

## **Impairment of emotional processing in Multiple Sclerosis: an event-related fMRI study**

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### **Introduction:**

Multiple Sclerosis (MS) is not only associated with sensory-motor deficits, but it may also present with an higher level impairment including both cognitive deficits and psycho-pathological symptoms. Previous functional MRI (fMRI) studies in patients with MS mainly focussed on motor and cognitive disabilities 1,2. Conversely, the psycho-pathological manifestations associated with MS have not been investigated yet. There is clinical evidence that MS patients exhibit significantly higher rates of anger, depression and pathological laughing and crying (PLC) when compared to healthy individuals 3,4. Aim of this study was to investigate, using fMRI, implicit and explicit emotional processing in MS patients.

### **Methods:**

Eighteen patients with relapsing-remitting (RR) MS [F/M ratio=7/11; Mean age(SD)=37.88(9.04) years; median (SD) EDSS score 2.5 (range 0.5-6)] and 13 healthy controls [F/M ratio=6/7; Mean age(SD)=34.46(8.59)] were recruited for this study. Each patient underwent neurological and psychological assessments before MR scanning 5. MRI included the collection of clinical scans (DE and FLAIR sequences), and EPI sequence with BOLD contrast for fMRI investigation. An event-related design was employed using a dedicated emotional paradigm. Subjects were presented with a set of different facial expressions to evoke three basic emotional states: anger, sadness and joy. An additional neutral emotional expression was added as control condition. Subjects were required to answer a specific question by button pressing, being presented with two different tasks, an implicit one concerned a gender discrimination, and an explicit involving an emotional facial expressions discrimination. MS lesions were outlined on proton density weighted scans using a semi-automated contouring technique, and T2-lesion loads were estimated for each patient. Functional data were processed using SPM5 and analyzed with the general linear model for event-related designs in a randomized-effect analysis.

### **Results:**

The mean T2-lesion load in MS patients was 5.22 (SD=4.96) mL. Psychological measures did not reveal any significant difference between MS patients and controls. However, MS patients showed significantly higher brain activation than controls in both negative emotional states (anger and sadness). Additional significant differences in each emotional condition were also observed according to the specific kind of task. Overall, the emotional valence discrimination task activated more limbic areas, whereas when asked to discriminate for gender, higher activation was observed in visual areas. When considering sad condition, a higher activation was found in MS patients compared to controls in the temporal cortex and limbic areas (including the hippocampus, and the amygdala) bilaterally (cluster-level  $p$  corrected  $<0.01$ ) (Figure 1). Both implicit and explicit anger conditions, showed an increased activation in the occipital areas of MS patients compared to controls (Figure 2). An opposite effect was observed in joy condition. In fact, healthy controls showed significantly (cluster-level  $p$  corrected  $<0.01$ ) higher bilateral activity in many limbic structures, including the hippocampus, the amygdala, the insula, and the posterior cingulate, and in the occipital and temporal areas (Figure 3).

### **Discussion:**

Our fMRI findings suggest that an abnormal emotional processing occurs in patients with MS. These abnormalities are consistent with previous clinical observations 4, and might reflect the underlying brain tissue damage. Interestingly, only negative emotions revealed significantly higher brain activity in MS patients compared to controls. Although our patients did not reveal actual signs of psychopathological impairment, this hyperactivation might explain the increased risk of developing psychopathological manifestations in MS. Consistently, the reduced activation for positive emotions found in MS patients might play a synergic role in inducing mood disorders.

Figure 1. Both implicit and explicit sad conditions in RR patients (green) compared to healthy volunteers (red).

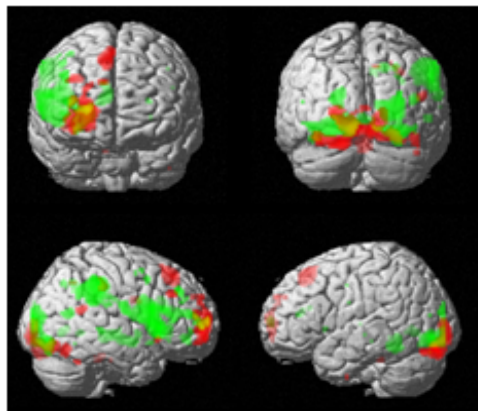


Figure 2. Both implicit and explicit anger conditions in RR patients (green) compared to healthy volunteers (red).

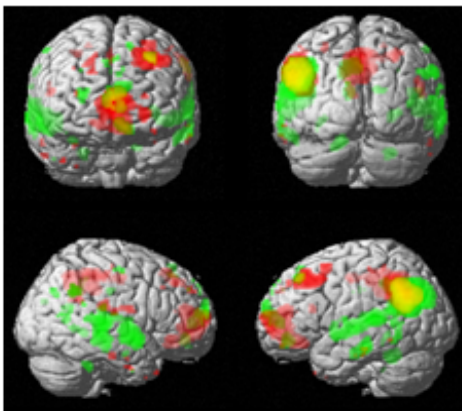
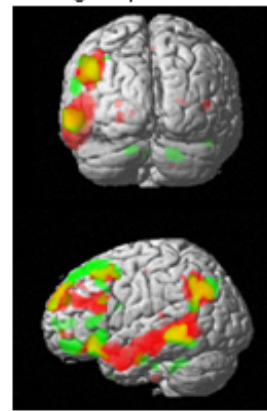


Figure 3. Both implicit and explicit joy conditions in healthy volunteers (red) compared to RR patients (green).



### **References:**

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