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Multiple sclerosis is associated with high trait anger: A case–control study

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ABSTRACT

Introduction: In recent years there has been a focus on health-related quality of life in multiple sclerosis (MS) and in particular the importance of non-motor problems such as fatigue, pain, depression, anxiety, and cognitive disorders. However, little attention has been focused on other negative emotions, such as anger. Our purpose was to evaluate whether trait anger (a predisposition to experience frequent and intense episodes of anger over time) is different between persons with and without MS after controlling for depression, anxiety, and other socio-demographic variables.
Methods: 157 consecutive MS patients were enrolled in the study and compared to eighty age, gender, and education-matched healthy controls. Participants were administered affective trait measures (Beck Depression Inventory, Beck Anxiety Inventory) and the trait anger measure (the Spanish adapted version of the State–Trait Anger Expression Inventory-2 [STAXI-2]).
Results: MS patients had significantly higher scores on anger intensity (state anger) and trait anger than did controls. They also had a trend to experience direct anger toward other persons or objects in the environment (higher anger expression-out score) and to hold in or suppress angry feelings (higher anger expression-in score). However, in a regression analysis that adjusted for different demographic and clinical variables, we found that diagnosis category (MS patient vs. control) was associated with none of the highest quartiles of STAXI-2 scores, except for the Trait Anger scale (odds ratios between 2.35 and 3.50).
Conclusions: The present study provides further evidence that MS is independently associated with high trait anger.

1. Introduction

The focus on health-related quality of life of MS in recent years has demonstrated the importance of non-motor symptoms. Among these, fatigue, pain, depression, anxiety, and cognitive disorders are among the most important [1–4]. However, although anger is one of the basic emotions, and deleterious consequences of anger on physical health have been well reported [5], only two studies have specifically been performed on the association between anger and MS [6,7]. In all these previous studies [6,7], unmeasured confounders, including demographic variables such as marital status and employment status, and the effects of medications with central nervous system activity (e.g., anxiolytics, stimulants, antipsychotics, antidepressants, antihistamines, and antiepileptic drugs) [8], may have influenced the results.

Anger is the emotion associated with attack/threat often associated with irritability and occasionally aggression [5,9]. It can be measured by the degree to which people have this mood and the characteristic means by which they express it [5,9]. The prolonged predisposition for frequent, often intense, long-lasting anger is a relatively enduring and stable personality attribute known as trait anger [5,9]. Anger expression, on the other hand, refers to how anger is managed, that is, whether it is expressed outwardly, held in, or controlled [5,9].

Both psychosocial and biological factors contribute to anger [5,9]. Yet the biological basis of anger is not fully known [5,9]. Serotonin, and perhaps serotonergic dysregulation, may be involved in the modulation of anger and aggressive behavior [10–12]. In this sense,

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biochemical studies have shown that MS patients are serotonergically depleted with the extent of cerebral depletion correlating with the degree of motor disability and a chronic progressive course [13,14]. In some studies drugs such as selective serotonin reuptake inhibitors (SSRIs) have been associated with changes in anger [15]. Given these observations, we hypothesized that modulation of anger might be affected in MS, and more specifically, that MS is associated with higher levels of trait anger. The little attention that has been focused on trait anger in MS encouraged us to conduct a case–control study to assess this relationship, using the Spanish adapted version of the State–Trait Anger Expression Inventory-2 (STAXI-2) [9,16,17]. Our analyses adjusted for several confounders, including socio-demographic variables and medications with central nervous system activity [8].

2. Methods

2.1. Participants

One hundred and fifty seven MS patients were consecutively recruited from January 2011 to June 2013 either from the MS Clinics at the University Hospital "12 de Octubre" (Madrid, Spain) or from the MS Association of Madrid, Spain. Patients studied had clinically definite MS by McDonald criteria [18,19], were stable (free from any exacerbation) at the time of study, and fluent Spanish speakers. A 20 minute interview was conducted on each MS patient in which information on age of MS onset and disease evolution was also obtained. Three neurologists with expertise in MS (JBL, ALF, and SMG) participated in the clinical assessment and applied the Kurtzke Expanded Disability Status Scale (EDSS) to rate the severity of disease (range = 0–10) [20]. For clinical course, two subgroups were defined: relapsing/remitting (RR) and progressive (secondary progressive [SP] or primary progressive [PP]). The Fatigue Impact Scale for Daily Use (D-FIS) was administered to measure subjective daily experience of fatigue in MS patients [21,22].

Patients taking high dose of corticosteroids at the time of the recruitment were temporarily excluded, and they underwent the emotional and neuropsychological batteries at least one month after the interruption of the drug treatment. Other exclusion criteria were as follows: institutionalized at the time of observation; major acute co-morbidities or any major serious chronic illness three months before inclusion (patients with a stable chronic medical conditions were included); and neurological illness other than MS, including dementia.

Eighty 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 among the relatives or friends of the health professionals working at the University Hospital "12 de Octubre" of Madrid (Spain). None of the controls recruited were consanguineous of the patients with MS involved in the present study. Each control was free of known neurological disorders. None of the control subjects had symptoms or a history of a neurological disorder (e.g., demyelinating disorders, cognitive impairment) and none had received a neurological diagnosis from a physician.

2.2. Procedure

All procedures were approved by the ethical standards committees on human experimentation at the University Hospitals "12 de Octubre" (Madrid). During recruitment, cases and controls were told that the purpose of the study was to complete a battery to assess both emotional status and neuropsychological status. After the study had been described to subjects, written (signed) informed consent was obtained from all enrollees.

2.3. Measurements

Symptoms of depression were assessed by the Beck Depression Inventory (BDI) [23]. The BDI is a widely used self-report measure of depressive symptoms that has been validated for MS and is recommended in this population of patients [24]. The range of responses to each depression symptom is 0–3 points, and a higher score means more severe depression (range from 0 to 63) [23]. Symptoms of anxiety were assessed by the Beck Anxiety Inventory (BAI) [25]. The BAI is a self-report questionnaire to assess the severity of symptoms of anxiety [25]. 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) [25]. The total score has a minimum of 0 and a maximum of 63 and higher scores indicate higher levels of anxiety [25].

Anger was assessed by the State–Trait Anger Expression Inventory-2 (STAXI-2) [9,17]. Participants rate themselves on 4-point scales for each item. In each case, higher scores indicate a greater level of anger and its suppression or expression [9,17]. The Spanish adaptation of the STAXI-2 was used: it includes 49 items (range 0 to 196), and it is organized into six scales (including five subscales) and an anger expression index that provides an overall measure of total anger expression [9,17]. The trait anger contains two subscales, T-Anger/T, which measures the general disposition toward angry feelings (angry temperament), and T-Anger/R, which measures the tendency to express anger when one is criticized (reaction to criticism) [9,17]. State anger (including the three subscales: feeling angry; feel like expressing anger verbally; and feel like expressing anger physically) assesses current anger as an emotional state [9,17]. Additional scales include anger expression-out, which measures expression of anger toward other persons or objects in the environment; anger expression-in, which assesses the holding in or suppression of angry feelings; anger control-out, which assesses the control of angry feelings by preventing the expression of anger toward other persons or objects in the environment; and anger control-in, which assesses the control of angry feelings by calming down or cooling off [9,17]. The final scale, the anger expression index, is a general index of the expression of anger. This index comes from the following formula: (anger expression-out + anger expression-in) − (anger control-out + anger control-in) + 36 [9,17].

A five-test neuropsychological test battery was administered to all subjects. Cognitive tests were conducted in a single session by experienced clinical neuropsychologists (VM, VP, AB, JFP, MIH, NC and UE, see Acknowledgments) during an interview on the week in what they had completed the aforementioned affective trait measures. All the neuropsychologists were blinded to STAXI-2, BDI and BAI results. The following neuropsychological tests were administered to all participants:

a) The Paced Auditory Serial Addition Test (PASAT)
   The PASAT measures working memory and speed of information processing. Both the 3-second and 2-second versions of the PASAT were administered [26]. The score was the total number of correct responses [26].
b) The Symbol Digit Modalities Test (SDMT)
   The SDMT is a test of sustained attention that measures information processing speed [27]. This test involves the substitution of digits for symbols as quickly as possible within a 90 second time frame. The score was the total number of correct items [27].
c) The Stroop Color–Word Trial
   The Stroop Color–Word Trial is a test of executive functioning that requires participants to inhibit a natural response (reading a word) and replaces it with another response (saying a color) [28]. Participants completed 45-s word naming, color naming, and color–word naming trials of a computer-based Stroop task. The score for this study was the number of correct responses in the color–word trial [28].
d) The Controlled Oral Word Association Test (COWAT) is a test that measures phonemic fluency [29]. Participants were provided three letters of the alphabet (F, A, and S), one letter at a time, and instructed to say as many words as possible that begin with this letter in a 60-second interval [29]. All responses were recorded verbatim.