Multiple Sclerosis and Related Disorders 37 (2020) 101418

Contents lists available at ScienceDirect

Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard

Original article

False memories in relapsing remitting multiple sclerosis patients: A preliminary investigation with the DRM paradigm

Marco Pitteri[a,1,*], Manila Vannucci[b,1], Stefano Ziccardi[a], Maddalena Beccherle[a], Carlo Semenza[c,d], Massimiliano Calabrese[a,*]

[a] Neurology section, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[b] Department of NEUROFARBA, Section of Psychology, University of Florence, Florence, Italy
[c] Department of Neuroscience (Padova Neuroscience Centre), University of Padova, Padova, Italy
[d] IRCCS San Camillo Hospital, Lido-Venice, Italy

ARTICLE INFO

Keywords:
Multiple sclerosis
False memories
Deese-Roediger-McDermott (DRM) paradigm
Semantic networks
Semantic memory

ABSTRACT

Background: Memory impairment is one of the most frequently and early detected impairment in multiple sclerosis (MS) patients. Several authors have argued that when a failure occurs in the retrieval of lexical information, this might be due to a reduction of the lexical pool, related to semantic memory. Here we further investigated memory alteration in MS patients, by focusing on memory distortions (i.e., false memories) for semantically-related material.

Methods: A group of 40 consecutive relapsing remitting MS (RRMS) patients and a matched control group of 40 healthy controls performed the Deese-Roediger-McDermott (DRM), a false memory task for lists of associated words.

Results: At recall, RRMS patients reported a reduced number of false recalls for semantically-related but non-presented items (i.e., critical false recalls) compared to HCs; at recognition, RRMS patients showed a reduced level of confidence for false recognitions of critical items.

Conclusion: We found a reduced susceptibility to false memories in RRMS patients compared to HCs. The potential mechanisms underlying this effect are discussed in light of the alterations in the structure of semantic memory.

1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system (CNS) (Lassmann, 2016), which represents the most common non-traumatic cause of disability in young adults. MS is characterized by white matter (WM) and grey matter (GM) demyelination, axonal injury, and neurodegeneration (Kutzelnigg and Lassmann, 2014), and its pathogenesis is complex and not yet fully understood (Olsson et al., 2017).

Cognitive impairment (CI) is a common consequence of MS (Amato et al., 2006a; Grzegorski and Losy, 2017), mainly associated with GM damage (Calabrese et al., 2009; Rocca et al., 2015), also visible in the long term (Eijlers et al., 2018; Pitteri et al., 2017). Among cognitive functions, learning and memory are one of the most frequently and early detected impairment in MS patients (Amato et al., 2001; Bobholz and Rao, 2003; Chiaravalloti and DeLuca, 2008; Sepulcre et al., 2006). Although extensively debated, the pathogenesis of memory dysfunction in MS is still unclear. A key challenge still facing research in this field is whether memory impairment arise from deficits in *acquisition, retrieval*, or *both*. To this regard, some authors argued that impaired *retrieval* process is responsible for long-term memory impairment (Beatty et al., 1993; Bobholz et al., 2006; Rao et al., 1993). Conversely, other studies suggested that dysfunctions of encoding and consolidation lead to memory deficits (DeLuca et al., 1998; Thornton et al., 2002). Finally, other studies suggested different mechanisms depending on the stage of the disease, with impairment in information retrieval in the early stage of the disease and additional impairments in the encoding phase as the disease progresses (e.g., Brissart et al., 2012).

A recent behavioral study by Abad et al. (2015) pointed out that when a failure occurs in the retrieval of lexical information, this might be because of a reduction of the lexical pool, related to semantic memory. By studying a large cohort of MS patients, the authors found

* Corresponding authors.
E-mail address: marco.pitteri@univr.it (M. Calabrese).
[1] These authors contributed equally to the present work.

https://doi.org/10.1016/j.msard.2019.101418
Received 25 February 2019; Received in revised form 16 July 2019; Accepted 25 September 2019

Table 1
Demographic and clinical characteristics of RRMS patients and HC. Mean ± SD was provided for continuous variables. EDSS: Expanded Disability Status Scale. Mdn ± range was given for EDSS. *P*-value with significant level of 0.05 was used.

	RRMS (=40)	HCs (=40)	*p*
Gender (M/F)	12/28	19/21	*.168*
MoCA (raw scores)	26.4 ± 2.3	26.0 ± 2.0	*.427*
Age (years)	41.6 ± 9.2	42.3 ± 8.9	*.739*
Education (years)	13.4 ± 2.7	13.9 ± 3.9	*.524*
EDSS	2 (0–7)*	/	
Disease duration (years)	9.0 ± 8.4	/	

* Considering that the range of EDSS in our sample of MS patients range from 0 to 7, we specify that only 1 patient had an EDSS score of 7, only 1 patient had an EDSS score of 6, and only 1 patient had an EDSS score of 5. If we did not consider the EDSS of these 3 patients, the EDSS of the remaining patients (n = 37) ranged from 0 to 3.5.

that the content of semantic networks from MS patients was noticeably inferior to that of the matched control networks, in terms of both nodes and edges (i.e., relationships between nodes), despite the network complexity and cluster hierarchy of related words seemed to be preserved. The authors concluded that semantic networks of MS patients were smaller, with fewer nodes and edges scattered in a narrower distribution than that of the controls.

These behavioral findings are in line with the results of neuroimaging studies which have shown that neurologic diseases are often associated with brain damage that may differentially affect short-term connections in the GM (due to direct damage of neurons or synapses) and long-term connections in the WM (Rocca et al., 2015). Specifically, for MS patients, Rimkus et al. (2018) have shown that single-subject GM networks have fewer connections compared to controls, with the most pronounced differences shown by patients with CI. Moreover, the authors observed GM network disruptions related to specific cognitive functions: they identified the most significant loss of GM connections in the bilateral fusiform gyrus and the mesial temporal-occipital regions, implicated in visual, categorical, and also semantic memory. Other imaging studies have also reported that networks become increasingly disorganized in MS patients as related to disease progression and that these measures might be related to CI (Riccitelli et al., 2011).

Semantic verbal fluency tests are the most common methods to quantify semantic memory; however, semantic verbal fluency tests, in addition to their lexical–semantic component, are affected by executive functioning since the task involves strategy generation, monitoring of strategy success, and inhibition of previous responses. As a consequence, the use of semantic verbal fluency tests cannot exclude the reflection of other levels of cognitive impairment outside the semantic domain (Abad et al., 2015), leaving unsolved the hypothesis of a primary semantic memory impairment in MS patients.

In the present study we capitalized on these findings and we further investigated memory alterations in MS patients, by focusing on memory distortions (i.e., false memories) for semantically-related material. To this aim we used the Deese-Roediger-McDermott paradigm (hereafter called DRM; Deese, 1959; Roediger and McDermott, 1995), a robust paradigm that investigates false memories for associatively/semantically-related neutral words. In the task, participants are required to learn lists of words constructed so that all the words in the list are associates of a word not presented in the list (i.e., critical word or critical lure; e.g., bed, rest, awake…all related to sleep). After each list is presented, participants are given a free recall task and they are instructed not to guess. After participants have learned and recalled numerous lists, they are given a final overall recognition test in which learned items from the lists are mixed with the critical words (e.g., sleep) and other unrelated distractors. Studies on healthy young adults have shown that the non-presented critical word is falsely recalled with relatively high probability (i.e., from 0.40 to 0.55 in different studies). At the recognition task, the false recognition rates of the critical words approximate the hit rate (i.e., rate of correct recognition) for studied items (i.e., from 0.80 to 0.85 in different studies). When asked to do a further "Remember/Know" judgment, in most cases (0.80 or more) participants claim to remember the presentation of the critical words as frequently as they do for studied (old) words (see for a review, Gallo, 2010). According to the activation-monitoring account (Roediger et al., 2001), false memories for critical words arise because of processes occurring at both encoding and retrieval levels: while participants are listening to the DRM list, the non-presented critical word may be mentally activated (either consciously or unconsciously), due to a spread of activation across the items within a semantic network, which converges on the non-presented critical representation. If the spreading activation process occurred for the critical item, at retrieval participants would be faced with a classic reality-monitoring problem (e.g., discrimination between sources of activation).

In this preliminary study we would investigate possible semantic networks alteration in MS patients by using the DRM paradigm. If alterations in the semantic network of MS patients are present, one might hypothesize that the activation of the critical word during the encoding phase was less likely, thereby resulting in a lower amount of false memories for critical words compared to healthy controls.

2. Methods

2.1. Participants

Forty consecutive relapsing remitting MS (RRMS) patients and a matched control group of 40 healthy controls (HCs) took part in the present study. Inclusion criteria for the experimental group were diagnosis of RRMS (Polman et al., 2011), no concomitant neurological or other pathological health conditions, no relapse in the last six months before the testing phase, no substance abuse or other concomitant medications. Inclusion criteria for HCs were absence of cognitive impairment, assessed with the Montreal Cognitive Assessment (MoCA) test (Santangelo et al., 2015), absence of neurological or psychiatric conditions, and no substance abuse or medications. RRMS and HCs were recruited at the Multiple Sclerosis Center of Verona University Hospital (Verona, Italy). Demographic and clinical characteristics of the participants are provided in Table 1.

Each patient underwent a neurologic examination (including the evaluation of the expanded disability status scale, EDSS; Kurtzke, 1983) and a neuropsychological assessment consisting of the Italian version of the Brief Repeatable Battery (BRB) of neuropsychological tests (Amato et al., 2006b) and the Stroop Test (Caffarra et al., 2002).[2] Tests' scores were classified as failed according to the cut-off (fifth percentile) derived from the Italian normative data. Depression, anxiety, and stress were evaluated with the Depression Anxiety Stress Scale (DASS-21; Bottesi et al., 2015).

The study was approved by the Verona University Ethics Committee and written informed consent was obtained from all participants prior their participation in the study.

[2] The BRB is composed of tests of verbal learning and delayed episodic memory recall (Selective Reminding Test, SRT), visuo-spatial learning and delayed memory recall (10/36 Spatial Recall Test, SPART), visual information processing speed and attention (Symbol Digit Modalities Test, SDMT), auditory information processing speed, attention, and calculation (PASAT), and semantic verbal fluency on double category (word list generation, WLG). The ST is considered a measure of attention and in particular of executive functions, such as the inhibition of automatic response domain.

2.2. Stimuli

The learning phase consisted of 4 lists, each composed of 12 semantically related words. The words of each list were strongly associated with a critical item not included in the list (the *critical lure*) (see Supplemental Material). For example, for the words "hot", "snow", "winter", "ice" etc., the critical item is "cold". The recognition phase consisted of other 4 lists, composed of 12 words each (see Supplementary Materials).

The 4 lists used for the learning phase showed a probability to recall the critical item of 52% (first list), 44% (second list), 34% (third list), and 42% (fourth list). Besides, the 4 lists used for the recognition task showed a probability to recognize the critical item of 60% (first list), 53% (second list), 35% (third list), and 42% (fourth list). The total number of words used during the recognition phase was 32: 12 from the lists previously presented (3 from each of the 4 lists, in particular in position 1, 5, 8 of the serial order of presentation), 4 critical items associated with the words previously presented (1 from each of the 4 lists), 4 critical items associated with the words not previously presented (1 from each of the 4 lists), 12 new words belonging to the lists not previously presented (4 weakly associated with the lists presented and 8 completely not related with the lists presented; all of them were presented in position 1, 5, 8 of the serial order of presentation of each list).

2.3. Procedure

Participants were seated in comfortable position and tested individually in a quiet room. During the learning phase, participants were asked to listen to an electronic male voice that pronounced the 12 words of each list (lapse of 2 s between each word). Immediately after, they were asked to recall orally as many words as possible within 60 s. The study-recall cycle was repeated for all the 4 lists of words. No feedback was given to the participants regarding the accuracy of responses.

After the 4 cycles, there was a brief time interval (about 2 min) and then the participants (patients and HCs) performed the recognition task: during this phase, the examiner read the list of 32 words, listed in a pseudorandomized order, and for each word participants had to say whether the pronounced word was already presented earlier or not. For each response, participants had also to express their confidence level in a scale ranging from 1 (low confidence) to 5 (high confidence).

The experimental session was audio recorded to allow an accurate off-line analysis of the patients' responses.

2.4. Statistical analysis

Mann–Whitney *U*-tests were performed to investigate the difference between RRMS and HCs. In the recall task, the total number of critical false recalls, the total number of correct recalls, the total number of intrusions (non-critical false recalls), and the accuracy (proportion of correct recalls on the total number of recalls) served as dependent variables. In the recognition task, the number of correct recognitions (hits), the number of false recognition of critical words (false alarms to critical words), and the number of false recognition of new words (false alarms to non-critical words, which included false recognition of new-non related words and false recognition of new-weakly related words) served as dependent variables. Confidence ratings for each of these variables also served as dependent variables in the recognition task.

Spearman's correlation analyses were carried out between disease duration and significant dependent variables derived from the Mann-Whitney *U*-tests. Since we did not expect a role of EDSS on DRM performance, we did not take into account the correlation between false memories independent variables with that of physical disability (EDSS).

Table 2
RRMS patients' neuropsychological performance. Mean ± SD was provided for each test.

	RRMS (=40)	Mean ± SD	Patients scores below the cut-off
BRB	SRT-LTS	45.2 ± 12.9	3
	SRT-CLTR	34.6 ± 15.4	5
	SRT-D	8.2 ± 2.9	8
	SPART	21.5 ± 5.2	0
	SPART-D	7.1 ± 2.2	1
	SDMT	48.9 ± 12.8	6
	PASAT-3	42.2 ± 11.4	5
	PASAT-2	30.5 ± 10.0	4
	WLG	25.3 ± 5.6	2
Stroop Test	Stroop-EIT	14.3 ± 7.5	2
	Stroop-EIE	0.4 ± 0.6	0

3. Results

MS patients and HCs did not differ in gender, age, education, and global cognitive functioning (see Table 1). MS patients were classified as having normal cognition (0 failed subtest), mild cognitive impairment (up to 2 failed subtests), and severe cognitive impairment (at least 3 failed subtests) considering both the BRB and the Stroop Test (see Pitteri et al., 2017). Following this classification criterion, 21 (52.5%) MS patients were classified as having no cognitive impairment, 15 (37.5%) as having mild cognitive impairment, and 4 (10%) as having severe cognitive impairment. No patients were considered as having emotional distress as assessed by the DASS-21 (all scores were below the cut-off of clinical relevance). Detailed results about neuropsychological performance of RRMS patients are shown in Table 2.

3.1. Recall task

Results showed a significant difference between RRMS and HCs in the total number of critical false recalls ($p = .009$, $r = 0.29$): RRMS reported fewer critical false recalls (Median ± range = 1 ± 3) than HCs (Median ± range = 2 ± 4). No significant differences between the two groups were found in the other measures, that is the number of correct recalls ($p = .671$), the number of intrusions (non-critical false recalls) ($p = .988$), and accuracy ($p = .209$) (Fig. 1).

No significant correlation between the total number of critical false recalls and the years of disease duration ($p = .281$) was found.

3.2. Recognition task

No significant difference between the two groups were found in the number of correct recognitions (hits; $p = .224$), the number of false recognition of critical words ($p = .207$), and the number of false recognition of new words ($p = .956$).

With respect to confidence ratings, results showed a significant difference between RRMS and HCs in the confidence ratings of false recognition of critical words ($p = .019$, $r = 0.26$): RRMS were less confident about the critical false recognitions (Median ± range = 4.5 ± 2) than HCs (Median ± range = 4.75 ± 4). No significant difference between the two groups was found in the other confidence ratings, that is correct recognitions (hits; $p = .630$) and false recognition of new words ($p = .814$) (Fig. 2).

No significant correlation between the confidence ratings of false recognition and the years of disease duration ($p = .901$) was found.

3.3. Subgroup analysis

The group of RRMS patients included some patients with verbal memory or sematic memory deficits. As a matter of safety, since 10 RRMS patients performed below the cut-off in the test of verbal memory (i.e., the SRT) and 2 RRMS performed below the cut-off in the test of

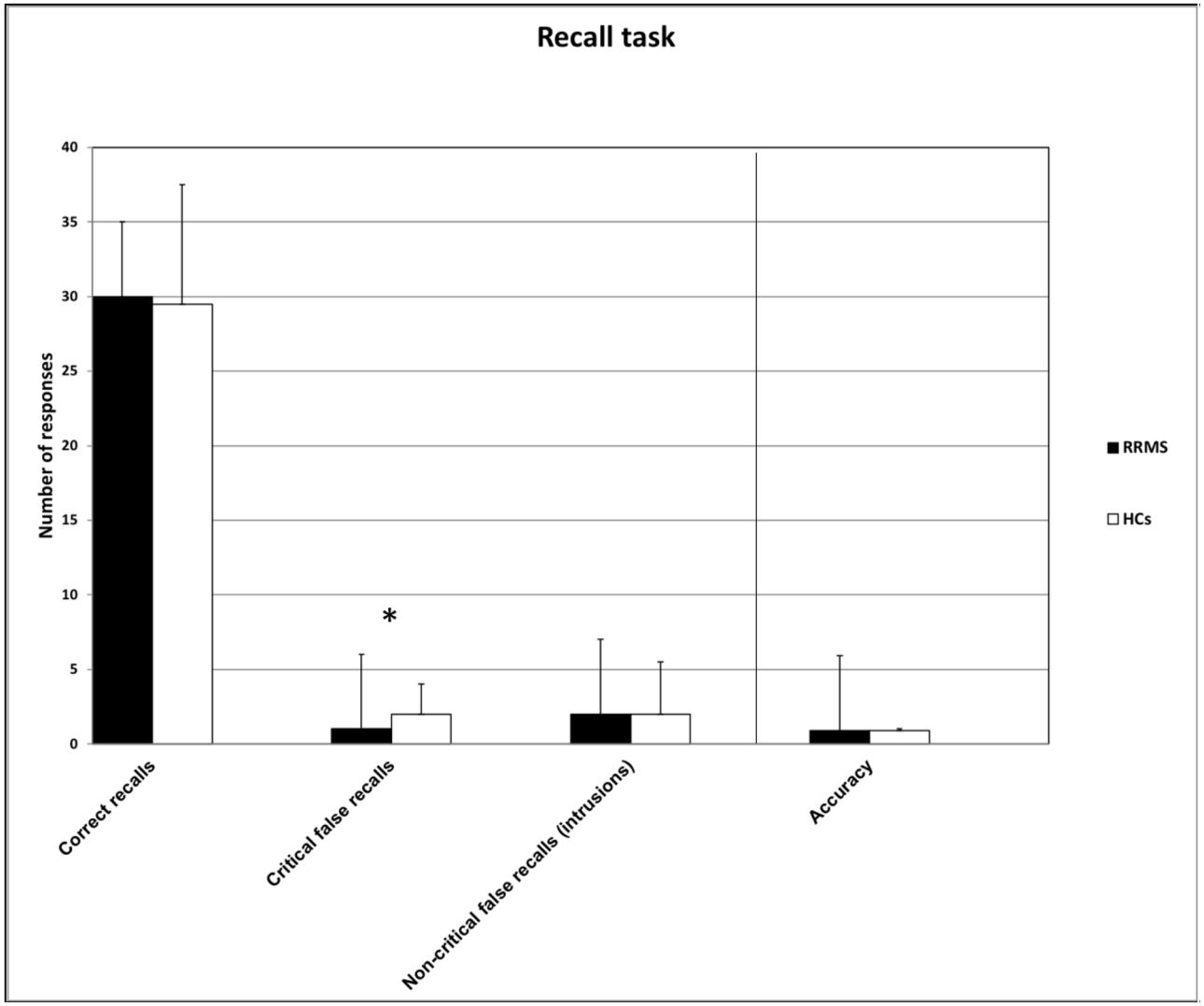

Fig. 1. Median scores of responses in the recall phase of the DRM paradigm. Error bars represent range of scores. Black bars: RRMS patients; white bars: HCs. Significance: $*=p < .05$.

semantic fluency (i.e., the WLG), we ran the same analyses excluding these 12 patients (new $n = 28$). The two groups (RRMS vs. HCs) did not differ in age ($p = .54$) and education ($p = .91$). At the recall task, the results confirmed a significant difference in the total number of critical false recalls between the two groups ($p = .024$, $r = 0.27$). Also at the recognition task, the results confirmed a significant difference in the confidence ratings of false recognition of critical words ($p = .029$, $r = 0.26$) between the two groups. No other comparisons reached the statistical significance (all $p > 0.05$).

4. Discussion

The present study aimed at investigating veridical and false memory for associatively/semantically related material in MS patients, by using the Deese/Roediger–McDermott false memory paradigm (DRM; Deese, 1959; Roediger and McDermott, 1995). The results showed that the group of RRMS patients were less likely to falsely recall highly related but non-presented items (critical false recalls) than the group of HCs. Moreover, at the recognition task, RRMS patients showed a reduced level of confidence for false recognitions of critical items.

To the best of our knowledge, this is the first report describing memory distortions, and specifically false memories for semantically-related words, in a group of RRMS patients. The most interesting finding of our study is the reduced susceptibility to this kind of false memories in RRMS patients compared to HCs.

Such an effect could possibly be due to alterations in the semantic memory networks in MS patients. To this regard, a recent study by Abad et al. (2015) has shown that MS patients are characterized by an alteration in the connectivity of semantic networks that involves reduced number of nodes (words) and links (significant associative relationship between words), besides reduced cohesive force of the network. On the basis of functional efficacy of semantic networks (Goñi et al., 2011), a higher number of nodes means a higher number of information stored in the semantic memory, while a higher number of connections between nodes represents an indicator of the ability to retrieve information.

In the light of these findings, we suggest that the reduced number of critical false recalls found in the group of RRMS patients might arise from alterations in the structure of semantic memory. In RRMS patients, the alteration of semantic networks might interfere with the activation of semantic associates from the list words during the acquisition phase, thereby reducing the likelihood of critical false recalls.

In the recognition task, the two groups did not differ in the number of false recognitions for critical items but differed in their level of confidence: RRMS patients were less confident in their false recognitions for critical items than HCs. Nevertheless, the two groups exhibited

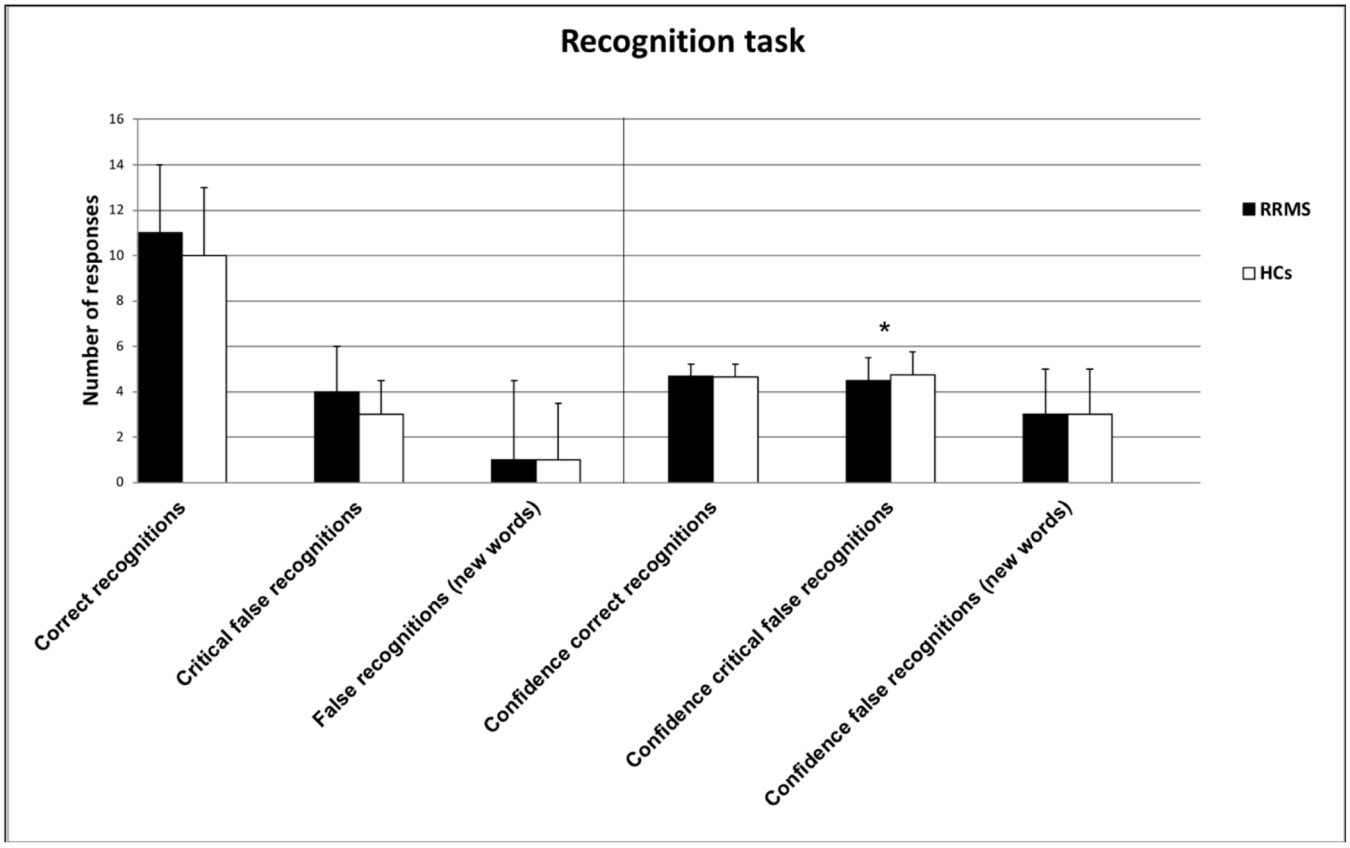

Fig. 2. Median scores of responses in the recognition phase of the DRM paradigm. Error bars represent range of scores. Black bars: RRMS patients; white bars: HCs. Significance: * = $p < .05$.

similar levels of confidence in their correct recognition responses to learned items. Previous studies have shown that normal individuals experience false recognitions for critical items accompanied by *strong* feelings of recollection, as indicated by a high level of confidence (for a review, Roediger and McDermott, 2000). The reduced level of confidence for false recognitions reported by RRMS patients provided further support for the presence of a less robust false remembering in RRMS patients compared to HCs.

The reduced susceptibility to false memories for critical words shown by RRMS patients could not be ascribed to an impairment in verbal memory, since we could get the same pattern of results when we limited the analyses to the subgroup of patients without deficits in verbal memory and semantic fluency as assessed with the SRT and the WLG, respectively.

However, some limitations of the present study should be considered when interpreting the results. First, the sample size was relatively small, considering the high heterogeneity of clinical characteristics of MS patients: therefore, studies with higher number of MS patients, stratified considering MS type and other neurological characteristics, e.g., disease duration and disease type, are needed. Second, this study did not include analysis of advanced structural neuroimaging, which could shed light on the neuroanatomical organization that promotes semantic networks alteration associated with false memories.

Despite these limitations, the present study makes a first exploratory contribution to our understanding of semantic memory mechanisms and distortions shown by RRMS patients, a topic that has been neglected for a long time and that might have important implications also in clinical setting. To this regard, although it is well known that MS is characterized by neurodegeneration and demyelination, subtle cognitive changes and initial alterations in semantic networks might not be evident in classic neuropsychological examination. Including the DRM paradigm in the cognitive assessment might provide more sensitive information about the functioning of semantic memory networks in MS patients that might be associated with the course of degenerative processes underlying the disease.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

This study was approved by the local Ethic Committee (University of Verona, Italy).

Informed consent

The informed consent was obtained from all individual participants included in the study.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

Acknowledgements

We would like to thank all participants for their time and effort in taking part in the present study. We are grateful to Viola Miranda for her help in data collection.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.msard.2019.101418.

References

Abad, E., Sepulcre, J., Martinez-Lapiscina, E.H., Zubizarreta, I., Garcia-Ojalvo, J., Villoslada, P., 2015. The analysis of semantic networks in multiple sclerosis identifies preferential damage of long-range connectivity. Mult. Scler. Relat. Disord. 4 (5), 387–394.

Amato, M.P., Ponziani, G., Rossi, F., Liedl, C.L., Stefanile, C., Rossi, L., 2001. Quality of life in multiple sclerosis: the impact of depression, fatigue and disability. Mult. Scler. J. 7 (5), 340–344.

Amato, M.P., Zipoli, V., Portaccio, E., 2006a. Multiple sclerosis-related cognitive changes: a review of cross-sectional and longitudinal studies. J. Neurol. Sci. 245 (1–2), 41–46.

Amato, M.P., Portaccio, E., Goretti, B., Zipoli, V., Ricchiuti, L., Caro, M.F.De, …, Trojano, M., 2006b. The Rao's brief repeatable battery and Stroop test: normative values with age, education and gender corrections in an Italian population. Mult. Scler. J. 12 (6), 787–793.

Beatty, W.W., 1993. Cognitive and emotional disturbances in multiple sclerosis. Neurol. Clin. 11 (1), 189–204.

Bobholz, J.A., Rao, S.M., 2003. Cognitive dysfunction in multiple sclerosis: a review of recent developments. Curr. Opin. Neurol. 16 (3), 283–288.

Bobholz, J.A., Rao, S.M., Lobeck, L., Elsinger, C., Gleason, A., Kanz, J., Maas, E., 2006. fMRI study of episodic memory in relapsing-remitting MS: correlation with T2 lesion volume. Neurology 67 (9), 1640–1645.

Bottesi, G., Ghisi, M., Altoè, G., Conforti, E., Melli, G., Sica, C., 2015. The Italian version of the Depression Anxiety Stress Scales-21: factor structure and psychometric properties on community and clinical samples. Compr. Psychiatry 60, 170–181.

Brissart, H., Morele, E., Baumann, C., Debouverie, M., 2012. Verbal episodic memory in 426 multiple sclerosis patients: impairment in encoding, retrieval or both? Neurolo. Sci. 33 (5), 1117–1123.

Caffarra, P., Vezzadini, G., Dieci, F., Zonato, F., & Venneri, A. (2002.). Una versione abbreviata del test di Stroop: dati normativi nella popolazione Italiana.

Calabrese, M., Agosta, F., Rinaldi, F., Mattisi, I., Grossi, P., Favaretto, A., Perini, P., 2009. Cortical lesions and atrophy associated with cognitive impairment in relapsing-remitting multiple sclerosis. Arch. Neurol. 66 (9), 1144–1150.

Chiaravalloti, N.D., DeLuca, J., 2008. Cognitive impairment in multiple sclerosis. Lancet Neurol. 7 (12), 1139–1151.

Deese, J., 1959. On the prediction of occurrence of particular verbal intrusions in immediate recall. J. Exp. Psychol. 58 (1), 17–22.

DeLuca, J., Gaudino, E.A., Diamond, B.J., Christodoulou, C., Engel, R.A., 1998. Acquisition and storage deficits in multiple sclerosis. J. Clin. Exp. Neuropsychol. 20 (3), 376–390.

Eijlers, A.J., van Geest, Q., Dekker, I., Steenwijk, M.D., Meijer, K.A., Hulst, H.E., Geurts, J.J., 2018. Predicting cognitive decline in multiple sclerosis: a 5-year follow-up study. Brain 141 (9), 2605–2618.

Gallo, D.A., 2010. False memories and fantastic beliefs: 15 years of the DRM illusion. Mem. Cognit. 38 (7), 833–848.

Goñi, J., Arrondo, G., Sepulcre, J., Martincorena, I., de Mendizábal, N.V., Corominas-Murtra, B., Villoslada, P., 2011. The semantic organization of the animal category: evidence from semantic verbal fluency and network theory. Cogn. Process. 12 (2), 183–196.

Grzegorski, T., Losy, J., 2017. Cognitive impairment in multiple sclerosis–a review of current knowledge and recent research. Rev. Neurosci. 28 (8), 845–860.

Kurtzke, J.F., 1983. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology 33 (11), 1444–1452.

Kutzelnigg, A., Lassmann, H., 2014. Pathology of multiple sclerosis and related inflammatory demyelinating diseases. Handbook of Clinical Neurology 122. Elsevier, pp. 15–58.

Lassmann, H., 2016. Demyelination and neurodegeneration in multiple sclerosis: the role of hypoxia. Ann. Neurol. 79 (4), 520–521.

Olsson, T., Barcellos, L.F., Alfredsson, L., 2017. Interactions between genetic, lifestyle and environmental risk factors for multiple sclerosis. Nat. Rev. Neurol. 13 (1), 25.

Pitteri, M., Romualdi, C., Magliozzi, R., Monaco, S., Calabrese, M., 2017. Cognitive impairment predicts disability progression and cortical thinning in MS: an 8-year study. Mult. Scler. J. 23 (6), 848–854.

Polman, C.H., Reingold, S.C., Banwell, B., Clanet, M., Cohen, J.A., Filippi, M., …, Wolinsky, J.S., 2011. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. Ann. Neurol. 69 (2), 292–302.

Rao, S.M., Grafman, J., DiGiulio, D., Mittenberg, W., Bernardin, L., Leo, G.J., Unverzagt, F., 1993. Memory dysfunction in multiple sclerosis: its relation to working memory, semantic encoding, and implicit learning. Neuropsychology 7 (3), 364.

Riccitelli, G., Rocca, M.A., Pagani, E., Rodegher, M.E., Rossi, P., Falini, A., Filippi, M., 2011. Cognitive impairment in multiple sclerosis is associated to different patterns of gray matter atrophy according to clinical phenotype. Hum. Brain Mapp. 32 (10), 1535–1543.

Rimkus, C.M., Schoonheim, M.M., Steenwijk, M.D., Vrenken, H., Eijlers, A.J., Killestein, J., Tijms, B.M., 2018. Gray matter networks and cognitive impairment in multiple sclerosis. Mult. Scle. J 1352458517751650.

Rocca, M.A., Amato, M.P., De Stefano, N., Enzinger, C., Geurts, J.J., Penner, I.K., MAGNIMS Study Group, 2015. Clinical and imaging assessment of cognitive dysfunction in multiple sclerosis. Lancet Neurolo. 14 (3), 302–317.

Roediger, H.L., McDermott, K.B., 1995. Creating false memories: remembering words not presented in lists. J. Exp. Psychol. 21 (4), 803–814.

Roediger, H.L., McDermott, K.B., 2000. Distortions of memory. The Oxford Handbook of Memory. pp. 149–162.

Roediger III, H.L., Balota, D.A., Watson, J.M., 2001. Spreading activation and arousal of false memories. The Nature of Remembering: Essays in Honor of Robert G. Crowder. pp. 95–115.

Santangelo, G., Siciliano, M., Pedone, R., Vitale, C., Falco, F., Bisogno, R., …, Trojano, L., 2015. Normative data for the montreal cognitive assessment in an Italian population sample. Neurolo. Sci. 36 (4), 585–591.

Sepulcre, J., Vanotti, S., Hernández, R., Sandoval, G., Cáceres, F., Garcea, O., Villoslada, P., 2006. Cognitive impairment in patients with multiple sclerosis using the Brief Repeatable Battery-Neuropsychology Test. Mult. Scler. J. 12 (2), 187–195.

Thornton, A.E., Raz, N., Tucker, K.A., 2002. Memory in multiple sclerosis: contextual encoding deficits. J. Int. Neuropsychol. Soc. 8 (3), 395–409.