

## Social cognition in a cohort of Greek 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) which 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 compared to affective ToM. It was also found that the disease duration has an important impact on ToM.

**Conclusion:** Social cognitive deficits including theory of mind are an underestimated but important aspect of cognitive disorders in MS patients even with a lack of marked cognitive decline and disability with the potential effect of disease duration (short vs long evolution) on MS individuals' performance.

**Keywords:** Multiple sclerosis; RRMS; Social cognition; Theory of mind; Cognitive theory of mind; Affective theory of mind; Faux pas.

### Introduction

Multiple Sclerosis (MS) is an autoimmune, demyelinating, and neurodegenerative disease of the Central Nervous System (CNS). It is characterized by autoimmune processes, neuroinflammation, demyeli-

nation, neurodegeneration, and remyelination [1,2]. Relapsing-Remitting Multiple Sclerosis (RRMS) is the predominant phenotype of MS. It 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 in 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 in the last decades did cognitive deficits begin to be considered a frequent symptom of the disease [10].

One of the cognitive functions affected by the diffuse pathologic processes seen in 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 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, which 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 courses, 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 the 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].

Our study aimed 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 of the duration of RRMS and the gender of the patient on the ToM. We decided to study further this ability since only in 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 population.

## Materials and Methods

### Study population

Patients with a definite diagnosis of RRMS from the Multiple Sclerosis Outpatient Clinic of the 1<sup>st</sup> Department of Neurology, AHEPA University Hospital, took part in our study.

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

### Social cognitive testing

Our participants underwent the neuropsychological test that was selected to evaluate the global functioning of ToM and showed 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 to reduce their memory load. In 10 of the stories, a person commits a social faux pas, 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 one «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. 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, 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].

### 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, 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 it and were asked to pay attention to the examiner's narration and the following questions. The administration of the «Faux Pas» test took approximately 10 minutes.

### Results

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

### Demographic data

Twenty (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 ( $M.=42,55$ ,  $S.D.=12,62$ ) (Table 1), and the percentages were distributed in the following way: those aged 18-35 assembled 30% of the sample, the groups' 36-45 and 46-55 gather 25% respectively, and group age 56-65 20% (Table 2).

**Table 1:** Means and standard deviation.

N	Valid	18
Mean		42,55
Std. Deviation		12,622

**Table 2:** Age: Frequencies and percentages.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	18-35	6	30,0	30,0	30,0
	36-45	5	25,0	25,0	55,0
	46-55	5	25,0	25,0	80,0
	56-65	4	20,0	20,0	100,0
Total		20	100,0		

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

**Table 3: Education:** Frequencies and percentages.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Primary school graduate	1	5,0	5,0	5,0
	Junior high school graduate	1	5,0	5,0	10,0
	High school graduate	7	35,0	35,0	45,0
	Bachelor's degree	7	35,0	35,0	80,0
	Master's degree	3	15,0	15,0	95,0
	Doctor's degree	1	5,0	5,0	100,0
	Total	20	100,0	100,0	

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:** Frequencies 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	

### 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, and one participant answered incorrectly to only 1 out of 2 Control Stories. Therefore, both participants showed, to some degree, an enhanced ToM, since both attributed intentions to someone who had no intent.

**Table 5:** Frequencies and percentages of the 1<sup>st</sup> 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 3<sup>rd</sup> 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 2<sup>nd</sup> 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 4<sup>th</sup> 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 in 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 2<sup>nd</sup> 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 the 4<sup>th</sup> Faux Pas story.

		Frequency	Percent
Valid	Q5 and Q6 incorrect	1	9,1
	Q6 incorrect	-	-
	Q5 incorrect	5	45,5
	Total	-	-

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

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, 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.

## Discussion

Our study aimed 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 patient's gender and the duration of the disease on the Theory of Mind.

Regarding the relationship between ToM and RRMS, the results of our research showed that the performance of most participants was slight 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 in cognitive ToM ability in contrast with affective ToM. This finding is by 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, concerning the RRMS duration and ToM ability, the results of our research suggested that the disease's longer duration has worsened 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 relatively small sample size (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. In addition, future studies investigating the hyperfunction of ToM should be considered for better comprehending the function of ToM in MS.

Despite the limitations, the results of this study could be useful to both scientists and health professionals. Our research aimed 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 continuous and correct screening, 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].

## Conclusion

In conclusion, our research results align with existing literature suggesting that RRMS negatively affects ToM, especially cognitive ToM, even at early stages. We also conclude that the longer the duration of RRMS the greater the impairment of ToM. Given the impact of ToM on RRMS patients' QoL, it is important to not disregard the deterioration of social cognitive skills, which is parallel to physical disability, and to timely detect these deficits through screening and neuropsychological evaluation.

## Declarations

**Author contributions:** Conceptualization, D.D. and E.K.; methodology, M.L., and M. T.; validation, E.K., M.L., and M.T.; investigation, D.D. and M.L.; data curation, D.D. and M.L.; writing-original, D.D.; writing-review and editing, D.D., E.K., D.M. and M.T.; supervision, E.K., D.M. and M.T.; project administration, D.D., E.K., M.L., D.M. and M.T.; All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional review board statement:** The study was conducted by the Declaration of Helsinki and approved by the Ethics Committee of the Aristotle University of Thessaloniki (protocol number 77/15-4-2022).

**Informed consent statement:** Informed consent was obtained from all subjects involved in the study.

**Data availability statement:** The data presented in this study are available on request from the corresponding author.

**Acknowledgments:** The authors would like to thank the First Department of Neurology of AHEPA University Hospital of Thessaloniki for the valuable help on participant recruitment and for granting access to the clinic for the neuropsychological evaluation.

**Conflicts of interest:** The authors declare no conflict of interest.

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**Manuscript Information:** Received: September 16, 2024; Accepted: October 17, 2024; Published: October 31, 2024

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**Citation:** Koutsouraki E, Dagkonaki D, Loizou M, Moraitou D, Tsolaki M. Social cognition in a cohort of Greek patients with relapsing-remitting multiple sclerosis. *Open J Clin Med Case Rep.* 2024; 2295.

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