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Moral Cognition and Multiple Sclerosis: A Neuropsychological Study

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Abstract

Objectives: Recent literature proved that social cognition impairments may characterize the neuropsychological profile of Multiple Sclerosis (MS) patients. However, little is still known about moral cognition in MS. In this study, we evaluated non-social, social, and moral cognitive performances in 45 relapsing-remitting MS patients.
Methods: Patients underwent the Brief International Cognitive Assessment for Multiple Sclerosis battery, the Cognitive Estimation and Stroop tasks, the Ekman-60 Faces test, the Reading the Mind in the Eye and Story-based Empathy task. Additionally, a task of moral dilemmas including both "instrumental" and "incidental" conditions was administered to patients. Forty-five age-, gender- and education-matched healthy control subjects (HC) were enrolled for comparisons.
Results: The majority of patients (i.e., 77.6%) showed deficits at non-social tasks, particularly in the executive domains. A subset of MS sample (i.e., 24%) presented with emotion recognition and socio-affective processing impairments. Overall, MS patients showed comparable levels of moral judgment with respect to HC. The rate of yes/no response in resolution of moral dilemmas and scores of attribution of emotional valence were comparable between groups. Nevertheless, lower moral permissibility and emotional arousal, particularly for the instrumental dilemmas, characterized the MS profile. Significant correlations between the attribution of emotional valence to moral actions and mentalizing scores emerged.
Conclusions: Our findings expand current literature on MS supporting not only deficits in executive and socio-emotional domains but also low levels of permissibility of immoral actions and emotional detachment in the moral judgment process.

Keywords: Multiple sclerosis; Emotions/emotional processing; Moral cognition; Moral judgment

Introduction

Multiple Sclerosis (MS) is a chronic inflammatory disease affecting the central nervous system. It is associated with accumulating multifocal tissue damage, often leading to physical disability and cognitive impairments. These latter are reported in a high rate of patients, ranging from 40% to 70% (Chiaravalloti & DeLuca, 2008). Cognitive disorders are due to the heterogeneity of gray and white matter damage, i.e., "multiple disconnection syndrome" (Calabrese & Penner, 2007) and result in different neuropsychological patterns. Speed information processing, attention, learning and memory, and executive functions are frequently impaired (Chiaravalloti & DeLuca, 2008). In addition, recent studies proved emotion recognition, theory of mind and empathy deficits, which can be very consistent even in the early disease phases (Bora, Ozakbas, Velakoulis, & Walterfang, 2016; Chalah & Ayache, 2017). Notwithstanding this latter emerging literature exploring socio-emotional skills, moral cognition has been poorly investigated in MS (Gleichgerrcht, Tomashitis, & Sinay, 2015; Patil, Young, Sinay, & Gleichgerrcht, 2017).

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Morality is defined as the sets of values and habits that are adopted by a cultural group in order to orient its social conduct (Moll, Zahn, de Oliveira-Souza, Krueger, & Grafman, 2005). The ability to evaluate the actions made with respect to a set of virtues (i.e., "moral judgment") is measured through tasks involving moral dilemmas, i.e., situations where an agent cannot fulfill all applicable moral requirements. All the conscious mental processes that allow to transform a given information in order to reach a moral judgment is defined as "moral reasoning" (Moll et al., 2005). By evaluating a moral dilemma, it is also required to define the "moral acceptability/permissibility" of the leading character's behavior (e.g., completely morally inacceptable or acceptable) and to evaluate the experience by rating the relative "emotional valence" (e.g., pleasantness/unpleasantness) and "emotional arousal" (e.g., activation/calm). These emotional dimensions represent affective parameters that typically account for most of the variance in the final moral judgment (Lotto, Manfrinati, & Sarlo, 2014).

Preliminary evidence in MS (Gleichgerrcht et al., 2015; Patil et al., 2017) proved preserved moral judgment ability with reduced rating of moral acceptability and higher levels of emotional reactivity. MS patients showed an egocentric projection of the moral problem, which accounts for the overestimation of the rate of respondents that would deliver a similar judgment at the same dilemma (Gleichgerrcht et al., 2015). These authors (Gleichgerrcht et al., 2015) thus hypothesized in MS a shift of moral judgment towards a "non-utilitarian pattern". This behavior is mainly driven by an instinctual emotional aversion to harm other people (Greene, Nystrom, Engell, Darley, & Cohen, 2004; Greene, Sommerville, Nystrom, Darley, & Cohen, 2001). On the contrary, a detailed cost-benefit analysis of the specific moral situation usually results in a "utilitarian pattern" of moral judgment (Greene et al., 2001, 2004).

No study systematically explored the relationship between moral judgment and basic and social cognitive performances in MS. Literature suggests that fatigue, depression, anxiety, and alexithymia levels may influence performances at social cognition tasks (Chalah & Ayache, 2017) as well as deficits on basic cognitive abilities may account for lower socio-emotional scores (Cotter et al., 2016; Pottgen, Dziobek, Reh, Heesen, & Gold, 2013). The strength and the significance of these associations are still matter of debate. Although isolated social cognition impairments have been reported in a subset of MS patients with spared non-social performances (Pottgen et al., 2013), discrepancies in the cognitive demand among tasks may influence both the neuropsychological outcome and the reliabily of results across studies (Cotter et al., 2016). In this view, our research study was aimed at (1) analyzing the prevalence of non-social and social cognition disorders; (2) investigating moral judgment, moral acceptability/permissibility, emotional reactivity and emotional arousal at moral dilemmas; and (3) exploring the relationship among clinical, non-social, social, and moral variables in a sample of relapsing-remitting (RR) MS patients.

Materials and Methods

Subjects

Forty-five RR-MS patients (14 males; mean age 34.22 ± 7.65 years; mean education 13.42 ± 2.57 years; mean disease duration from the onset 9.72 ± 6.22 years) who were referred to the MS center, BioNeC, University of Palermo (Italy) were enrolled for the present study (Table 1). All patients were diagnosed with clinically definite MS, according to the revised McDonald criteria (Polman et al., 2011). Exclusion criteria included acute relapse or steroid treatment within the past month, and current/past psychiatric disease. Patients with severe cognitive deficits or comorbid medical conditions potentially interfering with cognitive functioning were excluded. Expanded Disability Status Scale (EDSS), Multiple Sclerosis Severity Score (MSSS) and Multiple Sclerosis International Quality of Life (MuSIQoL) assessed disease disability, clinical severity and quality of life. Fatigue Severity Scale (FSS) assessed fatigue in patients. Mood disorders were evaluated by means of the Hospital Anxiety and Depression Scale (HADS).

For statistical comparisons at the moral dilemmas task, we enrolled 45 age-, gender- and education-matched healthy controls (HC; 13 males; mean age = 33.04 ± 7.73 years; mean education=13.31 ± 3.08 years) who were recruited among siblings of elderly subjects from senior community centers. They underwent a clinical interview, a neurologic examination and a brief cognitive assessment in order to test cognitive efficiency. Medical history positive for neuropsychiatric disorders, positive neurologic examination, Mini Mental State Examination (MMSE) raw score <28, as well as verbal and visuospatial delayed memory performances below 25th percentile according to the Italian normative values, were exclusion criteria.

A preliminary pilot study on 10 patients and 10 healthy controls was performed in order to calculate the sample size. We used emotional arousal as variable of interest. According to the distribution of emotional arousal performances in MS patients (i.e., 5.25 ± 1.9) and controls (i.e., 6.5 ± 1.59), the sample size required to ensure the 90% chance of finding a significant difference at $\alpha = 0.05$ was 43 subjects per group. We thus included in the study 45 subjects per group.

Table 1. Demographic, clinical and neuropsychological features of the sample

	RR-MS	*HC*	Statistics
Demographic and clinical features			
Female/male ratio	31/14	32/13	$X^2(1) = 0.05$, n.s.
Age in years	34.22 ± 7.65	33.04 ± 7.73	$t(88) = 0.727$, n.s.
Education in years	13.49 ± 2.46	13.31 ± 3.08	$t(88) = 0.302$, n.s.
Disease duration in years	9.72 ± 6.22	—	—
Hospital Anxiety and Depression Scale – HADS total score	13.39 ± 6.88	—	—
Expanded Disability Status Scale – EDSS total score	2.06 ± 1.46	—	—
MS Severity Scale – MSSS total score	2.85 ± 2.59	—	—
MS International Quality of Life – MuSIQoL total score	73.52 ± 12.32	—	—
Fatigue Severity Scale	61 ± 35.18		
		% out of cut-off score[a]	*% borderline score*[a]
Basic cognitive and social cognition assessment			
BICAMS – SDMT subscale	47.4 ± 10.7	18%	—
BICAMS – CLVT-II subscale	49.3 ± 8.11	18%	—
BICAMS – BVMT-R subscale	25.47 ± 6.2	13%	—
Cognitive Estimation Task	16.84 ± 4.32	42%	13%
Stroop task – Interference effect of time	26.49 ± 5.18	2%	18%
Stroop task – Interference effect of errors	0.28 ± 0.72	2%	2%
Reading the Mind in the Eye – RME total score	25.27 ± 3.8	16%	—
Ekman-60Faces Test – Ek-60F total score	46.58 ± 6.11	11%	20%
Story-based Empathy task – SET total score	16.27 ± 2.02	0%	4%

RR-MS = Relapsing-Remitting Multiple Sclerosis; HC = Healthy Controls; BICAMS = Brief International Cognitive Assessment for Multiple Sclerosis; SDMT = Symbol Digit Modalities Test; CLVT-II = California Verbal Learning Test-II; BVMT-R = Brief Visuospatial Memory Test Revised.
[a]Percentage of patients obtaining a deficitary/borderline performance were computed according to the Italian normative values.

Basic Cognitive and Social Assessment

In order to test basic cognitive functioning, patients performed the Italian version of the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS). It is a widely used neuropsychological mini-battery designed to assess those cognitive domains that are more frequently impaired in MS (Goretti et al., 2014). It includes three subtasks: (1) speed of information processing (i.e., Symbol Digit Modalities Test; SDMT), (2) verbal (i.e., California Verbal Learning Test-2; CVLT2) and (3) visuospatial (Brief Visuospatial Memory Test-Revised; BVMT-R) learning and memory (Goretti et al., 2014). Patients performed also two additional executive tasks (i.e., Cognitive Estimation-CET (Della Sala, MacPherson, Phillips, Sacco, & Spinnler, 2003) and Stroop test (Caffarra, Vezzadini, Dieci, Zonato, & Venneri, 2002)) in order to better investigate executive domains that are often impaired in MS (Macniven et al., 2008; Taylor & O'Carroll, 1995).

Finally, a brief social cognition battery was administered to patients to explore emotion recognition (i.e., Ekman-60-Faces task; Ek-60F) and socio-affective processing (i.e., Story-based Empathy Task; SET and Reading the Mind in the Eye; RME) skills. In details, the Ek-60F assessed the ability of recognize basic emotions (i.e., anger, sadness, happiness, surprise, fear, disgust) from facial expressions (Dodich et al., 2014). A preliminary trial test was administered to exclude semantic deficits and visuo-perceptual disorders in patients. The SET is a non-verbal task standardized for the Italian population (Dodich et al., 2015). This test consists of two main experimental conditions, i.e. identifying intentions (SET-IA) and emotional states (SET-EA), plus a control condition entailing the inference of causality reaction based on knowledge about the physical properties of objects or human bodies (SET-CI). The RME is a test of affective mentalizing in which the subject is asked to choose which of four words best describes what a person is thinking or feeling just looking at the picture of the eye-region (Serafin & Surian, 2004).

All subjects gave informed consent to the experimental procedure, which was approved by the local Ethic Committee.

See Table 1 for details on demographic variables.

Experimental Moral Task

The task of moral dilemmas includes eight scenarios derived from Lotto et al. (2014). Each dilemma was presented as text in two phases. The first phase described the scenario, in which some kind of threat was going to cause death to a group of people. The second phase described a hypothetical resolution in which the participant, identifying him/herself as the main character, killed one individual to save the others, which otherwise would have died. Dilemmas were sub-grouped into

"instrumental" (i.e., the death of one person is a mean to save more people) and "incidental" (i.e., the death of one person is a foreseen but unintended consequence of the action aimed at saving more people) ones. Additionally, half of dilemmas involved the main character as also his life was at risk (i.e., self-involvement). See Table 2 for stimuli examples.

Participants were asked to indicate whether they would do the proposed action. Then, they were asked to judge how morally acceptable was the resolution (0 = not at all, 7 = completely), to attribute an emotional valence to the moral action (0 = totally unpleasant, 8 = totally pleasant) and to rate the emotional arousal (0 = totally calm, 8 = totally involved). Outcome variables were: (i) the rate of yes/no responses to the proposed resolution (i.e., moral judgment); the rating of (ii) moral acceptability, (iii) emotional valence and (iv) emotional arousal experienced during the decision-making process.

Statistical Analyses

First, we estimated in patients the prevalence of impaired (i.e., score below the 5th percentile), borderline (i.e., score between the 5th and 10th percentile) or unimpaired (i.e., score above the 10th percentile) performances according to the Italian normative values in both non-social and social tasks.

Then, we explored patient performances at moral dilemma task in comparison to the control group. Preliminarily, we explored the distribution for each variable with the Kolmogorov–Smirnov test. All moral variables did not significantly depart from normality ($p > .05$) with the exclusion of the rate of yes/no responses to the proposed resolution, which follows a binomial distribution.

Chi-squared test was used to analyze group differences in rate of yes/no responses at moral dilemmas. Mixed-ANOVA was computed to detect differences in the rating of moral permissibility, emotional valence and arousal experienced during the decision-making process, considering the effects of the type of dilemma and of the self-involvement as within-groups variables. In order to test the relationship between scores at moral dilemmas and basic/social cognitive scores or clinical variables Pearson ρ test was used. Statistical threshold was corrected for multiple comparisons using false discovery rate (FDR). Finally, regression analysis was performed to characterize the predictors of moral judgment in MS, using moral descriptors as dependent variables and clinical, basic and social cognition scores as independent ones. Analyses were conducted using IBM SPSS Statistics for Windows v20.0 (Armonk, NY IBM Corp.) with α set at 0.05.

Table 2. Examples of stimuli from moral dilemma task

Dilemma	Scenario	Resolution
Instrumental/Self-involvement	You are the fourth of five hikers in a mountain climb. The leader just secured his rope when the second hiker starts sliding down dragging all the others with him. The group, including you, falls for tens of meters and stops on the edge of a cliff. You are too many and too heavy, and the rope will not hold all that weight.	To lighten the weight, you cut the rope between you and the last hiker. You know he will fall and die, but you and the other two hikers will be safe.
Instrumental/Other-involvement	You are the supervisor of a team working on a very big lift. Six workers are operating in the elevator shaft. You and a colleague are at the top floor, in the motor room. Suddenly the winch breaks, and the cabin starts falling.	You push your colleague into the gears, so that his body will stop the motor and the cabin will not fall. You know he will die, but the other six workers will be safe.
Incidental/Self-involvement	You are a taxi driver and you are taking two passengers at night. It has been snowing for a couple of hours and the road are dangerously iced. You turn into an alley and suddenly you find an upset truck in the middle of the road. You start breaking but the brakes do not respond and the wheels start spinning loosing grip.	You briskly turn the car towards the side of the road. You see a pedestrian, and you know he will die hit by the car, but you and the two passengers will be safe.
Incidental/Other-involvement	You are a building worker who is maneuvering a crane on a building site. You have just started your day on the site, when you realize that the cable of the crane is about to break. Attached to the cable is an enormous steel beam that is directly above a crew of six who are working on the outside of a building in construction.	You move the arm of the crane a short distance to another area of the site. You know that there is a worker there who will be crushed by the steel beam and will die, but the other six workers will be unhurt.

One stimulus per type and condition has been reported (i.e., incidental vs. instrumental and self-involvement vs. other-involvement).

Results

Basic Cognitive and Social Impairments in MS Patients

The large majority of RR-MS patients (i.e., 77.6%) showed significant impairments in the basic cognitive functions evaluated by the BICAMS scale and/or with the executive tasks. In detail, the majority of such patients (i.e., 40% of the overall sample, 18/45 patients) presented an isolated dysexecutive syndrome with impaired CET score (i.e., $n = 12$), Stroop performance (i.e., $n = 5$) or both (i.e., $n = 1$). Eleven patients (i.e., 24.4%) showed deficits in two basic cognitive domains (i.e., executive plus one among speed information processing, verbal or visuospatial learning and memory), and an isolated non-executive cognitive deficit emerged in three further patients (i.e., 6.6%) who showed either speed information processing (i.e., $n = 2$) or verbal learning and memory (i.e., $n = 1$) impaired performance. An additional 6.6% (i.e., 3/45) presented severe multi-domain impairments at basic cognitive battery. See Table 1 for details.

Emotion recognition and processing were impaired in the 24% (i.e., 11/45) of the sample. Eight out of these 11 patients also showed impairments at the basic cognitive tasks. In addition, nine patients had a borderline performance at the Ek-60F test. Notably, scores on SET were globally normal in the overall sample, with only two patients showing borderline performances.

Moral Cognition Disorders in Patients Compared to Controls

Overall, the RR-MS sample showed preserved moral judgment ability. The rate of yes/no response in resolution of moral dilemmas ($X^2(1) = 0.006$, $p = .9$) and scores of attribution of emotional valence ($F(1,88) = 0.11$, $p = .74$) were comparable between groups. Compared to HC, patients showed a different level of moral permissibility ($F(1,88) = 14.56$, $p < .001$) and emotional arousal ($F(1,88) = 6.22$, $p = .015$) particularly in instrumental dilemmas, with a significant interaction between group and type of dilemma ($F(1, 88) = 4.7$, $p = 0.03$; Fig. 1 and Table 3).

Correlation analysis showed significant inverse association between emotional valence and SET global score ($\rho = -0.32$, $p < .05$), which however did not survive the correction for multiple comparison. No further correlations were found. No significant results emerged from regression analyses. Notably, at the individual level, a subset of MS patients ($n = 6$) unimpaired at basic and social tasks showed poor performances at the moral cognition task.

Discussion

In the last few years, the interest of researchers on the investigation of social and moral cognition in neurological disorders considerably increased. This is a rather new area of cognitive psychology still poorly explored in MS. In particular, the relationships between moral and social cognition and basic cognitive functioning or clinical MS phenotypes are unexplored. In

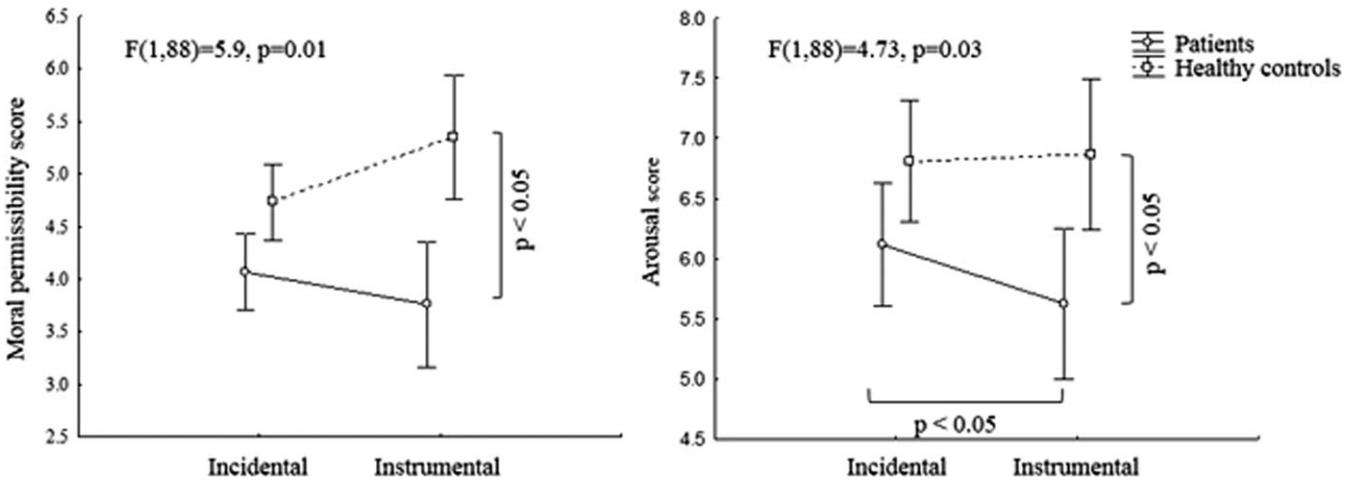

Fig. 1. Effect of interaction between type of dilemma (incidental vs. instrumental) and group (patients vs. controls) in scores of moral permissibility and emotional arousal.

Table 3. Performance at moral judgment task in RR-MS patients and healthy controls

Moral judgment										
	Type of dilemma					Type of dilemma				
	Incidental		Instrumental		Statistics	Incidental		Instrumental		Statistics
Group	RR-MS	HC	RR-MS	HC		RR-MS	HC	RR-MS	HC	
Affirmative response %	62%	64%	18%	16%	$X^2(1) = 0.1$[a] $X^2(1) = 0.3$[b]	33%	31%	48%	49%	$X^2(1) = 0.04$[c] $X^2(1) = 0.12$[d]
Moral permissibility	4.1 ± 1.4	4.7 ± 1.1	3.8 ± 2.5	5.3 ± 1.4	$F(1,88) = 5.9$*	4.1 ± 2.1	5.3 ± 1.2	3.8 ± 1.8	4.8 ± 1.1	$F(1,88) = 0.33$
Emotional valence	2.4 ± 1.1	2.3 ± 1.1	2.6 ± 1.1	2.2 ± 1.2	$F(1,88) = 0.04$	2.5 ± 1.2	2.5 ± 1.2	2.1 ± 1.1	2 ± 1.01	$F(1,88) = 0.01$
Moral arousal	6.1 ± 1.8	6.8 ± 1.6	5.6 ± 2.4	6.9 ± 1.8	$F(1,88) = 4.7$*	5.6 ± 2.3	6.7 ± 1.7	6.2 ± 2	6.9 ± 1.7	$F(1,88) = 2.6$

Comparison between RR-MS and HC in [a]incidental and [b]instrumental dilemmas, [c]self-involvement and [d]no self-involvement conditions.
RR-MS = Relapsing-Remitting Multiple Sclerosis; HC = healthy controls.

this study, we aimed to fill this lack of knowledge by exploring on a sample of RR-MS patients performances on moral dilemmas as well as non-social and social deficits and disease features.

Our data support the presence of low moral permissibility in MS. Patients harshly judged their moral behaviors, particularly in case of instrumental dilemmas. In agreement with previous authors (Gleichgerrcht et al., 2015), this shift of moral judgment towards a non-utilitarian pattern could be explained in the context of an unbalanced activation of ventromedial and dorsolateral prefrontal cortices. These brain regions are differently engaged in socio-emotional and basic cognitive processes and play crucial and mutually antagonistic roles in moral cognition processes (Greene et al., 2001, 2004). The utilitarian judgment, as compared to the non-utilitarian one, has been related to an increased activity in those brain regions associated with cognitive control, and thus to the dorsolateral prefrontal cortex (Greene et al., 2001, 2004). On the other side, a greater activity of the ventromedial prefrontal cortex, which is a key brain structure involved in socio-emotional processing (e.g., (Winecoff et al., 2013)) has been associated to instinctively emotional aversion to harm other people (Greene et al., 2001, 2004). The unbalance activation of these brain regions may thus influence moral stimuli processing in favor of a non-utilitarian decision strategy, as suggested by previous authors (Gleichgerrcht et al., 2015). However, in our sample, the rate of non-utilitarian resolution of the moral dilemmas did not differ between patients and controls ($X^2(1) = 0.006$, $p = .9$). Additional evidence from functional imaging studies are definitely required to better clarify whether moral decision difficulties in MS are related to specific regional brain damages.

Together with reduced moral permissibility, MS patients presented lower levels of emotional arousal compared to HC, particularly in the instrumental condition, suggesting an alteration in the emotional reaction rather than in the evaluation of moral dilemmas per se. This emotional detachment can be explained according to two different hypotheses. The presence of high levels of alexithymia (i.e., difficulties in identifying and describing the self-related emotional response) in MS may spoil the emotional reactivity experienced during the decision-making process related to moral dilemmas and thus result into a reduced emotional arousal (Gleichgerrcht et al., 2015). Besides, MS patients may implement coping strategies of emotional detachment during disease course in order to maintain their quality of life and obtain a better adaptation to the social context (McCabe, Stokes, & McDonald, 2009). The reduction of emotional arousal in our RR-MS sample did not agree with previous literature proving increased arousal response in patients (Gleichgerrcht et al., 2015). Differences between the structure of the moral scenarios used in this study and those applied by Gleichgerrcht and colleagues (Gleichgerrcht et al., 2015) may be responsible of result mismatch across studies. Even though the format of Gleichgerrcht's scenarios, derived by Greene (Greene et al., 2001, 2004), is more or less comparable to our, they present critical issues related to the reliability of the stimuli. Greene's scenarios have a significant number of confounding factors (e.g., emotive language or referral to close friends and family members) that affect some moral scenarios (Lotto et al., 2014). According to the item analysis reported by Lotto et al. (2014), the reactions to such items crucially drag the general effect at the task making the result poorly reliable.

A quarter of MS patients had impaired performances at both emotion recognition and socio-emotional processing tasks (see Table 1). A comparable number of patients had borderline emotion recognition Ek-60F test performance. These data suggest that socio-emotional deficits affect a large part of our patient sample (i.e., 20/45 had performances below the 10th percentile of the reference Italian population). No significant impairment of mentalizing ability emerged. Notably, in our RR-MS sample, emotionally-based social cognition (i.e., Ek-60F and RME) disorders were as frequent as executive deficits. This evidence certainly needs further confirmation on larger MS samples.

Reduced ability to recognize and share affective and mental states of others may affect emotional reaction to moral dilemmas contributing to enhance the aversion towards harming others (Gleichgerrcht et al., 2015). In agreement with this, we

found in patients a significant correlation between the emotional valence evaluation at moral task and the SET global score. Since both skills were preserved in patients, additional studies on healthy control subjects are mandatory to clarify whether this is a more general effect due to the nature of the two cognitive tasks.

At the individual level, a subset of MS patients with preserved socio-emotional skills showed poor performances at moral cognition task. This might suggests that these aspects may be somehow independent. To fortify this, moral and social cognition scores did not correlate each other and regression analysis on moral scores did not show any predictive value of basic and social performances. Further studies on different MS subgroups are needed to clarify this open question.

No correlation was found between moral or social scores and quality of life measured by MuSIQoL scale. We believe that this negative result should be interpreted considering the intrinsic features of this scale. It is indeed a reliable and valid instrument to evaluate disease-related quality of life, but it is certainly unbalanced in favor of the evaluation of the impact of motor disability in patient life. Thus, it suggests that current MS specific quality of life scale may not be useful to evaluate the impact of cognitive impairments in real life.

This study presents some limitations. First, since no information about alexithymia and empathic profile was available in our MS patients we did not test the hypothesized association (Gleichgerrcht et al., 2015) between reduced empathic abilities and lower level of moral permissibility. Then, although our results supports a damage of the thalamic–hippocampal–prefrontal circuit which is crucially engaged both in attention/executive, processing speed and memory abilities and in socio-affective and moral cognition skills (Kern et al., 2015), we cannot test the association between behavioral responses and the relative neural correlates. Finally, a larger sample size would have allowed in-depth analyses considering MS patients clinical heterogeneity.

In conclusion, the present study expand previous literature supporting emotional detachment and low acceptability of immoral actions in RR-MS, which are at least in part in relationship with socio-affective disorders. The correct perception and interpretation of socio-emotional signals, as well as a balanced reaction to moral problems, are key prerequisites to understand and predict others' behavior and plan adaptive social interactions. An unbalanced emotional reaction to moral situations may considerably influence real-life choices in MS patients, influencing employment decisions, partnership and family duties, as well as may affect the compliance to medical treatments.

Moral and social cognition represent crucial cognitive domains with relatively large effect on this chronic heterogeneous neurological condition. As proved by recent literature (see Chiaravallotti et al., 2015 for a review), maladaptive neuroplasticity occurs along the disease course in individuals with significant cognitive impairments and/or with disease progression. Functional changes due to non-invasive treatments for deficits in cognition have been shown in MS (Chiaravallotti et al., 2015). In this view, future ecological rehabilitative programs designed to treat emotionally-based social and moral cognitive disorders are to recommend.

Conflict of Interest

None declared.

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References

Bora, E., Ozakbas, S., Velakoulis, D., & Walterfang, M. (2016). Social cognition in multiple sclerosis: A meta-analysis. *Neuropsychology Review*, *26*, 160–172. doi:10.1007/s11065-016-9320-6.

Caffarra, P., Vezzadini, G., Dieci, F., Zonato, F., & Venneri, A. (2002). Una versione abbreviata del test di Stroop: dati normativi nella popolazione italiana. *Nuova Rivista di Neurologia*, *12*, 111–115.

Calabrese, P., & Penner, I. K. (2007). Cognitive dysfunctions in multiple sclerosis—A "multiple disconnection syndrome"? *Journal of Neurology*, *254*, II18–II21. doi: 10.1007/s00415-007-2006-5.

Chalah, M. A., & Ayache, S. S. (2017). Deficits in social cognition: An unveiled signature of multiple sclerosis. *Journal of the International Neuropsychological Society: JINS*, *23*, 266–286. doi:10.1017/S1355617716001156.

Chiaravalloti, N. D., & DeLuca, J. (2008). Cognitive impairment in multiple sclerosis. *Lancet Neurology*, *7*, 1139–1151. doi:10.1016/S1474-4422(08)70259-X.

Chiaravalloti, N. D., Genova, H. M., & DeLuca, J. (2015). Cognitive rehabilitation in multiple sclerosis: The role of plasticity. *Frontiers in Neurology*, *6*, 67. doi:10.3389/fneur.2015.00067.

Cotter, J., Firth, J., Enzinger, C., Kontopantelis, E., Yung, A. R., Elliott, R., et al. (2016). Social cognition in multiple sclerosis: A systematic review and meta-analysis. *Neurology*, *87*, 1727–1736. doi:WNL.0000000000003236.

Della Sala, S., MacPherson, S., Phillips, L., Sacco, L., & Spinnler, H. (2003). How many camels are there in Italy? Cognitive estimates standardised on the Italian population. *Neurological Sciences*, *24*, 10–15.

Dodich, A., Cerami, C., Canessa, N., Crespi, C., Iannaccone, S., Marcone, A., et al. (2015). A novel task assessing intention and emotion attribution: Italian standardization and normative data of the Story-based Empathy Task. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, *36*, 1907–1912. doi:10.1007/s10072-015-2281-3.

Dodich, A., Cerami, C., Canessa, N., Crespi, C., Marcone, A., Arpone, M., et al. (2014). Emotion recognition from facial expressions: A normative study of the Ekman 60-Faces Test in the Italian population. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, *35*, 1015–1021. doi:10.1007/s10072-014-1631-x.

Gleichgerrcht, E., Tomashitis, B., & Sinay, V. (2015). The relationship between alexithymia, empathy and moral judgment in patients with multiple sclerosis. *European Journal of Neurology: The Official Journal of the European Federation of Neurological Societies*, *22*, 1295–1303. doi:10.1111/ene.12745.

Goretti, B., Niccolai, C., Hakiki, B., Sturchio, A., Falautano, M., Minacapelli, E., et al. (2014). The Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS): Normative values with gender, age and education corrections in the Italian population. *BMC Neurology*, *14*, 171. doi:10.1186/s12883-014-0171-6.

Greene, J. D., Nystrom, L. E., Engell, A. D., Darley, J. M., & Cohen, J. D. (2004). The neural bases of cognitive conflict and control in moral judgment. *Neuron*, *44*, 389–400. doi:S0896627304006348.

Greene, J. D., Sommerville, R. B., Nystrom, L. E., Darley, J. M., & Cohen, J. D. (2001). An fMRI investigation of emotional engagement in moral judgment. *Science (New York)*, *293*, 2105–2108. doi:10.1126/science.1062872.

Kern, K. C., Gold, S. M., Lee, B., Montag, M., Horsfall, J., O'Connor, M. F., et al. (2015). Thalamic-hippocampal-prefrontal disruption in relapsing-remitting multiple sclerosis. *Neuroimage Clin*, *8*, 440–447. doi:10.1016/j.nicl.2014.12.015.

Lotto, L., Manfrinati, A., & Sarlo, M. (2014). A new set of moral dilemmas: Norms for moral acceptability, decision times, and emotional salience. *Journal of Behavioral Decision Making*, *27*, 57–65.

Macniven, J. A., Davis, C., Ho, M. Y., Bradshaw, C. M., Szabadi, E., & Constantinescu, C. S. (2008). Stroop performance in multiple sclerosis: Information processing, selective attention, or executive functioning? *Journal of the International Neuropsychological Society: JINS*, *14*, 805–814. doi:10.1017/S1355617708080946.

McCabe, M. P., Stokes, M., & McDonald, E. (2009). Changes in quality of life and coping among people with multiple sclerosis over a 2 year period. *Psychology, Health & Medicine*, *14*, 86–96. doi:10.1080/13548500802017682.

Moll, J., Zahn, R., de Oliveira-Souza, R., Krueger, F., & Grafman, J. (2005). Opinion: The neural basis of human moral cognition. *Nature Reviews. Neuroscience*, *6*, 799–809. doi:nrn1768.

Patil, I., Young, L., Sinay, V., & Gleichgerrcht, E. (2017). Elevated moral condemnation of third-party violations in multiple sclerosis patients. *Social Neuroscience*, *12*, 308–329. doi:10.1080/17470919.2016.1175380.

Polman, C. H., Reingold, S. C., Banwell, B., Clanet, M., Cohen, J. A., Filippi, M., et al. (2011). Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Annals of Neurology*, *69*, 292–302. doi:10.1002/ana.22366.

Pottgen, J., Dziobek, I., Reh, S., Heesen, C., & Gold, S. M. (2013). Impaired social cognition in multiple sclerosis. *Journal of Neurology, Neurosurgery, and Psychiatry*, *84*, 523–528. doi:10.1136/jnnp-2012-304157.

Serafin, M., & Surian, L. (2004). Il Test degli Occhi: uno strumento per valutare la" teoria della mente". *Giornale italiano di psicologia*, *31*, 839–862.

Taylor, R., & O'Carroll, R. (1995). Cognitive estimation in neurological disorders. *The British Journal of Clinical Psychology/the British Psychological Society*, *34*, 223–228.

Winecoff, A., Clithero, J. A., Carter, R. M., Bergman, S. R., Wang, L., & Huettel, S. A. (2013). Ventromedial prefrontal cortex encodes emotional value. *The Journal of Neuroscience*, *33*, 11032–11039. doi:10.1523/JNEUROSCI.4317-12.2013.