

Social Cognition in patients with Relapsing-Remitting Multiple Sclerosis

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Abstract: Background: Relapsing-Remitting Multiple Sclerosis (RRMS) is characterized by new or recurrent episodes of neurological dysfunction followed by partial or complete recovery. A remarkable non-motor symptom of the disease is the impairment of Social Cognition, and in particular the impairment of Theory of Mind (ToM) that shows the highest frequency of dysfunction; Objective: To quantify the deficits in both cognitive and affective ToM in patients with RRMS, and to analyze the relationship between ToM, longer disease duration and gender; Methods: In our study, we administered the «Faux Pas» test to 20 patients with RRMS to assess both cognitive and affective ToM; Results: Our patients showed more prominent deficits in cognitive ToM in comparison to affective ToM. It was also found that the disease duration has an important impact on ToM; Conclusions: RRMS affects ToM, especially cognitive ToM, whilst the longer the duration of RRMS the greater the impairment of ToM.

Keywords: multiple sclerosis; relapsing-remitting; social cognition; theory of mind; cognitive theory of mind; affective theory of mind; faux pas

1. Introduction

Multiple Sclerosis (MS) is an autoimmune, demyelinating and neurodegenerative disease of the Central Nervous System (CNS). It is characterized by autoimmune processes, neuroinflammation, demyelination, neurodegeneration and remyelination [1,2]. Relapsing-Remitting Multiple Sclerosis (RRMS) is the predominant phenotype of MS and is characterized by new or repeated episodes of neurological dysfunction, lasting from a few days to several months, followed by partial or complete recovery [3-5].

The symptoms of MS depend on the phenotype of the disease, as well as the location of the lesion. As the disease proceeds, symptoms become more permanent and can lead to progressive disability [6]. Clinical symptoms of MS include both motor and non-motor dysfunction [2,7]. One of the most important non-motor symptoms is cognitive impairment [8]. This symptom can occur in all stages of the disease, even the earliest, and can be a key factor of disability, social impairment and poor quality of life [9]. However, the non-motor symptoms are not given the same attention as the motor symptoms [2] and only the last decades did cognitive deficits begin to be considered as a frequent symptom of the disease [10].

One of the cognitive functions affected by the diffuse pathologic processes seen in the MS is social cognition [11,12]. Social cognition (SC) is defined as the neurocognitive ability required to process social information [13], and involves the encoding, representation and interpretation of information regarding other people and the self [14,15]. SC is a multi-dimensional construct that includes Theory of Mind (ToM), empathy, and social

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perception of emotions from prosody, facial and body gestures [14,16]. The two core aspects of SC are Facial Emotion Recognition and ToM, which collectively drive interpersonal skills [17], such as empathy, and may have important implications on social functioning [18].

One of the core aspects of SC is ToM, that is the ability to interpret and infer the intentions or feelings of others based on their behavior [11,19,20], and to understand that others have their own beliefs, intentions and emotions that may differ from one's own [21,22]. ToM consists of two components: cognitive ToM, which is the ability to understand the beliefs, thoughts and intentions of others, and affective ToM, which is the ability to understand the emotional state of others [15,23].

Social cognitive impairment is common in patients with MS and affects all stages of the disease and all types of clinical course, even Clinically Isolated Syndrome (CIS) [23], with ToM dysfunction, among SC aspects, showing the highest frequency of impairment [24], and mainly cognitive ToM [10]. Additionally, research shows that long disease duration, increasing disability and fast progression of the disease are factors associated with greater deficits in ToM [13,25], whereas regarding the gender differences in ToM, females appear to have less deficits in this ability in comparison to males [26]. Hence, recent studies highlight the presence of social cognitive deficits in MS as an unveiled signature of the disease pathology [27].

Social cognition has a huge impact on interpersonal communication and subsequently on quality of life (QoL) [5,16,28]. More specifically, social cognitive abilities are important for maintaining social relationships and, consequently, for preserving the wider social network, which contributes to the patient's QoL [13]. Humans are profoundly social beings, therefore successful social communication is essential for their well-being [23]. Additionally, preserved social cognition has been found to contribute to long-term maintenance of QoL [13]. Therefore, continuous and correct screening for such deficits is important to improve patients' QoL [16], as the early detection of the deficits and the adequate rehabilitation of social cognition could help patients enjoy a satisfying social life for a longer period [23].

Nevertheless, social cognitive impairment remains a neglected aspect of cognitive impairment in MS, even though there is potential prognostic significance for social functioning and QoL of patients with MS [17,18].

The aim of our study was to assess ToM in patients with RRMS and to investigate the differences between cognitive and affective ToM performance by administering the «Faux Pas» test. Furthermore, we studied the effect the duration of RRMS and the gender of the patient have on ToM. We decided to study further this ability since, only the last few decades have scientists begun to conduct research studies on SC in MS, and little is known about the impact of MS on SC regarding the Greek area.

2. Materials and Methods

2.1. Study population

Patients with a definite diagnosis of RRMS from the Special Multiple Sclerosis Outpatient Clinic of 1st Neurology Clinic of AHEPA University Hospital took part in our study.

Inclusion criteria for our patients were the age between 18-65 years old, the Northern Greek origin, the fluency in Greek, and the absence of other chronic diseases or any other psychiatric disorder.

2.2. Social cognitive testing

Our participants underwent the neuropsychological test that was selected to evaluate global functioning of ToM and shows sensitivity to the impairment of both cognitive and

affective ToM. Specifically, we administered the «Faux Pas» test validated and performed in Greek.

«Faux Pas» is a verbal test [16] that evaluates both cognitive and affective ToM [29]. In the test, the examiner reads aloud 20 short vignettes to the participant, who is at the same time given the written version of each story in front of them in order to reduce their memory load. In 10 of the stories, a person commits a social faux pas, an indecency, by unintentionally saying something distressing or offensive to another person. In the remaining 10 stories no faux pas is committed [10]. There is no time limit, therefore participants are allowed to read the stories as many times as necessary to fully comprehend them [30]. At the end of each story, the participant is asked whether anything inappropriate was mentioned [31]. Correct answers were rated 1, incorrect answers were rated 0 [17]. The maximum score at the «Faux Pas» test is 80 points [32].

A faux pas occurs when someone says something they should not have said, not knowing or realizing that they should not have said it. To understand that a faux pas has occurred, one must perceive two mental states: the cognitive state and the emotional state. In order to attribute a cognitive state, it must be understood that the person who says something socially inappropriate does not comprehend that he should not say it. Then, in order to attribute an emotional state of mind, it must be understood that the person hearing it would feel offended or hurt [33]. Thus, the «Faux Pas» test requires the simultaneous understanding of multiple mental states (i.e., intentions, emotions, beliefs) in everyday social situations [30].

Therefore, the «Faux Pas» test is a good measure of subtle ToM deficits [33]. In particular, cognitive ToM is assessed in the false belief question (question #5), which evaluates whether participants understand the false beliefs of the person who committed a faux pas, whereas affective ToM is assessed in the affective question (question #6), which evaluates whether participants understand how the person in the story would feel [30].

2.3. Data collection

In our study, we administered 4 vignettes of the «Faux Pas» test, two of which were control stories and the other two were faux pas stories. The stories were presented alternately, in order to avoid any influence the order of the story presentation might have on the study results.

The social cognitive assessment was held in person. Patients were tested individually. They were given a sheet with the «Faux Pas» stories printed on and were asked to pay attention to the examiner's narration and following questions. The administration of «Faux Pas» test took approximately 10 minutes.

3. Results

All statistical analyses performed in our research were carried out using the statistical software platform SPSS 27.

3.1. Demographic data

20 patients with RRMS voluntarily participated in the study. Specifically, the sample consisted of 9 men (45%) and 11 women (55%). The participants originated from the geographical regions of Macedonia and Thrace, and more precisely from the prefectures of Thessaloniki, Komotini and Florina.

The age of the participants ranged from 18 to 65 years old (M. = 43.94, S.D. = 12.53) (Table 1) and the percentages distributed in the following way: the group age 18-35 assembles 20% of the sample, the groups 36-45 and 46-55 gather 25% respectively, and group age 56-56 20% (Table 2).

Table 1
Means and Standard Deviation

N	Valid	18
	Missing	2
Mean		43,94
Std. Deviation		12,530

147
148

Table 2
Age: Frequencies and percentages

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	18-35	4	20,0	22,2
	36-45	5	25,0	27,8
	46-55	5	25,0	27,8
	56-65	4	20,0	22,2
	Total	18	90,0	100,0
Missing System	2	10,0		
Total	18	90,0		

149
150
151
152

Regarding the educational level of the participants, 35% of the sample consisted of high school graduates and 35% of bachelor's graduates, gathering together the majority of the participants (Table 3).

153

154
155
156

Table 3
Education: Frequencies and percentages

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Primary School Graduate	1	5,0	5,0
	Junior High School Graduate	1	5,0	10,0
	High School Graduate	7	35,0	35,0
	Bachelor's Degree	7	35,0	35,0
	Master's Degree	3	15,0	15,0
	Doctor's Degree	1	5,0	5,0
	Total	20	100,0	100,0

157
158
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Finally, regarding the professional status of the participants, most of the participants worked as civil servants (30%) and private employees (30%), however, a significant percentage of the participants were unemployed (20%) (Table 4).

Table 4
Profession: Frequency and percentages

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Civil Servant	6	30,0	30,0	30,0
	Private Employee	6	30,0	30,0	60,0
	Freelancer	1	5,0	5,0	65,0
	Unemployed	4	20,0	20,0	85,0
	Retired	3	15,0	15,0	100,0
	Total	20	100,0	100,0	

3.2. Neuropsychological Data

As shown in Table 5 and Table 6, almost all participants answered correctly to the Control Stories of the «Faux Pas» test. However, one participant answered incorrectly to both vignettes by recognizing a non-existent faux pas.

Table 5
Frequencies and percentages of the 1st Faux Pas Story

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Incorrect	1	5,0	5,0	5,0
	Correct	19	95,0	95,0	100,0
	Total	20	100,0	100,0	

Table 6
Frequencies and percentages of the 3rd Faux Pas Story

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Incorrect	2	10,0	10,0	10,0
	Correct	18	90,0	90,0	100,0
	Total	20	100,0	100,0	

As shown in Table 7 and Table 8, 8 participants respectively answered correctly to all questions of the Faux Pas Stories. However, in each faux pas story there was one participant who answered incorrectly to the vignette by not recognizing the existent faux pas.

Table 7
Frequencies and percentages of the 2nd Faux Pas Story

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	All answers incorrect	1	5,0	5,0	5,0
	3 answers incorrect	1	5,0	5,0	10,0
	2 answers incorrect	2	10,0	10,0	20,0
	1 answer incorrect	8	40,0	40,0	60,0
	All answers correct	8	40,0	40,0	100,0
	Total	20	100,0	100,0	

Table 8
Frequencies and percentages of the 4th Faux Pas Story

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	All answers incorrect	1	5,0	5,0	5,0
	2 answers incorrect	5	25,0	25,0	30,0
	1 answer incorrect	6	30,0	30,0	60,0
	All answers correct	8	40,0	40,0	100,0
	Total	20	100,0	100,0	

Moreover, to assess cognitive and affective ToM, we examined the participants' incorrect answers to the Faux Pas Stories, specifically the answers given at Question 5 (Q5) and Question 6 (Q6) of the vignettes, since Q5 evaluates the participant's ability to perceive if the faux pas happens unintentionally (cognitive ToM), and Q6 evaluates the participant's ability to perceive how the person in the story would feel (affective ToM).

As shown in Table 9, 6 participants answered incorrectly to Q5 of the first Faux Pas Story, 4 participants answered incorrectly to Q6, whereas one participant answered both Q5 and Q6 incorrectly.

Table 9
Frequencies and percentages of Q5 and Q6 in 2nd Faux Pas Story

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Q5 and Q6 Incorrect	1	9,1	9,1	9,1
	Q6 Incorrect	4	36,4	36,4	45,5
	Q5 Incorrect	6	54,5	54,5	100,0
	Total	11	100,0	100,0	

However, in the second Faux Pas Story, 5 participants answered incorrectly to Q5, and one participant answered both Q5 and Q6 incorrectly, with Q6 not having been answered incorrectly by the other 10 participants (Table 10).

Table 10
Frequencies and percentages of Q5 and Q6 in 4th Faux Pas Story

		Frequency	Percent
Valid	Q5 and Q6 Incorrect	1	9,1
	Q6 Incorrect	-	-
	Q5 Incorrect	5	45,5
	Total	11	100,0

Furthermore, to evaluate the relationship between ToM and the RRMS duration, we executed the Pearson Correlation Coefficient to find the statistically significant correlation between the disease duration and the «Faux Pas» test performance.

As shown in Table 11, there is a statistically significant negative correlation between the RRMS duration and the total performance at the «Faux Pas» test ($r = -.548, p < .05$), meaning that the participants who lived with RRMS for a longer period, performed worse at the «Faux Pas» test.

Table 11
Correlation between the variables

		Years living with RRMS	Total Score Faux Pas
Years living with RRMS	Pearson Correlation	1	-.548*
	Sig. (2-tailed)	-	.012
	N	20	20
Total Score Faux Pas	Pearson Correlation	-.548*	1
	Sig. (2-tailed)	.012	-
	N	20	20

*. Correlation is significant at the 0.05 level (2-tailed).

Moreover, we performed the Simple Linear Regression to predict the deficits in ToM depending on the duration of RRMS. In the statistical analysis, the RRMS duration was the predictor variable, whereas the ToM performance was the dependent variable.

Based on the results of the Simple Linear Regression analysis ($r^2 = .3, beta = -.548, t = -2.8, p < .05$) (Table 12), we concluded that the RRMS duration negatively predicts ToM deficits by 30%.

Table 12
Simple Linear Regression values

	r ²	beta	t	p-value
Years living with RRMS	.300	-.548	-2.777	.012

Finally, in order to detect the gender differences of RRMS participants at the «Faux Pas» test performance, we applied the Independent Samples t-test analysis. In the statistical analysis, the participants' gender was the grouping variable, whereas the total «Faux Pas» test performance was the test variable.

However, in our analysis we found no statistically significant effect of the RRMS patients' gender on ToM.

4. Discussion

The aim of our study was to investigate the relationship between Social Cognition (Theory of Mind) and Multiple Sclerosis (Relapsing-Remitting). Secondly, we wanted to examine the differences between RRMS patients' Cognitive Theory of Mind and Affective Theory of Mind in terms of the «Faux Pas» test performance. In addition, we aimed to study the effect of the patients' gender and the duration of the disease on Theory of Mind.

Regarding the relationship between ToM and RRMS, the results of our research showed that the performance of most participants was slightly to considerably deficient. Our finding is consistent with other studies, which suggest that RRMS shows deficits in ToM, even though not as great as the deficits due to progressive MS [13], and that ToM can be impaired even in the early stages of RRMS [14]. A possible interpretation of this finding could be the fact that the pathologic processes observed in RRMS, particularly the neurodegeneration that is present from the early stages of the disease, could be responsible for the impairment of ToM [34].

Moreover, concerning cognitive and affective ToM and RRMS, the participants of our research showed more deficits on cognitive ToM ability in contrast with affective ToM. This finding is in accord with existing literature referring to cognitive ToM ability being more impaired than affective ToM in patients with RRMS [10]. A probable explanation of this finding could be the fact that the brain regions associated with cognitive ToM (frontal regions) are affected earlier by RRMS than the brain regions associated with affective ToM (temporal regions) [28].

Furthermore, with respect to the RRMS duration and ToM ability, the results of our research suggested that the disease duration has a negative impact on ToM performance. This result is in line with other studies referring to more prominent deficits in ToM in patients with longer disease duration [23, 27]. One possible interpretation of this research finding could be the fact that the neurodegeneration occurring in RRMS has a significant impact on ToM functioning [11].

Finally, as far as the RRMS patients' gender and ToM ability are concerned, the non-statistically significant results of our analysis did not allow us to make any conclusions regarding the gender effect on ToM ability. However, this result is inconsistent with existing literature mentioning that women perform better than men at the «Faux Pas» test, thus demonstrating fewer deficits in ToM compared to men [26].

Several limitations of the present study are to be considered. One limitation of our study was the sample size that is relatively small (20 participants), due to the special conditions arising from the COVID-19 pandemic. The small sample size limits the validity of the results and any population generalizability. Another shortcoming was the small number of «Faux Pas» test Stories administered (4), which may not represent the participants' ToM ability to a large extent. Ultimately, a further limitation of our research was the cross-sectional type of study, as specific age groups were studied and compared in a specific period. This method does not allow the accurate demonstration of the changes over time. Future longitudinal research could be conducted to represent the social cognitive changes of MS patients occurring with time. Future research including the other phenotypes of MS is also needed to better understand the impairment of ToM, and subsequently the impairment of SC, in MS.

Despite the limitations, the results of this study could be useful to both scientists and health professionals. The aim of our research was to inform and raise awareness among experts regarding the social cognitive deficits of patients with MS, an aspect of the disease

that remains overlooked despite its prognostic value [17,18]. Therefore, it is necessary to integrate the evaluation of social cognition in the main neuropsychological assessment of MS patients, and encourage the continuous and correct screening, in order to facilitate the early detection of the deficits and to preserve the social cognitive ability for a longer period and, subsequently, the satisfactory QoL [13,16,23].

5. Conclusions

In conclusion, RRMS negatively affects ToM, especially cognitive ToM. We also conclude that the longer the duration of RRMS the greater the impairment of ToM.

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