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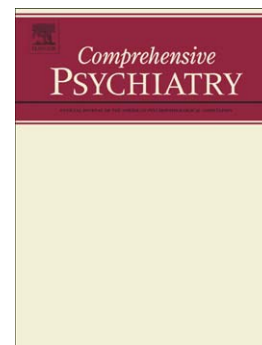
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Executive Function in Fibromyalgia: Comparing Subjective and Objective Measures

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Background: There is evidence to suggest the existence of an executive dysfunction in people diagnosed with fibromyalgia, although there are certain inconsistencies between studies. Here, we aim to compare executive performance between patients with fibromyalgia and a control group by using subjective and objective cognitive tests, analysing the influence of patient mood on the results obtained, and studying associations between the two measures. **Method:** 82 patients diagnosed with fibromyalgia and 42 healthy controls, matched by age and years of education, were assessed using BRIEF-A¹ as a subjective measure of executive functioning. A selection of objective cognitive tests were also used to measure a series of executive functions and to identify symptoms of depression and anxiety. **Results:** Patients with fibromyalgia perceived greater difficulties than the control group on all of the BRIEF-A scales. However, after adjustments were made for depression and anxiety the only differences that remained were those associated with the working memory scale and the Metacognition and Global Executive Composite index. In the case of the objective cognitive tests, a significantly worse overall performance was evidenced for the fibromyalgia patients. However, this also disappeared when adjustments were made for depression and anxiety. After this adjustment, fibromyalgia patients only performed significantly worse for the interference effect in the Stroop Test. Although there were no significant associations between most of the objective cognitive tests and the BRIEF-A scales, depression and anxiety exhibited strong associations with almost all of the BRIEF-A scales and with several of the objective cognitive tests. **Conclusions:** Patients with fibromyalgia showed executive dysfunction in subjective and objective measures, although most of this impairment was associated with mood disturbances. Exceptions to this general rule were observed in the impairment of working memory evidenced on the BRIEF-A scale and the inhibition impairment exhibited by the interference effect from the Stroop Test. The two types of measurement provide different yet complementary information.

Keywords: Fibromyalgia; executive functions; subjective cognitive dysfunction; depression; anxiety.

1. Introduction

¹ Behavioral Rating Inventory of Executive Function – Adult version

Fibromyalgia is a chronic disease belonging to the group of musculoskeletal diseases. It is characterized by the presence of generalized and diffuse pain, which is generally accompanied by other symptoms such as fatigue, restless sleep, depression and cognitive disorders [1]. Although pain is the main symptom of this disease, cognitive complaints are common in affected patients and contribute to an increased perception of disability and to this disease having a great impact on the quality of life of these patients [2].

The study of cognitive complaints associated with this disease has gained interest in recent years. These are now recognized as components of an independent symptom which must be studied as it causes patients increased suffering and discomfort [3]. Several studies have coincided in identifying the existence of cognitive dysfunction in fibromyalgia and in emphasizing problems associated with executive functions and, more specifically, with working memory processes and attentional and executive control [4–7]. However, some authors have failed to find such impaired performance in these components [8–10], while others have even concluded that the cognitive dysfunction observed in these patients could be explained by concurrent symptoms of depression [11,12].

The executive functions construct includes an extensive variety of cognitive processes including: inhibition, impulse control, working memory, affect regulation, motivation, planning, organization, decision-making, judgment, monitoring, problem-resolution, hypothesis generation, abstract thought and cognitive flexibility [13,14]. Research on executive functions has linked the presence of executive dysfunction to

performance in day-to-day activities and shown that executive dysfunction may significantly contribute to functional difficulties [15,16].

Executive functions have traditionally been assessed through the use of objective cognitive tests, with this requiring the breakdown of these executive functions into their different cognitive processes in order to identify which have been conserved and which have been impaired. However, in clinical practice, it has been shown that the breakdown of this complex cognitive process is artificial. Studies performed with patients suffering from neurological conditions have revealed that objective cognitive tests of executive performance largely fail to collect the integrated, multidimensional, priority-based decision-making that is often demanded in real world situations, exhibit poor ecologic validity, and do not identify executive disorders in day-to-day functioning [17–24]. However, another way to evaluate executive functions is through daily functioning questionnaires; these are subjective evaluations that are usually administered to patients, and/or their relatives, and that have shown greater sensitivity than objective cognitive tests for reflecting everyday situations. In fact, subjective and objective measurements of executive functions seem to evaluate different processes: objective cognitive tests may assess underlying executive abilities, while the daily functioning questionnaires assess the application of these abilities in daily life [25].

One daily functioning questionnaire that has acquired significant importance in recent years is the Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) [26], which measures problems in executive functions. This is a subjective measure, as it uses self-reported information to assess the impact of an individual's perceived executive functioning on their day-to-day behavior. The inventory has been validated in an extensive variety of populations and has shown a number of good

psychometric properties. Studies using this scale have shown that it offers a useful way to assess and detect executive dysfunction in patients with ADHD, schizophrenia, mild cognitive impairment, traumatic brain injury, hypersexuality and eating disorders, and in those who are pathological gamblers and ecstasy consumers, among others [14,27–33].

Our primary aim was to determine whether there were significant differences between patients suffering from fibromyalgia and controls with respect to a series of subjective and objective measures of executive functions and then to analyse the influence of patient mood on performance in certain specific measures. We were also interested in exploring associations between the different components of the subjective and objective measures used in the study in order to understand the relationships between them and to know whether both approaches could be applied to provide useful and complementary information. Our hypothesis was that patients with fibromyalgia would perform significantly worse than the control group in subjective and objective tests of executive functions and that mood symptoms would exhibit associations with the performance of both measurement strategies. We also hypothesized that we would find a lack of significant associations between subjective and objective measures.

1. Method

2.1. Participants

We carried out a cross-sectional, case-control observational study in which we invited 100 patients who had been diagnosed with fibromyalgia to participate. Of these, 18 were excluded (3 decided not to participate, 7 were ineligible because they did not

meet the entry criteria and another 8 subsequently revoked their consent). Our sample population finally consisted of 82 women diagnosed with fibromyalgia who were recruited from the Fibromyalgia Unit of the Hospital Santa Maria of Lleida and who met the classification criteria of the American College of Rheumatology (Wolfe et al. 1990). Recruitment was performed between August 2012 and November 2014. The exclusion criteria were: (a) a history of neurological disorders; (b) a history of diagnosed psychotic spectrum; (c) a current major depressive episode; (d) a history of dependence on psychoactive substances; (e) a low estimated IQ, with a standard score of less than 85 according to the Vocabulary subtest of the Wechsler Adult Intelligence Scale (3rd edition), WAIS-III [34]; (f) ongoing treatment with antipsychotic drugs, (g) cognitive global impairment at the dementia level, with a score of ≤ 24 on the Mini Mental State Examination [35]; and (h) the diagnosis of other chronic autoimmune rheumatic diseases. The control group consisted of 42 healthy female volunteers who were recruited from non-healthcare community settings and matched with the patient group by age and years of education at a ratio of 2:1. The exclusion criteria were the same as for the patient group, with the addition of the presence of any rheumatologic diagnosis and also of any psychiatric disease. The study was approved by the hospital's institutional ethics committee (Hospital Universitari Arnau de Vilanova – CEIC 1068) and the research was carried out in accordance with the Helsinki Declaration. Written informed consent was obtained from each participant prior to their participation in the study.

1.2. Clinical Measures

1.2.1. Subjective Assessment of Executive Function

A subjective assessment of problems of executive functions was conducted by applying the BRIEF-A scale, which is a self-administered, standardized questionnaire whose aim is to identify problems in everyday life that can be attributed to executive dysfunction [26]. BRIEF-A provides a combined score for executive function, the Global Executive Composite (GEC) and two indices: the Behavioral Regulation Index, which includes four subscales (Inhibit, Shift, Emotional Control and Self-monitor), and the Metacognition Index, which includes five subscales (Initiate, Working Memory, Plan/Organize, Self-monitor and Organization of Materials). This questionnaire also includes 3 validity scales that indicate whether respondents tend: to have an unusually negative response style (Negativity scale); to report highly unusual symptoms (Infrequency scale); or to answer similar items in an inconsistent manner (Inconsistency scale). A Negativity scale raw score of 6 or higher indicates a high degree of negativity, an Infrequency scale raw score of 3 or higher evidences atypical responses, and an Inconsistency scale score of 8 or higher suggests the presence of inconsistent responses. The BRIEF-A scale uses T scores for which the mean value for the normative population is fixed at 50, the standard deviation is 10, and higher scores indicate worse performances.

1.2.2. Objective Cognitive Assessment

For the objective cognitive assessment, we selected a group of neuropsychological instruments that had been used to measure various components of executive functions.

1.2.2.1. Phonological Fluency

We used a phonological verbal fluency test that measured the spontaneous production of words beginning with the letters P, M and R within a time limit of 60 seconds for each letter. This provided information about the ability of the updating function. Proper nouns, repetitions and variations were not admitted. In the original English language version of this test, F, A, and S were the letters most commonly used, but in the Spanish version, the letters P, M and R are used [36]. The score was the sum of all the admissible words.

1.2.2.2. Paced Auditory Serial Addition Task (PASAT)

This is another test which assesses working memory, but also sustained attention, auditory processing speed, calculation ability and stimulus competition filtering skill [37]. The subjects added up consecutive numbers ranging from 1 to 9 presented by an auditory tape and responded orally by giving their sum. As each digit was presented, the patients added this number to the one presented before it. The presentation rates were 3.0 seconds in trial 1 (PASAT 3.0) and 2.0 seconds in trial 2 (PASAT 2.0). The score for each trial was given by the number of correct responses to 60 different combinations.

1.2.2.3. N-back Paradigm.

This task assesses working memory and requires relevant pieces of information to be maintained and constantly updated. It was performed with the aid of a computer and the subjects were required to monitor a continuous sequence of digits and to respond whenever the stimulus presented was the same as the one presented in previous trials, in which n was either 2 (2-back condition) or 3 (3-back condition) [38]. The participants were instructed to respond to the correct answer as quickly and accurately as possible by pressing the computer spacebar key. Each trial consisted of a stimulus,

which was presented for 500 milliseconds, followed by an interstimulus interval of 1500 milliseconds. After this period, the next stimulus was presented. In each block, a series of black numbers, ranging from zero to nine, were randomly presented in the centre of a grey background. There were 30 stimuli within each condition, 6 of which were the correct targets. Each block consisted of a 2-back condition followed by a 3-back condition, with each one being presented three times. The outcomes were the total number of correct responses for each condition.

1.2.2.4. Trail Making Test

The Trail Making Test is a set of visual search and sequencing tasks involving motor speed, attention and the ability to alternate between categories (set-shifting) [39]. In TMT-A, subjects were asked to connect consecutive numbers (e.g., 1-2-3), whereas in TMT-B, they had to alternate between consecutive numbers and letters (e.g., 1-A-2-B). The scores were based on the amount of time taken to complete each part of the test. We were specifically interested in evaluating the set-shifting ability and to do this we calculated a derived score based on the difference between the score TMT-B and TMT-A scores.

1.2.2.5. Stroop Color and Word Test

The Stroop Color and Word Test [40] was used to assess interference inhibition ability. The test consists of using a Word Card with 100 colour words (red, blue and green) printed in black ink, a Colour Card with 100 Xs printed in blue, red or green ink, and a Colour-Word Card with 100 names of colours printed in incongruent colours. Participants are asked to read the words (on the Word Card) or to name the ink colour (on the Colour Card and Colour-Word Card), as quickly as possible and within a time

limit of 45 seconds. We assessed the inhibition ability by calculating the interference effect as the number of correct responses given in the Colour-Word Card test minus the number of correct responses in the Colour Card test.

2.2.2.6. Wisconsin Card Sorting Test

The computerized version of the Wisconsin Card Sorting Test-64 [41,42] was used to assess abstract reasoning and the ability to change cognitive strategies in response to changing environmental contingencies. The participants were asked to sort a series of cards bearing simple stimuli that were characterized by three relevant categories (colour form, and number) and to relate them to four reference cards. The rules for correctly sorting the cards were modified during the test (every time that the participant achieved 10 consecutive hits in a certain category). We used the total number of categories achieved as a measure of abstract reasoning and the total number of perseverative errors as a measure of cognitive flexibility. The number of categories achieved corresponded to the number of runs of 10 correct responses and the number of perseverative errors was given by the total number of times that the subject failed to change their sorting strategy after receiving negative feedback.

2.2.2.7. WAIS-III-R Vocabulary subtest

We used the scaled score from the vocabulary subtest of the Weschler-III scale [34] as a measure of premorbid intelligence. The participants were required to provide definitions of words presented in order of increasing difficulty.

1.2.3. Mood Assessment

The Spanish version of the Beck Depression Inventory (second edition: BDI-II) [43,44] was used to assess the intensity of depressive symptoms. The BDI-II consists of 21 items that assess emotional, behavioral and somatic symptoms associated with depression. In this test, the scores range from 0 to 63, with higher scores indicating greater depressive symptoms.

The Spanish version of the State-Trait Anxiety Inventory (STAI) [45,46], was used to evaluate the intensity of anxiety. This consists of two subscales, each composed of 20 items. The State subscale measures anxiety related to a specific situation or time-period (at the moment of questionnaire completion), while the Trait subscale measures relatively stable anxiety. The total scores range from 20 to 80 for each subscale, with higher scores indicating greater levels of anxiety.

2.3. Statistical Analysis

We used the SPSS 16 program for Windows (SPSS Inc.) to perform our statistical analyses. We analysed whether there were differences between the two groups in terms of age, years of education, premorbid intelligence and mood disturbances, using the Student's *t* test. We used multivariate analysis of variance (MANOVA) to establish the presence or absence of differences between the 2 groups for the BRIEF-A scale and also in the cognitive tests. We subsequently performed post-hoc univariate analysis and measured the size of the effect using the eta-squared coefficient (η^2), in which values of >0.01 , >0.06 and >0.14 were respectively defined as small, medium and large. We then repeated the multivariate analyses using BDI-II and STAI scores as covariates.

For the cognitive measures, we calculated standard normal Z-scores for fibromyalgia patient data based on our own control data and averaged these Z-scores to obtain the level of impairment. Individual Z-scores were calculated by the following formula: $Z = (\text{value}_{\text{patient}} - \text{mean}_{\text{controls}}) / \text{SD}_{\text{controls}}$. The BRIEF-A scores were converted into T scores, and T scores ≥ 65 were considered clinically elevated [26]. Then, we calculated the percentage of participants in each group who presented clinically elevated scores for this measure. We also used the Fisher's Exact Test to compare the results obtained for the 2 groups. We computed Pearson correlations to analyse the associations between the BRIEF-A subscales and the cognitive tests, and between these measures and BDI-II and STAI. Statistical significance was declared at $P < 0.05$.

3. Results

3.1. Sample characteristics

There were no significant differences between the two groups in terms of age, years of education or premorbid intelligence. However, the 2 groups differed significantly in their scores on the BDI-II and STAI scales ($p < 0.001$). The fibromyalgia patients exhibited higher scores on both scales, with a significant higher incidence of symptoms associated with depression and anxiety than the control group (Table 1).

3.2. Inter-group analyses for BRIEF-A

No subjects had elevated scores on the Infrequency and Inconsistency scales. The Negativity scale was elevated for 45 patients from the fibromyalgia group (54% of the patients in this group), whereas none of the control group showed elevated scores on this scale. The high scores registered on the Negativity scale for the fibromyalgia group may be related to the known negative response pattern of these patients, which is

associated with high psychiatric comorbidity rates, rather than to a lack of validity of their responses to this questionnaire. We found strong associations between the Negativity scale score and BDI-II ($r=0.75$, $p<.001$), STAI State ($r=0.66$, $p<.001$) and STAI Trait ($r=0.66$, $p<.001$). For all of these reasons and as none of the protocols produced elevated scores on any of the other validity scales, we chose to include these subjects in the subsequent statistical analyses.

The overall MANOVA for the BRIEF-A subscales revealed significant differences between the fibromyalgia patients and the control group, with a Wilks $\lambda=0.437$, $F(11.933)$, $p<0.001$, $\eta^2=0.56$, showing greater dysfunction amongst the fibromyalgia patients. Adding the BDI-II and STAI scores as a covariate in the multivariate analysis attenuated the effect of size but did not change the overall pattern of the results obtained, with a Wilks $\lambda=0.829$ and $F(1.843)$, $p=0.05$, $\eta^2=0.17$. Within the MANOVA, the omnibus univariate tests were significant for the Working Memory subscale ($p=0.002$), Metacognition Index ($p=0.036$) and Global Executive Composite Index ($p=0.037$), with a medium effect size for the Working Memory subscale and a small effect size for the Metacognition and Global Executive Composite Index (Table 2). When we also considered age and education, in addition to BDI-II and STAI scores, as potentially confounding variables in the multivariate inter-group analysis, a borderline p-value was observed: Wilks $\lambda=0.833$ and $F(1.758)$, $p=0.065$, which was attributable to the consequent unnecessary loss of statistical efficiency in the variability estimation. Even so, when we specifically considered individual subscales, the results obtained were similar in terms of their statistical significance.

To further investigate the clinical context, we examined the percentage of individuals in each of the 2 groups who had clinically elevated scores: with T scores of 65 or more [26]. In the fibromyalgia group, more than half of the subjects exhibited clinically

elevated scores on six (Inhibit, Shift, Emotional Control, Initiate, Working Memory and Plan) of the nine subscales. In contrast, in the control group, the Plan subscale was the one that contained the highest proportion of subjects with clinically elevated scores (24%), while the other scales showed lower proportions (0-16.7%). Comparisons between the 2 groups for the percentage of participants with clinically elevated scores revealed significant differences for all of the scales except that relating to Organization of Materials (Table 3).

3.3. Inter-group analyses for the objective cognitive measures

The MANOVA for the objective cognitive tests also revealed significant differences between the 2 groups (Wilks $\lambda=0.751$, $F(3.895)$, $p<0.001$, $\eta^2=0.249$), although these disappeared after adjusting for the BDI-II and STAI measures; the overall MANOVA was non-significant (Wilks $\lambda=0.841$, $F(1.357)$, $p=0.19$, $\eta^2=0.159$). Despite the results of the MANOVA, we applied a univariate test to study each measure independently and to assess in more detail some of the measures which had previously been reported to have significant associations [7,47]. We only found significant differences between the groups for the interference effect from the Stroop Test, which exhibited a small size effect ($p=0.03$, $\eta^2=0.05$ (Table 4).

3.4. Associations between BRIEF-A and objective cognitive measures

An analysis of the associations between scores for objective cognitive measures and BRIEF-A scale scores in the group of fibromyalgia patients showed a significant negative correlation for a 3-back test with several BRIEF-A scales; these included: Inhibit ($r=-0.34$, $p=0.003$), Shift ($r=-0.26$, $p=0.03$), Initiate ($r=-0.23$, $p=0.04$), Working memory ($r=-0.28$, $p=0.009$), and Plan scale ($r=-0.25$, $p=0.03$), as well as for the

Behavioral Regulation Index ($r=-0.27$, $p=0.01$) and Metacognition Index ($r=-0.24$, $p=0.04$). We also identified significant negative associations between the WCST-categories score, an objective cognitive measure, and the Working Memory scale from BRIEF-A ($r=-0.24$, $p=0.03$) (Table 5).

4. Discussion

On examining executive functioning in patients with fibromyalgia using subjective self-report measures and objective cognitive tests, we initially found significant differences with respect to the control group. Fibromyalgia patients generally exhibited worse levels of performance, although many of the differences appeared to be influenced by mood disturbances, since most of them disappeared after adjusting for depression and anxiety.

As expected, fibromyalgia patients exhibited higher scores than the control group for measurements of mood symptoms related to depression and anxiety. These results agree with the vast majority of studies undertaken with patients suffering from fibromyalgia; this would therefore seem to be a common feature in these patients [48–51]. The influence of mood symptoms in subjective ratings of cognitive functioning has also been reported in other populations. This has occurred in both subjective measures of general cognitive functioning [52–55] and in subjective measures of executive performance using BRIEF-A, in which they were the strongest predictors of subjective executive dysfunction [56,57]. Our results also paralleled those presented in the original validation of BRIEF-A, which reported a significant association between this scale and both the Beck Depression Inventory II and State-Trait Anxiety Inventory [26].

In the case of specific results relating to subjective measures, we found significant differences between groups for all of the BRIEF-A scales. This led us to conclude that these patients probably presented impaired executive functioning in their daily lives. However, when we wanted to separate the influence of mood on executive performance, we found that most of the perceived executive dysfunctions disappeared, leaving only differences between groups associated with the Working Memory Scale. As a result, these patients reported experiencing significant problems relating to this ability that were independent of the severity of their mood symptoms. These results were in line with those of several other neuroimaging studies and add to growing evidence that fibromyalgia patients tend to exhibit several abnormalities in their frontoparietal networks which, in turn, affect their working memory processes [58,59]. Functional impairment in these brain regions has also been widely associated with pain, anxiety and depression: symptoms that often occur together in people diagnosed with fibromyalgia [60–62].

The results for the objective cognitive tests were similar to those previously described, with there being significant differences between groups for all of the tests. The worst initial performances were associated with fibromyalgia patients, although most of the observed differences disappeared when we adjusted for depression and anxiety. In this case, once we had made adjustments for mood symptoms, the significantly worse performances by fibromyalgia patients only persisted for interference inhibition ability in the Stroop Test. No differences were identified between the other executive functions evaluated: updating, cognitive flexibility, working memory, abstract reasoning and shifting, once mood-related symptoms had been

isolated. These results were in line with those cited in recent publications on fibromyalgia and chronic pain by authors such as Cherry et al [47]. These authors also pointed to impairment of cognitive inhibition but not of either cognitive flexibility or verbal fluency in their sample of fibromyalgia patients, who were all assessed using objective cognitive measures. Glass et al [63], who used neuroimaging, also identified altered brain activity in response to a motor inhibition task in the group of patients with fibromyalgia. The study by Mercado et al [64] followed similar lines, with the authors reporting that fibromyalgia patients experienced specific problems of cognitive inhibition when they were assessed using an emotional Stroop task and event-related potentials. Finally, Berryman et al [65], who carried out a systematic review and made a meta-analysis of executive function in people with chronic pain, also found evidence of minor to moderate impairment in response inhibition.

The impaired cognitive inhibition mechanisms identified in the fibromyalgia patients was compatible with the hypothesis of hypervigilance to pain and to pain-related information that has already been extensively described in this population. This points to the existence of an attentional bias toward negative information and to difficulties in inhibiting thoughts that prevent fibromyalgia patients from carrying out other daily tasks [66,67].

Our results failed to identify any significant differences between objective cognitive measures of working memory after adjusting for depression and anxiety. This was in line with some previous studies which revealed that mood could explain the observed cognitive impairment [10–12]. Even so, our results differed from others that had reported impairments in working memory in fibromyalgia patients assessed using

objective cognitive tests [6,68,69]. Such differences may, however, have been attributable to the different configurations of the samples used in the studies, given that depressive symptomatology was an exclusion criterion in some of them. This is particularly noteworthy considering that the severity of depression in our sample was moderate or even severe.

Moreover, in the same way that we found some different results using subjective and objective measurements of executive functions, we also found a general lack of extensive significant associations between the two types of measures. The exception to this general tendency was the 3-back test, which correlated with several BRIEF-A scales and indices. The lack of extensive significant association between the two types of measures was expected and was in line with results obtained from several other studies; this would perhaps suggest that the subjective and objective measures could, in fact, measure different constructs [29,30,70]. In this regard, it should perhaps be added that several researchers have previously highlighted the fact that objective cognitive tests are designed to assess an isolated aspect of behavior, separating it from the influence that other variables might have on the same behavior. On the other hand, subjective measures, such as BRIEF-A, tend to evaluate the application of these skills in daily life, which often includes their interaction with an environment characterised by complex and multifactorial demands [25,71,72]. All of these results support the combined use of both types of measures to provide more comprehensive information about these patients. Special mention must also be made of the associations identified between the 3-back test and several BRIEF-A scales and indices. These may point to the 3-back test being an objective cognitive task with a high cognitive load that probably does not only evaluate a single, isolated aspect of working memory, but also the

inhibition, shift, initiation and planning abilities measured by BRIEF-A. In this regard, similar results were found by Garcia-Molina et al [20] in a study that was conducted with a group of individuals with moderate-to-severe TBI. They identified a limited number of associations between BRIEF-A and objective cognitive measures. The exception to this general situation was found with the Letter-Number Sequencing test, a working memory measure which correlated with many of the BRIEF-A scales and indices. More research is clearly needed in this area in order to elucidate the relations between objective cognitive measures of working memory and the different BRIEF-A scales.

Regardless of the possible reasons for the impairment of executive performance, we were also interested in knowing the clinical relevance of the perceived functioning in our sample and analysed the percentage of individuals in each group who reported clinically elevated BRIEF-A scores. In this case, we found that the clinical impact was significant. It revealed considerable differences between groups, with more than half of the fibromyalgia patients having experienced problems with: their control impulses (Inhibit scale); their ability to think flexibly and/or to accept different ways of solving problems (Shift scale); their ability to modulate emotional responses appropriately (Emotional Control scale); their ability to start tasks and/or to create problem-solving strategies (Initiative scale); their ability to hold in mind and simultaneously manipulate information (Working Memory scale); and their ability to anticipate future events and set goals (Plan scale). These results should be taken into account, because they demonstrate that fibromyalgia patients experience all of these problems in their daily lives and that it is very difficult to dissociate them from their mood. This perceived

executive dysfunction would also probably have an impact on their social, occupational and emotional performances, which would include poorer treatment adherence.

Several of the current limitations of this study need to be addressed. First, it may include a potential selection bias, given that it was not possible to randomise the selection of participants. Instead, it was the subjects themselves who decided whether or not to participate in the study. It is, however, worth mentioning that refusal to participate in the study was minimal, both amongst patients and members of the control groups. Further, there was similarly only a minor loss of cases during the assessment process. The high presence of depressive and anxiety symptoms in the group of fibromyalgia patients was also a limiting factor in this study, given its observational nature. Even so, we consider that it probably provides a faithful reflection of the current reality of fibromyalgia patients. However, for this reason, we would propose larger observational studies that should also include fibromyalgia patients who are not suffering from depression. Another limitation may be the high proportion of fibromyalgia patients with high scores in the Negativity scale of BRIEF-A, which was one of the three validity scales for this measure. However, as that none of the subjects scored highly on the other validity scales, we related the high level of negativity to the severity of the depressive symptoms reported by many fibromyalgia patients. Another limitation worth highlighting was the lack of control over the medication that the patients were taking. Although we excluded patients who were taking antipsychotic medication, others receiving treatment with anxiolytic agents and antidepressants were included in the study. It is, however, important to note that when patients were receiving treatments including anxiolytics, these were only administered at low doses. Finally, it must be underlined that this study has not included in its analysis the influence of other

relevant symptoms of fibromyalgia, such as the degree of pain, fatigue or sleep disorder, all of which can also affect cognitive functions. These factors should also be considered in future studies.

5. Conclusions

Using a combination of subjective and objective measures, we found that patients with fibromyalgia showed impairment in some components of their executive functions. The main functions affected were working memory and inhibition, and the effects noted could not be explained by mood. We would argue that subjective and objective measures can provide useful and complementary information to help us understand the scope of the executive dysfunction often exhibited by these patients. Mood disturbances, which tend to be very frequent in this disease, contribute to a worsening of the global executive dysfunction suffered by these patients and have a negative impact on their daily functioning. These results underscore the need to design and implement clinical interventions to address impaired cognitive functioning in these patients and to intervene on both the cognitive and mood levels in order to improve their functionality.

6. Conflicts of interest

The authors declare that they have no conflicts of interest.

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Table 1. Demographic and Clinical Characteristics for patients with fibromyalgia and controls

	Fibromyalgia		Controls		<i>p</i>
	Patients		(n = 42)		
	(n=82)				
	M	SD	M	SD	
Age (years)	45.24	5.31	45.88	6.30	.55
Education (years)	10.39	2.72	11.17	2.70	.13
WAIS-III Vocabulary ¹	10.48	3.70	11.21	1.60	.22
BDI-II	24.93	12.05	5.45	5.65	<.001
STAI State	36.55	11.26	16.59	9.19	<.001
STAI Trait	35.48	11.11	12.54	8.201	<.001

Notes. WAIS-III = Wechsler Adult Intelligence Scale 3r version; BDI-II = Beck Depression Inventory-II; STAI = State-Trait Anxiety Inventory

¹*Data are presented in mean scaled scores.*

Table 2. Means, standard deviations and group differences on BRIEF-A adjusted for BDI-II and STAI State and Trait scores

BRIEF-A Subscales	Fibromyalgia		Controls		<i>p</i>	η^2
	Patients		(n = 42)			
	(n=82)					
	M	SD	M	SD		
Inhibit	60.9	10.01	47.0	6.17	.17	.01
Shift	67.8	11.83	52.5	9.83	.56	.003
Emotional Control	68.2	12.25	54.2	11.25	.50	.004
Self-Monitor	59.13	11.70	51.1	9.31	.70	.001
Initiate	67.7	10.50	48.5	9.34	.07	.02
Working Memory	73.0	11.57	51.4	11.61	.002	.07
Plan/Organize	71.4	10.87	57.5	10.46	.77	.001
Task Monitor	52.9	9.09	43.9	6.96	.89	.000
Organization of Materials	53.7	11.82	46.9	9.03	.89	.000
Behavior Regulation Index	67.5	10.92	51.7	8.90	.49	.004
Metacognition Index	68.15	11.13	49.8	9.17	.03	.04
Global Executive Composite	68.7	10.10	50.2	8.65	.03	.04

Table 3. Prevalence rate comparisons for the percentage of individuals with clinically elevated BRIEF-A scores

BRIEF-A Subscales	Fibromyalgia Patients (n=82)	Healthy Controls (n = 42)	<i>p</i>
Inhibit	35.7	2.4	<.001
Shift	63.1	16.7	<.001
Emotional Control	60.7	16.7	<.001
Self-Monitor	23.8	4.8	.005
Initiate	60.7	4.8	<.001
Working Memory	76.2	16.7	<.001
Plan/Organize	71.4	23.8	<.001
Task Monitor	13.1	0	.009
Organization of Materials	13.1	7.1	.24
Behavior Regulation Index	61.9	7.1	<.001
Metacognition Index	57.14	4.76	<.001
Global Executive Composite	59.52	2.38	<.001

Notes. Clinically elevated BRIEF-A score = T-scores ≥ 65 [26]

Table 4. Z scores and group differences on neuropsychological measures adjusted for BDI-II score and STAI-State and Trait scores

	Fibromyalgia Patients (n=84)		Controls (n = 42)		<i>p</i>	η^2
	m	SD	m	SD		
z PMR	-.37	.74	-.006	.96	.37	.007
z PASAT 3.0	-1.09	1.72	.07	.99	.09	.03
z PASAT 2.0	-1.05	1.70	.04	.97	.16	.02
z 2-back	-.81	1.60	-.002	1.01	.54	.003
z 3-back	-.55	1.07	.03	.98	.45	.005
z TMT B-A	.11	.64	-.01	1.01	.80	.001
z SCWT, Interference Task	-.60	.64	-.01	1.01	.03	.05
z WCST categories	1.44	8.35	-.008	1.01	.18	.02
z WCST persever. responses	.22	.96	-.01	1.01	.98	.000

Notes: PMR = Phonemic verbal fluency test; PASAT3 = Paced Auditory Serial Addition Test version 3; PASAT2 = Paced Auditory Serial Addition Test version 2; TMTB-A = Trail Making Test, total difference part B minus part A; SCWT, Stroop Word and Color Test; WCST categories = Wisconsin Card Sorting Test, total categories accomplished; WCST persever responses = Wisconsin Card Sorting Test, total perseverative responses

Table 5. Spearman correlations between BRIEF-A scales and neuropsychological measures for Fibromyalgia Patients

	PMR	PASAT 3.0	PASAT 2.0	2-back	3-back	TMT B-A	SCWT Interf. T.	WCST categ	WCST per resp
Inhibit	.01	.00	.01	.22	-.337**	.15	.10	-.15	-.13
Shift	-.13	-.15	-.07	-.19	-.251*	.12	.06	-.17	-.02
Emotional Control	-.05	-.01	.04	-.06	-.14	-.01	-.09	-.06	-.05
Self-Monitor	-.06	.05	.07	-.12	-.12	-.04	.02	-.08	-.05
Initiate	-.17	-.08	-.07	-.18	-.233*	.15	.03	-.14	.17
Working Memory	-.12	-.09	-.05	-.18	-.295**	.07	.00	-.245*	-.01
Plan/Organize	-.15	-.04	-.03	-.19	-.248*	.00	.00	-.15	.00
Task Monitor	.13	-.01	.04	.08	-.09	.00	.07	-.11	.07
Organization of Mat.	.04	.08	.08	.13	.05	-.09	.08	-.11	-.04
Behavior Regulation I.	-.11	-.08	-.05	-.20	-.268*	.09	-.03	-.15	-.05
Metacognition Index	-.01	-.11	-.05	-.09	-.236*	.17	-.03	-.22	.06
Global Exec Comp.	-.12	-.01	.00	-.12	-.18	.03	.01	-.20	.01

Notes: PMR = Phonemic verbal fluency test; PASAT3 = Paced Auditory Serial Addition Test version 3; PASAT2 = Paced Auditory Serial Addition Test version 2; TMTB-A = Trail Making Test, total difference part B minus part A; SCWT Interf. T. = Stroop Word and Color Test, Interference Task; WCST categ = Wisconsin Card Sorting Test, total categories accomplished; WCST per resp = Wisconsin Card Sorting Test, total perseverative responses

* $p < .05$

** $p < .001$

Table 6. Spearman correlations between BRIEF-A scales and neuropsychological measures for Controls

	PMR	PASAT 3.0	PASAT 2.0	2-back	3-back	TMT B-A	SCWT Interf. T	WCST categ	WCST per resp
Inhibit	-.21	-.33*	-.28	.73	-.11	-.02	-.03	-.35*	.05
Shift	-.06	-.02	-.12	-.05	-.16	.28	-.05	-.21	.11
Emotional Control	-.05	.03	-.05	.14	-.02	.04	.00	-.27	-.05
Self-Monitor	-.01	-.19	-.28	.05	-.12	.23	.02	-.19	.18
Initiate	-.09	-.08	-.19	.17	-.07	.15	.14	-.02	.27
Working Memory	-.27	.02	-.09	.06	-.08	.23	.13	-.13	.14
Plan/Organize	-.08	-.28	-.14	.04	-.03	.29	.04	-.15	.10
Task Monitor	-.09	-.15	-.21	.11	-.12	-.02	.27	-.28	.31*
Organization of Mat.	-.19	-.37*	-.28	.03	-.22	.19	.25	-.07	.15
Behavior Regulation I.	-.09	-.08	-.22	.10	-.04	.15	.18	-.27	.11
Metacognition Index	-.16	-.16	-.22	.06	-.08	.21	.23	-.25	.31*
Global Exec Comp.	-.19	-.18	-.23	.05	-.17	.24	.12	-.29	.16

* $p < .05$