Can connectivity information from DTI improve cortical parcellation for resting-state analyses?

E. Baerends[1,2], H. Fonteijn[2], E. Shumskaya[2], and D. Norris[2]

[1]Technische Universiteit Eindhoven, Eindhoven, Netherlands, [2]F.C.Donders Centre for Cognitive Neuroimaging, Nijmegen, Netherlands

Introduction

In the last decade, there is increasing evidence that low frequency components of the BOLD response of functionally associated areas are correlated. Salvador et al.[1] have further developed this technique by performing a partial correlation analysis on the whole brain. This was done by parcellating the brain into subareas, using an anatomical template and by taking the averaged signal of these subareas as the starting point. A partial correlation analysis investigates whether a signal is correlated to another signal, when all other influences have been partialled out. This gives a unique insight in the functional hierarchy of the brain, while being in a putative resting state. A disadvantage of this approach is that the anatomical template is relatively coarse, which results in subareas containing multiple functionally different areas, which can potentially confound the assessment of these unique pair-wise connections.

Recently, it has also been shown possible to perform cortical parcellation on the basis of diffusion tensor imaging (DTI), using the working hypothesis that functionally segregated areas have distinct anatomical connectivity patterns. For example for supplementary motor area (SMA), it was shown [2,3] that pre-SMA and SMA proper can be discriminated by different connectivity profiles. The aim of this study was to use this parcellation method and the resulting subdivision to investigate whether more precisely defined cortical areas could improve the power of the partial correlation analysis.

Hypothesis

In a partial correlation analysis, dividing a larger region into 'sensible' subregions will increase the number of significant partial correlations. This is because unique connections of the subregions, which would not show up by analyzing the entire region, may show up if they are analyzed separately. Dividing a region into random subregions should not result in a higher number of significant partial correlations. Because SMA contains several functionally different areas and these areas can be characterized by their connectivity profiles, it was expected that subdividing SMA by incorporating information from DTI would result in a higher number of significant partial correlations.

Methods

Data acquisition: Four subjects were scanned using a Siemens Trio scanner at 3T, after informed consent was obtained. Diffusion-weighted data were acquired by using twice refocused spin-echo EPI sequence [4] with the following imaging parameters: TR 8300 ms, TE 93 ms, 60 slices, matrix size 96×96, resolution 2.0×2.0×2.0 mm, 64 directions, b-value 1000 s/mm^2, 1 volume without diffusion weighting, bandwidth 1954 Hz/pixel, scan time 9 min. Resting-state data were acquired by using gradient-echo EPI with the following imaging parameters: TR 1350 ms, TE 30 ms, 21 slices, matrix size 64×64, resolution 3.5×3.5×5.0 mm, distance factor 20%, 265 volumes, bandwidth 1816 Hz/pixel, scan time 6 min. Per subject 12 runs were measured, to have enough statistical power to obtain significant partial correlations on the subjects' level. During resting state subjects were instructed to stay awake with their eyes closed. A standard MPRAGE T_1-weighted anatomical image was also acquired.

Image analysis: Diffusion data were analyzed in FSL. These data were first corrected for eddy currents and head motion. Then probability distributions on fiber directions were calculated at each voxel. After this, probabilistic tractography could be performed from all n voxels in the ROI. This ROI was the SMA region of the AAL-template [5], transformed to the space of the diffusion data. For each voxel in the ROI this resulted in an image, treated as a vector, of connections to all other voxels in the brain. Between these vectors the correlations were calculated, resulting in an $n \times n$ matrix. This matrix was automatically clustered using a k-means algorithm (MATLAB). These clusters were transformed to standard space, to be used in the partial correlation analysis.

Resting-state data were realigned and normalized to the EPI-template in SPM2. Partial correlation analyses were then performed using the method described in Salvador et al. Two analyses were performed: one with the original AAL-template, where SMA is divided in left and right SMA, and one with the 'enhanced' template where left and right SMA are subdivided in pre-SMA (anterior) and SMA proper (posterior).

Results and Discussion

For all four subjects, SMA could be divided by their connectivity profiles in two (in three subjects) or three clusters (in one subject), comparable to the results of Johansen-Berg et al. and Anwander et al. Figure 1 shows this subdivision in one subject.

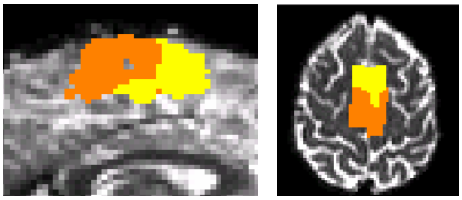

Figure 1. Parcellation of SMA by anatomical connectivity information (left: saggital view, right: axial view)

By using this anterior-posterior division in the resting state analysis, the number of significant partial correlations increased for all subjects. The mean number of areas connected to SMA by using the original template was 8.75, whereas using the parcellation based on DTI resulted in an average of 13.75 areas. The connections found for these four subjects seem to be functionally plausible. With this method also other areas of the original template can be subdivided, although the issue remains how to decide about the number of clusters and the level of parcellation.

In conclusion, the resting-state approach benefits from a finer defined parcellation. We have shown that providing this parcellation on the basis of DTI data is successful for SMA.

References: [1] Salvador, R. *et al*. *Cereb.Cortex* 15(9):1332-1342 [2] Johansen-Berg, H., *et al. PNAS* 101(36):13335-13340 [3] Anwander, A. *et al*. *Cereb.Cortex* May 2006 [4] Reese, T.G. *et al. MRM* 49(1):177-182 [5] Tzourio-Mazoyer, N. *et al. Neuroimage* 15(1):273-289