Neuroradiological characterization of multiple sclerosis patients with chronic pain

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Introduction and Purpose

Chronic pain is defined by the International Association for the Study of Pain as constant or intermittent daily pain, persisting for more than three months, without apparent biologic value. (1) Many studies have assessed the prevalence of pain in Multiple Sclerosis (MS), concluding that pain is one of the most disabling symptoms. Chronic pain in MS patients is often neuropathic in nature, although a clear-cut distinction with nociceptive pain is not easy. The aim of our study was to analyze the MRIs of MS patients with chronic pain in order to explore possible associations with lesion sites, on a voxel-by-voxel basis

Methods

We enrolled patients aged >18 years with MS in accordance with the 2010 McDonald criteria. All patients with a clinical diagnosis of depression or peripheral nerve disease were excluded. Neurostatus-certified neurologists assessed Kurtzke's Functional Systems and EDSS. We defined 'persistent pain' as a frequent or constant pain lasting longer than 3 months. Patients meeting criteria for persistent pain were included in the “Pain Group” (PAIN+). The other patients were included in the “No-PAIN Group” (PAIN-). We outlined lesions on FLAIR MRI scans using a semi- automated edge finding tool (JIM v. 6.0, Xinapse systems, Aldwincle, UK, http://www. xinapse.com). Total lesion volume (mL) and lesion number were recorded for each subject. To detect the association between lesion localization and persistent pain, images were analyzed with the Voxel- based Lesion Symptom Mapping (VLSM) methods implemented in the nonparametric mapping (NPM) software included into the MRIcron.(2)

RESULTS

We enrolled 208 MS patients (140 F, mean age 55.2 ± 9.4 years; 176 RR, 28 progressive MS; mean EDSS 2.0+2.0). In both groups (PAIN+ group: 96 patients and PAIN- group: 112 patients) lesion volume was correlated with clinical disability measured with EDSS (Spearman r: 0.442, p< 0.0001 in PAIN+ and Spearman r: 0.319, p=0.0014 in PAIN-). Lesions of the right dorsolateral prefrontal area were significantly more prevalent in patients without pain, whereas periventricular posterior lesions were significantly more prevalent in patients with persistent pain. (Figure)

CONCLUSIONS

Right dorsolateral prefrontal lesions may induce hypoalgesia, whereas posterior periventricular lesions may induce hyperalgesia in MS patients. It can be hypothesized that the hypoalgesia mechanism

s disease and the opposite of those occurring in anxious syndromes. Our data support a hemispheric asymmetry in pain perception and modulation.

Patients	n = 208
Age (years) (mean ± SD)	55.19 ± 9.4
Gender	
M (n, %)	68 (32.7)
F (n, %)	140 (67.3)
MS type	
CIS (n, %)	14 (6.7)
RR (n, %)	166 (79.8)
PP/SP (n, %)	28 (13.5)
Disease duration (years) (mean ± SD)	11.4 ± 8.4
Ongoing disease modifying treatment	
Glatiramer acetate (n, %)	53 (25.5)
Beta-interferon 1a/1b (n, %)	38 (18.3)
Dimethylfumarate (n, %)	4 (1.9)
Natalizumab (n, %)	24 (11.5)
Fingolimod (n, %)	12 (5.8)
Mitoxantrone/azathioprine/teriflunomide (n, %)	9 (4.3)
None (n, %)	68 (32.7)
EDSS (mean ± SD)	2.0 ± 2.0

Table
Demographic and clinical features of MS patients. EDSS = Expanded Disability Status Scale; SD = standard deviation; MS = Multiple Sclerosis; CIS = Clinically Isolated Syndrome; PP = Primary Progressive; SP = Secondary Progressive; M = Male; F = Female.

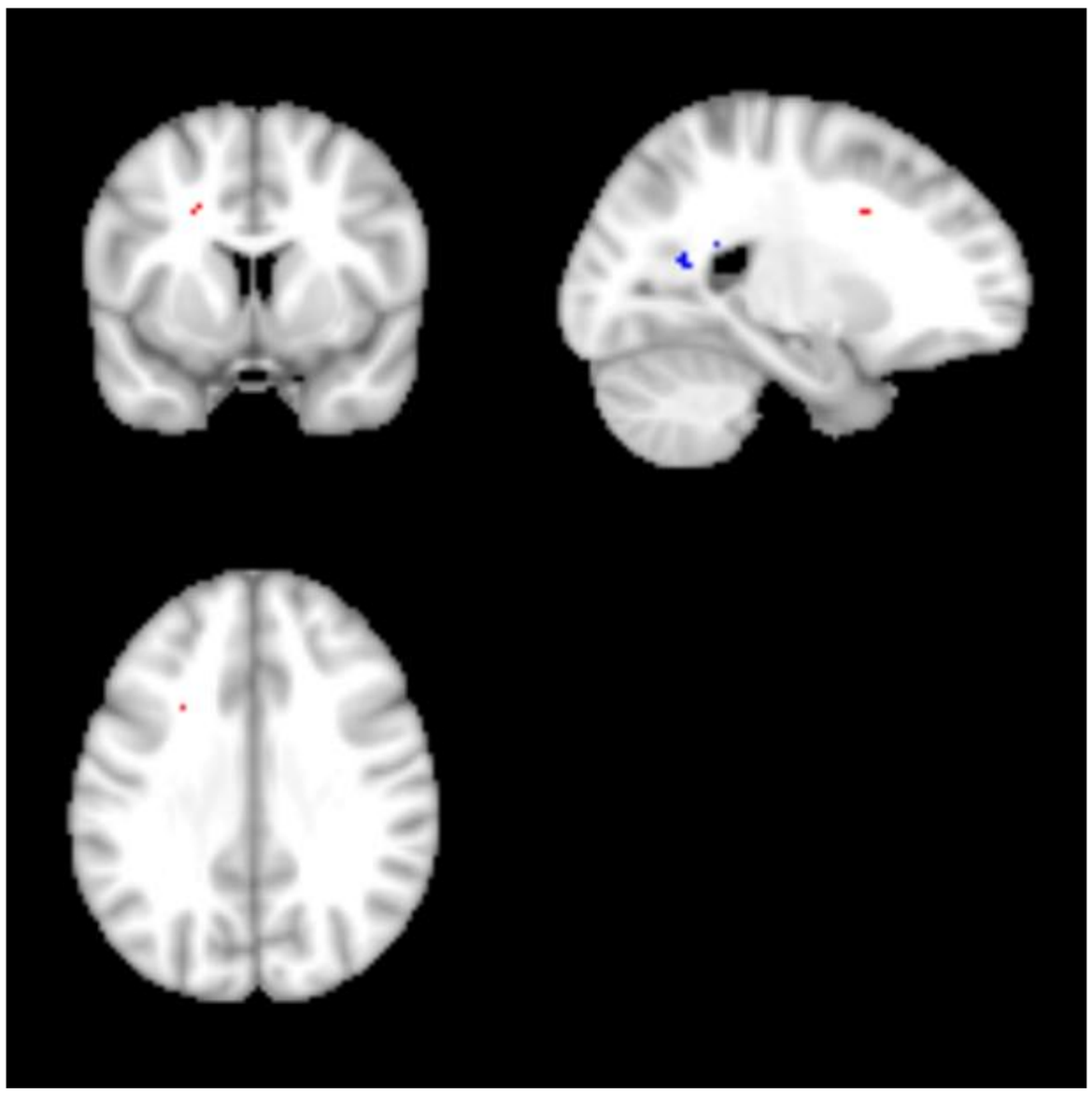

Figure
Lesions of the right dorsolateral prefrontal area significantly more prevalent in patients without pain (red) and periventricular posterior lesions significantly more prevalent in patients with persistent pain (blue). We used Brunner–Munzel test (3,000 permutations); Z> 3.35 (P <0.05).

DISCLOSURE

Domenico Plantone, Diana Ferraro, Francesca Vitetta, Anna Maria Simone, Virxhina Myftari, Patrizia Sola, Massimiliano Mirabella, Guido Primiano, Matteo Pardini, Catello Vollono: nothing to disclose

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