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THE ROLE OF METACOGNITION IN MULTIPLE SCLEROSIS: A CLINICAL STUDY AND ASSESSMENT OF POSSIBLE CORRELATION WITH ANXIETY, DEPRESSION AND COPING STRATEGIES.

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ABSTRACT

The current study aimed to explore the relationships between metacognition and anxiety, depression, and coping strategies in MS patients, compared to healthy subjects.
The study was conducted on a group of 50 MS patients and a control group of 50 healthy volunteers matched for gender, age, level of education and social status. Metacognitions were assessed with the Metacognitions Questionnaire-30, while anxiety and depression were assessed with the Hospital Anxiety and Depression Scale, and coping strategies were assessed with the Brief COPE.
Results did not show significant differences between metacognitive factors for MS patients and healthy subjects. However, we found specific, contrasting correlations between the MS group and the control group.
The results of this study could have some implications for clinical practice. Given the relationship between metacognitions and negative emotions, "psychological intervention", based on the metacognitive approach, could have positive effects on MS patients.

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1. Introduction

Multiple sclerosis (MS) is a neurodegenerative inflammatory disease of the central nervous system. Its pathophysiology is characterized by a demyelination of brain cells. The disease usually emerges in early adulthood, and clinical symptoms include motor deficits as well as cognitive and mental impairments. Common symptoms include double vision, loss of vision in one eye, muscle weakness, and trouble with sensation and/or coordination. MS causes a neurological disability that is thought to result from impaired immune mechanisms and neurodegeneration [1]. MS is the most frequent demyelinating disease with a high prevalence in North American and European populations (>100/100,000 inhabitants), whereas Eastern Asian and sub-Saharan African populations are infrequently affected (2/100,000 population) [2].
About 50% of MS patients show symptoms of depression following the diagnosis[3]. It has been shown that depression and anxiety can precipitate following MS diagnosis, and they can negatively affect patient compliance[4]. Inadequate coping strategies, insufficient social support and dysfunctional metacognitive abilities can exacerbate anxiety and depression[5]. Depression and anxiety in MS patients are positively correlated with cognitive dysfunction, lower quality of life and interpersonal difficulties[6].
Multiple sclerosis is associated with psychological and neuropsychological disorders, as well as anxiety, cognitive impairments, and depression[7].
In terms of metacognition and MS, patients perceive some changes in their cognitive function, although they often appear unaware of the actual degree of dysfunction [8]. The patients' perceived cognitive function is predicted by depression, anxiety, and level of disability, whereas objective cognitive performance in specific cognitive tests is not [9]. Moreover, there is a significant positive correlation between cognitive abilities and self-awareness of any executive dysfunction and disinhibition [10]. A recent study showed that patients with MS adopt a dysfunctional metacognitive strategy, and thus metacognition represents an important therapeutic tool[11]. The results of the metacognitive training program described showed significant improvements in MS patients in terms of coping self-efficacy, mood, perceived cognitive deficits, and quality of life. Another study reported that MS patients are less likely to adopt a

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problem-focused coping strategy, leading to a poorer psychological adjustment [12].

Executive functions seem to have an important role in the coping strategies of MS patients[13].

However, to our knowledge, no studies have explored the role of metacognition in terms of "the aspect of the information-processing system that monitors, interprets, evaluates and regulates the contents and processes of its own organization". From this point of view, dysfunctional metacognitive beliefs can be considered the basis for the development and maintenance of psychological disorders [14].

Some recent studies have explored metacognition in cancer patients during chemotherapy [15-16]. Another study has shown a relationship between metacognition and burnout in a sample of palliative care workers [17].However, more research is needed to investigate the role of psychological variables in the medical setting.

This study had three general objectives: (a) to verify the metacognitive differences between MS patients and healthy subjects; (b) to explore the relationships between metacognition and anxiety, depression, and overall distress in MS patients and healthy subjects; finally, (c) to explore the relationship between metacognition and coping strategies in MS patients and healthy subjects.

We hypothesized that: (a) there are no significant metacognitive differences between the two groups. In fact, many studies have shown the role of metacognitive factors as tools for predicting the development of psychological symptoms; (b) there are specific and significant correlations between cognitive confidence and anxiety, depression, and duration of disease. The cognitive confidence factor, which measures the subject's confidence in his/her attention and memory, could play an important role in MS patients; (c) there are some specific correlations between metacognitive factors and coping strategies in MS patients.

2. Material and methods

Participants

The study was conducted on a group of 50 MS patients aged 21-64 years (M = 39.58; SD = 11.41). The initial MS diagnosis was based on the revised McDonald criteria [18]. All patients were native Italian speakers and Italian nationals. The demographics and medical characteristics of the sample population are presented in Table 1. The sample consists of 33 women (66%) and 17 men (34%), and the level of formal education in was 12.50 years (SD = 3.12). Forty-six percent were married, and 54% of the enrolled patients were unemployed. Patients were treated with natalizumab (Tysabri) or interferon. Disability was measured with the Expanded Disability Status Scale (EDSS)[19]by an experienced neurologist. The results of the EDSS assessment ranged from 1.3 to 7 (M = 4.5), and the mean disease duration in the sample was 9.98 years (SD = 6.74). Forty-four participants had relapsing-remitting MS (RRMS), four had secondary progressive MS (SPMS), and two had primary progressive MS (PPMS).

The inclusion criteria were a MS diagnosis according to the revised McDonald criteria [18], and age of 18 years or over. Exclusion criteria were under 3 years of formal education, presence of a severe psychiatric disorder, history of alcohol/drugs abuse, presence of severe cognitive impairment, and exacerbation of symptoms during the four weeks prior to enrollment. The control group consisted of 50 healthy volunteers matched for gender, age, education level and social status, recruited among the general population. All control subjects underwent a psychological interview and were screened for mental disorders by an experienced clinical psychologist. Moreover, control group subjects had no history of psychiatric or neurologic disorders, as defined by DSM-5 [20].

Variables	
Gender (female), %	66
Age (years), mean (± SD)	39.58 (11.41)
Educational level (years), mean (± SD)	12.50 (3.12)
Disease duration (years), mean (± SD)	9.98 (6.74)
EDSS score, mean (± SD)	4.50 (1.93)
Relapsing-remitting MS, N (%)	44 (88%)
Secondary progressive MS, N (%)	4 (8%)
Primary progressive MS, N (%)	2 (4%)

Table 1 - Demographic and medical characteristics of patients with MS (*n* = 50)

Procedure

All patients were consecutively recruited at the neurological department of a hospital in southern Italy. The study was approved by the Ethics Committee for Medical and Health Research of the hospital in advance. Participants were informed that all data would be treated confidentially and used exclusively for research purposes. Before the beginning of the study, all participants gave written consent. All questionnaires were administered in a standardized order. Participants were not remunerated.

Collected data

Sociodemographic information included age, gender, educational level, nationality, and marital status.

Medical information included data on the disease and treatment history.

Metacognitions

Metacognitions were assessed with the Metacognitions Questionnaire-30 (MCQ-30)[21]. This is a 30-item self-report questionnaire, which measures a range of metacognitive beliefs and processes relevant to the vulnerability to and to the maintenance of emotional disorders. The items are rated on a 4-point Likert scale from 1 *('do not agree')* to 4 *('completely agree')*. The questionnaire includes the following five subscales (Cronbach's alpha scores derived from the sample of MS patients enrolled are reported in parentheses):

Cognitive confidence (CC; α = .86), which measures confidence in attention and memory;

Cognitive self-consciousness (CSC;α = .79), which measures the tendency to monitor one's own thoughts and focus attention inward;

Positive beliefs about worry (POS; α = .86), which measures the extent to which a person thinks that perseverative thinking is useful.

Negative beliefs about worry concerning uncontrollability and danger (NEG; α = .75), which assesses the extent to which a person thinks that perseverative thinking is uncontrollable and dangerous.

Beliefs about the need to control thoughts (NC; α = .79), which assesses

the extent to which a person believes that certain types of thoughts need to be suppressed.

A high score on each factor is considered dysfunctional. The MCQ-30 is a brief, reliable and valid self-report assessment tool for metacognitions [22]. In the present study, a validated Italian version of the MCQ-30 was used to assess metacognitive beliefs [23]. The results of the Italian MCQ-30, like the original version, indicated direct correlations between metacognitive factors (except for CSC) and state and trait anxiety, pathological worry, and obsessive-compulsive symptoms.

Anxiety and depression

Anxiety and depression were measured with the Hospital Anxiety and Depression Scale (HADS)[24-25]. This is a 14-item self-report scale that is divided into two dimensions, each composed of seven items. The two subscales provide a measure of anxiety (HADS-A) and depression (HADS-D). The HADS is specifically designed for assessing physically ill patients and is routinely used with medical outpatients. Respondents choose one from four responses to each item. Their responses are then summed within the two dimensions and a total score is obtained for each separate dimension, as well as both dimensions combined. Scores can range from 0 to 21 for each subscale, with high scores indicating higher levels of anxiety and depression. According to the developers of the HADS assessment, scores for the anxiety dimension and the depression dimension can be categorized as follows: 0–7, normal; 8–10, mild; 11–14, moderate; 15–21, severe. Moreover, the combined scores assess overall emotional distress and range from 0-42, with higher scores indicating more distress. The HADS has been employed among a wide range of clinical groups. The degree of reliability of the two factors in the present sample was good, with Cronbach's α of .75 for the depression subscale and .77 for the anxiety subscale.

Coping strategies

Coping strategies were assessed with the Brief COPE [26]. This is a 28-item self-report questionnaire, which measures different behaviors and cognitive activities involved with stress-related coping strategies. The items are rated on a 4-point Likert scale from 1 ('I haven't been doing this at all') to 4 ('I've being doing this a lot'). In this study, a validated Italian version of the Brief COPE was used to assess coping strategies. The Brief COPE consists of 14 conceptually distinct subscales, as follows (Cronbach's alpha scores derived from the present sample of MS patients and the items for each scale are given in parentheses).

Self-distraction (SD; α = .69; I've been turning to work or other activities to take my mind off things; I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping).

Active coping (AC; α = .60; I've been concentrating my efforts on doing something about the situation I'm in; I've been taking action to try to make the situation better).

Planning (PL; α = .70; I've been trying to come up with a strategy about what to do; I've been thinking hard about what steps to take).

Positive reframing (PR; α = .61; I've been trying to see it in a different light, to make it seem more positive; I've been looking for something good in what is happening).

Acceptance (AE; α =.70; I've been accepting the reality of the fact that it has happened; I've been learning to live with it).

Humor (HU; α = .78; I've been making jokes about it; I've been making fun of the situation).

Religion (RE; α = .90; I've been trying to find comfort in my religion or spiritual beliefs; I've been praying or meditating).

Use of emotional support (UE; α = .82; I've been getting emotional support from others; I've been getting comfort and understanding from someone).

Use of instrumental support (UI; α = .75; I've been getting help and advice from other people; I've been trying to get advice or help from other people about what to do).

Denial (DE; α = .69; I've been saying to myself "this isn't real"; I've been refusing to believe that it has happened).

Venting (VE; α = .62; I've been saying things to let my unpleasant feelings escape; I've been expressing my negative feelings).

Substance use (SU; α = .71; I've been using alcohol or other drugs to make myself feel better; I've been using alcohol or other drugs to help me get through it).

Behavioral disengagement (BD; α = .67; I've been giving up trying to deal with it; I've been giving up the attempt to cope).

Self-blame (SB; α = .65; I've been criticizing myself; I've been blaming myself for things that happened).

Subscale scores can range from a minimum of 0 to a maximum of 20. Higher total scores in the Brief COPE assessment indicate higher prevalence of the respective coping strategies.

Statistical Analysis

SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for data analysis. Data obtained from the research was checked and subsequently analyzed by a descriptive and inferential statistical analysis. Descriptive statistics, such as the means and standard deviations of the variables, are reported below. Relationships between metacognitions and the other variables were assessed with Pearson product-moment correlation coefficients. An absolute *r* value of .1 is considered as weak correlation, while an absolute value of .3 is considered as moderate, and of .5 is considered as a strong correlation[27]. Comparisons between MS patients and control subjects for metacognitions were carried out with Student's t-test. The levels of statistical significance were set at $p \leq .05$ and $p \leq .01$

3. Results

Descriptive Analysis and T-tests between the groups.

The descriptive statistics for the MCQ-30 scores and t-test results for the two groups are presented in Table 2. Table 2 also shows the cut-off point as per the Italian MCQ-30 validation sample [23]. The obtained results indicate that the scores of the MS patients are higher than those of the healthy control subjects. However, the scores of the two groups generally remain below or seldom exceed the cut-off value of the validated Italian MCQ-30. The results of the t-test for two independent samples (using the Bonferroni correction) did not show significant differences for metacognitions between MS patients and healthy subjects.

Variables	Ms patients	Healthy subjects	Cut-off*	t (df: 98)	p**
Cognitive confidence	12.02 (5.05)	10.10 (4.94)	9.94 (3.73)	1.92	.06
Positive beliefs	9.92 (4.61)	9.36 (3.98)	10.49 (3.92)	.65	.51
Cognitive self-consciousness	17.20 (3.54)	16.94 (3.19)	16.65 (3.19)	.39	.70
Negative beliefs	12.02 (3.90)	10.54 (3.35)	11.55 (3.97)	2.04	.05
Need to control thoughts	11.86 (4.01)	11.74 (2.91)	11.71 (3.26)	.17	.86
Total score	63.02 (13.58)	58.68 (13.29)	60.34 (12.00)	1.62	.11

**Mean values with standard deviations reported in parentheses from the Italian MCQ-30 validation sample [23].*
***with Bonferroni correction for six comparisons: $p < .008$.*

Table 2 - Descriptive statistics (mean values with standard deviations reported in parentheses) and t-test results for MCQ-30 for the two samples.

Relationships between variables

Tables 3 and 4 report Pearson correlation coefficients for the MCQ-30, HADS, and Brief COPE scores of the two groups. Table 3 also shows the correlation coefficients between the MCQ-30 scores and disease duration for MS patients.

The results presented in Table 3 show that most of the correlations between the MCQ-30 scores and the HADS scores range from moderate to strong for both samples.

In terms of potential relationships between the metacognitive factors and anxiety, the correlation between negative beliefs and the HADS anxiety score were highest for both samples. Anxiety was also correlated with the need to control thoughts, cognitive confidence, and positive beliefs about worry factors (moderate to strong positive correlations for both samples). These relationships between metacognitive factors and anxiety confirmed our hypothesis discussed earlier.

In terms of relationships between the metacognitive factors and depression, the correlation between the MCQ-30 scores and the HADS depression scores were contrasting for the two samples. We found a positive and moderate correlation between cognitive confidence and depression for MS patients, but not for control subjects. Moreover, negative beliefs were correlated positively with depression in MS patients but not in control subjects. Furthermore, a moderate positive correlation between cognitive self-consciousness and depression was observed in control subjects, but not in MS patients. Thus the results for metacognitions and depression appeared to differ markedly between MS patients and control subjects.

In terms of relationships between the metacognitive factors and overall distress, the correlation between negative beliefs and the HADS total score were highest for both samples. Overall distress (HADS TOT) was also correlated with cognitive confidence, and need to control thoughts. As shown in Table 3, correlations were moderate to strong for MS patients, and weak to moderate for control subjects. Moderate correlation between positive beliefs and HADS global score was also found for both samples. These results were in accordance with our expectations and with the initial hypotheses.

Finally, cognitive confidence was strongly correlated with disease duration in MS patients. This result is also coherent with our expectations.

Variables	HADS A		HADS D		HADS TOT		Disease duration (MS patients)
	MS patients	Control subjects	MS patients	Control subjects	MS patients	Control subjects	
Cognitive confidence	.41**	.38**	.38**	.14	.44**	.30**	.47**
Positive beliefs	.28*	.41**	.25	.15	.29*	.32*	.22
Cognitive self-consciousness	.17	-.03	-.08	-.38**	.04	-.20	.05
Negative beliefs	.58**	.53**	.37**	.17	.53**	.41**	.08
Need to control thoughts	.46**	.42**	.26	.12	.40**	.32*	.06

* $p < .05$; ** $p < .01$

Table 3 - Pearson *r* correlations between MCQ-30 and HADS scores for the two samples

Table 4 presents the Pearson correlation coefficients between Brief COPE and MCQ-30 for the two samples. The results show that most correlations between coping strategies and metacognitions range from weak to strong. Moreover, there are some discrepancies between the two samples. Cognitive confidence showed a moderate correlation coefficient with denial for both samples. Regarding the MS patients, there was a negative correlation between cognitive confidence and acceptance, while for the control sample, cognitive confidence was correlated with substance use (moderate positive correlation), behavioral disengagement (strong positive correlation), and self-blame (very strong positive correlation). In terms of relationships between positive beliefs and coping strategies, the two samples showed contrasting correlation coefficients.

Variable	CC		POS		CSC		NEG		NC	
	MS patients	Control subjects	MS patients	Control subjects	MS patients	Control subjects	MS patients	Control subjects	MS patients	Control subjects
SD	.12	.20	.23	.05	.07	.34*	.29*	.07	.25	.16
AC	-.02	.09	.24	.09	.36**	.27	.23	.03	.35**	.21
DE	.32*	.35*	.49**	.13	.04	.28*	.37**	.41**	.26	.29*
SU	.03	.28*	-.12	-.14	.11	-.19	-.20	-.03	.06	-.24
UE	-.02	-.06	.31*	.07	.05	.24	.11	-.09	.12	-.18
UI	-.01	.22	.20	.16	.17	.29*	.08	.19	.01	-.02
BD	.09	.49**	.13	.26	.01	-.22	.29*	.26	.25	-.07
VE	.25	.15	.41**	.13	.06	.26	.35*	.06	.18	-.06
PR	-.02	.10	.22	.10	.48**	.34*	.12	.13	.10	.01
PL	-.10	-.05	.27	.13	.41**	.42**	.23	-.12	.24	.13
HU	.25	.16	.25	.05	.10	.24	.13	.02	.23	-.01
AE	-.31*	.26	-.31*	.20	.38**	.30*	-.08	.08	.06	.22
RE	-.11	.11	-.11	.30**	.14	.16	.14	.39**	.08	.08
SB	.20	.65**	.20	.46**	-.12	.16	.26	.57**	.29*	.37**

Brief COPE = SD Self-distraction, AC Active coping, DE Denial, SU Substance use, UE Use of emotional support, UI Use of instrumental support, BD Behavioral disengagement, VE Venting, PR Positive reframing, PL Planning, HU Humor, AE Acceptance, RE Religion, SB Self-blame.
MCQ-30 = CC Cognitive confidence, POS Positive beliefs, CSC Cognitive self-consciousness, NEG Negative beliefs, NC Need to control thoughts.
** $p < .05$; ** $p < .01$*

Table 4 - Pearson *r* correlations between Brief COPE and MCQ-30 scores for the two samples

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For the MS patients, positive beliefs were related to use of emotional support (moderate positive correlation), acceptance (moderate negative correlation), venting (moderate positive correlation), and denial (strong positive correlation). For the control sample, positive beliefs were positively correlated with religion (moderate positive correlation), and self-blame (strong positive correlation).

Cognitive self-consciousness was positively correlated with acceptance, planning, and positive reframing for both samples. The correlation coefficients were positive and ranged from moderate to strong. Regarding the MS patients, cognitive self-consciousness was also related to active coping. On the other hand, we found a positive correlation between cognitive self-consciousness and use of instrumental support, denial, and self-distraction for the control sample. In terms of negative beliefs, there was a moderate positive correlation with denial for both samples. Negative beliefs were also related to self-distraction, behavioral disengagement, and venting (moderate positive correlations) for the MS patients, but not for the control sample. The results for the control sample show different correlations. Negative beliefs were positively related with religion (moderate positive correlation) and self-blame (strong positive correlation).

Regarding need to control thoughts, there was a positive and moderate correlation with self-blame for both samples. Need to control thoughts was positively correlated with active coping for the MS patients, and with denial for the control subjects.

4. Discussion

The current study aimed to explore the relationships between metacognitions, anxiety, depression, and coping strategies in MS patients, comparing them with healthy subjects. The results of this study are a valuable addition to the research on the application of metacognitive S-REF theory to understanding emotional distress and coping strategies in MS patients.

We hypothesized that there are no differences between MS patients and healthy subjects in terms of metacognitions. Previous studies have shown the role of metacognitions as vulnerability factors in predicting development of psychological symptoms [16]. In line with our initial expectations, results did not show significant differences in metacognitive factors between the two groups.

Another aim of this study was to examine the relationships between metacognitions and anxiety, depression, and overall distress in MS patients and healthy subjects. Past studies have found dysfunctional metacognitive beliefs to be positively associated with emotional distress [16]. Regarding MS patients, past studies has shown that the patients' perceived cognitive functioning is predicted by depression, anxiety, and level of disability [9]. However, to our knowledge, there are no previous studies on the relationships between metacognitions and anxiety and depression. The results of the current study show that cognitive confidence, positive beliefs, negative beliefs, and need to control thoughts are positively correlated with anxiety in both in MS patients and healthy controls. Contrary to our expectations, cognitive confidence and negative beliefs were positively correlated with depression for MS patients but not for healthy subjects. Cognitive self-consciousness, or the tendency to monitor one's own thoughts and focus attention inward, was negatively correlated with depression in healthy subjects but not in MS patients. A past study with a non-clinical sample population found that cognitive self-consciousness weakly predicted depression, but not anxiety [22]. Moreover, a recent study found that cognitive self-consciousness was not related with anxiety or depression in cancer patients undergoing chemotherapy [17].

Consistently with previous studies on metacognitions [23], in our two samples cognitive self-consciousness was not correlated with anxiety. The tendency to monitor one's own thoughts and focus attention inwards has a marginal role in the metacognitive model of psychopathology.

On the other hand, the cognitive confidence factor was positively and strongly correlated with disease duration in the MS sample. The other metacognitive factors did not show any significant correlation with disease duration in the MS sample. Hence, cognitive confidence has a central role for MS patients (e.g. ''my memory can mislead me at times'').

MS is a disease characterized by cognitive symptoms, such as deficits in complex attention, executive functioning, and long-term memory, that affect many aspects of daily life [10]. Therefore, the results of this study highlight the relationships between cognitive confidence, which measures a subject's confidence in his/her attention and memory, and the symptoms of emotional distress. Moreover, disease duration seems to precipitate this impairment.

Finally, the correlations between metacognitive factors and overall distress were similar for both the MS sample and the healthy sample. Cognitive self-consciousness was the only metacognitive factor that did not correlate with overall distress scores.

The third aim of this study was to explore the relationships between metacognitions and coping strategies in patients with MS and healthy subjects. The results of recent studies have shown a relationship between cognitive impairments, negative emotions, and dysfunctional coping strategies [28], although the nature relationship remains unclear. The results of this study suggest that there are specific, contrasting correlations between metacognitions and coping strategies for the MS patients sample and healthy subjects. Our study is the first published attempt to explore these relationships, to our knowledge.

Denial was found to be positively related with cognitive confidence for both samples, but only weakly. Regarding the healthy subjects, cognitive confidence was positively related with substance use and behavioral disengagement. Cognitive confidence was also positively and strongly correlated with self-blame.

Regarding the MS sample, cognitive confidence was only negatively (moderately) correlated with acceptance as a coping response.

Hence, cognitive resource limitations were negatively related with coping strategies based on acceptance. Acceptance was also negatively and moderately correlated with positive beliefs.

Moreover, positive beliefs about worry were positively correlated with denial, venting, and use of emotional support in MS patients. For the healthy subjects, positive beliefs were also correlated with coping strategies, albeit to a differing degree. Specifically, there was a moderate coefficient correlation between positive beliefs and religion, and self-blame.

Cognitive self-consciousness was positively correlated with positive reframing, planning, and acceptance for both samples. Additionally, there was a moderate and positive correlation between cognitive self-consciousness and active coping in MS patients, but not in healthy subjects. On the other hand, this metacognitive factor was positively correlated with self-distraction, use of instrumental support, and denial in healthy subjects, but not in MS patients. Negative beliefs about uncontrollability and danger were found to be positively and moderately

related to denial for both samples. Negative beliefs were weakly related to venting, behavioral disengagement, and self-distraction in MS patients. Contrastingly, negative beliefs were strongly correlated with self-blame and moderately correlated with religion.

Need to control thoughts was positively and moderately related to self-blame for both samples. Furthermore, need to control thoughts was related to active coping in MS patients, and denial in healthy subjects. With regards to MS patients, it is reasonable to think that the extent to which a patient believes that certain types of thoughts need to be suppressed can play a role in trying to improve their situation.

The results of this study may be affected by a number of limitations that should be addressed by future research. First, the sample under study was small and all patients were consecutively recruited in a neurological department. Therefore, the sample may not be representative of the entire clinical population of MS patients. However, patients were recruited according to the revised McDonald criteria [18],and a matching control sample in terms of gender, age, level of education and social status was employed for the study. Secondly, anxiety, depression and overall distress were measured with the HADS assessment[24-25], that does not take into account potential somatic symptoms. It was developed to assess emotional disturbances in medical sample populations. However, past studies have employed HADS to explore psychological symptoms in non-clinical samples [22]. Thirdly, there is a range of additional variables whose role we did not consider, such as social support, religiosity, employment, and area of residence. The quality of life (QOL) in these patients is not only determined by physical disability. In fact, variables such as the level of social support, area of residence, depression, level of education, employment, fatigue and religiosity contribute to determine a poor or good QOL.

For these reasons, this study needs replication to further examine the role of additional variables and metacognitions in MS patients. Furthermore, it might be worthwhile to change the study design to better explore the nature of the relationships found in this study.

If confirmed by future research, the results of this study could have implications in clinical practice. Cognitive behavioral approaches can be effective in helping patients with MS, but to date, there are no definite conclusions or standard practices for psychological interventions [29]. In this regard, a recent study has demonstrated the efficacy of a training program based on metacognition in MS patients [11]. Even though studies have explored the cognitive function in MS patients [8], the patient's perceived cognitive function[9] and its relationship with coping strategies, a metacognitive approach has not been operationalized in patients with MS. This study investigated the role of metacognitive S-REF theory in MS patients and its relationships with negative emotions and coping strategies. Given the relationship between metacognitions and negative emotions, a "psychological intervention" based on metacognitive therapy[16] could have positive effects on MS patients. In this perspective, a time-limited group therapy can be helpful for MS patients [30].

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