Resting State BOLD Fluctuations Reflect Impaired Functional Connectivity in Multiple Sclerosis.

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Introduction

It has been shown there are correlations in low-frequency temporal BOLD fluctuations between functionally related brain regions in normal humans(1,2). MS is a common demyelinating neurologic disorder. Progressive forms of MS often result in extensive destruction of the white matter within the spinal cord and brain. MS lesions can impair neuronal transmission through the affected white matter. Our hypothesis is that, if the observed correlations in low-frequency BOLD fluctuations are a reflection of functional connectivity, then MS patients with a large lesion volume should show abnormally low correlations between anatomic regions which are highly correlated in normal subjects.

Methods

Six strongly right-handed subjects, 2 normals and 4 patients with advanced MS were scanned using gradient echo EPI at 1.5T. (GE Medical Systems, Waukeshau, WI). A 7mm thick axial slice was acquired for each subject through bilateral precentral gyrus. BOLD-weighted data were acquired with the following parameters: acquisition: Gradient-recalled echo echoplanar, echo time=50ms, repetition time=250ms, flip angle=30^0, matrix= 64×64, field-of-view= 24cm $\times$ 24cm, receiver bandwidth=125kHz.

An acquisition of 1100 repetitions was acquired with the subject resting for the duration of the scan. A functional scan was then performed using an interleaving 32s tapping/32 s rest block paradigm lasting 320s. The timeseries data from the resting-state scan are then low-pass filtered to remove cardiac and respiratory fluctuations. An ROI is selected from regions of activation in the left precentral gyrus obtained from the block paradigm tapping scan. Timeseries from all pixels in the resting-state scan are then cross-correlated to the timeseries in the a priori-selected ROI. An empirical approach is used to convert the cross-correlation coefficient to a corrected Student's t that can be used to set similar confidence levels across subjects (2). The resulting map is used to determine anatomic regions with low-frequency fluctuations which are highly correlated to those of the left primary motor region.

Results and Discussion

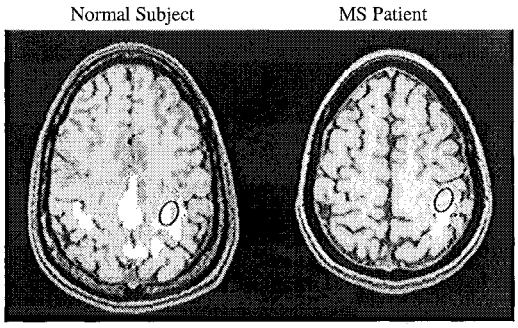

Figure 1

Figure 1 shows the regions of highest correlation (rendered in white) to the a priori-defined ROI (black ellipse) in left precentral gyrus for a normal subject and a patient with MS. Both normal subjects exhibited patterns of correlation similar to that shown on the left in Fig. 1. Three out of four MS patients showed dramatically lower correlation to regions outside of left precentral gyrus than the normal subjects, similar to that shown in the image on the right in Fig. 1. The implication of this finding is that the white matter lesions which characterize MS in MR images interfere with the physiologic mechanism that causes the observed correlations between functionally connected regions in normal subjects.

Conclusion

We have shown that the majority of MS patients studied exhibit abnormally low correlations in low frequency BOLD fluctuations between bilateral motor cortices when compared to normal subjects. This finding supports our hypothesis that impaired neuronal transmission through the white matter pathways of the brain will result in lower resting-state BOLD correlations between otherwise functionally connected anatomic regions.

References

1. Biswal, B., *et al.*, *Magn. Res. Med.*, 34,537, 1995.
2. Lowe, M.J. *et al. NeuroImage*, 7,119, 1998..