Resting State fMRI in Geriatric Depression Before and After Treatment

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Introduction

Previous studies have shown abnormal changes in the connectivity of default-mode network in patients with cognitive diseases such as schizophrenia, major depression and Alzheimer's disease. So far, no studies have investigated the default-mode network of elderly patients with late life depression (LLD), a disorder strongly associated with changes in frontal white matter. The fMRI data from simple sensory-motor tasks (e.g. finger tapping) have been used to assess the resting-state, under the assumption that the low cognitive load of the simple tasks does not disrupt the default-mode network [1][2]. Posterior cingulate cortex (PCC) has been shown to have consistently greater activity during resting state than during cognitive tasks and is hypothesized to constitute a core node in the default-mode network [1]. Thus, the PCC has often been used as a seed region to identify the default-mode network. In this study, we compared the default-mode networks among elderly controls, and patients with LLD before and after treatment, through the resting-state connectivity of PCC on a simple finger-tapping task.

Subjects

Twenty-four subjects participated in this study. Subjects were all cognitively unimpaired. Twelve right-handed healthy elderly subjects, 8 males, age = 69.00 ± 6.54 years, MMSE = 28.91 ± 1.08, HDRS = 1.45 ± 1.57 and MDRS = 140.66 ± 2.77. Twelve elderly patients, 5 males, 10 right-handed, age = 67.91 ± 5.71 years, MMSE = 28.00 ± 3.46, HDRS =19.75 ± 4.07 and MDRS = 137.00 ± 5.40. Follow-up scans were performed on 7 patients after 3 months of antidepressant medication treatment. SCID-IV evaluation information changed for the 7 patients before/after treatment: MMSE 26.71± 4.15/27.60± 2.88, HDRS 20.00± 5.20/6.00± 4.32, and MDRS 136.83± 7.47/133.83± 9.54.

The subjects were scanned on a 1.5T GE Signa scanner using a one-shot spiral pulse sequence (TR=2000 ms, TE = 35 ms, flip = 70,FOV = 24cm) while performing a 24-trial 5-min finger-tapping visual motor task (stimulus "tap" appeared every 12s and remained for 1s). A high-resolution SPGR image was also acquired on each subject for co-registration.

Methods

The subject's SPGR images were mapped to a standard MNI template Colin27 using a fully deformable model [3], and the functional images were normalized into the common space using the computed deformations. A Gaussian smoothing filter (6 mm full width at half maximum) was used on the normalized images to reduce the spatial noise and then a band-pass filter ([.01 .1] Hz) was used to extract the resting-state signal, which also effectively removed the linear trend in the data.

A 3x3x3 element 6 connected 2.5D erosion was performed on the PCC from the AAL atlas on Colin27 (Fig. 1 a). This led to a 12-voxel ROI centered in the PCC (Fig.1 b).

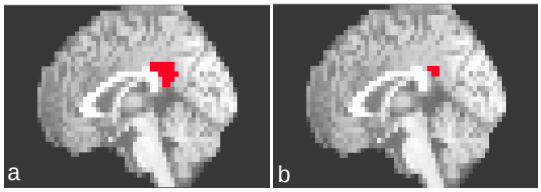

Fig. 1. Original PCC and the eroded centered ROI on Colin27.

The reference time-series for a given subject was computed by averaging the time-series across the 12-voxel PCC ROI. The reference time-series was then correlated with the time-series of each voxel in the brain using 3dDeconvolve (AFNI)[4] to generate a whole-brain correlation map.

Results

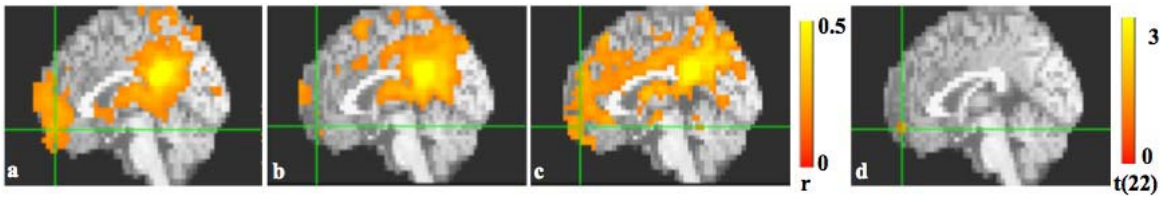

Fig. 2. Mean default-mode correlation maps for elderly controls (a), LLD patients before (b) and after treatment (c). Group comparison between elderly controls and LLD patients before treatment (d).

Within-group: For each group (controls and patients), the correlation maps were statistically compared to the baseline 0 using a 1-sample t-test. All groups demonstrated the expected default-mode network of activity, with significant medial prefrontal and anterior cingulate correlation (joint height and extent threshold of $p < 0.01$, via Monte Carlo simulations (AlphaSim, AFNI)), but the patient groups (both before and after treatment) show less medial prefrontal activation in comparison to the controls. However, due to power issue (different numbers of subjects per group), the mean default-mode correlation maps (rather than the t-maps) are shown in Fig. 2 with threshold $r > 0.18$, elderly controls (a), LLD patients before (b) and after treatment (c).

B*etween-group:* The correlation maps from different groups are statistically compared using 2-sample t-test (controls vs patients, pantients before vs after treament, controls vs patients after treatment). Significantly lower default-mode network activity was found in the LLD patients than the healthy elderly controls, with a joint height and extent threshold of $p < 0.05$ and a cluster size of 105, as shown in Fig. 2(d). Increased resting-state correlations in the medial prefrontal cortex was observed in the patients after treatment, compared to patients before treatment, with $p < 0.05$ and a cluster size of 83 (fail to survive the cluster size of 105 for a corrected $p < 0.05$). Interestingly, compared to controls, higher correlation was found in patients after treatment with $p < 0.05$ and cluster size of 21, which also fail to survive the extent for a corrected $p < 0.05$.

Conclusion:

Overall, our results show that the default-mode functional connectivity of patients with LLD is significantly lower than that of elderly controls in the prefrontal cortex region for a corrected $p < 0.05$. We suspect that the decrease in functional connectivity is a functional correlate of the damage to frontal white matter tracts, which has previously been reported in LLD. Our current results do not show statistically significant differences between the patients after treatment and patients before treatment or between patients after treatment and controls. Thus, it remains unclear whether the functional connectivity changes in LLD persist after effective treatment.

Reference:

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