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The relationship between dimensions of mental health and alexithymia in multiple sclerosis patients

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ABSTRACT

Objectives: The emotional correlates of multiple sclerosis have been the source of empirical interest in recent years. Studies have indicated that alexithymia as well as anxiety and depression are of central importance in this regard. The purpose of the present study was to continue this line of investigation regarding the relationships between alexithymia and mental health problems in patients with multiple sclerosis. More specifically, this study examined whether, and if so to what extent alexithymia significantly accounts for mental health problems in multiple sclerosis patients over and above the effect of the disease itself. The possible role of alexithymia as a moderating variable between multiple sclerosis and mental health difficulties was also investigated. In addition, the current study investigated mental health problems and alexithymia in greater depth by focusing on specific mental health problems that is, somatic complaints, anxiety, social dysfunction and depression as well as each of the component dimensions of alexithymia, that is, difficulty identifying feelings, difficulty describing feelings, and externally oriented thinking.

Methods: Forty patients with multiple sclerosis were compared to forty healthy individuals on the General Health Questionnaire-28 and the Toronto Alexithymia Scale-20.

Results: Alexithymia, especially difficulties identifying feelings, contributed to a substantial extent over and above multiple sclerosis per se in predicting all forms of psychopathology. The alexithymia dimension of difficulty describing feelings was found to moderate the relationship of multiple sclerosis with anxiety, so that the relationship between anxiety levels and difficulty describing feelings is different in multiple sclerosis patients than in healthy individuals. Finally, the alexithymia dimension externally oriented thinking was related to social dysfunction for all participants but to greater degree for multiple sclerosis patients.

Conclusion: These to date unprecedented results have important implications regarding psychological treatment of patients with MS.

1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory neurodegenerative disease of the central nervous system that affects 2.3 million people worldwide (National Multiple Sclerosis Society, 2011). Demyelination and axonal loss lead to symptoms such as impaired balance, sensory deficits, motor we akness and urinary disturbance. It typically appears between 20 and 40 years of age and is the most common non-traumatic cause of disability in young adults (Chalah et al., 2020). It is more prevalent in women than men (Brown et al, 2014).

The emotional correlates of the disease have been a source of empirical and clinical interest for a number of years leading to a significant body of research on patients with MS (Boeschoten et al., 2017). Psychiatric problems have been found to affect up to 95% of patients at some point during their lifetime (Chalah and Ayache, 2017). Depression has been found in up to 50% of patients (Corallo et al., 2019; Patten et al., 2017; Solaro et al., 2018). Anxiety appears to affect up to 57% of the MS population (Butler et al., 2016; Pham et al., 2018). The inter-relationship between anxiety and depression has also been noted (Chalah and Ayache, 2017; Eboni et al., 2018).

In recent years, the growing body of literature on this topic has increasingly focused attention on the implication of alexithymia in patients with MS (Chalah and Ayache, 2017). Alexithymia is a psychological characteristic that involves difficulty in identifying and describing feelings, restricted imagination, and an externally oriented style of thinking that has been linked to various psychological and physical disorders (Luminet et al., 2018). It has been suggested that alexithymia is a non- specific risk factor for various physical and

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psychological problems (Taylor, 2004). Some researchers consider it as a stable personality trait and/or as a state of mind in reaction to stressful conditions (Parker et al., 1998; Smith et al., 1992). Others suggest it is comprised of two dimensions, affective and cognitive, having to do with diminished levels of emotional experience and deficits in cognitive processing of emotions respectively (Bermond et al., 2007).

Increasing attention has been given to the idea that relationship between alexithymia and executive functions, particularly the specific dimension of social cognition (Chalah and Ayache, 2020; Chalah and Ayache., 2017; Di Tella et al., 2020; Raimo et al., 2017; Vermeulen et al., 2018; Santorelli and Ready, 2015). Executive functions are the cognitive processes needed to control goal- oriented behavior (Diamond 2013) Social cognition is a multidimensional construct comprised of the processes involved in dealing with social situations that have to do with the recognition and understanding of others mental states, and to experience empathy towards others, which is also linked to the theory of mind- ToM (Adolfs, 2009; Chalah and Ayache, 2017). Studies with non-clinical populations have demonstrated that alexithymia and executive function, particularly social cognition are closely related, and that the ability to recognize others emotions relies on the ability to recognize one's own (Di Tella et al., 2020). In the MS population, neuropsychological studies have noted social cognitive deficits in patients with MS, but the findings regarding the relationships between social cognition, disease characteristics and cognitive domains are to date contradictory. Moreover, the relationship between social and nonsocial cognition is a source of scientific controversy, as some studies have yielded contrasting results leading some researchers to assert that the two are integrally related while others argue that the two are separate domains of function (Batista et al., 2018; Chalah and Ayache, 2020; Dulau et al., 2017). In a recent review of the neuroimaging literature on social cognition in MS patients Chalah and Ayache (2020) conclude that there is evidence of an altered brain network underlying social cognition deficits in patients with MS, but that the limitation of studies to date underscore the need for further research to understand the phenomenon of social cognition in patients with MS.

In the MS patient population, alexithymia is estimated to vary between 10% and 53% in contrast to the general population prevalence of 10% to 20.7% (Chalah and Ayache, 2017). (moved sentence). Studies have demonstrated a significant relationship between alexithymia and various dimensions of multiple sclerosis (Chalah and Ayache, 2017). For example, an association between alexithymia disease severity and relapse has been documented (Stojanov and Stojanov, 2020). A number of investigations have focused more specifically on the relationships between alexithymia, depression and anxiety in patients with MS (Briones-Buixassa et al., 2017; Eboni et al., 2018). However, the results of these studies have yielded interesting but conflicting results. Chalah et al. (2020) found no significant association between alexithymia, anxiety and depression. In other studies with MS patients, a positive correlation was found between depression and alexithymia (Bodini et al., 2008; Chahraoui et al., 2008; 2014; Eboni et al., 2018; Gay et al., 2010; Cecchetto et al., 2014; Mosson et al., 2014) but a negative correlation was found in other investigations (Dulau et al., 2017; Gay et al., 2017). Similarly, anxiety was found to be positively correlated with alexithymia in some (Briones-Buixissa et al., 2017; Chahraoui et al., 2008, 2014; Eboni et al., 2018; Gay et al., 2010; Gay et al., 2017; Mosson et al., 2014) but not in other research (Dulau et al., 2017; Prakash et al., 2019). In a recent longitudinal study, alexithymia was found to be more highly correlated with anxiety in comparison to depression over time (Chahraoui et al., 2014). However, research to date has not examined the possible role of alexithymia as a moderating variable that is, affecting the way (s) that multiple sclerosis impacts on psychopathology. The need for further research regarding these relationships has been noted particularly in view of both their physical and psychological correlates in patients with MS.

Most recently, within the larger framework of interest in executive function and social cognition, attention has turned to the relationships between alexithymia, executive function and social cognition, in patients with MS. As noted by their review by Chalah and Ayache (2017) a number of studies point to the idea that alexithymia may underlie deficits in social cognition. The investigations to date have yielded interesting but cosnflicting results (Cecchetto et al., 2014; Dulau et al., 2017; Gleichgerrcht et al., 2015; Patil et al., 2016; Prochnow et al., 2011; Raimo et al., 2017). In two studies of recognition of facial emotion, a facet of social cognition, although MS patients had lower levels of facial recognition than their healthy counterparts, no correlation was found between alexithymia and facial emotion recognition (Cecchetto et al., 2014; Prochnow et al., 2011, 2013). In contrast, Dulau et al. (2017) found no differences between MS and healthy participants regarding facial emotion recognition or alexithymia, nor any correlation between alexithymia and any cognitive variable. However, Raimo et al. (2017) found that MS patients had significantly more difficulty than healthy controls in certain aspects of social cognition, that is understanding and interpreting other people's beliefs, intentions and emotions. Interestingly MS patients were less able than controls in specific domains that is, in detecting deception and cheating, and in recognizing envy and embarrassment. However, they did not differ in recognizing happiness, sadness anger fear and disgust. For both MS and healthy participants, recognition of others emotions was significantly linked to alexithymia. These findings have led Chalah and Ayache (2017) to propose that impaired ability for facial emotion recognition might be specific to social cognition deficits in MS patients, independent from alexithymia. Moreover, these authors consider that in view of the contrasting findings to date, it is still unclear whether alexithymia is a result of MS pathological change, whether it is an effect of the psychological distress generated by the disease, or due to a combination of both factors.

The purpose of the present study was to investigate the relationships between alexithymia, anxiety, depression and other mental health problems in greater depth in this population by examining the contributions of multiple sclerosis and alexithymia in predicting basic dimensions of psychological disorders. More specifically, we examined whether and if so, to what extent alexithymia significantly accounts for mental health problems in MS patients over and above the effect of MS in statistically predicting the aforementioned problems. We also investigated whether and if so to what extent alexithymia functions as a moderating variable between MS and mental health difficulties, that is whether, and if so, how alexithymia affects or changes the relationship between MS and mental health problems, for example by amplifying or attenuating the effect of MS on mental health problems in the MS population.

Moreover, the current study investigated mental health problems and alexithymia in greater depth by focusing on specific mental health problems that is, somatic complaints, anxiety, social dysfunction and depression. We also looked at each of the component dimensions of alexithymia, that is, difficulty identifying feelings (DIF), difficulty describing feelings (DDF) and externally oriented thinking (EOT) as these dimensions appear to have different relationships with variables related to MS and to psychopathology (Briones-Buixassa et al., 2017; Chahraoui et al., 2015).

2. Method

2.1. Participants

Forty patients with a definitive diagnosis of multiple sclerosis according to McDonald's criteria were recruited from of the outpatient neurological clinic of the Naval Hospital of Athens. Forty healthy individuals matched for gender and age with the patient group were recruited from the hospital staff, including nursing and administrative staff but excluding physicians. Exclusion criteria for both groups were

(a) history of alcohol and drug abuse, (b) psychiatric illness apart from major depression for the patient group, (c) diagnosis of any chronic disease other than MS (d) visual, motor or severe cognitive disorder as assessed by the neurologists through clinical examination, the EDSS scale for the MS group, that could interfere with the assessment procedure and (e) for the MS group, having a relapse during the last 2 months. Patients completed the questionnaires of the research after having met their doctor. The control group completed the forms at the hospital after their work in an office provided by the research team of this study. All participants signed informed consent forms. The study was approved by the hospital's bioethics committee and was conducted in accordance with the Declaration of Helsinki.

2.2. Measures

2.2.1. Sociodemographic and clinical data

Demographic data (gender, age, education) were provided by the patients while clinical data (disability status, medication, type of disease, disease duration, medical history etc.) were provided by the doctor responsible for them. Disability was assessed by Expanded Disability Status Scale (EDSS; Kurtzke, 1983).

2.2.2. Mental health

Mental health was assessed with General Health Questionnaire-28 (GHQ; Goldberg and Hillier, 1979), which has 28 items scored for 0 for absence of symptoms or 1 for presence. It is comprised of four scales namely somatic complaints, anxiety /insomnia, social dysfunction, depression and a total score of overall psychopathology index. It has been standardized for the Greek population (Garyfallos et al., 1991) and for this research the internal consistency of the four factors was high (Cronbach's alpha, somatic complaints = 0.82, anxiety = 0.83, social dysfunction = 0.88, severe depression = 0.88, overall psychopathology index = 0.92).

2.2.3. Alexithymia

Alexithymia was assessed with the Toronto Alexithymia Scale–20 TAS (Bagby et al., 1994; Taylor, 2004), which includes four scores: three for separate aspects, that is Difficulty in Identifying Feelings (DIF), Difficulty in Describing Feelings (DDF) and Externally Oriented Thinking (EOT)as well as a Total Alexithymia Score. The TAS is a 20 item scale and each item is scored with a 5-point Likert scale ranging from 1 (totally disagree) to 5 (totally agree). TAS has been recently validated psychometrically in Greece (Tsaousis et al., 2010). For the sample of this research, the internal consistency of the three aspects was adequate (Cronbach's alpha, DIF = 0.78, DDF = 0.69, EOT = 0.64).

2.3. Statistical analyses

Analyses were conducted with SPSS Version 22.0. We first performed exploratory analyses by comparing means of the aspects of alexithymia with Student's *t*-test and computing the Pearson correlation coefficients between dimensions of alexithymia and mental health for the MS and the control group, separately. We then used hierarchal multiple regression analyses (enter mode) for the prediction of dimensions of mental health, namely somatic complaints (SOM), Anxiety (ANX), Social Dysfunction (SOC) and Depression (DEP), as well as the Overall Psychopathology Index (TOT). In these analyses, predictors were entered in four sequential blocks as follows: (1) age and gender, (2) presence of MS (group) as a predicting variable, (3) the dimensions of alexithymia, and (4) the interaction of dimensions of alexithymia with MS. Each interaction term was tested in a separate regression model in order to account for multicollinearity. This statistical handling allows for assessing the effect of alexithymia on mental health over and above the effect of MS, as well as potential moderation of alexithymia in the relationship between MS and mental health. We decided not to use the total alexithymia score so that we would have the opportunity to assess the contribution of its different aspects to the prediction models, as they seem to be differentiated (Chahraoui et al., 2015).

Table 1
Sociodemographic and disease data of research participants (N = 80).

Variables	MS Diagnosis							
	No				Yes			
	M	*SD*	min	max	*M*	*SD*	min	*Max*
Age	43.28	12.03	16	66	43.02	11.70	15	64
Years of Education	12.87	3.81	6	16	13.70	3.14	6	16
Years of illness					8.72	8.61	0.17	31
Disability Level					2.63	1.16	1	6

3. Results

3.1. Sociodemographic data

On Table 1, sociodemographic and disease related characteristics are presented. In both groups, male-female ratio was 25% (10) and 75% (30) a ratio similar to the one in the MS population. Similar to the frequency of MS types in this population were also the disease types in the sample, that is 67,5% (27) RR, 20% (8) SP and 12,5% (5) PP. According to these results it would appear that the MS group was representative of the MS population with respect to gender and MS type.The two groups did not differ significantly concerning age, t (78) = 0,10, p = 0,925 and years of education, t (75,20) = −1,06, p = 0,294.

3.2. Mean comparisons of alexithymia aspects

As shown on Table 2, MS patients scored higher in all aspects of alexithymia, that is DIF, DEF, EOT and total score. Effect sizes, according Cohen's d coefficient ranged from medium (EOT = 0.60) to high (TOT = 0.92).

3.3. Correlation of alexithymia with mental health

As shown on Table 3, there were some differences in the pattern of relationships of alexithymia with mental health for the two groups. The most prominent were those between DIF and somatic complaints (r = 0.49, p < .01 for MS and r = 0.19, n.s. for the control group), between DIF and social dysfunction (r = 0.40, p < .05 for MS and r = 0.13, n.s. for the control group), between DDF and depression (r = 0.34, p < .05 for MS and r = 0.17, n.s. for the control group), and between EOT and the overall psychopathology index (r = 0.33, p < .05 for MS and r = 0.09, n.s. for the control group). Although none of the aforementioned or any other pair of correlation coefficients differed in a statistically significant manner, one can assume that there is a tendency for the aspects of alexithymia to exhibit stronger association with mental health issues in the presence of MS.

Table 2
Means and standard deviations of alexithymia aspects for the presence of MS diagnosis.

TAS	MS diagnosis				*t*	*df*	*Cohen's d*
	No		Yes				
	M	*SD*	*M*	*SD*			
DIF	14.52	4.21	19.10	7.39	−3.40***	61.98	0.77
DDF	11.05	3.86	14.42	4.75	−4.49***	78	0.79
EOT	23.85	4.88	26.78	4.97	−2.66**	78	0.60
TOT	49.42	9.18	60.30	14.15	−4.08***	66.91	0.92

Note. ** p < .01, *** p < .001.

Table 3
Pearson correlation coefficients between the aspects of alexithymia and the aspects of mental health issues separately for the control ($N = 40$) and the multiple sclerosis group ($N = 40$).

	GHQ SOM	ANX	SOC	DEPR	TOT
TAS	Pearson *r*	Pearson *r*	Pearson *r*	Pearson *r*	Pearson *r*
MS					
DIF	.49**	.48**	.40*	.41**	.56***
DDF	.23	.24	.32*	.34*	.35*
EOT	.24	.27	.38*	.16	.33*
Control					
DIF	.19	.41**	.13	.24	.34*
DDF	.38*	.49**	.52**	.17	.51**
EOT	.12	.05	.34*	−0.21	.09

Note. *$p <$ .05, **$p <$.01, ***$p <$ .001. MS: Multiple Sclerosis. Control: Control group.

3.4. Statistical prediction of mental health

In the first step of the hierarchical multiple regression models the demographic variables of gender and age did not show a significant contributionin the prediction of somatic complaints, $F(2, 77) = 0.26$, n.s.; anxiety, $F(2, 77) = 0.26$, n.s.; social dysfunction, $F(2, 77) = 0.18$, n.s.; depression, $F(2, 77) = 0.37$, n.s.; or the overall psychopathology index, $F(2, 77) = 0.17$, n.s. Therefore, we decided not to include them in the final models presented below for reasons of parsimony.

As shown on Table 4, all predictions concluded in significant results. The total variance of the dependent variables explained for each model was 39% for somatic complaints, 37% for anxiety, 33% for social dysfunction, 23% for depression, and 47% for the overall psychopathology index. MS contributed significantly in the prediction of all dimensions of psychopathology. The amount of explained variance ranged between 13% for depression to 30% for somatic complaints and overall psychopathology. In the next step, the dimensions of alexithymia explained an additional amount of variance that was significant in all analyses and ranged between 13% for somatic complaints and 20% for overall psychopathology. Specifically, DIF positively predicted all GHQ dimensions. EOT had a significant positive effect only on social dysfunction ($\beta = 0.24, t = 2.01, p = .048$). DDF did not have a significant contribution in the prediction of any GHQ dimension. It is noteworthy that the effect of MS on mental health problems decreased when alexithymia was entered in the equation, although the effect of MS nonetheless remained significant. With respect to the prediction of depression specifically, MS no longer had a significant impact when the dimensions of alexithymia were accounted for. The aforementioned results suggest that the effect of MS on mental health is partially explained by the dimensions of alexithymia.

In the last step of the regression models we tested for the interaction of alexithymia by MS in the prediction of psychopathology. Only the interaction of DDF by MS was significant, $F(1, 74) = 4.57$, $p = 0{,}036$, $\Delta R^2 = 0.04$. As shown on Fig. 1, MS patients reported more anxiety than the healthy controls. This difference is amplified at low levels of DDF, while at high levels of DDF the association of MS with anxiety is attenuated.

Table 4
Prediction of mental health from MS and the aspects of alexithymia.

	Dependent Variables (GHQ)				
Predictors	SOM beta	ANX beta	SOC beta	DEP beta	TOT beta
Step 1					
MS	0.55***	0.44***	0.45***	0.36**	0.55***
ΔR^2	0.30	0.20	0.20	0.13	0.30
Step 2					
MS	0.39***	0.26*	0.27**	0.22	0.35***
DIF	0.34**	0.39**	0.24*	0.30*	0.39***
DDF	0.01	0.07	0.07	0.19	0.09
EOT	0.10	0.06	0.24*	−0.11	0.09
ΔR^2	0.13	0.18	0.16	0.14	0.20

Note. * $p < .05$; ** $p < .001$; *** $p < .001$.

4. Discussion

The current study focused on investigating the relationship between alexithymia and specific forms of psychopathology in patients with MS as well as the possible role of alexithymia as a moderating variable in relation to these dimensions of psychopathology. Our basic findings, briefly summarized now, and then explained in detail later in the text are as follows. As was expected, MS was related to higher levels of all forms of psychopathology which is line with a significant number of studies to date indicating that patients with MS demonstrate higher levels of psychopathology than people without the disease (Boeschoten et al., 2017; Chalah and Ayache, 2017; Corallo et al., 2019; Patten et al., 2017; Solaro et al., 2018). MS patients exhibited higher levels of alexithymia, as well, another finding in line with the majority of other research findings (Chalah and Ayache, 2017). However certain findings of our study have not been reported in the literature to date. Firstly, alexithymia, especially difficulties identifying feelings (DIF) contributed to a substantial extent over and above MS in predicting psychopathology. Secondly, we found that difficulty describing feelings (DDF) moderates the relationship of MS with anxiety, so that the relationship between anxiety levels and difficulty describing feelings is different in MS patients than in healthy individuals. Finally, we found that externally oriented thinking (EOT) was related to social dysfunction for patients with MS.

More specifically, the results of the present study confirm previous findings of significant relationships between alexithymia, psychological difficulties and multiple sclerosis found in some previous studies (Briones-Buixassa et al., 2017; Chalah and Ayache, 2017; Eboni et al., 2018) although not all (Chalah et al., 2020). In our study, alexithymia, and in particular, difficulty identifying feelings (DIF) was related to all mental difficulties over and above disease impact on psychopathology. This may be due to the fact that this is the dimension most integrally involved with affect regulation which is in return related to psychopathology (Bagby et al., 1994). The difficulty identifying feelings dimension (DIF) was independent of MS in predicting somatic complaints, anxiety, social dysfunction and overall psychopathology index.

The one exception was that of depression. In this case, when both alexithymia and MS were taken into account, difficulty identifying feelings (DIF) rather than MS predicted depression. This is in line with the findings to date that alexithymia is a major predictor of depression in patients with multiple sclerosis (Gay et al., 2010) and that difficulty identifying feelings (DIF) is the specific dimension of alexithymia in that is the most critical in this regard (Bodini et al., 2008). Our findings are consistent with those of Chahraoui et al. (2014) who found that difficulty identifying feelings (DIF) and difficulty describing feelings (DDF) were related to anxiety and depression.

We were particularly interested in the finding that difficulty in describing feelings (DDF) moderates the relationship of MS with anxiety, so that MS patients differed from their healthy peers with respect to the relationship between difficulties in describing feelings and degree of anxiety. Although MS patients had higher levels of anxiety than healthy participants overall, the difference in anxiety varied depending upon the difficulty in describing feelings. As difficulty in describing feelings decreases, difference in anxiety between the groups increases, with MS patients showing more anxiety than healthy controls. In other words, the easier it is for MS patients to describe their feelings, the more anxiety they report, in contrast to their healthy peers who do not report more anxiety when they can describe feelings more easily. This difference in anxiety between the groups significantly decreases as difficulty describing feelings increases. As difficulty in describing feelings

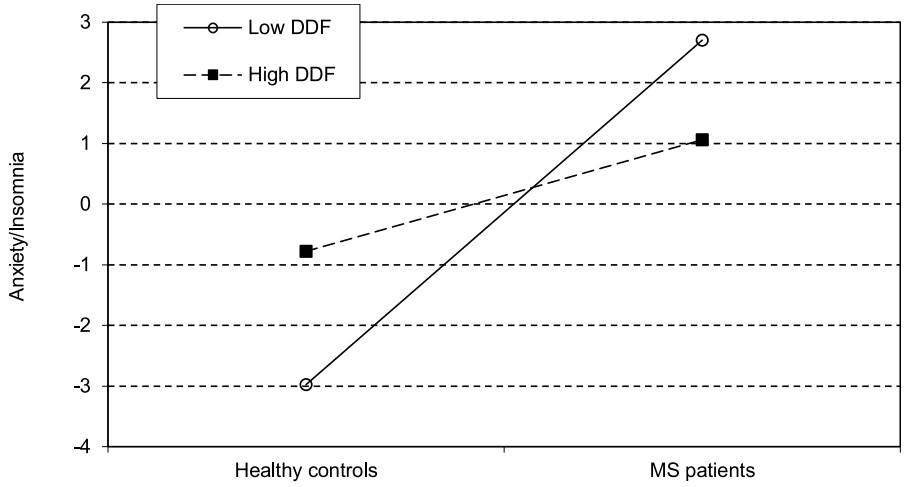

Fig. 1. Interaction of MS by DDF in predicting anxiety.

increases, patients with MS show levels of anxiety similar to that of healthy peers. This finding to the best of our knowledge is unprecedented to date. In terms of possible explanations for this finding it might at first glance seem that the greater ability to express feelings would enable patients with MS to acknowledge their anxiety. However, according to this line of thinking it would follow that greater ability to express feelings would be related to acknowledgement of other forms of psychopathology such as social dysfunction and depression which is not in fact the case. These findings are also counter to expectation from a social cognition perspective that would predict that higher levels of social cognition would be related to lower levels of anxiety.

A second explanation for this finding involves the psychodynamic position regarding the defensive use of alexithymia may explain this phenomenon. It has been suggested that alexithymia may be a primary, dispositional characteristic that develops from the earliest years, as a reaction to cope with stress albeit a maladaptive one, that increases the possibility of vulnerability to somatic outbreaks. From this viewpoint alexithymia is a response to pain, a defense mechanism that protects the individual against painful inner experience (Bronstein, 2011; Gubb, 2013; Taylor and Bagby, 2013). Thus, when this defense functions less well, the individual experiences more distressing feelings such as anxiety (Chahraoui et al., 2015; Gay et al., 2010). In the case of patients with MS, the emotional discomfort connected with the disease could well trigger alexithymic defenses including inhibition in expressing feelings. When this defensive inhibition is less effective, that is, the feelings are more easily expressed, the anxiety which would be warded off if the defense was operating effectively, is then experienced. Some questions remain however such as to why this particular aspect of alexithymia, i.e. difficulty describing feelings would be more affected rather than difficulty in identifying feelings. Perhaps our finding points to an inability to control the expression of feelings that is related to anxiety in the specific case of patients with MS.

Another question that arises is why anxiety rather than the other mental health problems would be affected. On possible explanation may have to do with the salient relationship between anxiety and alexithymia in patients with MS that has been documented in numerous studies. A stronger relationship has been documented between the two than between alexithymia and depression (Chahraoui et al., 2014), and in fact anxiety has been found to predict depression (Gay et al., 2017). Anxiety has been linked to greater impairment (Jones et al., 2014) as well as to illness relapse (Potogas et al., 2008). Moreover, previous longitudinal research on patients with MS has indicated that while depression decreases over time, anxiety does not, and it has been posited that the unpredictability of the disease is integrally involved in maintaining a high-level of anxiety (Chahraoui et al., 2014). This may in part explain why in the present study difficulty in describing feelings was related to anxiety but not other painful affects such as depression.

Our finding that externally orientated thinking was related to the social dysfunction dimension of mental health has also not been reported in previous research. This dimension on the General Health Questionnaire assesses the capacity to function in everyday life with a sense of accomplishment and satisfaction as indicated by the following questions “been managing to keep yourself busy and occupied”, “been taking longer over the things that you do”,“felt on the whole that you were doing things well”, “been satisfied with the way you are carrying out your task”, “felt capable of making decisions about things” “felt you were playing a useful part in things”, “been able to enjoy your day to day activities”. In our study, greater difficulty in these domains was associated with a stronger tendencies for externally oriented thinking for both healthy and ill participants, but more strongly associated for people with MS. This was an unexpected and counter intuitive finding given that one would expect that individuals who focus on external reality would be more efficient in executing their daily life responsibilities. One explanation for our finding is that individuals, who have greater difficulties functioning in everyday life do not have the internal strength to function beyond externally oriented thinking, that is, to delve more deeply into themselves or the inner experiences of others which could be psychologically taxing. Maintaining an external orientation could be a way of trying to cope with the demands of everyday living. This may have particular significance in the case of people with MS who are more burdened by daily life responsibility due to their physical condition. It is also possible that the correlation between social dysfunction and externally oriented thinking may be explained by a third variable common to both for example, a general difficulty or inability with coping with internal and external demands of life.

A case in point could be a non-social cognitive domains have to do with executive functions. Perhaps difficulties in these domains may underlie difficulties in coping with everyday demands and thus create pressure for the individual to focus on the external rather than the internal world. This may also indicate a possible difference between social and non-social cognition since neither difficulty identifying feelings nor difficulty expressing feelings- aspects of alexithymia and social cognition - were associated with social dysfunction.

The results of our study have important implications regarding psychological intervention for people with MS. It would appear that many of these patients have certain psychological vulnerabilities that must be taken into account in their treatment. With respect to the difficulty in describing feelings, to the extent that greater ease in describing feelings is associated with greater anxiety, caution is clearly indicated in psychotherapy with MS with respect to emphasis that is traditionally given to verbalization of inner experience particularly

emotions. Whereas with many if not most patients, such verbalization is associated with fewer symptom and improved psychological functioning, this does not appear to be the case with MS patients. Therapists should be aware of the relationship between describing feelings and increase in anxiety, respecting the potentially necessary defensive nature of a difficulty in describing feelings and intervene accordingly. Similarly, the relationship between externally oriented thinking and social dysfunction must be taken account in treatment approaches. To the extent that many forms of psychotherapy focus on internal processes, and on increasing awareness of these processes, it seems critical to consider that such an approach could be problematic or even harmful for patients with MS. Alternatively, it is possible that a treatment involving a decrease in externally oriented thinking could lead to improvement in carrying out daily responsibilities. In general, however, it appears that certain parameters must be considered carefully in the psychological treatments of patients with MS.

This study has certain limitations that must be noted. Although the total N of participants reaches or nearly meets some of the classical (e.g., Green, 1991) and more recent (e.g., Jenkins and Quintana-Ascencio, 2020) rules-of-thumb for conducting multiple regression analysis, it is the purposeful sampling procedure that urges for replication studies due to its non-random nature. The generalizability may also be limited given that the subjects were Greek, and cultural factors appear to play a significant role with respect to experience and expression of alexithymic characteristics (Chalah and Ayache, 2017; Dere et al., 2013; Le et al., 2002). Further study of all these variables is indicated to deepen understanding of the relationship between alexithymia and mental health in patients with multiple sclerosis.

CRediT authorship contribution statement

Anna L. Christopoulos: Conceptualization, Supervision, Writing - original draft, Writing - review & editing. **Antonios Poulios:** Conceptualization, Methodology, Formal analysis. **Vassilis Pavlopoulos:** Formal analysis, Writing - review & editing.

Declaration of Competing Interest

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References

Adolf, R., 2009. The social brain: neural basis of social knowledge. Annu. Rev. Psychol. 260, 693–716.
Bagby, R.M., Taylor, G.J., Parker, J.D.A., 1994. The twenty-item toronto alexithymia scale – II: convergent, discriminant and concurrent validity. J. Psychosom. Res. 38, 33–40.
Batista, S., Freitas, S., Afonso, A., et al., 2018. Theory of mind and executive functions are dissociated in multiple sclerosis. Arch. Clin. Neuropsychol. 33, 541–551.
Bermond, B., Clayton, K., Liberova, A., Luminet, O., Maruszewski, T., Ricci Bitti, P., Rimé, B., Vorst, H., Wagner, H., Wicherts, J., 2007. A cognitive and an affective dimension of alexithymia in six languages and seven populations. Cogn. Emot. 21, 1125–1136. https://doi.org/10.1080/02699930601056989.
CBodini, B., Mandarelli, G., Tomassini, V., Tarsitani, L., Pestalozza, I., Gasperini, C., Lenzi, G.L., Pancheri, P., Pozzilli, C., 2008. Alexithymia in multiple sclerosis: relationship with fatigue and depression. Acta Neurol. Scand. 118, 18–23. https://doi.org/10.1111/j.1600-0404.2007.00969.
Boeschoten, R.E., Braamse, A.M.J., Beekman, A.T.F., Cuijpers, P., van Oppen, P., Dekker, J., Uitdehaag, B.M.J., 2017. Prevalence of depression and anxiety in multiple sclerosis: a systematic review and meta-analysis. J. Neurol. Sci. 372, 331–341. https://doi.org/10.1016/j.jns.2016.11.067.
Briones-Buixassa, L., Milà, R., Arrufat, F., Aragonès, J., Bufill, E., Luminet, O., Rona Moss-Morris, R., 2017. A case control study of psychosocial factors and their relationship to impairment and functionality in multiple sclerosis. J. Health Psychol. 24 (8), 1023–1032.
Bronstein, C., 2011. On psychosomatics: the search for meaning. Int. J. Psychoanal. 1, 173–195. https://doi.org/10.1111/j.1745-8315.2010.00388.
Butler, E., Matcham, F., Chalder, T., 2016. A systematic review of anxiety amongst people with multiple sclerosis. Mult. Scler. Relat. Disord. 10, 145–168. https://doi.org/10.1016/j.msard.2016.10.003.
Cecchetto, C., Aiello, M., D'Amico, D., Cutuli, D., Cargnelutti, D., Eleopra, R., Rumiati, I.R., 2014a. Facial and bodily emotion recognition in multiple sclerosis: the role of alexithymia and other characteristics of the disease. J. Int. Neurol. Soc. 20, 1004–1014.
Chahraoui, K., Dieu, E., Moreau, T., 2015. Psychopathology of alexithymia and multiple sclerosis. In: Brochet, B. (Ed.), Neuropsychatric Symptoms of Inflammatory Demyelinating Diseases. Springer International Publishing, Switzerland, pp. 195–211.
Chahraoui, K., Duchene, C., Rollot, F., Bonin, B., Moreau, T., 2014. Longitudinal study of alexithymia and multiple sclerosis. Brain Behav. 4 (1), 75–82.
Chahraoui, K., Pinoit, J.M., Viegas, N., Adnet, J., Bonin, B., Moreau, T., 2008. Alexithymia and links with depression and anxiety in multiple sclerosis. Rev. Neurol. (Paris) 164 (3), 242–245.
Chalah, M.A., Ayache, S.S., 2020. A scope of the social brain in multiple sclerosis: insight from neuroimaging studies. Cogn. Behav. Neurol. 33, 90–102.
Chalah, M.A., Ayache, S.S., 2017. Alexithymia in multiple sclerosis: a systematic review of literature. Neuropsychologia 104, 31–47.
Chalah, M., Lefaucheura, J.B., Créange, A., Ayache, S.S., 2020. Corticospinal inhibition and alexithymia in multiple sclerosis patients–an exploratory study. Mult. Scler. Relat. Disord. 41, 1–5.
Corallo, F., Lo Buono, V., Genovese, R., Palmeri, R., Di Cara, M., Rifici, C., Sessa, E., D'Aleo, G., Galletti, F., Bonanno, L., Marino, S., 2019. A complex relation between depression and multiple sclerosis: a descriptive review. Neurol. Sci. 8, 1551–1558. https://doi.org/10.1007/s10072-019-03889-1.
Dere, J., Tang, Q., Zhu, X., Cai, L., Yao, S., Ryder, A.G., 2013. The cultural shaping of alexithymia: values and externally oriented thinking in a clinical sample. Compr. Psychiatry 54, 362–368.
Di Tella, M., Adenzato, M., Catmur, c., Miti, F., Castelli, L., Ardito, R., 2020. The role of alexithymia in social cognition: evidence from a non clinical population. J. Affect. Disord. 273, 482–492.
Dulau, C., Deloire, M., Diaz, H., Saubusse, A., Charre-Morin, J., Prouteau, A., Brochet, B., 2017. Social cognition according to cognitive impairment in different clinical phenotypes of multiple sclerosis. J. Neurol. 264, 740–748.
Eboni, A.C.B., Cardoso, M., Moreira Dias, F., da Gama, P.D., Gomes, S., Magno Goncalves, M.V., Machado, S.C.N., da Nobrega Jr., A.W., Parolin, M.F.K., Paz, S.C., Ruocco, H.H., Scorcine, C., Siquineli, F., Spessotto, C.V., Tauil, C.B., Yara Fragoso, Y.D., 2018. High levels of Alexithymia in patients with multiple sclerosis. Dement. Neuropsychol. 12 (2), 212–215.
Garyfallos, Karastergiou, A., Adamopoulou, A., Moutzoukis, C., Alagiozidou, E., Mala, D., Garyfallos, A., 1991. Greek version of the general health questionnaire: accuracy of translation and validity. Acta Psychiatr. Scand. 84, 371–378.
Gay, M.C., Bungener, C., Thomas, S., Vrignaud, P., Thomas, P.W., Baker, R., Montel, S., Heinzlef, O., Papeix, C., Assouad, R., Montreuil, M., 2017. Anxiety, emotional processing and depression in people with multiple sclerosis. BMC Neurol 17I (43). https://doi.org/10.1186/s12883-017-0803-8.
Gay, M.-.C., Vrignaud, P., Garitte, C., Meunier, C., 2010. Predictors of depression in multiple sclerosis patients. Acta Neurol. Scand. 121, 161–170.
Gleichgerrcht, E., Tomashitis, B., Sinay, V., et al., 2015. The relationship between alexithymia, empathy and moral judgment in patients with multiple sclerosis. Eur. J. Neurol. 22, 1295–1303.
Goldberg, D.P., Hillier, V.F., 1979. A scaled version of the general health questionnaire. Psychol. Med. 9, 139–145. https://doi.org/10.1017/s0033291700021644.
Green, S.B., 1991. How many subjects does it take to do a regression analysis. Multivar. Behav. Res. 26 (3), 499–510. https://doi.org/10.1207/s15327906mbr2603_7.
Gubb, K., 2013. Psychosomatics today: a review of contemporary theory and practice. Psychoanal. Rev. 100, 103–142. https://doi.org/10.1521/prev.2013.100.1.103.
Jenkins, D.G., Quintana-Ascencio, P.F., 2020. A solution to minimum sample size for regressions. PLoS ONE 15 (2), e0229345. https://doi.org/10.1371/journal.pone.0229345.
Jones, K.H., Jones, P.A., Middleton, R.M., Ford, D.V., Tuite-Dalton, K., Lockhart-Jones, H., Peng, J., Lyons, R.A., John, A., Gareth Noble, J., 2014. Physical disability, anxiety and depression in people with MS: an internet-based survey via the UK MS register. PLoS ONE 8, e104604. https://doi.org/10.1371/journal.pone.0104604.
Kurtzke, J.F., 1983. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology 33, 1444–1452.
Le, H.N., Berenbaum, H., Raghevan, C., 2002. Culture and alexithymia: mean levels, correlates and role of parental socialization of emotion. Emotion 2, 341–361.
Luminet, O., Bagby, R.M., Taylor, G.J., 2018. Alexithymia: Advances in Theory, Research & Clinical Practice. Cambridge University Press, Cambridge, U.K.
Mosson, M., Peter, L., Montel, S., 2014. Impact of physical activity level on alexithymia and coping strategies in an over-40 multiple sclerosis population: a pilot study. Rev. Neurol. (Paris) 170, 19–25.
Patten, S.B., Marrie, R.A., Carta, M.G., 2017. Depression in multiple sclerosis. Int. Rev. Psychiatry 5, 463–472. https://doi.org/10.1080/09540261.2017.1322555.
Parker, J.D., Taylor, G.J., Bagby, R.M., 1998. Alexithymia: relationship with ego defence and coping styles. Compr. Psychiatry 39 (2), 91–98.
Patil, I., Young, I., Sinay, V., Gleichgerrcht, E., 2016. Elevated moral condemnation of third party violation in multiple sclerosis patients. Soc. Neurosci. 1–22.
Pham, T., Jetté, N., Bulloch, A.G.M., Burton, J.M., Wiebe, S., Patten, S.B., 2018. The prevalence of anxiety and associated factors in persons with multiple sclerosis. Mult. Scler. Relat. Disord. 19, 35–39. https://doi.org/10.1016/j.msard.2017.11.003.
Potogas, C., Mitsonis, C., Watier, L., Dellatolas, G., Retziou, A., Mitropoulos, P., Sfagos, C., Vassilopoulos, D., 2008. Influence of anxiety and reported stressful life events on relapses in multiple sclerosis: a prospective study. Mult. Scler. 9, 1262–1268. https://doi.org/10.1177/1352458508095331.
Prakash, R.S., Schirda, B., Valentine, T.R., Crotty, M., Nicholas, J.A., 2019. Emotion dysregulation in multiple sclerosis: impact of depression and anxiety. Mult. Scler.

Relat. Disord. 36, 101399.
Prochnow, d., Hoing, B., Kleiser, R., Lindenberg, R., Wittsack, H., Schafer, R., et al., 2013. The neural correlates of affect reading an fMRI study on faces and gestures. Behav. Brain Res. 237, 270–277.
Prochnow, D., Donell, J., Schafer, R., Jorgens, S., Hartung, H., Franz, et al., 2011. Alexithymia and impaired facial affect recognition in multiple sclerosis. J. Neurol. 258, 1683–1688.
Raimo, S., Tojano, L., Papaccena, S., Alaia, R., Spitaleri, D., Grossi, D., Santangelo, G., 2017. Neuropsychological correlates of theory of mind deficits in patients with multiple sclerosis. Neuropsychology 1-11.
Santorelli, G.D., Ready, R., 2015. Alexithymia and executive function in younger and older adults. Clin. Neuropsychol. 29, 938–955.
Smith, M., Daurat, A., Pariente, P., Sifneos, P.E., 1992. French translation of schalling-sifneos personality scale revised and Beth Israel questionnaire, 2 evaluation tools of alexithymia. Encephale 18, 171–174.
Solaro, C., Gamberini, G., Masuccio, F.G., 2018. Depression in multiple sclerosis: epidemiology, aetiology, diagnosis and treatment. CNS Drugs 2, 117–133. https://doi.org/10.1007/s40263-018-0489-5.
Stojanov, J., Stojanov, A., 2020. A cross-sectional study of alexithymia in patients with relapse-remitting form of multiple sclerosis. J. Postgrad. Med. 66 (1), 23–27.
Taylor, G.J., Bagby, S., 2004. Alexithymia: 25 years of theory and research. In: Nyklíček, I., Temoshok, L., Vingerhoets, A. (Eds.), *Emotional Expression and Health: Advances in theory, Assessment and, Clinical Applications*. Brunner Routledge, New York, pp. 138–154.
Taylor, G.J., Bagby, R.M., 2013. Psychoanalysis and empirical research: the example of alexithymia. J. Am. Psychoanal. Assoc. 1, 99–133. https://doi.org/10.1177/0003065112474066.
Tsaousis, I., Taylor, G., Quilty, L., Georgiades, S., Stavrogiannopoulos, M., Bagby, R.M., 2010. Validation of a Greek adaptation of the 20-item Toronto alexithymia scale. Compr. Psychiatry 51, 443–448.
Vermeulen, N., Domachowska, I., Nielsen, K., 2018. Memory and executive functions in alexithymia. 2018. In: Luminet, Olivier, Bagby, R., Michael, Taylor, Graeme, J. (Eds.), Alexithymia: Advances in Research, Theory, and Clinical Practice. Cambridge University Press, New York, NY, US, pp. 78–89. xxiv, 352. https://doi.org/10.1017/9781108241595.007.