birth cohort and The Ethical Committee of the University of Oulu approved the study. The average age of the subjects was 33 (+/- 0.3) years at the imaging day and schizophrenia diagnoses were validated using DSM-III-R criteria. 15 schizophrenia and 37 control subjects were imaged, after drug screening there were 12 schizophrenia subjects left for analysis. GE 1.5T Sigma EchoSpeed MRI scanner with a birdcage coil was used in imaging. Six axial slices (96 x 96 matrix, 10 mm thickness, 5 mm spacing) were acquired using a GR-EPI sequence (TR 2000 ms, TE 40 ms, 90 flip angle). Eighty-two resting-state volumes were obtained. Head motion was minimized with pillows and ear pads were used to diminish auditory noise. Subjects were asked simply to rest quietly with their eyes closed. Standard SPM preprocessing procedures, including realignment, normalization and smoothing, were performed prior to running the ICA. For each subjects' resting-state scan FSL's MELODIC with component number estimation was used to calculate independent components. A template-matching procedure was used to select the independent components in each subject that best matched each of three networks: visual, auditory, and default-mode [3]. The template for each network was derived from the same dataset but using group ICA of all subjects performed with GIFT. Selected best-fit components were entered into a second level random-effects analysis in SPM. Presented activation maps were overlaid onto a standard structural template image (MNI/ICBM).

Results:

The default-mode network activity of the control subjects was found to be virtually identical to previous analyses [2,3]. A new inversely correlated source component was detected using a {−1} SPM contrast of the default mode network. The inversely correlated signal source was detected bilaterally in temporal and frontal lobes in close proximity with the primary auditory cortex, partly presented on bottom left in Fig.1. Schizophrenics presented three distinct defects in default mode network activity. Resting-state activity in the posterior cingulate cortex (PCC) and hippocampi was reduced compared to the controls (see Fig.1, top panel). Anterior cingulate cortex (ACC) activity on the right was also reduced. Secondly, the most prominent difference in the inverse correlation maps was the absence of the ventral temporal inverse correlations that could be detected in the controls, on the bottom of Fig.1. Thirdly, in half (6/12) of the schizophrenics the best-fit default mode component was fused to either the visual (4) or auditory signal source (2). This fusing of the components was detected in only 5 controls.

Discussion:

Schizophrenia reduces the normal resting state signal sources of the default mode areas by causing anatomical variation between the subjects or totally altering the signal sources. The new inverse correlation signal related to the default mode network shows significant deficit in the schizophrenics suggesting defects in functional connectivity in schizophrenics. Also a non-Gaussian signal source seems to fuse the resting state activity of the primary sensory regions and default mode network together.

References:

[1] Biswal, *et al.*, Magn Reson Med 1995, 34:537-541.
[2] Beckmann, *et al.*, Philos Trans R Soc Lond B Biol Sci. 2005, 29;360(1457):1001-13
[3] Greicius, *et al.* PNAS 2004, 30;101(13):4637-42
[4] Boksman, *et al.*, Schi Res 2005, 75: 247– 263
[5] Greicius, *et al.* PNAS 2003, 100:253-258
[6] Fox, *et al.* PNAS 2005, 27:9673-9678
[7] Fransson, *et al.* Hum Brain Mapp 2005, 26:15-29
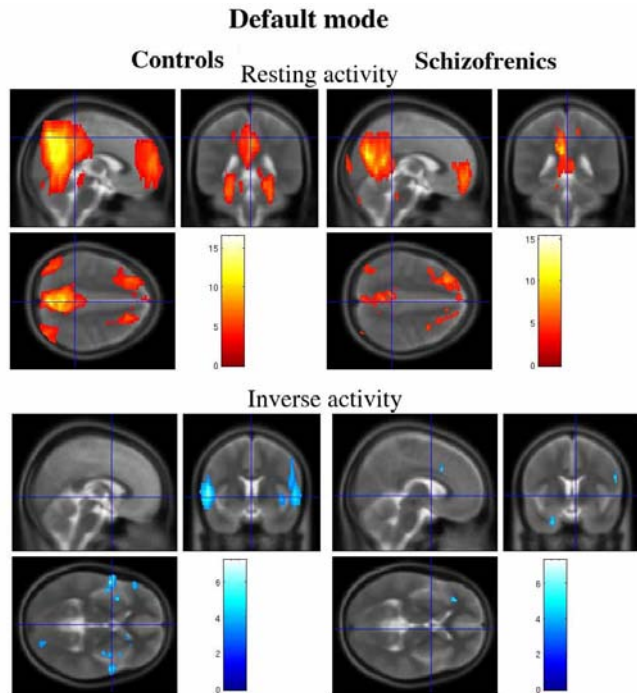
Figure 1. Resting-state, default-mode network activity {1} and its inverse {-1} SPM contrasts (p<0.003, voxel cluster size > 9)