

## Anxiety and depression in patients with multiple sclerosis: The mediating effects of perceived social support

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#### Abstract

#### Background

Social support has been identified as a buffering or intervening variable in stressful life events. Research has demonstrated that greater social support is associated with better mental health in multiple sclerosis (MS), but little is known about its links to specific aspects of mental health. We therefore investigated if and how perceived social support modulates depression, anxiety and fatigue in patients with MS.

#### Methods

We recruited 112 patients with MS from three French hospitals and administered a demographic and clinic interview, and self-report measures of perceived social support (Multidimensional Scale of Perceived Social Support), depression and anxiety (Hospital Anxiety and Depression Scale), and fatigue (Fatigue Severity Scale). We then analyzed the relationships between these domains using path analysis.

#### Results

The causal path model provided an excellent fit for the data ( $\chi 2 = 9.8$ , p = 0.778, standardized root mean square residual = 0.043, comparative fit index = 1.00). Results indicated that the level of social support from friends is a predictor of anxiety symptomatology. Thus, anxiety may have both a direct and an indirect impact on fatigue and depression levels.

#### Conclusions

This study highlights the important roles played by perceived social support and anxiety in MS. These should be key pharmacological and non-pharmacological targets for optimizing patient care.

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Keywords: perceived social support, anxiety, depression, multiple sclerosis

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#### 1. Introduction

Multiple sclerosis (MS) is characterized by the occurrence of widespread lesions or plaques in the brain and spinal cord (Compston and Coles, 2008). Because of these lesions and their unpredictable locations, MS has a broad range of motor, visual, cognitive, and neuropsychiatric symptoms.

Owing to the physiopathology of the disease and its unpredictable course, psychological and psychiatric disorders are common features of MS. Relative to individuals with similar degrees of disability, patients with MS have an elevated incidence and prevalence of psychological and psychiatric symptoms (Beiske et al., 2008; José Sá, 2008; Kinsinger et al., 2010; Marrie et al., 2015). MS also has psychosocial consequences, disrupting life goals, employment, relationships, and daily living activities (Morrow et al., 2010; Simmons, 2010; Smith and Arnett, 2005).

Depression and anxiety are among the most common psychiatric disorders in MS, and their association increases the risk of suicide. *Depression* concerns 26-55% of patients, according to the literature, with a lifetime prevalence of around 50% (Feinstein et al., 2014; Patten et al., 2017; Siegert and Abernethy, 2005; Wood et al., 2013). Severe depression is more prevalent in MS (15.7%) than it is in either the general population (7.4%) or patients with other chronic diseases (9.1%), suggesting a direct effect of the disease on depressive symptoms (Chwastiak et al., 2002; Patten et al., 2003; Sadovnick et al., 1996). Although the etiology of depression in MS remains unclear, it appears to stem from the interaction of biological, psychological and social factors. High levels of *anxiety* can occur even in the early stages of MS, with prevalence rates ranging from 43% to 70% (Butler et al., 2016; Boeschoten et al., 2017; Chahraoui et al., 2008; Korostil and Feinstein, 2007; Montel and Bungener, 2007; Wood et al., 2013). Both depression and anxiety are associated with increased thoughts of selfharm, impaired social functioning, lower quality of life, and more somatic complaints, leading to greater utilization of healthcare services (Al-Asmi et al., 2015; Feinstein et al., 1999; Wollin et al., 2013). Gay et al. (2017) and Gay, Vrignaud, Garitte, and Meunier (2010) showed that anxiety and functional status (disability) are independent predictors of depressive symptoms, with anxiety being a strong predictor. This relationship is modulated by social support and alexithymia (Gay et al., 2010).

Given the impact of anxiety and depression on disease course, health, and quality of life, research has focused on the factors that protect against them and predict their emergence. Illness-related factors (severity of disability, extent of neurological lesions, disease duration) are often weaker predictors of psychosocial adjustment (Chwastiak et al., 2002) than psychological factors (Kirchner and Lara, 2010; Thomas et al., 2006). Among these, social support is an important contributor to positive social adjustment (Dennison et al., 2009).

Social support refers to the emotional, instrumental and informational support that people receive from others to cope with their stressful life events. Social support providers include family members, friends and significant others. Significant others include coworkers, healthcare professionals and other patients. Social support influences morbidity, mortality, and quality of life in both the general and chronic disease populations (Bruchon-Schweitzer and Boujut, 2014). It has a direct and positive effect on physical and mental health and/or acts as a buffer, protecting against the negative effects of stressful life events. In patients with MS, lower social support is associated with higher anxiety and depression, and lower quality of life (Dennison et al., 2009). Although social support is frequently studied in MS, little is known about either the nature of its relationship with mood and emotional factors or differences according to provider (e.g., relative, friend, or healthcare professional). Some studies showed that poor perceived support from friends and family members was strongly associated with depressive symptomatology (Jensen et al., 2014; McIvor et al., 1984). More recently, social support was found to be significantly related to mental health outcomes regardless of the source of that support (Koelmel et al., 2017). Krokavcova et al. (2008) showed that social support from significant others has a positive impact on perceived physical health, while that from family and friends had a positive impact on perceived mental health.

Given recent findings indicating that anxiety predicts depression in MS (Gay et al., 2017, 2010), together with the acknowledged role of perceived social support in depression and mental health, we explored whether perceived social support predicts the relationship between anxiety and depression in MS, using path analysis. We also took fatigue and disability into account, as several studies have highlighted the impact of these variables. We considered perceived social support from three sources: family members, friends, and significant others. Better knowledge of how these different variables interact could inform the design of psychological and therapeutic education programs aimed at preventing anxiety and depression.

#### 2. Method

#### 2.1 Participants

We recruited 112 patients with clinically definite MS (Polman et al., 2011) during their regular appointments at three French hospitals (Reims University Hospital, Porte Verte Hospital in Versailles, de Rothschild Ophthalmology Foundation in Paris). Exclusion criteria were (a) history of alcohol or drug abuse, (b) history of major psychiatric illness other than major depressive episode, (c) history of a neurological disorder other than MS, (d) significant visual or motor impairment that would interfere with testing, and (e) relapse within the past 6 weeks.

#### 2.2 Measures

#### 2.2.1 Sociodemographic and clinical variables

Patients were asked to provide basic demographic information, including their sex, age, education level, marital status, and employment status. Clinical and disease-specific variables (level of disability, type of MS, and time since diagnosis) were obtained by neurologists. Patients' level of disability was measured with the Expanded Disability Status Scale (EDSS; Kurtzke, 1983).

#### 2.2.2 Perceived social support

The Multidimensional Scale of Perceived Social Support (MSPSS, Zimet et al., 1990) is a self-report questionnaire with 12 items assessing perceived social support from family, friends and significant

others, rated on a 7-point Likert-like scale ranging from 1 (*Strongly disagree*) to 7 (*Very strongly agree*). Each of the three sources is probed by four items, and subscores range from 4 to 28. A high subscore indicates high perceived social support. The French version of the MSPSS (Denis et al., 2015) is a reliable and valid measure with high internal consistency (Cronbach's alpha > .90).

#### 2.2.3 Anxiety and depression

The Hospital Anxiety and Depression Scale (HADS, Zigmond and Snaith, 1983) is a widely used selfassessment instrument for determining the severity of depressive and anxiety symptoms. It comprises 14 items: seven for depression and seven for anxiety. Each item is rated on a 4-point Likert-like scale ranging from 0 to 3, yielding subscores of 0-21. A subscore of 0-7 indicates the absence of anxious/depressive symptoms, a subscore of 8-10 indicates the presence of moderate symptoms (i.e., doubtful cases), and a subscore of 11 or above indicates numerous symptoms of anxiety/depression (i.e., confirmed cases). The French version of the HADS (Untas et al., 2009) has good reliability and discriminant validity (Cronbach's alphas > .80). The HADS was developed specifically for use in medically ill populations characterized by *potential somatic confounders*, including MS (Honarmand and Feinstein, 2009). We selected it because the absence of items assessing somatic symptoms (fatigue, insomnia, impaired concentration, pain) limits false positive findings.

#### 2.2.4 Fatigue

The Fatigue Severity Scale (FSS, Krupp et al., 1989) is a nine-item self-assessment questionnaire originally used to assess fatigue among patients with MS or systemic lupus erythematosus. Participants indicate the fatigue they experienced in different situations during the previous week on a 7-point Likert scale ranging from 1 (*Strongly disagree*) to 7 (*Strongly agree*). The final score represents the mean value of the nine items. A high FSS score indicates a high level of fatigue. The FSS has good internal consistency (Cronbach's alpha = 0.88) and good test-retest reliability (r = 0.84).

#### 2.3 Procedure

After providing demographic information and being assessed on the EDSS by an experienced neurologist, participants completed three self-report measures of perceived social support, depression and anxiety, and fatigue. These took about 30 min to complete. The study was approved by the medical research committee and ethics committee (S.C. 3396) of Tarnier-Cochin Hospital, Ile-de-France. All participants gave their written informed consent, and the study was conducted in accordance with the Declaration of Helsinki.

#### 2.4 Statistical Analyses

We used SPSS Version 21.0 for Macintosh to undertake the descriptive and correlational analyses, and AMOS 20.0 for Windows to perform the structural equation modelling for the path analyses.

We used descriptive statistics to summarize these data, *t*-test to compare MSPSS, FSS, and HADS scores between the progressive (PMS) and relapsing remitting MS (RRMS) forms and Pearson correlation coefficients to explore the relationships between the variables of interest. Path analysis was used to estimate the strength of the direct and indirect relationships between the variables of interest with perceived social support as predictors and anxiety and depression primary outcomes. Variables were introduced into the model if they were significantly correlated with perceived social support, anxiety and/or depression (see Table 3). Model fit statistics included the Satorra-Bentler chi-squared test (SB $\chi^2$ ), standardized root mean square residual (S-RMR), root mean square error of approximation (RMSEA), comparative fit index (CFI), and goodness-of-fit index (GFI), which measured the proportion of the variance/covariance explained by the model.

#### 3. Results

#### 3.1 Sociodemographic and Clinical Characteristics

A total of 112 patients with MS met the inclusion criteria. However, two were excluded from the analyses, owing to incomplete responses. Of the 110 participants who provided usable data, 70 patients (63.6%) had the relapsing-remitting form of MS and 40 (36.4%) a progressive form (Lublin et al., 2013): 17 (15.4%) had primary progressive MS, and 23 (21%) secondary progressive MS. The participants' details are given in Table 1.

#### [INSERT TABLE 1 HERE]

#### 3.2 Descriptive data for the self-report measures

Descriptive and comparison data for the self-report questionnaires are provided in Table 2.

The mean MSPSS score (M = 5.40, SD = 1.17) was comparable to that found in both the general population (M = 5.80, SD = 0.86; Zimet et al., 1988) and the MS population (M = 5.34, SD = 1.25; Osborne et al., 2007). There was no effect of sex on either the total mean score, t(108) = 0.93, p = .35, or the three mean subscores: family, t(108) = 1.68, p = .09, friends, t(108) = 0.58, p = .56, and significant others, t(108) = -0.13, p = .89. Due to the small number of participants in each progressive form, we have grouped primary and secondary progressive forms into a single group. The PMS and RRMS groups did not differ significantly on the total MSPSS score or the three mean subscores: family, friends, and others.

The mean HADS depression subscore was within the normal range (M = 6.35, SD = 4.03), suggesting that most participants did not have depression: 62% of participants scored below 8 (no depression symptoms), 21% scored between 8 and 10 (possible symptoms), and 17% scored above 10 (probable symptoms). The mean HADS anxiety subscore (M = 9.01, SD = 4.24) indicated that patients had possible anxiety symptoms: 37% of participants scored below 8 (no anxiety symptoms), 27% scored between 8 and 10 (possible symptoms), and 36% scored above 10 (probable symptoms). The PMS and RRMS groups did not differ significantly on HADS total score. However, the two groups differ significantly on the HADS anxiety and depression subscales. The HADS anxiety subscale showed a significantly higher level of anxiety symptoms in the RRMS group than among the PMS while the HADS depression subscale showed a significantly higher level of depressive symptoms in the PMS group.

The mean FSS score of patients with MS (M = 5.48, SD = 1.42) in this study was similar to that found for patients with MS in other studies (e.g., M = 4.66, SD = 1.64; Valko et al., 2008) and higher than that of healthy controls (e.g., M = 3, SD = 1.08; Valko et al., 2008). No differences between PMS and RRMS patients were observed on the mean FSS score.

#### [INSERT TABLE 2 HERE]

# **3.3** Correlation between perceived social support, anxiety, depression, fatigue, and disease severity

The total MSPSS score was significantly negatively correlated with both the HADS-A and HADS-D subscores, but not with FSS, EDSS or disease duration. HADS-A was positively correlated with HADS-D and FSS, but not with EDSS or disease duration. HADS-D was positively correlated with both FSS and EDSS, but not with disease duration. Finally, FSS, EDSS, and disease duration were correlated. These results are summarized in Table 3.

[INSERT TABLE 3 HERE]

# 3.4 Relationships between perceived social support, anxiety, depression, fatigue, and functional status

To test our hypothesized model, we undertook a path analysis, using the maximum likelihood estimation on AMOS 20 (see Fig. 1). This analysis served to confirm the known direct links between anxiety, fatigue, EDSS and depression, and to explore the direct effects of the three types of perceived social support on anxiety and depression. Disease duration was not included in the model since it did not correlate with social support; depression and anxiety (see Table 3).

Given the non-normality of our data, we used a bootstrap resampling approach to obtain robust statistics in SEM (Nevitt & Hancock, 1998). Thus, rather than using the usual maximum likelihood-based p-value to assess overall model fit, we used and presented the Bollen-Stine bootstrap to provide the correct p-values for the chi-square statistic (Bollen & Stine, 1992). According to criteria, the CFI must be above .95, the S-RMR below .08, and the RMSEA below .08, for a model to be deemed

satisfactory. Moreover, according to Jöreskog and Sörbom (1993), the GFI must be above .90 for the model to be acceptable. Our model showed a good fit with the data,  $SB\chi^2(7) = 4.02$ , *Bollen-Stine* p = .745 (for information: *usual* p = .778), GFI = .99, CFI = 1.00, RMSEA = .000 and S-RMR = .034. Figure 1 presents the standardized values of the regression coefficients. All the values are significant at p < .05.

#### [INSERT FIGURE 1 HERE]

As shown in Figure 1, anxiety directly triggered depression symptoms ( $\beta = .27, p < .05$ ) and contributed to fatigue symptoms ( $\beta = .32, p < .001$ ) which, in turn, heightened depression symptoms ( $\beta = .30, p < .001$ ). We found an identical result for the EDSS, which directly triggered depression symptoms ( $\beta = .23, p < .01$ ) and contributed to fatigue symptoms ( $\beta = .41, p < .001$ ) which, in turn, enhanced depression symptoms ( $\beta = .30, p < .001$ ). This suggests that fatigue plays a mediating role in the relationships between anxiety and depression, and between EDSS and depression.

Concerning perceived social support, we observed three different relationships: perceived social support from family had no effect on either anxiety ( $\beta = -.15$ , ns) or depression ( $\beta = .04$ , ns), perceived social support from others was directly negatively linked to depression symptoms ( $\beta = -.19$ , p < .05) but not anxiety ( $\beta = .01$ , ns), and perceived social support from friends was directly negatively linked to anxiety ( $\beta = -.27$ , p < .05) but not depression ( $\beta = -.15$ , ns). As anxiety was connected to depression, perceived social support from friends probably had an indirect effect on depressive symptomatology via anxiety.

To test for the mediating role of fatigue in the relation between anxiety and depression, we performed a bootstrap analysis (5000 iterations) and checked the indirect confidence index (ICI), which proved to be significant (p = .001), indicating some kind of mediation. To determine whether this mediation was full or partial, we checked the direct confidence index (DCI) and found that it was also significant (p =.015), albeit less strongly so. Fatigue was therefore a partial mediator of the relation between anxiety and depression. We used the same process to test for the role of fatigue in the relation between EDSS and depression. The ICI was significant (p = .001), as was the DCI (p = .009), albeit more weakly, thus indicating that fatigue was a partial mediator. Finally, we used the same process to test for the mediating role of anxiety in the relation between perceived social support from friends and depression. The ICI (p = .021) was significant, but not the DCI (p = .096), indicating that anxiety was a full mediator.

#### 5. Discussion

We sought to explore the relationship between perceived social support, anxiety, and depression in patients with MS, postulating that perceived social support is predictive of the relationship between anxiety and depression. Our main goal was to explore the role of perceived social support from three different sources (relatives, friends, and significant others) as a predictor of the relationship between anxiety and depression in MS, using path analysis.

First, prevalence rates for anxiety and depression in our study were similar to those reported in the literature, with around 17% of patients displaying clinically significant depressive symptoms, and around 36% clinically significant anxiety symptoms (Boeschoten et al., 2017). Anxiety and depression prevalence rates vary widely across studies. This may be due in part to the instruments that are used (e.g., (semi)structured interview vs. cut-off on a self-report scale). A recent review and meta-analysis showed a mean prevalence of 20.6 (range: 9.3-76.4) for depression and a mean prevalence of 34.2 (range: 15.4-54.1) for anxiety, with measures similar to those used in our study (i.e., cut-off scores on self-report scales) (Boeschoten et al., 2017).

In our study, anxiety and depression were strongly associated, and were both correlated with fatigue and perceived social support, in accordance with the literature (Butler et al., 2016). We found that depression was associated with disability (EDSS), unlike anxiety and perceived social support. Anxiety, depression and perceived social support were not correlated with disease duration. Studies examining the links between depression or anxiety and clinical variables such as disability and disease duration have yielded inconsistent results, with some reports confirming positive associations and others not (Beiske et al., 2008; Butler et al., 2016; Chwastiak and Ehde, 2007; Jones et al., 2014). These seemingly controversial results could be due to the heterogeneity of the clinical characteristics

of the MS samples and the cross-sectional design of the studies. For example, levels of anxiety and depressive symptoms are thought to be higher in the early years of the illness, after which they decrease (Wood et al., 2013).

In line with Gay et al. (2010, 2017), we found that anxiety was a strong predictor of depression, both directly and indirectly. Fatigue played a partial mediating role in the relationship between anxiety and depression. Anxiety caused depression and increased symptoms of fatigue, which in turn increased the depressive symptoms. With regard to perceived social support, its effects on anxiety and depression symptoms varied according to its source.

While perceived social support from friends had a direct effect on anxiety symptoms, perceived social support from significant others had a direct effect on depressive symptoms. Furthermore, perceived social support from friends had an indirect effect on depressive symptoms. The relationship between perceived social support from friends and depression was fully mediated by anxiety. This result suggests that perceived social support from friends reduces anxiety symptoms which, in turn, reduce depressive symptoms. However perceived social support from family had no effect on anxiety or depression in our sample. This result is surprising, and may stem from the fact that participants were asked to rate perceived *social support of the family* without distinguishing between close and distant relatives. This term may therefore have been too broad, resulting in more heterogeneous responses, compared with those for perceived social support from friends/others, where participants focused solely on persons of interest.

These findings confirm the strong relationship between anxiety and depression, and the partial mediating role of fatigue in this relationship (Butler et al., 2016; Gay et al., 2017, 2010). They highlight the role of social support according to its provider, in particular, the role of low perceived social support from friends as a predictor of anxiety symptoms. This seems to be supported by a prospective study showing that patients with high social support are less anxious (Butler et al., 2016). Our study had several limitations. First, its cross-sectional design meant that issues of causality could not be adequately addressed. Moreover, although we used a bootstrap resampling approach to obtain

robust statistics, our results should be viewed with caution given the relatively small MS sample size. Prospective studies with larger samples are needed to confirm our results. Second, we measured perceived social support from different providers, but had no information about whether this support was emotional, functional, or informational. Different types of social support may have different effects on emotional and mood variables, just as different sources of social support seem to have, with emotional support seeming to play the most important role, especially in anxiety (Bruchon-Schweitzer and Boujut, 2014). Third, the size of our sample did not allow us to conduct a research on the different forms of MS. It would be interesting to replicate this study with more participants by distinguishing the MS subtypes because the profiles could be different according to clinical characteristics of the disease for example. Indeed, some studies show that patients with a PMS are more depressed than those with a RRMS (Lorefice et al., 2015). Finally, our study focused primarily on anxiety, depression, fatigue, and perceived social support, even though other factors are known to play a role in anxiety and/or depression. Coping, perceived stress, social variables, and personality may modulate the relationship between anxiety and depression, and could be included in our causal model. These variables could help explain the amount of variation in depression not captured by the variables of interest. Further studies with more participants with MS are needed to introduce other variables without reducing statistical power.

In summary, several studies have shown that social support is predictive of the physical and mental dimensions of health-related quality of life in MS, but little is known about its links with other variables that contribute to quality of life, such as anxiety and depression. Our findings confirm the role of anxiety as a predictor of depression, and the roles of perceived social support from friends in anxiety and perceived support from others in depression. Different types of social support are clearly necessary to different dimensions of mental health in patients with MS.

Anxiety and social support should be considered as important pharmacological (for anxiety) and/or non-pharmacological (for anxiety and social support) therapeutic targets for reducing or even preventing depressive symptoms. Anxiety is commonly reported in MS-more so than depression-, but remains undertreated (Beiske et al., 2008), even though it affects many domains, including cognition,

treatment adherence, illness symptoms, and quality of life (Butler et al., 2016). Social support also plays a role in many factors that can improve quality of life, such as action-oriented and problemsolving coping styles. A recent meta-analysis on interventions for depression and anxiety in MS (Fiest et al., 2016) failed to find any controlled study of the effectiveness of psychological and pharmacological treatments. This suggests that further research is needed on the impact of anxiety on patients with MS, and more systematic use should be made of existing anxiety-focused interventions.

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#### **Conflict of interest**

The authors declare that they have no conflicts of interest affecting this article.

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#### Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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## TABLES

### Table 1

Sociodemographic and Clinical Characteristics of Patients with MS

	Mean (SD)	Range
Demographic data		
Age in years	44.93 (12.70)	21-86
Education in years	13.16 (3.07)	9-17
Sex	F: 76 (69%)	
	M: 34 (31%)	
Marital status		
Married	66 (60%)	
Single	26 (24%)	
Divorced	16 (14%)	
Widow(er)	2 (2%)	
Employment status		
Employed	60 (54%)	
Unemployed	22 (20%)	
Invalidity	28 (26%)	
Children		
With	71 (65%)	
Without	39 (35%)	
Clinical data		
Median EDSS score	4	0-8.5
Disease duration in years	10.92 (8.72)	0-40

*Note*. EDSS = Expanded Disability Severity Scale.

## Table 2

	RRMS	PMS	All group		
	(n = 70)	( <i>n</i> = 40)	( <i>n</i> = 110)		
	Mean (SD)	Mean (SD)	<i>p</i> -value	Mean (SD)	Range
Total MSPSS	5.52 (1.04)	5.18 (1.34)	.14	5.40 (1.17)	1.58-7
MSPSS – Family	5.47 (1.45)	5.22 51.62)	.50	5.38 (1.51)	1-7
MSPSS – Friends	5.18 (1.40)	4.80 (1.62)	.19	5.04 (1.49)	1.25-7
MSPSS – Others	5.92 (1.11)	5.48 (1.37)	.07	5.76 (1.22)	2-7
Total HADS (0-42)	15.49 (7.82)	15.90 (6.89)	.77	15.64 (7.21)	1-33
Depression subscale (0-21)	5.58 (3.56)	7.67 (4.49)	.04	6.35 (4.03)	0-16
Anxiety subscale (0-21)	9.61 (3.99)	7.90 (4.49)	.008	9.01 (4.24)	0-21
FSS	15.90 (6.89)	15.49 (7.82)	.06	5.48 (1.42)	1-7

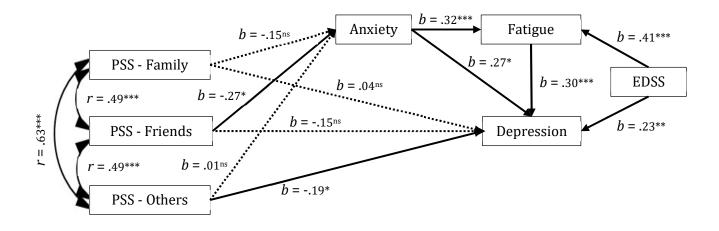
### Descriptive and Comparison Data for Self-Report Measures

*Note.* MSPSS = Multidimensional Scale of Perceived Social Support; HADS = Hospital Anxiety and Depression Scale; FSS = Fatigue Severity Scale.

	MSPSS Friends	MSPSS Others	HADS-A	HADS-D	FSS	EDSS	DD
MSPSS Family	0.48***	0.62***	27*	24	08	10	07
MSPSS Friends	_	0.47***	34**	37***	03	03	03
MSPSS Others	-	-	- .33***	21	12	09	07
HADS-A			_	.42***	.29**	07	01
HADS-D			_	_	.49***	.35***	.19
FSS			_	_	_	.39***	.23*
EDSS			_	_	_	_	.36***

Table 3 Pearson Correlation Coefficients of Perceived Social Support, Anxiety, Depression, Fatigueand Disease Severity

*Note.* MSPSS = Multidimensional Scale of Perceived Social Support; HADS = Hospital Anxiety and Depression Scale; FSS = Fatigue Severity Scale; EDSS = Expanded Disability Severity Scale; DD = disease duration. \* p < .05. \*\* p < .01. \*\*\* p < .001.



*Note.* Dotted lines represent nonsignificant pathways and solid lines significant ones. \* p < .05; \*\* p < .01; \*\*\* p < .001.

Model fit statistics: *X*<sup>2</sup> (*df*) = 4.02 (7); *p* = .778; GFI = .990; CFI = 1.00; RMSEA = .000; S-RMR = .034.

Figure 1: The causal path model. The values on the arrow represent the standardized path coefficients (*r values*: coefficients of correlation between the variables; *b* values: standardized regression weights)