Analysis of cortical metabolism in multiple sclerosis: a 3T 18F-FDG PET/MRI study

A. Favaretto1, D. Cecchin2, D. Poggial1, M. Margoni1, A. Lazzarotto1, A. Riccardi1, F. Bu2, P. Gallo1

1. Multiple Sclerosis Center – Veneto Region (CeSMuV). Department of Neurosciences, University Hospital of Padua
2. Unit of Nuclear Medicine, Department of Medicine – DIMED, University of Padova

Background
The cortex is severely damaged in multiple sclerosis (MS). Cortical atrophy can be demonstrated in some patients at clinical onset and its progression associates with physical and cognitive disability. Once established, atrophy is irreversible. Whether a cortical metabolic dysfunction may precede atrophy in very early disease phases has not been investigated yet. Recently, a fully integrated Positron Emission Tomography/Magnetic Resonance Imaging (PET/MRI) system that allows the measurement of the absolute glucose metabolic rate in the cortex has become available.

Objectives
In this pilot, explorative study we investigated cortical metabolism in MS patients and its possible association with structural measurements, as cortical thickness, by means of a fully integrated 3T-PET/MRI system. Our aim was to find possible differences in cortical metabolism between MS patients at clinical onset and Relapsing-remitting multiple sclerosis (RRMS) patients with long disease duration and clinical evidence of cortical dysfunction.

Methods

Patient population
28 patients were enrolled in the study: 13 Clinically isolated syndromes/early relapsing-remitting multiple sclerosis (CIS/eRRMS) with a very short disease duration and no sing of cognitive impairment, and 15 RRMS patients with a long disease duration and clinical evidence of cognitive dysfunction (table 1). The two groups were selected in order to avoid possible age-related bias (no significant differences in mean age).

All patients underwent neurological examination with Expanded Disability Status Scale (EDSS) and neuropsychological assessment with Rao's Brief Repeatable Battery of Neuropsychological Tests (BRB-NT). Patients were considered cognitively impaired if their neuropsychological assessment showed at least 1 test with z-score <-2 or 2 tests with z-score <-1.5.

Results
As expected, the structural analysis of cortex by means of Freesurfer showed a significant difference between RRMS and CIS/eRRMS patients. Considering macro-anatomical areas, cortical thickness was significantly lower in RRMS compared to CIS/eRRMS in left frontal (p=0.16), parietal (p=0.03) and occipital (p=0.02) lobes and in right frontal (p=0.019) and parietal (p=0.01) lobes. A more detailed regional analysis performed on 86 cortical areas (33 for each brain hemisphere) found a significant difference in 13/33 cortical areas in the right hemisphere and in 8/33 in the left one (p<0.04), with CIS/eRRMS showing higher thickness than RRMS patients. Surprisingly, no significant difference in cortical aMgRglu was found between RRMS and CIS/eRRMS groups except for the right paracentral area (p=0.04) and the left parietal lobe (p=0.05). These results disclose an unexpected homogeneity in cortical metabolism between the two patients subgroups, despite their important differences in cortical thickness and clinical profile (figure 2).

To investigate the association between cortical metabolism and thickness we performed a correlation analysis on all cortical areas of Desikan Killiany atlas. Only in RRMS group significant positive correlations were found in some cortical areas between cortical thickness and aMgRglu, whereas no correlation was found in CIS/eRRMS group (figure 3).

Conclusions
This study shows that CIS/eRRMS and RRMS have similar values of cortical metabolism despite they significantly differ in cortical thickness. This suggests that a metabolic dysfunction probably precedes MRI detectable structural damage in the cortex of MS using Freesurfer. This metabolic abnormality is secondary to local inflammation or precede the immunopathological process occurring in MS cortex deserves further investigation. The identification of morphometrically normal but hypometabolic areas in very early disease phases may have important pathological and clinical consequences.