

Cognitive Functional Patterns in the Early Stages of MS Patients Using fMRI

S. N. Miri Ashtiani, H. Behnam, M. R. Daliri, M. Mehrpour, G. A. Hossein-Zadeh
Biomedical Engineering Department, School of Electrical Engineering,
Iran University of Science and Technology, Tehran, Iran.

ABSTRACT

The structural damages exist in the brain of multiple sclerosis (MS) patients can cause dysfunction of physical or cognitive abilities in MS patients. Cognitive deficits are frequently found in early phases of MS patients. These impairments include many different cognitive domains such as attention, memory, executive functions and information processing speed that seems they can lead to alternations in connectivity. Brain's functional connectivity changes related to specific cognitive tasks can be investigated with blood oxygenation level dependent (BOLD) functional magnetic resonance imaging (fMRI).

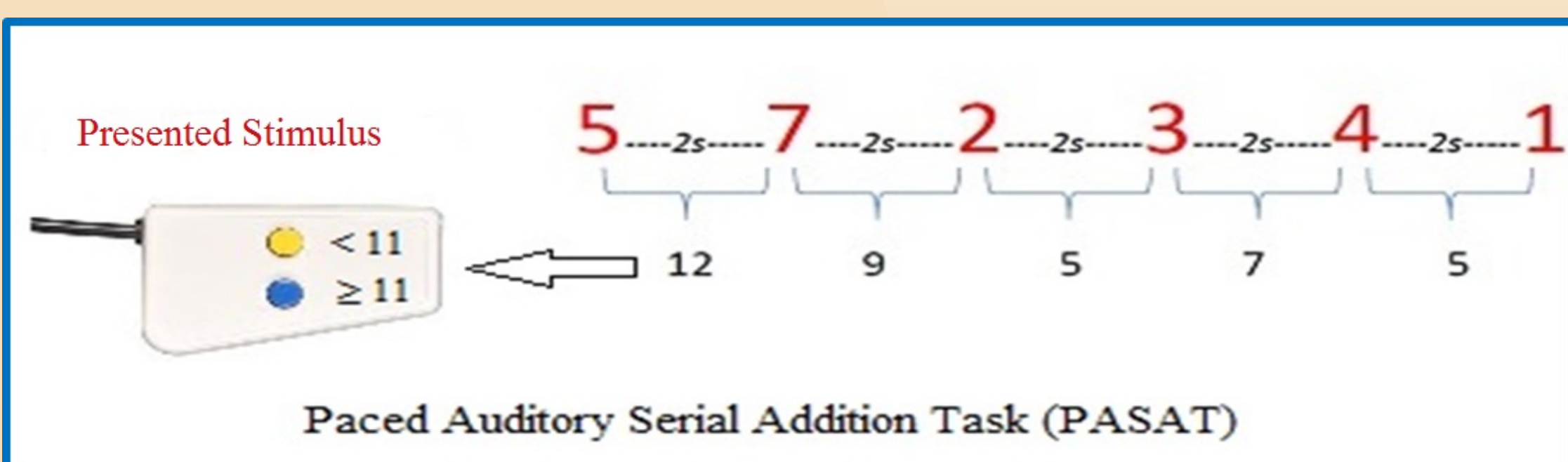
In this study, we applied fMRI data to study the activation patterns relevant neural hemodynamic responses during attention and working memory task using 3.0 Tesla scanner. Patients with clinically isolated syndrome (CIS) and clinically definite relapsing-remitting MS (RRMS) in the early stages and healthy subjects matched for age, years of education and handedness were scanned during Paced Auditory Serial Addition Task (PASAT) in Persian version. During PASAT task, a random series of single numbers was presented in an auditory way, and the subjects were required to add each digit to the one immediately preceding it and reported the result by pressing the response box keys in comparing with target number. fMRI data were preprocessed using FSL software. The analysis of preprocessed data hence was based on the analytical method of general linear model (GLM) which is the most widely used approach to analyze and inference of fMRI data.

According to this method, the time series of each voxel is statistically related to task paradigm corresponding to the repetition, in a temporal succession, consequently to which phases of activation and baseline phases are alternated. The results indicate that BOLD signal intensity changes could follow the specific model of temporal sequence of cognitive task as well and accordingly show the altered patterns of activity related to cognitive functions between two groups. These finding also suggest the feasibility of fMRI to monitor early cognitive impairments during disease progression.

Investigation of fMRI changes during a cognitive task in early MS patients with respect to healthy subjects

METHODS

Subjects	CIS and RRMS	Healthy Control
Gender, F/M	6/1	8/4
Handedness	Right-handed	Right-handed
Age range (years) (median)	20 < 27 - 44 ≤ 45 (35.28)	23 - 40 (30.58)
Disease duration (months) (median)	8 - 96 (3 years)	-
EDSS score	≤ 3	-



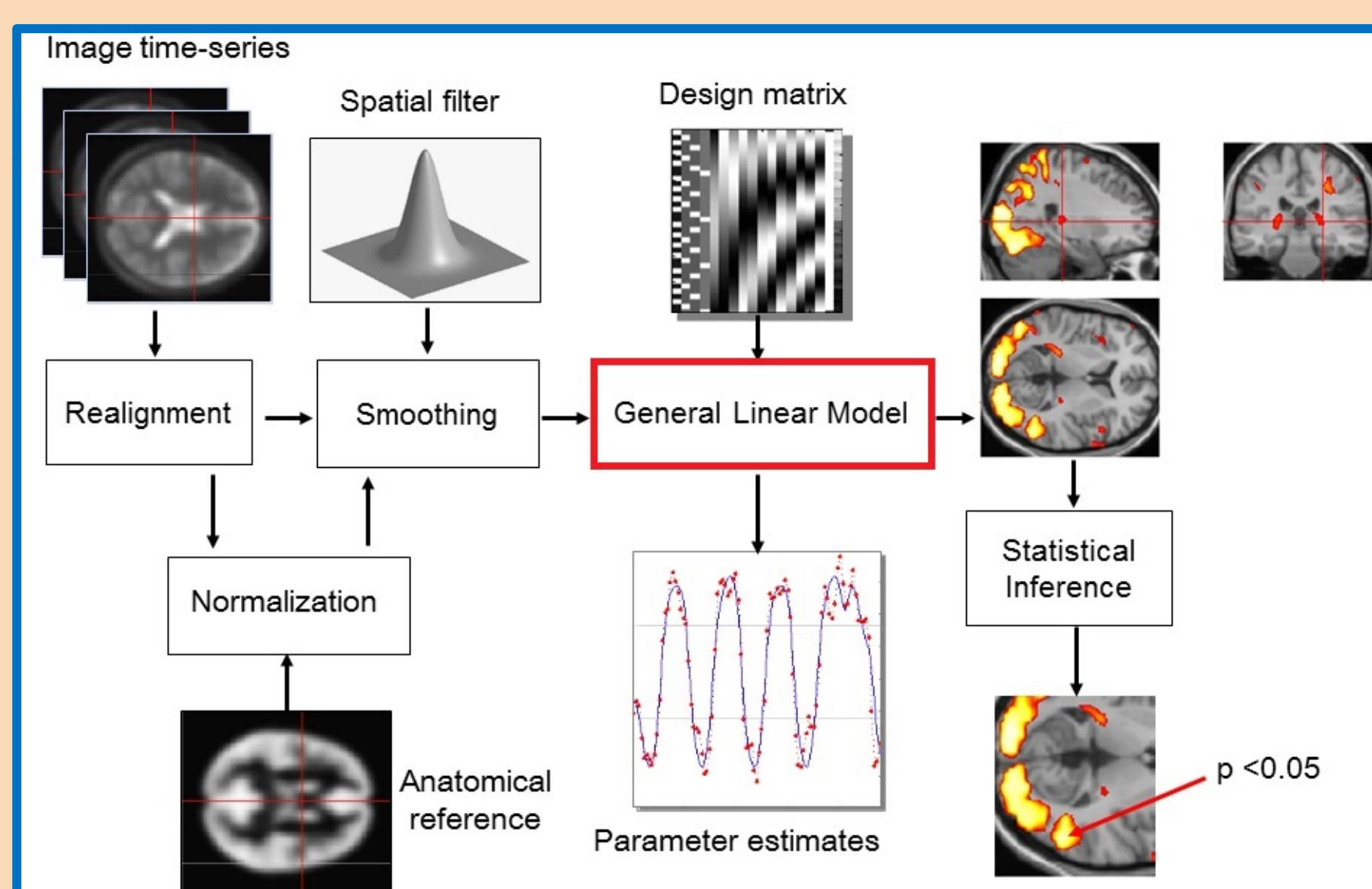
Functional MR images : echo planar imaging (EPI) sequence

TR = 2 s, TE = 30 ms, FOV = 192 mm², FA = 90°, matrix size = 64 × 64, voxel size = 3 × 3 × 4 mm³, 30 slices per volume, slice thickness = 4 mm, 180 volumes.

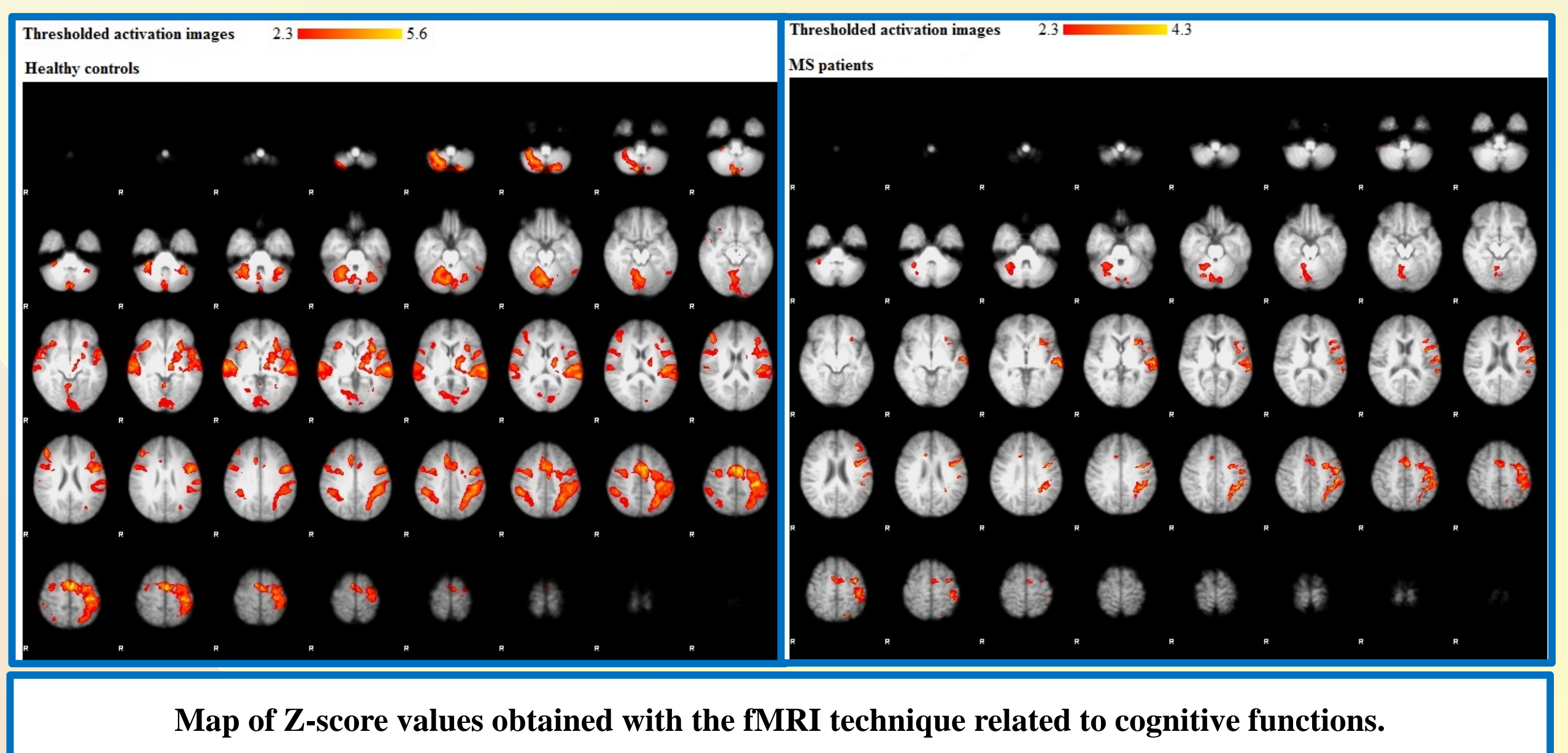
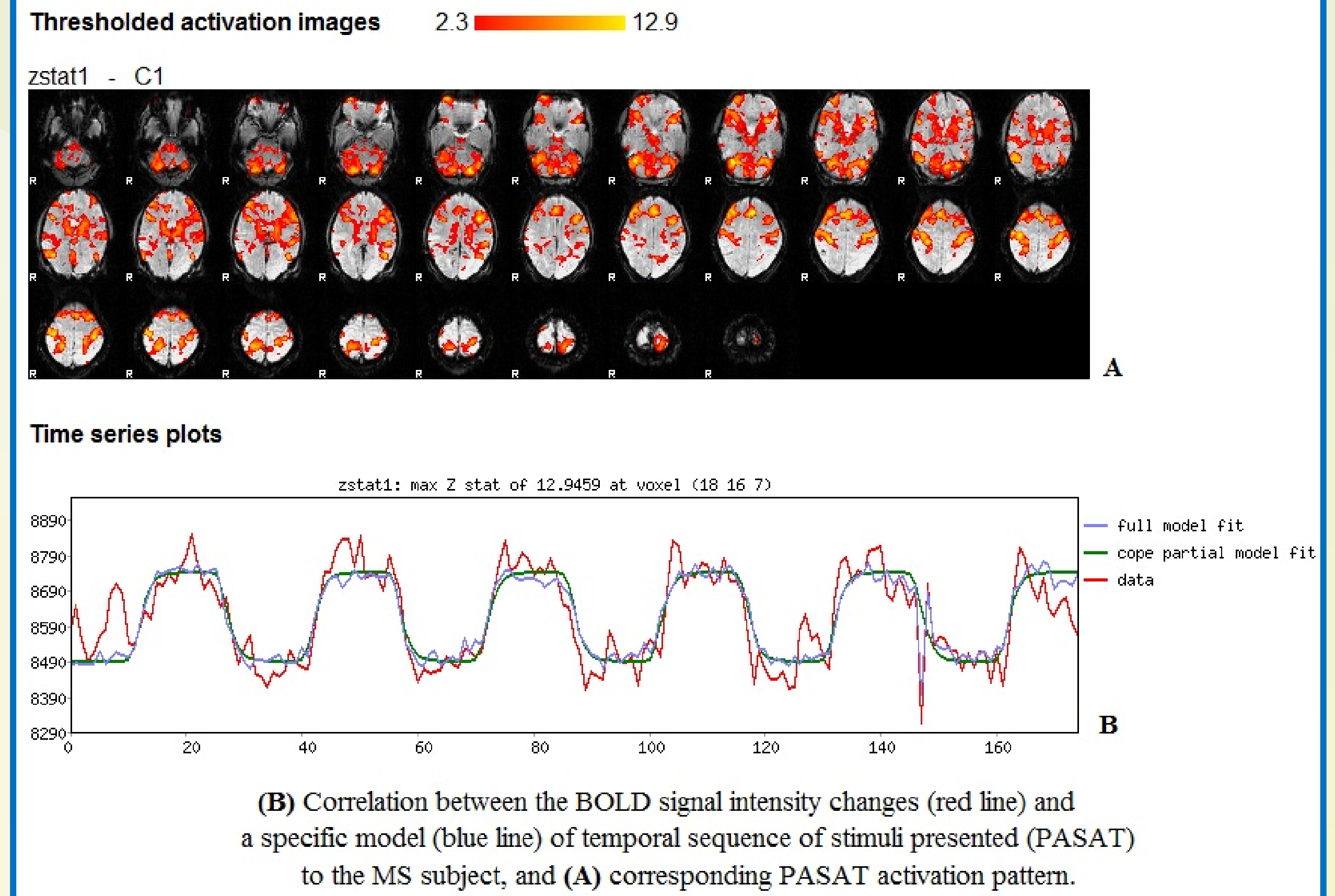
structural images: high resolution three dimensional T1-weighted MPRAGE sequence

TR = 2.53 s, TE = 3.44 ms, FA = 7°, matrix size = 256 × 256, voxel size = 1 × 1 × 1 mm³, 176 sagittal slices with thickness = 1 mm.

fMRI Data Analysis



RESULTS



CONCLUSIONS

- Our results in this study, show that early MS patients indicate altered patterns of activation during execution of cognitive tasks requiring working memory, attention and information processing speed.
- Patients in the early phases of disease had decreased activations of several areas located in the frontal, parietal and temporal lobes compared to the control group.
- The task we used was useful for identifying of alternations in connectivity relevant cognitive deficits in early MS patients and might also be consider for investigating of rewiring of cognitive brain networks in the future studies.

REFERENCES

J. V. Schepdom, J. Gielen, J. Laton, M. B. D'hooghe, J. D. Keyser, G. Nagels (2014), "Graph theoretical analysis indicates cognitive impairment in MS stems from neural disconnection," *NeuroImage: Clinical*, vol. 4, pp. 403-410.

C. Mainero, F. Caramia, C. Pozzilli, A. Pisani, I. Pestalozza, G. Borriello, L. Bozzao, P. Pantanob (2004), "fMRI evidence of brain reorganization during attention and memory tasks in multiple sclerosis," *NeuroImage*, vol. 21, pp. 858- 867.

C. Potagas, E. Giogkarakı, G. Koutsis (2008), "Cognitive impairment in different MS subtypes and clinically isolated syndromes," *Journal of the Neurological Sciences*, vol. 267, no. 1-2, pp. 100-106.

M. P. Amato, E. Portaccio, B. Goretti (2010), "Cognitive impairment in early stages of multiple sclerosis," *Neurological Sciences*, vol. 31, supplement 2, pp. S211-S214.

L. B. Strobera, S. M. Rao, J. C. Lee, E. Fischer, R. Rudick (2014), "Cognitive impairment in multiple sclerosis: An 18 year follow-up study," *Multiple Sclerosis and Related Disorders*, vol. 3, no. 4, pp. 473-481.

L. B. KJraç, Ö. Ekmekçi, N. Yüceyar, A. S. Kocaman (2014), "Assessment of Early Cognitive Impairment in Patients with Clinically Isolated Syndromes and Multiple Sclerosis," *Behavioral Neurology*, vol. 2014.

M. A. Rocca, P. Valsasina, H. E. Hulst, K. Abdel-Aziz, C. Enzinger, A. Gallo, D. Pareto and et. al. (2014), "Functional Correlates of Cognitive Dysfunction in Multiple Sclerosis: A Multicenter fMRI Study," *Human Brain Mapping*, vol. 35, pp. 5799-5814.

O. L. Gamboa, E. Tagliazucchi, F. von Wegner, A. Jurcoane, M. Wahl, H. Laufs, U. Ziemann (2013), "Working memory performance of early MS patients correlates inversely with modularity increases in resting state functional connectivity networks," *NeuroImage*, vol. 94, pp. 385-395.