BOLD fMRI responses during cognitive tasksin Multiple Sclerosis and effects of angioplasty

Buracas G[1], Ponec D[2], Gooding J[2], Saxon R[2], Haacke M[3], Sauder H[4], Hubbard D[4]

[1]Dept Radiology, University of California, San Diego, [2]North County Radiology, San Diego, [3]Wayne State U, Detroit MI, [4]Applied fMRI Institute, San Diego

Abstract

Introduction

There is renewed interest in the hypothesis that multiple sclerosis may be associated with impaired clearance or insufficient CNS venous drainage - chronic cerebrospinal venous insufficiency (CCSVI). FMRI BOLD offers the possibility to evaluate both neuronal population responses and cortical hemodynamics. Specifically, venous drainage from cortex can be assessed directly by measuring the component of the BOLD hemodynamic response (HDR) known as the venous undershoot.

Methods

20 patients with multiple sclerosis and 20 normal controls were studied by functional MRI. The cognitive task was designed to activate a maximum number of cortical and subcortical regions while still being intuitive to an untrained person. The MS patients were re-tested after undergoing internal jugular venoplasty. MR venography, flow quantification and fMRI were conducted on a Siemens 3T scanner.

Results

In healthy control subjects, the task evoked activation in an extensive set of brain areas (task-positive network), including visual, parietal, temporal and frontal cortices. In MS patients the task showed significantly reduced (30-70%) activations compared to normal controls. The default (task-negative) network, in particular the medial prefrontal, posterior cingulate and cuneus cortices, also showed pronounced differences in MS patients

compared to the normal controls. Specifically, these areas were not suppressed during task performance in contrast to the expected suppression seen in the normal controls. The time course of the BOLD response showed greater decay and a more pronounced undershoot as compared to the control group. Venoplasty resulted in recovery of the task-negative effects in the default network such that the comparison between controls and post-venoplasty MS patients showed no significant differences (t-test, $p<0.05$). The pair wise t-test of pre- and post-venoplasty activations confirmed that the default network suppression was increased post-venoplasty as compared to pre-venoplasty in the same subjects. The task-positive network on the other hand, did not show significant changes as a result of the procedure.

Conclusions

The finding of significant differences between normal controls and MS patients in BOLD response patterns associated with a cognitive task in both task-positive and task-negative cortical networks sheds light on neuronal mechanisms of cognitive impairment in MS patients. Most remarkably, the inhibition of the default network appears to be impaired in posterior parietal and anterior medial prefrontal cortex and this impairment is reversed and in fact normalized by venoplasty. Since BOLD response is a function of cerebral blood flow and volume, and also oxygen metabolism rate, the reduced BOLD responses in both task positive and task-negative networks may reflect not only altered neuronal function but also change in cortical venous blood volume in MS. Thus the recovery of the suppression in the default network by angioplastic treatment may reflect recovered neuronal and/ or vascular function. Moreover the increase in the venous undershoot component of the BOLD response in MS as compared to controls and its reduction after venoplasty provides evidence of impaired clearance and CNS venous insufficiency and holds out the promise that this method may provide an objective diagnostic test.

References

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