APPLIED NEUROPSYCHOLOGY: ADULT
https://doi.org/10.1080/23279095.2022.2122828

The cumulative effect of fibromyalgia symptoms on cognitive performance: The mediating role of pain

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ABSTRACT

Fibromyalgia (FMS) is a chronic condition that encompasses widespread pain associated with cognitive impairment and significant emotional distress related to functional disability. This study aimed to obtain evidence of the role of pain in the effect of time since FMS diagnosis and cognitive performance using a novel online protocol of neuropsychological evaluation since the COVID-19 pandemic has challenged traditional neuropsychology testing leading to the need for novel procedures transitioning to tele-neuropsychology. A sample of 70 adult women was evaluated (50 with FMS and 19 controls) using online questionnaires that evaluated pain and executive functioning (impulsivity, inhibition control, monitoring, and planning). Afterward, participants were evaluated by trained neuropsychologists in a 30 min online session using virtually adapted cognitive tests: the Hopkins Verbal Learning Test (memory), the Symbol-Digit Modalities Test (attention and speed processing), the F-A-S test (verbal fluency), and Digit Span tests (working memory). We found that the time of FMS diagnosis has an effect on cognitive functioning predominantly mediated by pain. Our results point out the role of pain as a mediator on cognitive performance, specifically in executive functions which are directly affected by the cumulative effect of the time of diagnosis. Furthermore, the importance of considering a broader perspective for assessment and treatment including novel procedures *via* tele-neuropsychology.

KEYWORDS
Executive functions; fibromyalgia (FMS); mediation model; pain; tele-neuropsychology

Introduction

Fibromyalgia (FMS) is a chronic syndrome characterized by complex symptomatology, the core of which is generalized and persistent musculoskeletal pain that also comprises fatigue, sleep disturbances, morning joint stiffness, depression, and anxiety (Bennett, 2009; Schmidt-Wilcke & Diers, 2017). This syndrome is one of the most common causes of widespread chronic pain and is a common condition in the general population (Jones et al., 2015; Queiroz, 2013). The worldwide prevalence of FMS is between 2 and 5%, regardless of the territory, and it mainly affects women (Juuso et al., 2013). Despite lacking studies in Chile, a similar prevalence is estimated, with predominance in women as well (MINSAL, 2016). Several studies across cultures and ethnicity showed that ∼90% of patients with FMS are women (Bengtsson et al., 1986; Choudhury et al., 2001; Nishikai, 1992; Wolfe et al., 1990). Population studies have also exhibited a female predominance in the prevalence of this syndrome (Heidari et al., 2017; Wolfe et al., 1995; 2018). The reasons or mechanisms for such differences in prevalence between women and men are not well understood yet (Heidari et al., 2017). Recent studies suggest the disparity in prevalence between men and women may be lower as previously thought (Vincent et al., 2013; Wolfe et al., 2018) because men are less likely to identify symptoms and be diagnosed with FMS. Additionally, it has been proposed that FMS is more prevalent in women because involves a set of interconnected variables interplay of biology, psychology, and sociocultural factors (Wolfe & Rasker, 2021; Yunus, 2001).

On the other hand, FMS has been associated with the suffering of physical and emotional trauma and a history of post-traumatic stress (Bradley, 2009; Semiz et al., 2014). Its impact on quality-of-life compromises physical, psychological, and social domains (Campos et al., 2012; Lee et al., 2017), including performing adequately in the work context (Palstam & Mannerkorpi, 2017).

Additionally, cognitive impairments in FMS patients have been reported, such as forgetfulness, concentration difficulties, and/or mental slowness. These impairments are known as fibrofog and are considered among the most severe symptoms of the disease (Kravitz & Katz, 2015). Several affected cognitive functions have been identified in a variety of studies, such as attention and memory (Montoro et al., 2015;

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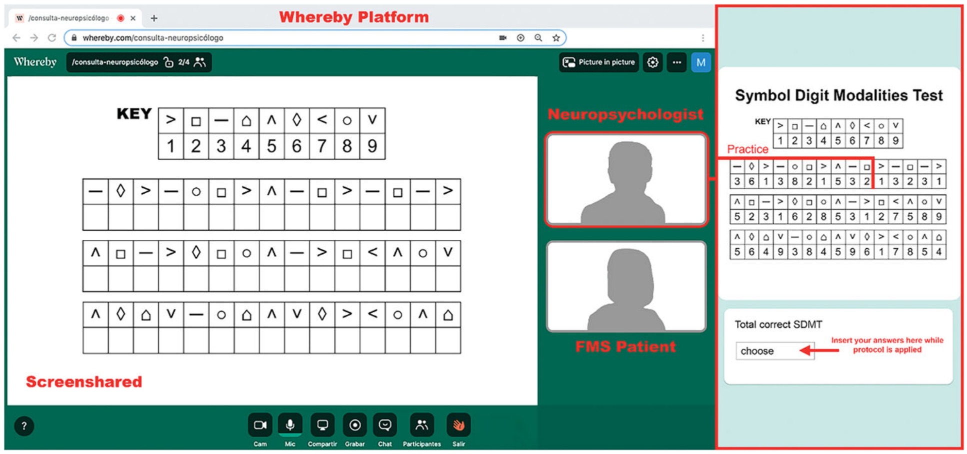

Figure 1. Representative neuropsychological online protocol. A trained neuropsychologist explained and guided the cognitive evaluation to FMS and control groups through the Whereby platform.

Bar-On Kalfon et al., 2016), and cognitive processing speed (Bar-On Kalfon et al., 2016). Furthermore, executive function impairment has also been confirmed, including planning (Cherry et al., 2014), abstract thinking (Verdejo-García et al., 2009), and cognitive flexibility (Gelonch et al., 2016). In this line, a recent meta-analysis that included 37 FMS case studies and controls concluded a decrease in the performance of memory, attention, processing speed, and mainly executive functions (Bell et al., 2018).

The mechanisms underlying the origin of the aforementioned impairments are not well understood yet. However, the Neurocognitive Model of Attention to Pain might provide a theoretical framework to understand and test whether the pain interferes with attention processes. According to this model, any cognitive dysfunction in the context of chronic pain is the result of the interference between attention focused on both the peripheral input (pain) and the goal-directed activity (Legrain et al., 2009; Teodoro et al., 2018; Wu et al., 2018). In other words, pain and high interoceptive monitoring might lead to reduced attention performance in cognitively demanding tasks or activities, in turn increasing the susceptibility to distraction and slowing down the information processing, interfering with cognitive function (Teodoro et al., 2018). However, how the cumulative effect of FMS symptoms on cognitive performance has not been described yet. In other words, we propose that the time since FMS diagnosis might have a direct effect on cognitive functioning mediated by pain.

Besides, the current emergency due to COVID-19 has challenged the traditional neuropsychology settings of evaluation among other clinical settings leading to the need for novel procedures, such as tele-medicine and tele-neuropsychology. Thus, new telematic protocols to assess psychological functioning in population that might have problems with presential consulting has become crucial (Kitaigorodsky et al., 2021; Rochette et al., 2021; Salinas et al., 2020). There are interesting initiatives in this regard. For example, Kitaigorodsky et al. (2021) have developed a tele-neuropsychology protocol for the cognitive assessment of older adults. Additionally, Ransom et al. (2020) studied the feasibility of pediatric tele-neuropsychology and provided recommendations, such as focusing on screening and shorter batteries more than a full traditional neuropsychological evaluation. However, tele-neuropsychological evaluation for the FMS patients' population remains as a challenge since there are particularities that must be addressed.

In the present study, we aimed to examine the cumulative effect of FMS symptoms (using time since diagnosis as a variable) on cognitive performance and to test the potential role of pain, using a novel online protocol of neuropsychological evaluation.

To do this, a group of FMS patients and controls were evaluated via a synchronic online evaluation with trained neuropsychologists using traditional virtually adapted cognitive tests (Figure 1).

We hypothesize that our protocol allows to show that, in agreement with the Neurocognitive Model of Attention to Pain, there is an effect of the time since diagnosis on cognitive impairment in executive functions (Legrain et al., 2009; Teodoro et al., 2018; Wu et al., 2018) mediated by pain. Figure 2 presents the hypothesized model in which pain plays a mediating role in the relationship between time since diagnosis and cognitive performance.

Hence, we expect that the cumulative effect of FMS symptoms over time results in impaired cognitive performance. Additionally, we expect an indirect effect mediated by the increase in pain reported by patients. Our results will contribute to the scientific body of knowledge and the clinical field since they may impact the development of clinical guidelines and health personnel training. Likewise, it is possible to promote and develop public policies that benefit patients with FMS, considering that there is still an underconsideration of these cases (Wolfe et al., 2019).

Materials and methods

Study design

This was a case-control observational study conforming to the STROBE Guidelines ("Strengthening the Reporting of Observational Studies in Epidemiology") (Vandenbroucke

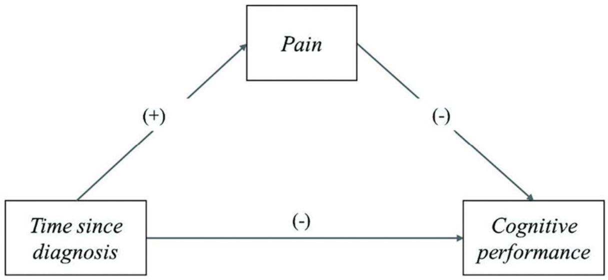

Figure 2. Hypothesized mediation model.

et al., 2007). The sampling technique was convenience and non-probabilistic. All the procedures were carried out remotely in tele-neuropsychology format (Bilder et al., 2020) due to the health emergency caused by the COVID-19 pandemic.

Participants

Data was collected from seventy right-handed and Chilean adult women. From the total sample, there was a group of fifty women diagnosed with FMS between 22 and 64 years old (mean age = 44.05, $SD = 8.71$) and nineteen healthy women as a paired-match (sex, age, nationality, demographic similarities) control group between 19 and 53 years old (mean age = 40.63, $SD = 9.79$). There were no differences between the FMS and control group in age ($p = .16$; Table 1) and education (control group, mean = 13.89 years of education, $SD = 5.21$; FMS group, mean = 13.74 years of education, $SD = 4.68$; $p = 0.90$; Table 1). The sample size followed the gold standard reported in the meta-analysis by Bell et al. (2018). Patients with FMS were diagnosed by a specialist following the 2016 diagnostic criteria for fibromyalgia (Wolfe et al., 2016, 2019) and were recruited from Fibromyalgia Associations located in distributed regions of Chile, while participants belonging to the control group were recruited based on demographic similarities with patients. Exclusion criteria for the control group were neurological or psychiatric disorders and medical background of severe somatic diseases. This study involved human participants and was approved by Ethics Committee of the Universidad Santo Tomás, Antofagasta, Chile. ID reference number: 01/2021. Participants gave informed consent to participate in the study before taking part.

Table 1. Sociodemographic, clinical characteristics, and levels of pain of FMS and control groups.

	FMS		Control			
	$N = 51$		$N = 19$			
	M/N	*SD/%*	*M/N*	*SD/%*	*p*	*d/V*
Characteristic						
Age	44.05	8.71	40.63	9.79	0.16	−.38
Education (in years)	13.74	4.68	13.89	5.21	0.90	−.03
Time since diagnosis						
Less than a year	2	2.85	–	–		
1 year	4	5.71	–	–		
2 years	13	18.57	–	–		
3 years	6	8.57	–	–		
More than 3 years	26	37.14	–	–		
Marital status						
Single	13	25.49	10	52.63	0.08	.34
Married	15	29.41	7	36.84		
Divorced/separated	14	27.45	1	5.26		
Widowed	1	1.96	0	0.00		
Cohabitating	8	15.68	1	5.26		
Occupation						
Unemployed	9	17.64	2	10.52	0.26	.27
Retired	6	11.76	0	0.00		
Housework	12	23.52	3	15.78		
Active w/ medical license	7	13.72	3	15.78		
Active w/o medical license	17	33.33	11	57.89		
House and family						
Single	2	3.92	1	5.26	0.84	.14
w/ Partner	3	5.88	1	5.26		
w/ Partner and children	17	33.33	9	47.36		
w/ Partner, children, and other	7	13.72	2	10.52		
Other	22	43.13	6	31.57		
Clinical data						
Diabetes (yes)	3	6.00	0	0.00	0.27	.13
CVA (yes)	1	1.42	0	0.00	0.53	.07
Hypertension (yes)	9	17.64	1	5.26	0.18	.15
Thyroid disease (yes)	15	29.41	6	31.57	0.86	.02
Physical pain						
Head	6.02	3.21	2.94	3.00	<.001**	−.97
Nape	6.37	3.58	1.15	2.34	<.001**	−1.58
Behind the neck	7.31	2.90	1.78	2.34	<.001**	−1.94
Face	3.45	3.34	0.36	0.95	<.001**	−1.05
Neck	6.68	2.89	2.42	2.43	<.001**	−1.59
Shoulders	7.49	2.83	2.26	3.01	<.001**	−1.81
High back	7.49	2.88	2.52	3.00	<.001**	−1.70
Middle back	6.60	2.94	2.05	2.91	<.001**	−1.55
Lower back	7.39	2.96	2.78	2.99	<.001**	−1.54
Shoulders	7.49	2.83	2.26	3.01	<.001**	−1.81
Hands	6.90	3.30	1.05	2.24	<.001**	−1.91
Wrist	6.60	3.00	1.05	1.47	<.001**	−2.06
Chest	3.82	3.63	0.57	1.46	<.001**	−1.01
Ribs	3.76	3.45	0.52	1.61	<.001**	−1.05
Hips	6.54	3.44	1.57	2.52	<.001**	−1.54
Thighs	6.17	3.50	0.78	2.14	<.001**	−1.68
Buttocks	4.94	3.33	1.26	2.62	<.001**	−1.16
Knees	6.45	3.31	1.89	2.97	<.001**	−1.41
Tibias	5.17	3.76	0.26	0.80	<.001**	−1.50
Shinbone	5.35	3.83	0.26	0.80	<.001**	−1.53
Feet	5.76	3.49	0.73	1.24	<.001**	−1.64
Total pain	113.64	45.36	25.89	25.43	<.001**	−2.13

M: mean; *SD*: standard deviation; *d*: Cohen's *d*; *V*: Cramer's *V*; FMS: fibromyalgia syndrome; CVA: cerebrovascular accident.
$^{**}p < 0.001$.

Measures

Sociodemographic questionnaire

We designed an open-ended and multiple options questionnaire instrument that measures general demographic characteristics (age, medications, illnesses, schooling, history of mental disorders, and medical background, among other aspects).

Dysexecutive Questionnaire (DEX-Sp) (Pedrero Pérez et al., 2009)

The DEX-sp is a brief and easy-to-complete Likert-type self-report test with twenty items, and five response options between "never" (0 points) and "very often" (4 points) used to estimate executive dysfunction. This test assesses abstract thinking, planning, insight, temporal sequencing, impulse control, response inhibition, decision-making, as well as the presence of fables, impulsivity, euphoria, apathy, aggressiveness, restlessness motor, superficial affective responses, perseverance, distractibility, and disregard for social rules (Norris & Tate, 2000). This scale presents good psychometric properties and has been validated in the Spanish-speaking population (Pedrero Pérez et al., 2009).

Visual analog scale of pain (VAS)

The VAS is a subjective measure of acute and chronic pain intensity. Scores are recorded by making a handwritten mark on a 10-cm line representing a continuum between "no pain" and "the worst pain imaginable." The VAS is a reliable and valid scale for many patient populations (Karcioglu et al., 2018). A value lower than 4 on the VAS means mild or mild-moderate pain, while a value between 4 and 6 implies moderate-severe pain. A value higher than 6 implies the presence of very intense pain.

Hopkins Verbal Learning Test (HVLT) (Arango-Lasprilla, Rivera, Garza, et al., 2015)

The HVLT is a verbal memory test consisting of a 12-item word list composed of three semantic categories, which subjects should recall after the list has been read to them. This procedure is repeated three times. Twenty-five minutes later, subjects are asked to recall the list of words again. Then, for a yes/no recognition, a list of 24 words is read, which consists of the 12 original/target words, six distractors from the same semantic categories, and six unrelated distractors. This test provides scores for a learning curve, long-term memory, and recognition/discrimination. The HVLT is a valid instrument in the Latin American Spanish-speaking adult population with good psychometric properties (Arango-Lasprilla, Rivera, Garza, et al., 2015).

Symbol-Digit Modalities Test (SDMT)

The SDMT measures sustained attention and speed of information processing (Spreen & Strauss, 1998) consisting of nine digits paired with symbols underneath. Participants are asked to provide the corresponding number for each symbol for 90 s. The SDMT is a valid instrument in the Latin American Spanish-speaking adult population with good psychometric properties (Arango-Lasprilla, Rivera, Rodríguez, et al., 2015).

F-A-S test

These tests evaluate executive functions since they demand participants to be flexible, organize information, provide effort, and control inhibition when it is needed (Olabarrieta-Landa et al., 2015). To evaluate these complex cognitive functions, we used the phonological and semantic fluency tasks, which both have been validated and normalized in the Latin American Spanish-speaking adult population with good psychometric properties (Olabarrieta-Landa et al., 2015).

Phonological verbal fluency (PVF)

This test aims to ask participants to create as many words as possible, beginning with a specific letter (F, A, S) for 60 s. If a participant does not respond within 10 s, the examiner gives prompts (Olabarrieta-Landa et al., 2015).

Semantic verbal fluency (SVF)

This test demands participants to produce items that belong to a given category (e.g., animals) within 60 s. The participants are also provided with prompts for this test when they do not respond within 10 s (Olabarrieta-Landa et al., 2015).

Digit Span tests

These are verbal tasks, with stimuli presented auditorily. These tests aim to assess attention (Digit Span Forward) and working memory capacity (Digit Span Reverse) (García-Morales et al., 1998).

Digit Span Forward

In this test, the experimenter says a sequence of digits (one digit per second); at the end, the participant is asked to repeat the digits back to the experimenter in the same order that was given. The task begins with a few digit sequences, and then the number of digits increases.

Digit Span Reverse

This version of the test has the same structure as the *Digit Span Forward*. The difference is that the participant is asked to repeat the digits in reverse order which requires manipulation of information, thus working memory function.

Procedure

The study was conducted at the School of Psychology of the Universidad Santo Tomas (UST), in Antofagasta, Chile, from March to December 2021. After the ethics committee of the Universidad Santo Tomás approved the research project (CEC-UST 01/21), this was formally presented at the Fibromyalgia Association of Chile. Women diagnosed with FMS members of the association along the country were voluntarily recruited. Afterward, patients were contacted to confirm computer or tablet availability with an internet connection. Subsequently, they received an online form that included a brief description of the research, informed consent, sociodemographic questionnaire, medical history, and the instruments: DEX-Sp, and VAS scales.

After the first data collection, the second part of the process was to conduct the online neurocognitive protocol on the same day consisting of the HVLT, SDMT, F-A-S, and Digit Span tests performed by trained neuropsychologists blinded to the diagnosis. The evaluation protocol lasted ∼30 min and was applied through the Whereby platform.

Later, the control group with similar characteristics as the FMS patient group was recruited. The control group was evaluated following the same procedure aforementioned. Finally, once all data were collected, statistical analyses were performed (Figure 3).

As shown in the STROBE flow chart, 31.8% of the potentially eligible FMS subjects were included in the study. Furthermore, 19 subjects without fibromyalgia who did not present exclusion criteria were added. In total, 70 subjects

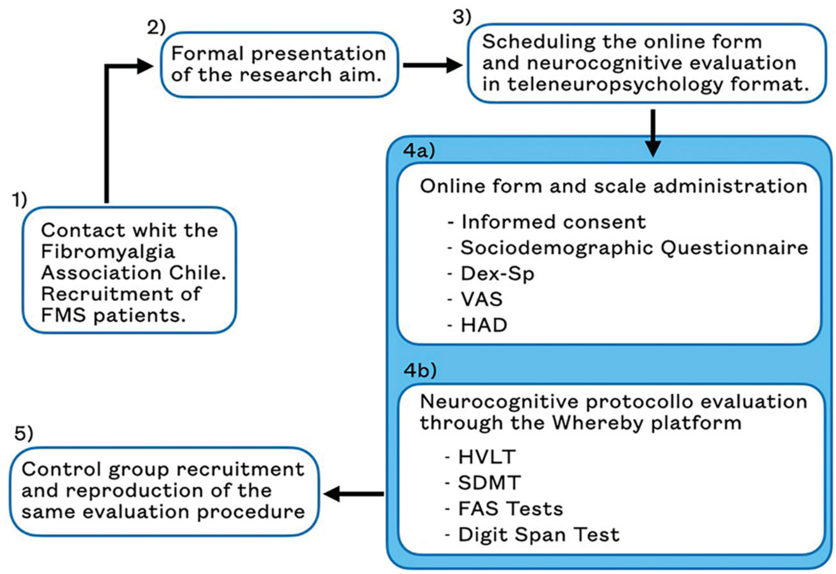

Figure 3. Scheme of the procedure.

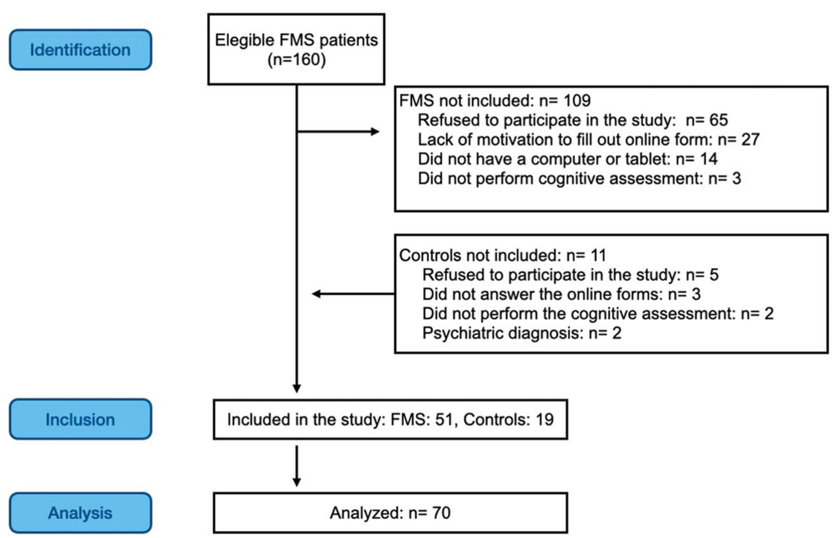

Figure 4. Participants' selection STROBE flowchart.

were analyzed (FMS = 51, Controls = 19). The reasons for exclusion are detailed in the diagram (Figure 4).

Data analysis

The student's *t*-test was used to compare all variables between groups. Additionally, Cohen's d test was performed to estimate the size effect. Moreover, we conducted the Chi-square test and the Cramer's *V* test for nominal variables, respectively. Afterward, we selected cognitive variables, specifically those related to executive functioning, based on these results. These groups of statistical analyzes were performed using the SPSS 25 statistical software synchronized with JASP, considering a significance threshold of $p < 0.05$. Samples with missing data were excluded from the analysis (see Strobe Flow Chart, Figure 3).

To present evidence about the mediating role of pain in the relationship between the time since FMS diagnosis and cognitive performance, we have performed two types of analysis. Firstly, we conducted Pearson correlations analyses between the four variables considered in the study: Time since FMS diagnosis, level of pain, performance in SDMT, and score in DEX-sp questionnaire. This allowed to compare the results obtained from the bivariate relationships between the variables, with the interaction effects obtained from the mediation analyses. In one stage, we will present the results of the mediation analyses. To do this, we have performed two analyses, using SDMT, DEX-sp, and SVF measures as dependent variables, respectively. In the three models, we have defined the time since diagnosis as the independent variable and the measure of subjective pain reported as the mediating variable. Both results have been obtained using the model 4 of "PROCESS" (Hayes, 2013), with bootstrapping of 5,000 random samples to obtain the estimation errors (SE).

Table 2. Cognitive performance and dysexecutive symptoms standardized by age and education (z-score).

	FMS		Control			
	$N=51$		$N=19$			
	M	*SD*	*M*	*SD*	*p*	*d*
Memory						
HVLT learning	−0.51	0.93	−0.28	0.64	0.330	.42
HVLT recall	−0.38	0.94	−0.02	1.02	0.171	.37
Language						
Phonological fluency	0.86	1.20	1.11	1.17	0.442	.20
Semantic fluency	−0.00	1.14	1.19	0.65	<.001**	1.15
Executive functions						
SDMT	−1.45	0.70	−0.67	1.16	<.001**	.91
Digit Span Test Forward	−1.28	0.82	−0.92	0.63	0.084	.47
Digit Span Test Inverse	−0.57	0.89	−0.32	0.83	0.289	.28
DEX disorganization	2.34	1.53	−0.01	0.87	<.001**	−1.70
DEX impulsivity	1.47	1.41	−0.08	1.17	<.001**	−1.14
DEX dysexecution total	2.14	1.55	−0.05	1.06	<.001**	−1.52

M: mean; *SD*: standard deviation; *d*: Cohen's *d*; FMS: fibromyalgia syndrome; HVLT: Hopkins Verbal Learning Test; SDMT: Symbol Digits Modalities Test; DEX: Disexecutive Questionnaire.
**$p < 0.001$.

Results

We found no significant differences between groups in sociodemographic characteristics. Table 1 shows a summary of the sociodemographic and clinical descriptive statistics. To analyze physical pain differences, we performed statistical comparisons showing that FMS patients exhibited higher levels of generalized physical pain (Table 1).

Cognitive performance was evaluated in different domains. Interestingly, we found no differences in memory performance and phonological fluency. However, the executive functions exhibited impairment in the FMS group. Specifically, the semantic fluency (SVF) and the attention are measured using the Symbol-Digit Modality test (SMDT). Additionally, the executive functions evaluated using the self-rating Dysexecutive Questionnaire (DEX-Sp) also showed higher dysexecutive symptoms in impulsivity and disorganization. Table 2 shows the statistical comparisons between groups in cognitive performance and dysexecutive symptoms.

Table 3 presents the bivariate correlations between the variables considered in the study. Five findings are important to highlight in these results. First, there is a moderate to the high relationship between *time since diagnosis* and *pain* ($r=.678$). Second, there is a moderate to low relationship between the *SDMT* measure with *time* ($r=-.333$) and *pain* ($r=-.433$), which are negative in both cases. Third, there is a moderate to high relationship between *DEX* score with *time since diagnosis* ($r=.595$) and *pain* ($r=.626$). Fourth, the results show that there is no significant correlation between the *SDMT* and *DEX* measures. Finally, the SVF showed a moderate and negative correlation between *time* ($r=-.463$) and *pain* ($r=-.510$).

Figure 5 presents the results from the estimation of the two mediation models obtained. The upper panel (Figure 5a) presents the mediation model that considers the SDMT measure as the dependent variable. The results of this model support the existence of a complete simple mediation model (Ato & Vallejo, 2011) since the direct effect (c') is non-significant (−.071). These results contrast with the bivariate

Table 3. Bivariate correlations between time of diagnosis, pain, SDMT, DEX, and SVF.

	Pain	SDMT	DEX	SVF
Time	.678*	−.333*	.595*	−.463*
Pain		−.433*	.626*	−.510*
SDMT			−.227	.389*
DEXT				−.454*

SDMT: Symbol-Digits Modalities Test; DEX: Dysexecutive Questionnaire; SVF: semantic verbal fluencies.
*$p < .05$.

correlations, which showed a significant and negative correlation between the *time since diagnosis* and the SDMT score ($r=-.333$; $p<.05$). This finding shows us the spurious relationship between both variables, which is fully explained by the mediating effect of the subjective perception of pain.

The 5b panel (Figure 5b) shows the mediation model that incorporates *DEX* measure as a dependent variable. Unlike the previous model, this result supports the existence of a simple partial mediation model (Ato & Vallejo, 2011) since, on one hand, there is a direct effect of *time* on *DEX*, and on the other hand an indirect effect through the mediation of *pain*. Even when the mediation model presents a significant relationship between *time* and *DEX*, these results also contrast with those obtained by the bivariate relationships. In the mediation model, the direct relationship between *time* and *DEX* decreases significantly compared to that obtained by the bivariate correlations, going from moderate to high (.595) to rather low (.316). Therefore, a significant proportion of the observed relationship between *time* and DEX can be explained by the mediating role of pain.

Finally, the lower panel 5c (Figure 5c) shows the result of semantic fluency measured by SVF test. As the SDMT measure, the results support the existence of a total mediation model. Once again, the relationship between the time since diagnosis and dysexecutive function is fully explained by the mediating role of pain.

In summary, these results show the importance of the mediating role of pain in the relationships observed between the cumulative effect of time since FMS diagnosis and cognitive performance.

Discussion

In this study, the cognitive performance and pain of FMS patients were evaluated using a novel online protocol. We found impairment in executive functions or high-order cognitive functions for the FMS group, specifically in SDMT, Semantic Fluency, and DEX. FMS patients exhibited semantic fluency impairment suggesting semantic access difficulties, which involve executive action to retrieve information from long-term memory (Fisk & Sharp, 2004). This result is in line with studies showing deficits in this area (Di Tella et al., 2015).

To test our cumulative effect on the cognitive performance hypothesis we performed mediation analyses in which three mediation models were obtained indicating that *pain* plays a mediator role between *time since diagnosis* and cognitive performance. Specifically, in the first model, there was a spurious relationship between the time and SDMT score

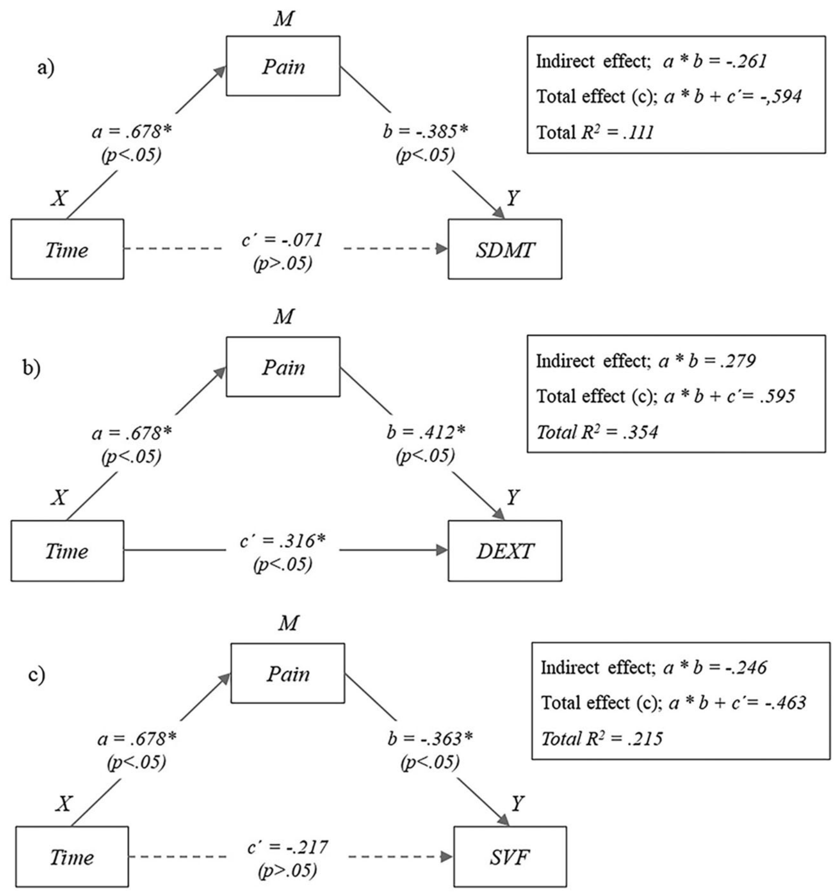

Figure 5. Results of the two estimated mediation models. (a) Cognitive performance in Symbol-Digit Modalities Test (SDMT), (b) Dysexecutive Questionnaire (DEX), and (c) Semantic Fluency test (SVF).

in which we found that the effect was explained by the mediator role of pain. In the second model, we found that *time since FMS diagnosis* has a direct effect on dysexecutive symptoms measured by DEX which is also mediated by pain. Finally, in the third model, we found that the *time since diagnosis* and semantic fluency impairment was fully explained by the mediating role of pain.

Our results are in line with the Neurocognitive Model of Attention to Pain which states that pain interferes with attentional processes. Specifically, attention is disrupted leading subjects to focus on peripheral sensations (pain) reducing the focus on goal-directed activity and producing lower performance in cognitively demanding tasks consequently (Legrain et al., 2009; Teodoro et al., 2018; Wu et al., 2018) which, according to our results, the lower performance increases when the pain is chronic. Studies that have focused on attention in patients with FMS have provided evidence in agreement with the hypothesis that chronic pain interrupts attentional processing showing that there is an attentional impairment to some extent, mainly related to pain, which is markedly present in FMS (Harker et al., 2011). This topic has been investigated in a variety of pathologies associated to chronic pain, concluding that pain is a sensory process that entails an attentional demand acting in competition with other stimuli that also require attention (Eccleston & Crombez, 1999; Legrain et al., 2009; Moriarty et al., 2011). Moreover, Grace et al. (1999) confirmed the existence of attentional deficits in FMS, but only in tasks with high attentional demands (executive control). Finally, Dick et al. (2008) evaluated attention using the Test of Everyday Attention (Evans & Preston, 2011) in a group of women with FMS and three other groups: a control group, patients with rheumatoid arthritis, and patients with musculoskeletal pain. When the effect of pain was controlled, all the differences observed between the groups in different attentional tests disappeared, concluding that pain had a crucial role in explaining the deficit in attentional functions in FMS. In summary, most studies agree that patients with FMS have deficits in cognitive tasks that require greater attentional efforts (Dick et al., 2008; Grace et al., 1999; Miró et al., 2011).

This study has some limitations. We evaluated only women from an urban context; thus, these findings are not extrapolatable to other groups, such as men with FMS or people from rural zones. Some evidence regarding differences between men and women with FMS in cognitive performance has been reported. Segura-Jiménez et al. (2016) showed that men with FMS exhibited better performance in working memory tests (using PASAT), whereas memory performance (using RAVLT) was better in women compared to men. Another line of research is the effect of effort on cognitive performance (Bar-On Kalfon et al., 2016), where decreased cognitive effort may reflect fatigability or a feeling of limited resources to achieve the goal in a given task. Bar-

On Kalfon et al. (2016) found that a higher proportion of men with FMS scored as low-effort compared with women with FMS. Furthermore, they found a significant interaction between gender, effort, and cognitive performance, specifically in attention and processing speed. Although, these results must be taken with caution since the low sample size of men in the Bar-On Kalfon et al. (2016) study. In contrast, Miró et al. (2015) found no difference in attentional function between men and women with FMS. However, attention deficit was associated with worse daily functioning in women with FMS (Miró et al., 2015). Hence, we strongly recommend for future research including other social groups (for instance, men and rural groups) to strengthen the results and subsequent interpretations. We believe that obtaining insight into the gender and/or sex differences in these factors and the underlying pathophysiologic mechanisms is of clinical relevance. Further research is needed for a better understanding of the gender and sex difference in FMS. Moreover, we recommend studying the mediation of pain on cognitive function in elderly population because those are limited (Minerbi & Fitzcharles, 2021; Defillo-Draiby & Page, 2016) and may shed light on how time since diagnosis might have an effect on cognitive performance mediated by pain in this specific population.

Another consideration is the telematic evaluation context. Due to previous evidence regarding the effect of the evaluation situation (Ployhart & Ehrhart, 2003; Ployhart et al., 2003), studies are needed to evaluate the effects on the validity of the different forms of application (attendance and telematics) from an Item Differential Functioning (DIF) analysis approach.

In summary, our results show that Chilean women with FMS exhibit subjective and objective cognitive impairments, predominantly in executive functions or high cognitive demanding tasks which are mediated by pain. This finding was in line with our predictions since it has previously been reported that physical pain reduces attention capacity, affecting overall cognitive performance (Teodoro et al., 2018), which agrees with the Neurocognitive Model of Attention to Pain (Legrain et al., 2009).

Acknowledgments

We want to thank the Fibromyalgia Association Chile (Asociación Fibromialgia Chile) for kindly helping us in contacting their members.

Ethical approval

This study involved human participants and was approved by the Ethics Committee of the Universidad Santo Tomás, Antofagasta, Chile. ID reference number: 01/2021. Participants gave informed consent to participate in the study before taking part.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This work was in part supported by the Agencia Nacional de Investigación y Desarrollo under Grant FONDECYT de Iniciación number: 11220009.

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Data availability statement

Data are available upon reasonable request.

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Appendices

Sociodemographic questionnaires and self-report scales

Online form and scale administration

https://docs.google.com/forms/d/e/1FAIpQLSexZeM5D0wzqK08E8xj09LqpAB_Wg2cKZ5nS1dPwjSwZPBURg/viewform?usp=sf_link

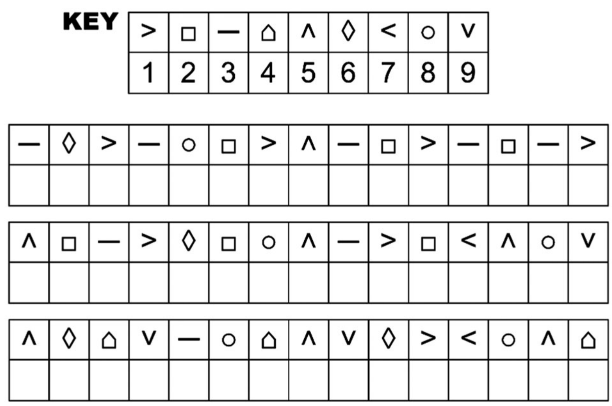
This online form was sent to the participants who orally agreed to participate in the study. In this virtual form, they gave their informed consent and answered questions about fibromyalgia, time since the first diagnosis, contact information, sociodemographic aspects, illness, and dysexecutive symptoms (DEX-sp).

Fibrocog: cognitive online evaluation

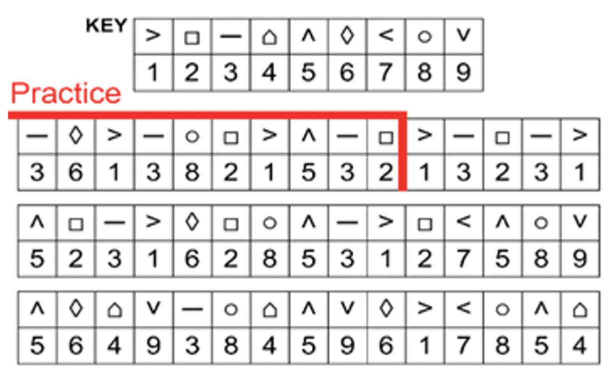
In a virtual meeting using the Whereby platform (https://whereby.com/), trained neuropsychologists blinded to the diagnosis evaluated the participants using cognitive tests and they scored performance on the following form:

https://docs.google.com/forms/d/e/1FAIpQLSexOXDBBVZtGGu5ke31m52wb0C92nu4XnytAMCTt25WFoHgA/viewform?usp=sf_link

The protocol sequence started with the Hopkins Verbal Learning Test (HVLT), encoding, and learning phase. Subsequently, Digit Span tests, forward and reverse, were administered. Afterward, participants were informed that a stimulus on the screen will be shared. Then, the following representative stimulus of the Symbol Digit Modalities Test was presented:



After confirming that the participant could see the stimulus on the screen, an instruction was given (see the instructions described in the link form). Participants were asked to practice on the first 10 boxes. Afterward, they were instructed to verbalize as many numbers associated with their corresponding symbol. The examiner scored correct answers and errors successes based on a guideline found in the same online form.



After, the spontaneous delayed recall phase of the HVLT was administered. The examiner registered the correct answers in the online form.

Finally, the phonological and semantic verbal fluency tests were administered and the number of words for each test was registered on the online form as well.