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*Brief communication*

# Altered bodily self-consciousness in multiple sclerosis

Elena Nava[1]*, Flavia Mattioli[2], Chiara Gamberini[1], Chiara Stampatori[2], Fabio Bellomi[2], Chiara Turati[1], Ruggero Capra[3] and Nadia Bolognini[1,4]

[1]Department of Psychology & NeuroMi-Milan Center for Neuroscience, University of Milan-Bicocca, Italy
[2]Neuropsychology Unit, ASST Spedali Civili, Brescia, Italy
[3]MS Center, ASST Spedali Civili, Brescia, Italy
[4]IRCSS Istituto Auxologico Italiano Laboratory of Neuropsychology, Milan, Italy

In this study, we assessed the impact of multiple sclerosis (MS) on bodily self-consciousness (BSC) using the Rubber Hand Illusion. Patients with MS showed a dissociation between body ownership and self-location: they did report an explicit ownership of the rubber hand, but they did not point towards it, showing a defective ability of localizing body parts in space. This evidence indicates that MS may affect selective components of BSC, whose impairment may contribute to, and even worsen, the functional disability of MS.

Multiple sclerosis (MS) is the most common immune-mediated demyelinating disease of the central nervous system in young adults, featured by different cognitive impairments (Chiaravalloti & DeLuca, 2008). Disorders of bodily self-consciousness (BSC) may be also present and contribute to the neurological disability, psychological distress and health-related quality of life in MS. For instance, even if mildly disabled and in a quite stable mood, patients with MS tend to report significantly higher worries about their body, such as a worse body appraisal, sexual problems and fears about physical deficits (Pfaffenberger *et al.*, 2011). However, whether and to what extent BSC is altered in MS is still unknown. The issue is worth being investigated considering the high incidence of sensorimotor impairment and the multifaceted nature of cognitive decline encountered in MS, and the growing body of evidence showing that BSC disorders are intrinsically linked to pain, sensory and motor deficits in many neurological diseases (Moseley & Flor, 2012).

Bodily self-consciousness relies on efficient multisensory integration of bodily signals (e.g., Serino *et al.*, 2013). Specific multisensory brain areas appear intrinsically intertwined with the immune system, and some studies indicate that immune-mediated diseases such as MS could impair multisensory integration, potentially disrupting BSC (Costantini, 2014). Here, we explored BSC in MS using the Rubber Hand Illusion (RHI, Botvinick & Cohen, 1998), which has been effectively used to assess and manipulate BSC

**Correspondence should be addressed to Elena Nava, Department of Psychology, University of Milan-Bicocca, Piazza dell'Ateneo Nuovo 1, 20126 Milan, Italy (email: elena.nava@unimib.it).*

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in many pathological conditions (Bolognini, Russo, & Vallar, 2015). The RHI allows to dissociate two components of BSC: the subjectively reported experience of sensing our body and its single parts (bodily ownership), and the more automatic process of localizing and keeping track of body parts in space (self-location, Serino *et al.*, 2013).

## Methods

### Participants

Twenty-six patients with a relapsing remitting type of MS (mean age = 44.31; *SD* = 12.29, females = 17), and 26 healthy controls, with no history of neurological or psychiatric diseases (mean age = 43.96, *SD* = 11.95, females = 13) were recruited; all participants were right-handed (except one patient with MS who was matched with one left-handed healthy control).

Patients with MS were recruited according to the following criteria: mean Expanded Disability Status Scale $\leq 6$, normal vision, the absence of severe motor arm and hand impairment (Medical Research Council scale < 3/5) or sensory deficits in the upper limbs at clinical examination, and the absence of cognitive decline (Mini-Mental State Examination > 24). They did not have any clinical relapse in the previous year, were not affected by major psychiatric disorders and did not take antidepressant or psychoactive drugs. Nineteen patients were under immunomodulatory treatment (natalizumab, $N = 2$; interferon beta, $N = 9$; dimethyl fumarate, $N = 2$; teriflunomide, $N = 1$; copolymer, $N = 4$; no drugs, $N = 7$).

All participants signed an informed consent prior to testing, and patients also gave consent for their clinical records to be used in the current study. The study was approved by the Ethical Committee of the University of Milan-Bicocca (Milan, Italy) and by the Ethical Committee of the ASST Spedali Civili (Brescia, Italy), in conformity with the Helsinki Declaration. Table 1 illustrates the demographic and clinical features of patients with MS.

### Stimuli and procedure

A life-sized plastic rubber left hand was placed in front of the participants, while the participant's left hand was prevented from being seen by applying a wooden platform at the right side of the left hand. The illusion induction consisted in stroking the participant's left non-dominant hand and the rubber hand with two paintbrushes in either a synchronous or asynchronous fashion, for about 60 s and repeated for three times. To assess self-location, before and after the illusion induction, participants performed a task measuring the proprioceptive drift, namely the perceptual change in the position of the real hand towards the rubber hand (see Botvinick & Cohen, 1998). To assess body ownership, after the RHI induction, a 5-item questionnaire was administered, comprising three items designed to reflect the strength of the embodiment ('I felt as if the rubber hand was my own hand'; 'I felt the strokes of the paintbrush in the location where the rubber hand was'; 'It seemed as though the touch I felt was caused by the paintbrush touching the rubber hand') and two other questions ('I felt as if my own hand had turned rubberish'; 'I felt as if I had more than two hands') that served to control for the suggestibility of the participants (see Botvinick & Cohen, 1998). Responses to the questions were collected using a 5-point Likert scale (points between −2 and +2).

**Table 1.** Demographic and clinical data of patients with MS

| Group | Age | Gender | Length of illness [years] | Neuropsychological assessment (Test scores from rao's brief repeatable battery) | | | | | | | | | EDSS | Upper-limb strength | Tactile sensitivity |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | SRT-LTS | SRT-CLTR | SRT-D | SPART | SPART-D | SDMT | PASAT 3″ | PASAT 2″ | WLG | | | |
| S | 50 | M | 28 | 40.8 | 19.16 | 8.03 | 11.71* | 3.28* | 41.76 | 34.86 | 38.88 | 32.44 | 6 | +/– | + |
| | 45 | M | 7 | 22.2* | 14.4* | 4.8* | 12.9 | 5.3 | 41.2 | 30.5 | 19.75 | 24.2 | 1.5 | +/– | + |
| | 45 | F | 16 | 45.2 | 37.8 | 8.9 | 14.6 | 3.5* | 29.5* | 28.4* | 0* | 15* | 1.5 | + | + |
| | 33 | F | 1 | 34.53 | 27.32 | 6.9 | 25.3 | 8.36 | 54.86 | 46.5 | 22.2 | 28.85 | 2 | +/– | + |
| | 53 | F | 11 | 32 | 22 | 8 | 20 | 7 | 60 | 58 | 41 | 32 | 2 | + | +/– |
| | 58 | F | 30 | 0* | 0* | 2.1* | 11.5* | 4.7 | 4.1* | 0* | n.s. | 8.9* | 6 | +/– | + |
| | 31 | F | 5 | 29.96 | 16.16 | 6.28 | 24.52 | 10.18 | 50.44 | 32.38 | 0* | 15.88* | 2.5 | +/– | +/– |
| | 47 | F | 30 | 48.16 | 32.07 | 3.9 | 18.78 | 3.92 | 32.38 | 53.9 | 38.33 | 19.8 | 2 | + | + |
| | 58 | F | 3 | 39.37 | 31.41 | 4.4* | 15.7 | 4.9 | 42.61 | 23.6 * | n.s. | 17 | 3 | +/– | + |
| | 44 | M | 6 | 54 | 42 | 9 | 30 | 10 | 61 | 64 | 47 | 26 | 1.5 | + | + |
| | 24 | F | 1 | 48.3 | 29.9 | 7.5 | 25 | 9.7 | 66.3 | 50.6 | 29.1 | 32.9 | 2 | + | + |
| | 48 | F | 4 | 40.8 | 37.53 | 8.7 | 20.4 | 9.8 | 58.4 | 48.3 | 37.2 | 35.9 | 1 | +/– | + |
| | 30 | F | 0 | 34.15 | 29.36 | 7.87 | 25.94 | 9.28 | 61.64 | 39.49 | 20.75 | 27.88 | 1 | + | + |
| A | 56 | F | 23 | 37.09 | 28.29 | 7.99 | 22.69 | 6.65 | 49.68 | 36.81 | n.s. | 31.37 | 2.5 | +/– | + |
| | 47 | F | 3 | 29.3 | 22.3 | 7.5 | 10.2* | 2.3* | 35.2 * | 14.1* | 0* | 18.9 | 2.5 | + | + |
| | 26 | M | 1 | *na* | | | | | | | | | 0 | + | + |
| | 56 | M | 32 | 58.7 | 46.8 | 9.6 | 30.6 | 9.6 | 53.4 | 54.4 | 35.9 | 20.1 | 3 | +/– | +/– |
| | 62 | M | 4 | 24.16 | 11.07* | 6.88 | 22.78 | 7.92* | 41.38 | n.s. | n.s. | 8.88* | 3.5 | + | + |
| | 57 | M | 13 | 35.2 | 29.8 | 7.9 | 20.7 | 7.6 | 49.6 | 41.5 | 28.9 | 20.12 | 0 | + | + |
| | 48 | F | 4 | 40.8 | 37.53 | 8.7 | 20.4 | 9.8 | 58.4 | 48.3 | 37.2 | 35.9 | 1 | + | + |
| | 36 | F | 16 | 30.55 | 26.91 | 7.08 | 21.31 | 4.41 | 55.27 | 42.19 | 16.9 | 21.88 | 1.5 | + | + |
| | 59 | M | 7 | 28.96 | 13.15* | 5.28 | 20.52 | 7.18 | 58.44 | 51.38 | 46.56 | 24.12 | 2 | + | + |

*Continued*

**Table 1.** (*Continued*)

| Group | Age | Gender | Length of illness [years] | Neuropsychological assessment (Test scores from rao's brief repeatable battery) | | | | | | | | | EDSS | Upper-limb strength | Tactile sensitivity |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | SRT-LTS | SRT-CLTR | SRT-D | SPART | SPART-D | SDMT | PASAT 3″ | PASAT 2″ | WLG | | | |
| | 53 | F | 22 | 35.17 | 23.78 | 6.88 | 23.6 | 5 | 43.5 | 52 | 29 | 21 | 3 | + | + |
| | 19 | F | 1 | 42.2 | 31.1 | 7.9 | 25.8 | 9.9 | 53.4 | 32.9 | 5.3* | 17.9 | 2 | + | +/− |
| | 31 | M | 7 | 34.16 | 31.07 | 2.88 * | 8.78* | 1.92* | 42.38 | 6.98* | n.s. | 23.12 | 2 | + | + |
| | 36 | F | 2 | 36.4 | 32.2 | 8.1 | 23.4 | 8.8 | 67.1 | 33.7 | 20.3 | 21.9 | 0 | + | + |

*Note*. The acronyms indicate: S = Synchronous RHI group, A = Asynchronous RHI group, M/F=Male/Female, SRT-LTS = Select Reminding Test – Long-Term Storage, SRT-CLTR = Select Reminding Test – Consistent Long-Term Retrieval, SRT-D = Select Reminding Test – Delayed Recall, SPART = Spatial Recall Test, SPART-D = Spatial Recall Test – Delayed Recall, SDMT = Symbol Digit Modalities Test, PASAT 3/2″ = 3/2-intervals Paced Auditory Serial Addition Task, WLG = Word List Generation, EDSS [range 0–7.5] = Expanded Disability Status Scale, na = not available, * = Pathological score, + = normal, − = deficit, +/− = minor deficit.

Both healthy and MS individuals entered in two experimental groups, one receiving the synchronous RHI (13 of 26 healthy controls: mean age = 42.69; 13 of 26 patients with MS: mean age = 43.54), one receiving the asynchronous RHI (13 healthy controls: mean age = 45.23; 13 patients with MS: mean age = 45.08). The use of this between-subjects design was motivated by pilot experiments conducted in our laboratory showing that one stroking condition may influence the other.

The two groups (synchronous vs. asynchronous RHI) of patients with MS were first compared by means of paired *t*-tests to detect differences with respect to their age, length of illness and severity of cognitive deficits assessed with the Rao's battery. The questionnaire data were analysed with Kruskal–Wallis non-parametric ANOVAs, and the proprioceptive drift with a mixed ANOVA.

## Results

The two MS patients groups were comparable with respect to their clinical and demographic features (all $p$s $> .2$).

With respect to the questionnaire, every illusion question reached significance (Q1: $H = 29.42$, $p < .001$; Q2: $H = 29.95$, $p < .001$; Q3: $H = 36.44$, $p < .001$). Post hoc multiple comparisons showed differences between synchronous and asynchronous stimulations in both patients with MS and controls, in every illusion question (all $p$s $< .02$, Figure 1). Hence, both healthy and patients with MS receiving the synchronous, but not the asynchronous stroking, reported feelings of embodiment over the rubber hand, with no difference between MS and controls ($p > .9$). With respect to the control questions, no

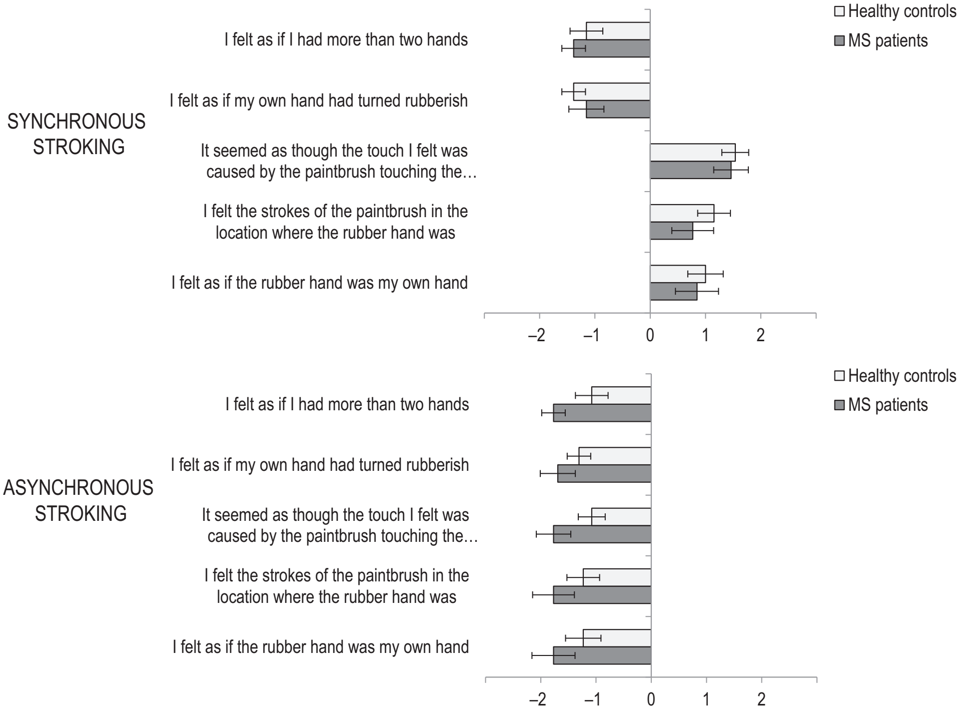


**Figure 1.** Questionnaire rating of patients with MS and healthy controls following synchronous (upper panel) and asynchronous (lower panel) stroking. Error bars indicate standard error of the mean.

difference was found within and across patients with MS and controls (C1: $H = 2.33$, $p = .51$; C2: $H = 5.35$, $p = .15$).

Analysis on the proprioceptive drift showed a significant session by group interaction ($F_{3,48} = 7.54$, $p < .001$, Figure 2a). Patients with MS of the synchronous group did not recalibrate their own hand towards the rubber hand (pre- vs. post-RHI, post hoc Bonferroni comparisons, $p > .9$), contrary to healthy controls of the synchronous group who showed the typical proprioceptive drift (pre- vs. post-RHI, and post-RHI of controls vs. patients with MS for synchronous RHI, all *p*s $< .001$). No proprioceptive drift was detected in controls and patients with MS of the asynchronous groups (all *p*s $> .2$, Figure 2b). Noteworthy, patients with MS and healthy controls showed similar accuracy in the pointing task before the RHI ($p = .5$), hence excluding that the post-stroking differences in recalibration of hand position between MS and controls were due to different motor capabilities at baseline (pre-RHI).

## Discussion

Our findings show that only the self-location component of BSC is altered in MS, while the subjective feeling of owning the rubber hand is preserved. Self-location relies upon

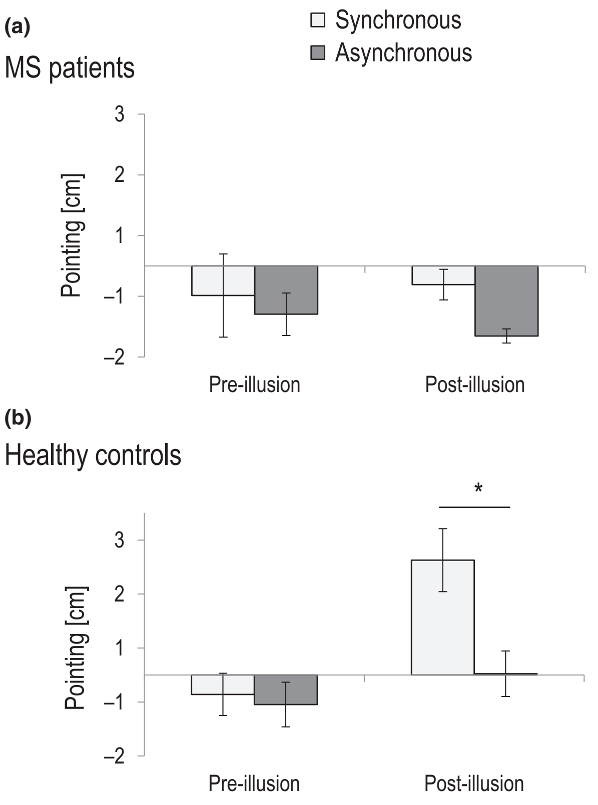


**Figure 2.** Pointing task following synchronous and asynchronous stroking for patients with MS (panel a) and healthy controls (panel b). Asterisks indicate a significant difference between pre- and post-illusion pointing. Error bars indicate standard error of the mean.

multisensory interactions and allows seen and felt touches to 'fuse' the real and rubber hand together (Serino *et al.*, 2013). The lack of recalibration of perceived hand position towards the rubber hand in patients with MS could result from an impaired multisensory processing that follows the damaged myelin attacked by the immune system. Such immune-mediated demyelination, by interrupting the flow of information within uni- and multisensory brain areas, and between such areas and the body, may alter BSC by primarily affecting its self-location component, while leaving unaltered the sense of body ownership. This last component requires additional top-down processes, which seem more resistant to the multifocal damage brought about by MS. A recent study investigating BSC through the RHI in the autoimmune Coeliac Disease (CD, Finotti & Costantini, 2016) found a similar dissociation between body ownership and proprioceptive drift: following the synchronous RHI, patients with CD had the illusory sense of owning the rubber hand but they showed an amplified proprioceptive drift, as compared to healthy controls. The different direction of the abnormal proprioceptive drift (amplified in CD, absent in MS) could be due to the different pathophysiology affecting sensory transmission in the brain.

Dysfunctions of BSC, as indexed by the RHI, were reported even in stroke patients. However, at variance of patients with MS, stroke patients showed stronger illusory effects, as assessed with both the self-report questionnaire and the proprioceptive drift (Bolognini, Ronchi, Casati, Fortis, & Vallar, 2014; Burin *et al.*, 2015; Llorens *et al.*, 2017). The more focal lesion caused by stroke may promote a plastic reorganization in the cerebral network involved in body representation and multisensory integration, which would induce an abnormal fusion of multisensory inputs (Bolognini, Convento, Rossetti, & Merabet, 2013), in turn amplifying both of the two components of the RHI: self-location and body ownership. Conversely, the degenerative white matter lesions of MS would primarily interrupt the transmission and interaction of sensorimotor signals necessary for localizing the body in space. It is also noteworthy that while our patients with MS did not have severe motor impairments (see Table 1), stroke patients tested in previous studies had hemiparesis or hemiplegia (Bolognini *et al.*, 2014; Burin *et al.*, 2015; Llorens *et al.*, 2017). This evidence further supports the role of movement in developing and maintaining a coherent sense of body ownership (Burin *et al.*, 2015; Llorens *et al.*, 2017).

In conclusion, the immune-mediated demyelination of the central nervous system featuring MS alters BSC by affecting its self-location component, while leaving unaltered the sense of body ownership.

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