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Cognitive Performance in Women Aged 50 Years and Older With and Without Fibromyalgia

Barbara J. Cherry,[1] Laura Zettel-Watson,[1] Renee Shimizu,[2] Ian Roberson,[1] Dana N. Rutledge,[3] and Caroline J. Jones[4]

[1]Department of Psychology, California State University, Fullerton.
[2]Department of Psychology, University of California, Los Angeles.
[3]School of Nursing and
[4]Department of Health Science, California State University, Fullerton.

Objectives. Persons with fibromyalgia (FM) report having cognitive dysfunction. Neuropsychological performance was compared across a variety of domains in 43 women with FM (M_{age} = 63 years) and in 44 women without FM (M_{age} = 65 years).

Method. Measures included explicit memory (Consortium to Establish a Registry for Alzheimer's Disease [CERAD] immediate/delayed recall, delayed recognition), aspects of executive function including interference/inhibition (Stroop Color/Word test), working memory (Digit Span Forward/Backward), set-shifting/complex sequencing (Trails B), monitoring (verbal fluency: naming animals), processing speed (Trails A, Digit Symbol Substitution Coding), and problem solving (Everyday Problems Test).

Results. Women with FM performed more poorly than controls on executive function (Stroop Color/Word) and one processing speed measure (Digit Symbol Substitution Coding).

Discussion. Results partly support altered cognitive function in FM. Mixed findings across cognitive domains among individuals with or without FM is consistent with the literature and suggest that factors beyond those typically controlled for (e.g., heterogeneity in FM) may be influencing findings. Future research is warranted.

Key Words: Cognition—Chronic pain—Executive functions—Fibromyalgia—Processing speed.

FIBROMYALGIA (FM) is a chronic widespread pain disorder currently affecting about 2% of the U.S. population, with a female to male ratio of approximately 9:1 (Mease, 2005; Wolfe, Ross, Anderson, Russell, & Hebert, 1995). Although FM has been diagnosed among children and adolescents, the mean age for diagnosis is 47 years, with prevalence increasing with age (Lawrence et al., 2008; Wolfe et al., 1995). Common symptoms associated with FM include fatigue, stiffness, sleep problems, cognitive dysfunction, and mood disturbances (Bennett, Jones, Turk, Russell, & Matallana, 2007; Katz, Heard, Mills, & Leavitt, 2004). A major concern among many individuals with FM is the perception of declines in cognitive functioning. Prominent cognitive complaints include poor concentration, trouble remembering things, reduced ability to process information, and problems performing during cognitively demanding situations and tasks (Arnold et al., 2008; Bennett et al., 2007; Glass, 2006). For example, Katz and colleagues (2004) explored subjective symptoms of cognitive declines by examining 114 patients, 57 with FM and 57 with a non-FM rheumatic disease. FM participants were more likely to report memory decline, mental confusion, and difficulties with speech than the non-FM group, despite both groups experiencing chronic pain.

Despite consistent subjective cognitive complaints, objective measurement of neuropsychological performance has produced mixed results across cognitive domains. For example, a variety of studies have examined explicit memory performance (Grace, Nielson, Hopkins, & Berg, 1999; Leavitt & Katz, 2006; Luerding, Weigand, Bogdahn, & Schmidt-Wilcke, 2008; Park, Glass, Minear, & Crofford, 2001), different aspects of attention/executive function/working memory (Cherry, Weiss, Barakat, Rutledge, & Jones, 2009; Dick, Eccleston, & Crombez, 2002; Dick, Verrier, Harker, & Rashiq, 2008; Glass et al., 2011; Grace et al., 1999; Leavitt & Katz, 2006, 2008; Luerding et al., 2008; Seo et al., 2012; Sletvold, Stiles, & Landrø, 1995; Veldhuijzen, Sondaal, & Oosterman, 2012), decision making (Apkarian et al., 2004; Verdejo-García, Lopez-Torrecillas, Calandre, Delgado-Rodriguez, & Bechara, 2009; Walteros et al., 2011), and processing speed (Cherry et al., 2009; Grace et al., 1999; Park et al., 2001; Sletvold et al., 1995), with some studies showing declines in particular domains, whereas others do not (Schmidt-Wilcke, Wood, & Lürding, 2010). In our study, we hoped to clarify some of these inconsistencies using a slightly larger sample size and by assessing a variety of domains within women both with and without FM. Most of the research comparing

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objective cognitive performance in individuals with FM versus controls has used sample sizes ranging from 15 to 36 for the FM group. Moreover, these same studies have done comparisons in individuals aged between 30 and 50 years. Our study may be the first to evaluate older adults, with an overall mean age of 64 years for participants.

Cognitive deficits in FM have sometimes been likened to accelerated aging (Glass & Park, 2001; Park et al., 2001). To explore this, Park and colleagues (2001) assessed three different groups of women (23 participants with FM, M_{age} = 47.8 years, 23 healthy age-matched participants, and 22 participants approximately 20 years older than the other two groups) on processing speed, working memory, long-term recall, memory recognition, verbal fluency, and vocabulary. When FM participants were compared with age-matched participants, women with FM performed more poorly on free recall and recognition, working memory, and verbal knowledge domains, were slightly worse for verbal fluency, and no different in processing speed. When FM participants were compared with women 20 years older, performance was comparable on free recall and recognition, working memory, and verbal fluency, but FM participants demonstrated faster processing speed. Finally, FM participants' performances were poorer in verbal knowledge tasks when compared with the older adult controls (Park et al., 2001).

Although results comparing FM with non-FM participants on various domains of cognitive/neuropsychological function have been mixed, those measures that assess aspects of attention/executive function consistently show impairment in persons with FM. Executive function refers to a number of cognitive processes (related to attention and frontal lobe function) that serve to control or supervise other operations (e.g., inhibition, task switching, and monitoring; Miyake, Friedman, Rettinger, Shah, & Hegarty, 2001; Woodruff-Pak, 1997). Therefore, the purpose of this study was to evaluate objective cognitive performance as part of a larger study of physical/cognitive function in adults aged 50 years and older with or without a diagnosis of FM (Jones, Rutledge, & Aquino, 2010). We predicted that cognitive measures most closely related to attention/executive function such as the Stroop Color/Word and Digit Span tasks would be most likely to show differences based on FM status.

Methods

Participants

In the larger study (Jones et al., 2010), community-dwelling participants with and without FM were asked to participate. Recruitment strategies included an advertisement sent to local FM support groups, senior centers and senior housing facilities, and phone calls/e-mails to people from databases from two university centers (FM and Chronic Pain; Gerontology). Participants were at least 50 years old, community-residing, and functionally independent. Exclusion criteria included the following: (a) inability to walk for 6 minutes without assistance, (b) medical conditions considered dangerous for submaximal exercise by the American College of Sports Medicine guidelines (Dwyer & Davis, 2007), and (c) physician advice not to exercise. Those with FM brought documentation from their physician showing that they met the American College of Rheumatology (ACR) 1990 FM criteria (Wolfe et al., 1990). Participants followed approved university consent procedures.

Findings related to the physical performance measures are reported elsewhere (Jones et al., 2010). For this study, only women who scored greater than or equal to 25 on the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975; used to screen for potential dementia) were considered; this guaranteed some baseline homogeneity regarding orientation to time and place, language, and basic attention and recall skills. Qualified female participants who completed all required questionnaires and cognitive assessments were considered for inclusion. We next matched our FM to non-FM controls based on age in years such that both mean age and variability were not significantly different between groups. This resulted in 43 individuals with FM (M_{age} = 63 years) and 44 non-FM controls (M_{age} = 65 years) in the present analyses (refer to Table 1 for complete demographic information).

Instruments

Demographics, symptoms, and medications.—Demographic information (using an investigator-developed questionnaire) was obtained on age, gender, education, ethnicity, medical history, and medications (Table 1). In addition, rating scales (from 0 to 10, with 10 being most severe) from the National Fibromyalgia Association Questionnaire (NFAQ; Bennett et al., 2007) were included to evaluate 19 symptoms (e.g., pain, fatigue) typical of FM symptomatology (Table 2). Finally, participants were administered a self-report measure to assess their current level of physical activity using the Rapid Assessment of Physical Activity (RAPA; Topolski et al., 2006) on a scale from 0 to 5 with 0 being sedentary and 5 being active. Medication lists from participants were coded by a registered pharmacist using American Hospital Formulary Service (AHFS) categories for pharmacologic–therapeutic classification (AHFS, 2007) and the number of medications per category were recorded (Table 3).

Neuropsychological measures.—Mini-Mental State Examination. MMSE (Folstein et al., 1975) is a 30-point questionnaire that assesses aspects of orientation, concentration, and memory and was used to screen for potential dementia.

Consortium to Establish a Registry for Alzheimer's Disease (CERAD) 10-item word list. The CERAD (Morris, Mohs, Rogers, Fillenbaum, & Heyman, 1988) 10-item word list (explicit memory) was used to assess immediate (three

Table 1. Demographic Characteristics

	FM (n = 43)			Non-FM (n = 44)		
Characteristics	Mean	*SD*	Range	Mean	*SD*	Range
Age (years)	63.0	7.2	50–85	64.8	7.3	50–82
Education (years)	16.5	2.6	14–20	17.1	2.7	12–20
Race (%)						
Caucasian	88.4			86.4		
African American	4.7			0.0		
Asian/Pacific Islander	0.0			11.4		
Multiracial	7.0			2.3		
Comorbidities (number of participants with)						
Nonrheumatoid arthritis	27			11		
High blood pressure	23			17		
Osteoporosis	15			6		
Neuropathies	14			0		
Cancer	11			11		
Other neurological conditions	11			1		
Stroke	4			1		
Other health problems	35			23		
Body mass index	28.2	8.1	16–55	27.1	5.3	19–45
Physical activity (0 = sedentary to 5 = active)	4.0	1.3	0–5	4.5	0.8	1–5

Table 2. Mean Ratings (*SD*) and Ranges for Top FM Symptoms

	FM (n = 43)			Non-FM (n = 44)		
Symptoms	Mean	*SD*	Range	Mean	*SD*	Range
Stiffness	7.0	2.8	0–10	2.2	2.5	0–9
Not feeling rested after sleep	6.5	2.8	0–10	2.4	2.8	0–10
Fatigue	6.4	2.4	1–10	1.8	1.6	0–7
Pain	6.3	2.5	0–10	1.6	1.8	0–7
Trouble staying asleep	6.0	3.1	0–10	2.6	2.5	0–10
Concentration problems	5.5	2.7	0–9	1.3	1.9	0–9.5
Forgetfulness	5.3	2.8	0–10	2.0	1.9	0–8
Trouble falling asleep	4.9	3.5	0–10	2.0	2.8	0–10
Anxiety	4.4	3.0	0–10	1.9	2.5	0–10
Depression	4.2	3.2	0–9	1.1	2.3	0–9.5

trials) and (10–15 minutes) delayed recall, plus a 20-item delayed recognition trial.

Stroop Color/Word test. Participants completed the Stroop Color subtest (Stroop C: read 112 words) and Stroop Color-Word subtest (Stroop CW: name 112 font colors) to assess interference/inhibition after a cursory screening for color blindness. Time to completion (in seconds) rather than number correct was used as the dependent variable to provide a wider range of scores (Trennery, Crosson, DeBoe, & Lever, 1989).

Digit Span Forward and Backward. Digit Span Forward and Backward (Wechsler Memory Scale-III; Wechsler, 1997) were used to assess working memory performance. Longest correct scores were used as measures, with a range of 0–9 for Digit Span Forward and a range of 0–8 for Digit Span Backward.

Trails A, B. Time to complete parts A and B of the Trail Making task were used to assess processing speed (Trails A; Army Individual Test Battery; United States Army, 1947; Lezak, 1995) and set-shifting/complex sequencing (Trails B; Lezak, 1995; Sánchez-Cubillo et al., 2009).

Naming animals. Verbal fluency/monitoring was measured by having participants name as many animals as possible in 60 seconds, with responses audiotaped and double scored to ensure accuracy (Morris et al., 1988).

Digit Symbol Substitution Coding. Participants used a code table to write in as many symbols as possible within 120 seconds, with the number of correct responses completed used as a measure of processing speed (Wechsler Adults Intelligence Scale-III; Wechsler, 1997).

Everyday Problems Test. Selected items from the Everyday Problems Test were used to assess participants' ability to solve problems associated with daily living. Eighteen questions in a multiple choice format pertaining to problems about financial, transportation, and medical/medication domains were used with number of correct responses (0–18) as the score (Willis, 1990; Willis & Marsiske, 1993).

Table 3. Medication Information

Medication	FM (n = 43)		Non-FM (n = 44)	
	Number of individuals	Number of prescriptions	Number of individuals	Number of prescriptions
Analgesics	19	38	1	2
Anemia	1	1	0	0
Antianxiety	16	20	5	6
Anticonvulsants	9	9	0	0
Antidepressants	22	30	6	6
Antihistamine	1	1	1	2
Antipsychotic	2	2	0	0
Cardiovascular	29	50	20	36
CNS stimulants	1	1	1	1
Coagulation	—	—	—	—
Dermatology	3	3	2	5
Diabetes	2	4	3	6
ENT	1	1	2	2
Estrogen	14	17	6	12
GI	6	7	3	3
Infections	4	4	2	4
Mania	—	—	—	—
Migraine	2	2	3	3
Muscle relaxants	11	11	0	0
Neoplasms	0	0	3	3
Oral contraception	—	—	—	—
Respiratory	5	5	5	10
Thyroid	12	12	8	9
Other	11	13	15	16

Note. FM = fibromyalgia.

Procedures

Following telephone screening for inclusion and exclusion criteria, eligible participants were scheduled for two appointments. They were mailed the study consent form and questionnaires to complete prior to the first appointment and were called as a reminder the day before assessments.

At the first appointment, research assistants reviewed consents and questionnaires for completeness. Following this, participants met briefly with the lead investigator to address any concerns and receive her thanks; they then received reminder cards for second appointments.

Prior to the second assessment, reminder calls included instructions for participants to wear comfortable clothing and shoes, refrain from heavy exertion and alcoholic beverages, and take normal medications for 24 hours preceding the appointment. Also discussed were eating a light meal an hour before arrival, and for those with FM, rescheduling in case of severe FM symptoms.

On the second study day (within 5 days of the first appointment), participants again met with the lead investigator who reviewed the study purpose and procedures and answered questions. Participants (10–16 per session) had their blood pressure, height, weight, and waist circumference measured, and then assembled in a common room to be greeted, receive instructions for the day, and complete the 18-item Everyday Problems Test and the RAPA. Following this, half were assigned to private rooms with a trained tester to individually complete the battery of neuropsychological measures first; the other half completed physical performance measures first. Task order for the cognitive assessments was the same for all participants: MMSE, CERAD immediate recall trials 1–3, Stroop Color/Word test, Digit Span Forward and Backward, Trails A and B, CERAD delayed recall and recognition, naming animals, and Digit Symbol Substitution Coding. Due to individual differences, participants took from 30 to 60 minutes to complete the cognitive battery.

Statistical Analysis

Descriptive statistics were computed for demographic information. Chi-square analyses for nominal variables and independent samples t tests for continuous variables were used to determine group differences (FM vs. non-FM). Preliminary correlations were conducted among the 13 neuropsychological measures and three symptom clusters (described later) for FM and non-FM groups to examine any significant associations, as well as for neuropsychological measures and medication classifications. We also considered body mass index (BMI) and self-report physical activity (as measured by the RAPA) in the same fashion (physical activity level was significantly less for FM compared with non-FM participants, p = .026). Criteria for inclusion in subsequent regressions for these variables were based on $\alpha = 0.01$ to account for multiple analyses. Cognitive performance differences between women with and without FM were analyzed using analyses of covariance (ANCOVA) with FM status as the independent variable, each cognitive measure as a dependent variable, and age as the covariate to account for the wide age range within each group. For a priori ANCOVAs, the α was set at 0.05.

Results

Tables 1, 2, and 3 provide demographic, symptom, and medication information for FM and non-FM groups, respectively. As expected, FM participants reported significantly greater FM-related symptoms than non-FM participants (Table 2). Specific to the present investigation, in terms of subjective cognitive experiences, the FM participants, as compared with the non-FM participants, reported greater concentration problems (M = 5.5 vs. M = 1.3) and forgetfulness (M = 5.3 vs. M = 2.0).

Correlations Between Symptom Clusters, Medications, BMI, Physical Activity, and Neuropsychological Measures

Based on findings by Rutledge and colleagues (2009), symptom clusters were created for *Core Symptoms* (the sum of scores from 0 to 10 for pain, stiffness, and fatigue), *Distress* (the sum of scores for depression and anxiety), and *Sleep Problems* (the sum of scores for trouble falling asleep

and trouble staying asleep). Correlations between neuropsychological measures and the three symptom clusters were then conducted for FM and non-FM participants separately, with no significant correlations found. Correlations between neuropsychological measures and medication classifications were also not significant. (Not reported but can be obtained from the first author upon request.) No symptom or medication met criteria for inclusion in analyses, nor did BMI or physical activity level.

ANCOVAs were conducted both with and without those reporting "other neurological conditions" and "stroke" as comorbidities (16 persons with FM and 2 non-FM had these conditions). The same pattern of effects was found for all analyses; therefore, results include these individuals.

Table 4 shows the means and standard deviations for each neuropsychological measure for FM and non-FM groups. Univariate ANCOVAs were conducted for each of the neuropsychological measures with age as the covariate and FM status as the independent variable.

Consortium to Establish a Registry for Alzheimer's Disease 10-Item Word List

Three measures of explicit memory were examined using the CERAD 10-item word test. The number of items correctly recalled in each of three trials were summed and used as a measure of immediate recall. Delayed recall and delayed recognition of the 10 items were also evaluated. For immediate recall, delayed recall, and delayed recognition, no significant effect of FM status was found after controlling for the effect of age. However, significant main effects of age after adjusting for FM status were found for immediate recall, $F(1, 84) = 13.63$, $p < .001$, partial $\eta^2 = .140$, for delayed recall, $F(1, 84) = 9.96$, $p = .002$, partial $\eta^2 = .106$, and for delayed recognition, $F(1, 84) = 4.02$, $p < .048$, partial $\eta^2 = .046$. Specifically, older participants obtained lower memory scores on immediate recall, delayed recall, and delayed recognition in comparison with younger participants.

Table 4. Performance Means (Standard Errors) Adjusted for Age for FM and Non-FM Groups Across Cognitive Domains

	M (*SE*)	
	FM	Non-FM
Interference/inhibition[a]		
Stroop C time (s)	61.1 (1.8)	58.4 (1.7)
Stroop Color/Word time (s)*	155.3 (5.3)	137.8 (5.2)
Working memory[a]		
Digit Span Forward (longest score)	10.0 (0.3)	10.0 (0.3)
Digit Span Backward (longest score)	6.3(0.3)	7.2 (0.3)
Processing speed		
Trails A time (s)	39.1 (2.3)	34.1 (2.2)
Set-Shifting/Complex Sequencing[a]		
Trails B time (s)	83.0 (5.2)	78.7 (5.0)
Verbal fluency, monitoring[a]		
Animals (#named)	19.6 (0.2)	19.3 (0.2)
Problem solving[a]		
Everyday Problems Test (#correct)	14.5 (0.4)	15.4 (0.4)
Processing speed		
Digit Symbol Substitution (#correct)**	57.7 (2.4)	68.2 (2.3)
Explicit memory		
Immediate recall trials 1–3 (#correct)	21.0 (0.6)	21.0 (0.6)
Delayed recall (#correct)	6.7 (1.9)	6.5 (1.8)
Delayed recognition (#correct)	19.6 (0.2)	19.3 (0.2)

Note. FM = fibromyalgia.
[a]Considered aspects of attention/executive function
Significant differences per group at *$p < .05$ and **$p < .005$.

Stroop Color/Word Test

Completion times for two measures were examined as follows: (a) reading color words on the Stroop C task and (b) naming the font color of words written in different colors on the Stroop Color/Word task. After adjusting for the effect of age, Stroop C completion times were not significantly different between FM and non-FM participants. However, there was a significant effect of FM status on Stroop Color/Word completion time after adjusting for differences in age, $F(1, 83) = 5.50$, $p = .021$, partial $\eta^2 = .062$, such that those participants with FM were slower to complete the task. Additionally, when adjusting for the difference in FM status, there was a significant effect of age on Stroop CW completion time, $F(1,83) = 8.21$, $p = .005$, partial $\eta^2 = .090$, such that older participants were slower to complete the task.

Digit Span Forward and Backward

Working memory span length was assessed using the Digit Span Forward and Digit Span Backward scores. Although no main effect of FM status was found for the Digit Span Forward score, there was a significant effect of age when adjusting for the difference in FM status, $F(1, 84) = 6.52$, $p = .013$, partial $\eta^2 = .072$, such that older participants had shorter spans than their younger counterparts. For Digit Span Backward scores, there was a main effect of FM status trending toward significance after adjusting for the effect of age, $F(1, 84) = 3.85$, $p = .053$, partial $\eta^2 = .044$, such that those with FM had shorter spans than those without FM. However, there was no significant effect of age.

Trails A, B

Trails A assessed processing speed; Trails B evaluated set shifting/complex sequencing There was no significant effect of FM status on either Trails A or B after adjusting for the effect of age. However, there was a significant main effect of age for Trails A after adjusting for the difference in FM status, $F(1, 84) = 10.89$, $p = .001$, partial $\eta^2 = .115$, as well as for Trails B, $F(1, 84) = 6.03$, $p = .016$, partial $\eta^2 = .068$. Older compared with younger participants took longer to complete both tests.

Naming Animals

After adjusting for the effect of age, there was no significant effect of FM status on verbal fluency and monitoring, but there was a significant main effect of age after adjusting for FM status, $F(1, 84) = 3.96$, $p = .050$, partial $\eta^2 = .045$, such that older participants named fewer animals than younger participants.

Digit Symbol Substitution Coding

Processing speed was measured by the number of items correctly coded in 2 minutes on the Digit Symbol Substitution Coding. There was a significant effect of FM status on the Digit Symbol Substitution Coding score after controlling for the effect of age, $F(1, 84) = 9.89$, $p = .002$, partial $\eta^2 = .105$, such that those with FM coded fewer digits than those without FM. There was also a significant effect of age after adjusting for differences in FM status, $F(1, 84) = 12.92$, $p = .001$, partial $\eta^2 = .133$, such that older participants coded fewer digits than younger participants.

Everyday Problems Test

No significant effects of FM status or age were found on the Everyday Problems Test score, used to measure problem solving.

Discussion

In our study of women aged 50 and older, FM versus non-FM differences were found on two measures of attention/executive function (Stroop Color/Word, Digit Span Backward [trend]) as well as processing speed as measured by Digit Symbol Substitution Coding. In contrast, group differences were not found for other aspects of attention/executive function: working memory (Digit Span Forward), set-shifting/complex sequencing (Trails B), verbal fluency/monitoring (naming animals), or problem solving (Everyday Problems Test), or an additional measure of processing speed (Trails A); although for most of these tasks, the pattern of performance was still better for non-FM than FM women. One exception was the measure of explicit memory (CERAD 10-item word list); scores for recall and recognition were not different for FM versus non-FM participants. Thus, inconsistencies remain even with a slightly larger sample and a variety of cognitive measures.

A number of studies have demonstrated deficits in tasks involving attention/executive function for persons with FM (Apkarian et al., 2004; Dick et al., 2002, 2008; Glass & Park, 2001; Glass et al., 2011; Grace et al., 1999; Park et al., 2001; Sephton et al., 2003; Verdejo-García et al., 2009). Executive function refers to multiple cognitive operations such as inhibition, working memory, set-shifting/switching, and monitoring (Miyake et al., 2001; Woodruff-Pak, 1997). As we had predicted, performance on Stroop Color/Word was significantly different for FM versus non-FM participants. That is, FM participants took longer than non-FM controls to complete this task, reflecting declines in the ability to inhibit distracting information. This is consistent with studies using similar methods to assess this aspect of executive function such as the Paced Auditory Serial Addition Task (Grace et al., 1999; Leavitt & Katz, 2006; Sletvold et al., 1995), the Wisconsin Card Sort Test (Verdejo-García et al., 2009), the Test of Everyday Attention (Dick et al., 2002; 2008), and a go/no-go temporal orienting paradigm (Correa, Miró, Martínez, Sánchez, & Lupiáñez, 2011; Veldhuijzen et al., 2012).

Digit Span Backward but not Digit Span Forward approached significance between the two groups. Span measures are typically used to assess working memory or the ability to hold information in short-term memory for manipulation. No differences were found in this study, consistent with Leavitt and Katz (2006). Park and colleagues (2001), however, did find poorer performance in FM participants for reading and computational span tasks, and Dick and colleagues (2008) found differences based on FM status for a reading span task. Seo and colleagues (2012) found both poorer accuracy and longer reaction times in FM versus non-FM participants for an *n*-back task for other than 0-back trials. These types of span tasks (as well as Backward vs. Forward Digit Span) place more demand on attention/executive function (manipulation, monitoring) than tasks that merely require the correct ordering of numbers such as the forward span used in this study.

Neither Trails B, which reflects aspects of set-shifting/complex sequencing and is thus a measure of attention/executive function, was significantly different based on FM status nor was naming animals (verbal fluency/monitoring) impaired in FM compared with control participants, although prior research on fluency tasks has demonstrated differences (Glass & Park, 2001; Park et al., 2001). Kemper and McDowd (2008) suggest that naming items from a category reflects not only semantic access but also requires attention/executive function in the monitoring of output. The high level of education in both our groups may contribute to the lack of differences found here.

Performance on tasks assessing processing speed showed deficits in FM compared with non-FM participants for Digit Symbol Substitution Coding. Trails A, which involves sequencing (of numbers) as quickly as possible but not switching between numbers and letters, may also be considered a measure of processing speed, but FM versus non-FM participants were not significantly different. These results are consistent with previous findings by Sletvold and colleagues (1995), who found no differences on Trails A but found significantly slower processing speed in FM compared with normal control participants using Digit Symbol Substitution Coding. Neither Grace and colleagues (1999) nor Park and colleagues (2001) found differences using somewhat similar tasks (Symbol Digit Modalities Test, and number, pattern, and letter cancellation tests, respectively).

There are subtle differences in these tasks even though they are purported to assess the same construct. For example, Digit Symbol Substitution Coding is probably more difficult than Trails A and may therefore provide enough variability to actually demonstrate group differences.

Explicit memory differences based on FM status using a 10-item word list to assess immediate recall, delayed recall, and delayed recognition were not found. Grace and colleagues (1999) used a similar word-list paradigm (Rey Adult Verbal Learning Test) and also found no differences, whereas Park and colleagues (2001) did. Interestingly, studies that employed other verbal memory measures such as logical memory (story rather than word recall) and paired associates learning from the Wechsler Memory Scale-Revised did find memory deficits in FM participants compared with controls (Grace et al., 1999; Leavitt & Katz, 2006). In addition, some research has suggested that explicit memory performance might be moderated by executive function ability, and it might be this rather than explicit memory per se that is reflected in performance differences between FM and controls (Grandfield et al., 2011).

Problem solving did not differ based on FM status in our study based on scores from the Everyday Problems Test. Problem-solving and decision-making tasks require attention/executive function in the processing of everyday activities and warrant further study. For example, both FM and non-FM chronic pain participants performed more poorly on the Iowa Gambling task compared with nonpain controls (Apkarian et al., 2004; Verdejo-García et al., 2009; Walteros et al., 2011). Due to time constraints, only three of seven domains were tested using the Everyday Problems Test. The full 42-item questionnaire may have provided a more sensitive measure of problem solving than the 18 items used in this study.

Because of the number of symptoms associated with FM that could independently influence cognitive processing, we initially investigated the relationship between our neuropsychological measures and *Core Symptoms* (pain, stiffness, fatigue), *Distress* (depression and anxiety), and *Sleep Problems* (trouble getting to sleep and staying asleep). Although some studies suggest that symptoms such as pain levels or depression explain the differences in cognitive performance between FM and non-FM groups (e.g., Dick et al., 2008; Sephton et al., 2003; Suhr, 2003), we found no such relationship. We also looked at medications, but no medication classification was significantly different across groups. Finally, correlations between BMI and physical activity levels with cognitive measures did not warrant inclusion of these measures in analyses.

Age was included as a covariate in all analyses due to the range of ages within groups (50–85 years in our FM group and 50–82 years in the non-FM group). Covariate analyses revealed significant differences in age (with younger outperforming older adults) for Stroop Color/Word, Digit Span Forward, Trails A and B, Digit Symbol Substitution Coding, and explicit memory measures (immediate recall, delayed recall, delay recognition); this is consistent with prior literature (Ardila, 2007; Darowski, Helder, Zacks, Hasher, & Hambrick, 2008; Fabiani, 2012). Thus, as FM participants age, risk for cognitive decline may be additive, especially for domains such as attention/executive function and processing speed.

Two symptom measures provided an opportunity to compare subjective perception of cognition to actual performance. Participants were asked to rate concentration problems and forgetfulness on scales from 0 to 10, with higher scores indicating more perceived impairment. Associations only reached criteria ($\alpha = 0.01$) when all participants were combined. Those reporting more problems with concentration had slower processing speed as measured by Digit Symbol Substitution Coding, $r = -0.29$, $n = 87$, $p = .006$ and poorer verbal fluency (naming animals), $r = -0.31$, $n = 87$, $p = .004$. Those reporting more forgetfulness also had slower processing speed as measured by Digit Symbol Substitution Coding, $r = -0.32$, $n = 87$, $p = .003$. Although these objective measures do not map directly onto concentration and forgetfulness, findings suggest that individuals (both FM and non-FM) may be mindful that it is becoming more difficult for them to process information.

Limitations of this study include self-selected samples of persons with and without FM. Both groups were highly educated and motivated enough to submit to multiple tests of both cognitive and physical performance. No attempt was made to screen for dementia in terms of daily functioning, so some individuals could have had mild cognitive impairment not detected by the MMSE; this could have particularly affected some of the memory measures. Although sample size in our study was larger than some past studies, certain cognitive variables may not have been significantly different due to lack of power. Subtle differences in many measures may exist and be clinically meaningful, yet may not be detected with small to medium sample sizes. In addition, because cognitive assessments were embedded within a larger study, this restricted the time allowed for assessment in order to minimize test burden, which influenced the selection of measures used.

Challenges in assessment of FM patients include consideration of multiple symptoms and medications (Rutledge et al., 2009; Suhr, 2003). Participants with FM appear to be a somewhat heterogeneous group (Wilson, Starz, Robinson, & Turk, 2009), and even within the same individual(s), there are good days and bad days, which might influence performance on certain measures. Our results, along with the mixed findings across cognitive domains in comparisons of individuals with and without FM (Schmidt-Wilcke et al., 2010), suggest that factors beyond those typically controlled for in current studies may be influencing FM participants. For example, variables such as comorbidities (e.g., hypertension, diabetes), decreased

physical activity levels, and increased prevalence of obesity may also influence cognitive performance (Cherry et al., 2009, 2012; Jefferson, Paul, Ozonoff, & Cohen, 2006; Lista & Sorrentino, 2010). This study attempted to control for some of these by evaluating associations between cognitive measures and symptoms, medications, BMI, and self-reported physical activity. Preliminary analyses also considered hypertension as a grouping variable but was dropped due to lack of significance.

In conclusion, neuropsychological assessment in a variety of cognitive domains in a group of FM versus non-FM participants (M_{age} = 63 and 65 years, respectively) found that performance on attention/executive function (interference/inhibition, working memory as measured by Stroop Color/Word and Digit Span Backward [trend]) and processing speed (as measured by Digit Symbol Substitution Coding) was significantly poorer for FM compared with control female participants. Inconsistencies in findings across studies may be due to sample size issues, participant comorbidities, subtle differences in measures purported to test the same construct, and/or potential heterogeneity in the FM population. They may also reflect the heterogeneity of cognitive performance trajectories in aging, where individual variance may outweigh aggregate variance (Small, Dixon, & McArdle, 2011).

Future research is warranted to parse these various components of cognitive function in clearer fashion. Moreover, factors that contribute to better cognitive performance should be explored, such as the influence of health habits, psychosocial factors, and health status (Cherry et al., 2009; Jorm, Anstey, Christensen, & Rodgers, 2004). Also needed is research that capitalizes on knowledge of biomarkers that share potential mechanistic links with cognitive performance (Macdonald et al., 2011). Inconsistencies in results across studies in various cognitive domains using neuropsychological assessment suggest that (a) more sensitive paradigms to assess potential information processing deficits in FM are warranted and (b) exploration of the possibility of heterogeneous groups within the FM population is needed (Follick, Zettel-Watson, Rutledge, Jones, & Cherry, 2012; Wilson et al., 2009) as cognitive function may be different across these potential subgroups. Finally, the possibility of differential aging effects on cognition among persons with FM needs to be explored.

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Correspondence

Correspondence should be addressed to Barbara Cherry, PhD, Department of Psychology, California State University, Fullerton, P.O. Box 6846, Fullerton, CA 92834–6846. E-mail: bcherry@fullerton.edu.

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