Mental Health Issues in Multiple Sclerosis Patients and Healthy Controls and Their Association with Disease Related Factors

A. Poulios[1], A. L. Christopoulos[1], D. K. Kitsos[2*] and K. I. Voumvourakis[2]

[1]Department of Psychology, University of Athens, School of Philosophy Athens, Greece.
[2*]Department of Neurology, Attikon University hospital, University of Athens, Medical School, Athens, Greece.

Authors' contributions

The authors contributed equally to the design of the study

ABSTRACT

Purpose: To investigate the mental health problems of multiple sclerosis (MS) patients, and the relationship between mental health, MS variables and disability status.
Methods: The sample consisted of 80 participants, 40 MS patients and 40 Healthy Controls matched for gender, age and socioeconomic status. There were 30 (75%) women and 10 (25%) men, 27 (67.5%) Relapsing Remitting Multiple Sclerosis (RRMS) patients, 8 (20%), Secondary Progressive (SP) patients and 5 (12.5%) Primary Progressive (PP) patients in the MS group, 26 (65%) of those were on systemic treatment. The General Health Questionnaire-28 (GHQ-28) was used to screen for mental health issues. Disability status was assessed with the Expanded Disability Status Scale (EDSS).
Mean comparisons were performed using Student's *t* test while effect sizes were estimated by Cohen's *d* coefficient. Percentage ratio differences were tested using *chi-square tests*, corrected by *Fischer's exact test* for 1 *df*. Correlations were investigated using Pearson's *r* coefficient.
Results: MS patients exhibited significantly more mental health problems than the healthy controls. The effect size of the presence of positive MS diagnosis ranged from large to very large with respect to overall psychological distress as well as with respect to the following different dimensions of psychological distress: somatic symptoms, anxiety - insomnia, social dysfunction and severe depression. There were significantly more MS

Corresponding author: Email: greeknite@gmail.com;

patients who could be diagnosed with mental health disorders (non psychotic disorders of axis I, DSM-IV-TR). Finally, no aspects of mental health impairment were significantly correlated with disease variables or disability status.

Conclusions: Mental health problems in MS patients are evident and frequent. As they are independent of illness duration, medication or disability, special care should be taken in treating mental health problems in MS patients.

1. INTRODUCTION

Mental health problems are very common in MS patients in comparison to the general population and to individuals with other diseases that cause similar disability [1,2]. Mental health problems are evident during the whole course of illness and many of them do not recede if not treated properly [3,4]. Despite the fact that they are a treatable factor that in many cases has a greater impact on the quality of life than even disability levels, psychological problems are often not diagnosed and consequently not treated in a multi-disciplinary context, as proposed by contemporary studies [2,5,6,7,8,9].

Mental health problems may have direct impact on the disease course, through their psycho-neuroimmunological effects [2,10,11]. Mental health problems also have indirect impact on the disease course due to their negative effect on adjustment and compliance with the medical recommendations [2,12].

The most common forms of psychopathology and psychosocial dysfunction are depression, anxiety and associated disorders as well as social and interpersonal dysfunction [2,13,14]. Other forms of psychopathology are also evidenced, such as various mood disorders, somatoform disorders and sometimes, in cases of severe neural degeneration, psychotic episodes and disorders of impulse control and personality disorders [2].

The pathophysiology of MS is related to the causes of psychopathology, especially depression [2,8,15]. Moreover, many psychosocial factors related to the disease are also considered causes of psychopathology, indicating that a bio-psychosocial approach is necessary in developing a treatment plan [2,8,12]. The fact that, according to research findings, psychopathology is not directly associated with disease related factors, such as duration or disability levels, lends further support to this hypothesis [15].

2. MATERIAL AND METHODS / EXPERIMENTAL DETAILS / METHODOLOGY

Purpose: (a) To investigate the presence of mental health problems and their frequency in a Greek sample of MS patients in comparison with healthy controls. (b) To investigate the existence of correlation between mental health issues and various illness and disability related factors, as well as some central socio-demographic factors.

The sample consisted of 80 participants, 40 MS patients (the first 40 patients enrolled in the MS dpt of Attikon University hospital, Athens, Greece within 12 weeks) and 40 healthy controls. Gender, age, $t(78) = 0.10$, $p = 0.925$, and years of education, $t(75.20) = -1.06$, $p = 0.294$, were controlled for the two groups of participants. On table 1 demographic and disease variables are shown. Regarding the type of disease for the MS group, 67.5% (27

participants) were RR cases, 20% (8 participants) were SP cases and 12.5% (5 participants) were PP cases. It should be noted that gender percentages and type of disease were quite similar to the ones of the MS population with the exception of the SP cases whose frequency in our study was rather lower than that of the MS population.

Table 1. Sample demographic and disease variables (N = 80)

Variables	Group[†]							
	Control				**MS**			
	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
Disease duration					8.72	8.61	0.17	31
EDSS score					2.63	1.16	1	6
Medication[‡]					65% (26 participants)			

Note. [†]Gender analogy is 25% (10 participants) male and 75% (30 participants) female for both groups. Disease subtypes are 67.5% RR, 20% SP, 12.5% PP.[‡] 26 of the 40 patients were under injectable treatment for ≤1y. 77% IF beta 1α, 12% IFbeta -1β, 11% glatiramer acetate.
M: Mean, SD: Standard Deviation

Mental health problems were assessed by the *General Health Questionnaire – 28* (GHQ-28) [16]. It is a widely used instrument, psychometrically sound and appropriate for organic illness, including MS [17,18,19,20,21,22]. This instrument yields a total score that reflects global psychological dysfunction and distress and additionally assesses four component domains of mental health problems: somatic complaints (mainly somatisation and fatigue symptoms), anxiety and insomnia, social dysfunction and severe depression.

The assessment is made in terms of mean scores for the separate domains and the total mental health problems (with higher scores indicating more psychological dysfunction). Assessment can also be used for screening purposes, using cut-off scores to identify patients who have non-psychotic mental health problems.

Disability status of MS patients was estimated by the *Expanded Disability Status Scale* (EDSS) which assesses physical and neurological disability in MS patients [23]. The rating is done by a neurologist who assesses pyramidal, cerebellar, brainstem, cognitive and emotional function. Scores may range from 0 to 10, where 0 indicates absence and 9.5 indicates maximum presence of functional systems' disability.

Patients examined in the tertiary care Neurology Clinic of the University General Hospital Attikon were asked to participate in the study. All patients had a confirmed diagnosis of MS according to known criteria (McDonald proposed criteria 2010) and were asked to sign an informed consent form. Participation was voluntary and anonymous.

26 of the 40 patients were under injectable treatment. 20 of them were receiving IF-beta 1α, 3 of them were receiving IF-beta 1β and the last 3 were receiving glatiramer acetate. All the 26 patients were receiving treatment for ≤1 year. No statistically significant correlation was found amongst treatment and mental health issues.

The patients were assessed in many areas, including mental health by a clinical psychologist. Patients were also assessed when necessary by a more than 10 years of practice psychiatrist. Only one case of psychotic behaviour illness was found and not

included in the sample. The present study is a pilot presenting the first results from a screening procedure of the aforementioned assessment.

A comment from the reviewers was that "This study is a prevalent estimation of health related symptoms. Both MS and psychological problems are dynamic measures, changing from one period to another. Repeated measures of GHQ-28 would be relevant to correlate to socio-demographic measures. None of the selected measures would be expected to correlate with GHQ-28 with only one prevalent measure. I.e. a methodological problem"

Only two patients were receiving psychiatric medication concerning mood disorders and none were in ongoing treatment with a mental health professional. Patients who participated reported no positive psychiatric history before the MS diagnosis while none reported substance use. Patients with a diagnosis of an additional chronic physical or psychotic mental illness (as GHQ-28 is not appropriate for its diagnosis [17,22]) were excluded from the study. Each MS patient was matched for age, sex and years of education with volunteers (healthy blood donor at the hospital) from the community. Exclusion criteria included 1.Psychotic disorder (as assessed clinically by clinical psychologist and psychiatrist), 2.Substance abuse, 3.Concomitant chronic and/or acute disease, 4.Serious cognitive impairment (MS patients only)

Mean comparisons were performed using Student's *t* test while effect sizes were estimated by Cohen's *d* coefficient. Percentage analogy differences were tested using *chi-square tests*, corrected by *Fischer's exact test* for 1 *df*. Correlations were determined using Pearson's *r* coefficient.

3. RESULTS AND DISCUSSION

The mean comparisons of the mental health variables resulted in all cases in statistically significant results, with the MS group having more problems in comparison with the healthy controls. MS positive diagnosis effect size ranged from large to very large effect, in the case of physical problems (see table 2).

Table 2. Means and standard deviations of mental health problems of healthy controls and MS patients

	Group				t	df	Cohen's d
	Control		MS				
	M	SD	M	SD			
Somatic Problems	4.53	2.75	9.10	4.46	-5.52***	64.93	1.25
Anxiety & Insomnia	5.35	3.07	9.10	4.71	-4.22***	67.04	0.96
Social Dysfunction	6.08	2.35	8.45	3.86	-3.32***	64.34	0.75
Severe Depression	1.12	2.43	4.00	4.72	-3.43***	58.34	0.78
Overall mental problems	17.08	7.89	30.65	14.31	-5.25***	60.73	1.17

*Note. *** p < 0.001.t: t value of student's t-test, df :degrees of freedom*

There were also significantly more MS patients than healthy controls that, according to the mental health screening, could be diagnosed with mental health problems, both in overall mental health problems as well as in the discrete domains (see table 3).

Table 3. Absolute and relevant frequencies of the presence of mental health problems for the healthy controls and the MS patients

	Healthy Controls		MS patients		Total		χ^2 (df = 1, N = 80)
	f	%	f	%	f	%	
Physical Problems	8	20	29	72.5	37	46.3	22.18***
Anxiety & Insomnia	7	17.5	26	65	33	41.3	18.62***
Social Dysfunction	5	12.5	21	52.5	26	32.5	14.59***
Depression	2	5	12	30	14	17.5	8.66**
Overall mental problems	7	17.5	27	67.5	34	42.5	20.46***

*Note. ** p < 0,01, *** p < 0,001.*

No significant correlations were found between mental health and the demographics of gender, age, years of education and family status.

Moreover, no statistically significant correlations between mental health and years of disease, medication and disability, as measured by the EDSS were obtained (see table 4).

Table 4. Correlation coefficients (Pearson r) between mental health and disease-related factors (N = 40)

Pearson r	Disease duration	Medication	EDSS
Somatic Complaints	-0,06	-0,01	-0,14
Anxiety & Insomnia	-0,03	-0,13	-0,18
Social Dysfunction	0,14	0,21	0,17
Severe Depression	0,23	-0,04	0,08
Overall mental problems	0,09	-0,00	-0,03

4. DISCUSSION

In line with other relevant studies [1,2], MS patients exhibited significantly higher levels of both overall psychological distress and mental health issues in their specific investigated aspects than the healthy controls. Furthermore, the fact that 67,5% of the MS patients, versus 17,5% of the healthy controls, were positive according to the screening of presence of mental health disorders shows that not only do they exhibit higher levels of psychological problems, but also that the majority of MS patients could be diagnosed with some kind of psychiatric non-psychotic axis I disorder.

In terms of the discrete domains of mental health issues, somatic problems were significantly higher in the MS patients with 72,5%, versus 20% of the healthy controls being positive for diagnosis of some kind of somatic complaints disorder. Of special interest is the fact that this scale did not correlate significantly with the EDSS score, which suggests that MS patients report more somatic problems than those measured by the EDSS. Additionally, as the somatic complaint scale has many items assessing symptoms like those of chronic fatigue syndrome [20], the fact that MS scored significantly higher in comparison to the healthy controls may reflect the quite common fact that fatigue symptoms are very common in these patients [18].

The finding that MS patients present high levels of anxiety and insomnia are in line with the results of other studies [2,8]. Actually, the fact that 65% of the MS patients, versus 17,5% of the healthy controls, were found positive in the screening of anxiety disorders is in accord with the finding of similar studies that anxiety disorders may be even more common in MS patients than depression [2], which is considered the most common psychiatric disorder presented by MS patients.

Indeed, despite the fact that depression was higher in MS patients than the healthy controls (30% of the investigated patients were positive in the screening of some kind of depressive disorder, versus 5% of the healthy controls) this percentage is somewhat lower than the one found in other studies [2]. One explanation of this finding could be that on one hand, GHQ estimates rather severe forms of depression [16,21] and thus maybe some patients with milder forms of depression forms were underestimated. Moreover, according to Mohr and Cox [8] the kind of depression MS patients present is not the same as the major depressive disorder most scales estimate. It seems that symptoms such as anger, generalised distress and tension are more profound in these patients rather than sadness [8].

Regarding social dysfunction, MS patients present more difficulties (52.5%) than healthy controls (12.5%). Thus, this domain should not be underestimated as, according to contemporary research findings [5,6], social dysfunction has a severe negative impact on the quality of life of the investigated patient population while good social functioning is an important protective factor of the disease's impact.

It is interesting that none of the disease-related variables was significantly correlated with the various investigated aspects of mental health problems or with overall mental health problems. Despite the fact that the size of the sample was rather small, this finding is in accord with previous results according to which psychological difficulties MS patients are quite stable over time and are quite often independent of disability severity [4,14,15]. Apparently, medication may improve the illness's effects but does not, at least directly, ameliorate mental health problems.

4.1 Limitations and Future Directions

One basic limitation of the current study is the relatively small sample. Undoubtedly, the fact that there were statistically significant findings with very low *p* values and that the MS sample was representative of the MS population, lends support to the reliability of the presented findings. However, a larger sample would enhance the rigour of the findings' significance and would provide the opportunity to investigate more aspects of multiple sclerosis such as relationships between the variables under investigation and the different types of MS.

Our study is considered a pilot study hence at that time we did not have data on possible cognitive impairment of our sample apart from the EDSS assessment. Further research should include many more variables concerning cognitive impairment so as to highlight any correlation with mental health problems

It would add to the presented results to use additional measures to assess mental health and other important variables such as fatigue. Perhaps, more importantly, other factors that create mental health problems or even moderate or mediate their relationship to MS should be looked for given that disease factors investigated were not significantly correlated with

mental health issues. Such factors of interest include personality traits, social support, and specifically located brain lesions.

It would also be interesting to compare MS patients with patients with other diseases, both neurological, i.e. MS like disorders, and other autoimmune and generally chronic diseases that cause similar disability.

Lastly, since MS patients appear to have significant psychological problems, interventions of various kinds should be planned and assessed with respect to their effectiveness.

5. CONCLUSION

MS patients present more psychological problems than healthy controls. This difference appears to be clinically significant in view of the effect size coefficients. In fact, according to our findings, it is likely that more than 50% of MS patients could be diagnosed with some kind of psychiatric disorder. Given that is mental health issues are independent of central disease related factors and that many studies [4,5,8,15] indicate that psychological problems have a greater negative impact on the quality of life of MS patients, sometimes even greater than even disability, it would appear that special care should be taken in specifically treating such problems, most probably with both medical and psychological interventions. Such treatment could help with symptoms of mental health issues and additionally help these patients adjust to their disease, cope with the challenges the disease presents and cooperate with medical treatment [5].

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CONSENT

Not applicable.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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