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Anxiety and depressive symptoms in caregivers of multiple sclerosis patients: The role of information processing speed impairment☆

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ABSTRACT

Background: Multiple sclerosis (MS) patients have high rates of complications and disability, including cognitive impairment, that often, impact on caregivers' emotional health. Clarification may help identify improved supportive strategies for both caregivers and patients.
Objective: We aimed to analyse whether MS domain-specific cognitive impairment can influence the severity of psychiatric symptoms of MS caregivers.
Methods: Patients with definite MS ($n = 63$) and their corresponding caregivers ($n = 63$) were recruited. In addition, 59 matched controls were enrolled for establishing normative cognitive data. Each patient underwent a complete neuropsychological testing for cognitive impairment and thorough clinical assessment, including data of disability status (EDSS), affective and emotional symptoms (depression, anxiety, anger) and fatigue. Psychiatric symptoms of the caregivers were assessed with the Beck Anxiety Inventory (BAI) and the Beck Depression Inventory (BDI).
Results: In logistic regression analyses, even after controlling for other MS-related symptoms, cognitive deficits, namely impairment on Symbol Digit Modalities Test ($OR = 8.03$, 95% $CI = 1.27–25.33$, $p = 0.027$) and on the Paced Auditory Serial Addition Test ($OR = 6.86$, 95% $CI = 1.07–21.97$, $p = 0.042$), were significant and independent predictors of more severe caregivers' depressive symptoms.
Conclusions: Information processing speed impairment is independently associated with more severe depressive symptoms of caregivers of MS patients, thereby reflecting a further deterioration of family setting.

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1. Introduction

Since multiple sclerosis (MS) is a chronic and incapacitating disease, providing care for a person with MS has considerable deleterious effects on the caregiver's psychological health [1–5]. Several studies have shown that MS caregivers have higher levels of distress [6], strain [7], and perceived burden [2], as well as significantly lower health-related quality of life (HRQoL) than healthy subjects [3,8,9]. However, some topics require further research. First, clear understanding of the MS-related characteristics specifically linked to anxiety and depression in caregivers is lacking. This would allow a better understanding of what MS-related symptoms influence family stress and resilience. Patients and caregivers are often concerned about cognitive symptoms but they do not always agree if it is significant [10].

The impact of MS-related cognitive impairment on caregivers' psychological symptoms has been documented in only two previous studies. Figved et al. [6] found that cognitive impairment in patients with MS was associated with caregivers' distress and HRQoL, even after controlling for level of disability. In particular, impairment on the Paced Auditory Serial Addition Test (PASAT) and impairment on Symbol Digit Modalities Test (SDMT) were significant predictors [6]. Chipchase at al. [11] found that problems with everyday memory and activities of daily living were associated with carer strain. Strained carers perceived strain to be a consequence of memory problems [11]. Furthermore, we have recently shown that caregivers' HRQoL was strongly influenced by slowed information processing speed of MS patients [3].

Given the paucity of studies in this area, our objective was to analyse to what extent MS-related cognitive impairment influences the severity of caregivers' psychiatric symptoms through a comprehensive approach

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☆ Authors' contributions Andrés Labiano-Fontcuberta collaborated in: 1) the conception, organization and execution of the research project; 2) the statistical analysis design; and; 3) the writing of the manuscript first draft and the review and critique of the manuscript.Alex J. Mitchell in: 1) the conception, organization and execution of the research project; and 2) the review and critique of the manuscript.Sara Moreno-García collaborated in: 1) the review and critique of the manuscript.Julián Benito-León collaborated in: 1) the conception, organization and execution of the research project; 2) the statistical analysis design; and; 3) the review and critique of the manuscript.

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where demographic, clinical, cognitive and psychosocial factors were all considered simultaneously. On the basis on our previous work, in which cognitive impairment was found to predict worse caregivers' HRQoL, we hypothesised that even when all known MS-related disabilities were accounted for, MS cognitive impairment would strongly influence self-report indices of caregivers' anxiety/depressive symptoms.

2. Methods

1. Study design and subjects

The study group consisted of 63 MS patients, their corresponding caregivers and 59 matched controls. MS patients were consecutively recruited from either the MS Clinics at the University Hospital "12 de Octubre" (Madrid, Spain) or from the MS Association of Madrid, Spain.

The inclusion criteria for patients were as follows: 1) having a definite diagnosis of MS; [12] 2) being stable (free from any exacerbation) at the time of study; 3) having a level of disabilities that implied they needed some extra care to manage by themselves and; 4) being able to complete a neuropsychological assessment. Patients were excluded if 1) they were in an acute phase or a relapse of the illness; 2) were suffering severe illness not related to MS; 3) were diagnosed with dementia, according to *Diagnostic and Statistical Manual of Mental Disorders (DSM) IV* criteria [13].

As to the family caregivers, defined in this work as anyone who provided informal care including basic (e.g. bathing and dressing) or instrumental activities (e.g. cooking and housework) of daily living on a regular basis, the selection criteria were: 1) living with the patient (or being in daily contact), and being responsible for caring for the patient; and 2) voluntarily caregiving.

To determine normative neuropsychological data, fifty nine age, gender and education-matched healthy controls were recruited either from relatives of patients who came to the neurological clinics for reasons other than MS (e.g., headache, dizziness) or amongst the relatives or friends of the health professionals working at the University Hospital "12 de Octubre" of Madrid (Spain).

3. Measurement instruments

1. Caregivers

Symptoms of depression were assessed by the Beck Depression Inventory (BDI) [14]. The choice of responses to each depression symptom is 0–3 points, and a higher score indicates more severe depression (range from 0 to 63). Between the different versions of the BDI, BDI-IA was applied [15]. Its standardized cut-off scores differentiate four categories of severity: 0–9 = no depression; 10–16 = mild depression; 17–29 = moderate depression; and 30–63 = severe depression [14].

To assess the severity of symptoms of anxiety, the Beck Anxiety Inventory (BAI) was used [16]. The BAI is a self-report questionnaire in which respondents are asked to rate how much each of the anxiety symptoms of the questionnaire bothered them, on a scale ranging from 0 (not at all) to 3 (severely, I could barely stand it) [16]. The total score has a minimum of 0 and a maximum of 63 and better scores indicate better levels of anxiety [16]. Suggested cut-off values for this instrument are as follows: 0–7 = no anxiety; 8–15 = mild anxiety; 16–25 = moderate anxiety; and 26–63 = severe anxiety [16].

2. MS patients

1. Neuropsychological assessment

Five neuropsychological tests were administered both to MS patients and their matched healthy controls: The Symbol Digit Modalities Test (SDMT); [17] the Paced Auditory Serial Addition Test (PASAT); [18] the Stroop Colour-Word Trial; [19] and the Controlled Oral Word Association Test (COWAT) [20]. In addition, subjects were asked to generate as many different animals as possible in 1 min to test semantic verbal fluency [21].

2. Psychiatric assessment

Both BAI and BDI were included to explore the level of anxiety and depressive symptomatology, respectively. Given recent findings regarding the presence of a disturbed pattern of anger emotion in MS patients [22], it was also interesting to include anger measurement as an independent MS-related psychological variable. Anger was assessed by the Spanish adaptation of the State-Trait Anger Expression Inventory-2 (STAXI-2) [22,23]. Among the different six scales that compose STAXI-2, three were particularly suitable to address the objectives of our study: State Anger, Trait Anger, and Anger-Out scales [15,16]. The State Anger scale is a 15-item scale designed to measure the intensity of angry feelings at a particular time [15,16]. The Trait Anger Scale is a 10-item scale designed to measure how an individual is disposed to experience frequent, intense and long-lasting anger [15,16]. The Anger-Out is a 6-item scale that measures the tendency to express anger through aggressive behaviour toward other people or objects [15,16]. Each item response consists of a 4-point Likert type scale ranging from 1 "almost never" to 4 "almost always." and in each case, higher scores indicate a greater level of anger or its expression [15,16].

3. Disability and fatigue assessment

Kurtzke Expanded Disability Status Scale (EDSS) [24] was applied to rate the disability status of each patient. The Fatigue Impact Scale for Daily Use (D-FIS) was administered to measure subjective daily experience of fatigue in MS patients [25,26].

4. Procedures

A structured interview was conducted for each MS patient providing information regarding demographic data, comorbidity, medications, age of MS onset, and disease evolution. Clinical and neurological examination, including scoring of the EDSS, was also performed. Cognitive tests were conducted in a single session by experienced clinical neuropsychologists (VP, VM, AB, JFP, MIH, NC and UE, see Acknowledgements) during an interview on the week in what they had completed the aforementioned psychiatric measures. All the neuropsychologists were blinded to BDI, BAI and STAXI-2 results.

Each caregiver was given a comprehensive questionnaire containing demographic and caregiving-related data as well as BAI and BDI tests, which would have to be refilled at their home.

All subjects provided written informed consent and the University Hospital "12 de Octubre" (Madrid, Spain) Committee of Ethics approved the study.

5. Statistical analyses

The data were analysed using the SPSS Version 21.0 (SPPS Inc, Chicago, IL, USA). All tests were two sided, and significance was accepted at 5% level (alpha = 0.05).

Normative neuropsychological data were derived from the group of healthy volunteers. *Z* scores were based on the means and standard deviations (SD) of this group. We defined cognitive impairment as a *Z* score $\leq$ 1.5 SD below the mean of any of the five neuropsychological tests. When assessing cognitive functioning, the interference of possible confounders should be always taken into account and thus, demographic and clinical characteristics of MS patients were compared according to their cognitive status.

Univariate correlations were used to investigate the relationship between each neuropsychological test and anxiety (BAI scores) and depressive (BDI scores) symptoms of caregivers. As no significant relationship was observed between domain-specific cognitive functioning and BAI scores, anxiety of caregivers was not considered further in the analysis (see below).

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