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Characterization of Fibromyalgia Symptoms in Patients 55 to 95 Years Old: a Longitudinal Study Showing Symptom Persistence with Suboptimal Treatment

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Abstract

BACKGROUND—Fibromyalgia (FM) has been understudied in the elderly population, a group with particular vulnerabilities to pain, reduced mobility, and sleep disruption.

AIMS—To characterize FM symptoms and treatments in a cohort of older subjects examined over time to determine the extent to which current, community-based treatment for older FM patients is in accord with published guidelines, and effective in reducing symptoms.

METHODS—A longitudinal, observational study of 51 subjects with FM (range 55 to 95 years) and 81 control subjects (58 to 95 years) performed at Banner Sun Health Research Institute in Sun City, AZ. Serial history and examination data were obtained over a 6-year period. FM data included medical history, medications, physical examination, tender point examination, neuropsychological testing, sleep and pain ratings, the Physical Function Subscale of the Fibromyalgia Impact Questionnaire, and other standardized scales to evaluate depression and other psychiatric symptoms, and cognitive and functional impairment.

RESULTS—Pain and stiffness that interfered with physical activity, sleep, and mood were reported by 80% or more of subjects. Over time, pain involved an increasing number of body areas. Over half of subjects were treated with NSAIDs, one-quarter with opioids, and one-quarter with estrogen. Few were treated with dual-acting antidepressants or pregabalin.

DISCUSSION—In this cohort of elders with suboptimally treated FM, substantial persistence of symptoms was seen over time. In general, recommended treatments were either not used or not tolerated.

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CONCLUSIONS—Age-appropriate treatments as well as education of primary care providers are needed to improve treatment of FM in the older population.

Keywords

fibromyalgia; elderly; geriatric; treatment

INTRODUCTION

The pace of fibromyalgia research has accelerated since the first publication of diagnostic criteria for this syndrome by the American College of Rheumatology in 1990 [1]. In spite of demonstrable progress, there is still relatively little known about fibromyalgia (FM) as it affects the elderly population [2,3], a group that could be expected to have particular vulnerabilities to pain, reduced mobility, and sleep disruption. FM was once believed to be a condition specific to middle-aged women, but in fact the prevalence of the syndrome is now known to increase with age, at least through the eighth decade [4]. Symptoms are seen to wax and wane over time, but rarely remit completely, so that affected patients can be expected to grow old with the condition [5].

Only six clinical research reports on FM in the elderly population have been published since 1988, when Yunus and colleagues reported the results of the only prospective study to date [6]. Yunus compared 31 elderly subjects to 63 younger subjects with FM in a clinic population, and found that the condition was often unrecognized in elders, treated with inappropriate medications such as steroids, and persistent at one-year follow-up [6]. Santos and colleagues found a community prevalence of FM in elders living in Sao Paulo of 5.5%, and noted that problems related to chronic pain were more severe among those with FM than those with other widespread pain conditions [3].

Four other studies reported the results of surveys or record reviews showing that elders with FM were more depressed and less physically active than elders without FM [7], and that the burden of symptoms was either reduced with increasing age [8], or remained high [2,9]. Associated problems of sleep disruption and isolation at home because of pain also were reported [2,9]. No studies have addressed the extent to which elderly patients are receiving adequate treatment for FM based on published guidelines, or longitudinally assessed change in symptoms in this population.

Current treatment recommendations for FM in non-age selected patients emphasize a multipronged approach, including effective communication and patient education, aerobic exercise, cognitive-behavioral therapy, and specific medications [10,11]. Based on available evidence, the U.S. Preventive Services Task Force strongly recommended duloxetine, milnacipran, pregabalin, and amitriptyline, and also recommended cyclobenzaprine, gabapentin, fluoxetine, and paroxetine [12]. The Task Force made no recommendation regarding opioids, tramadol, benzodiazepines, NSAIDs, magnesium, guaifenesin, DHEA, thyroxine, melatonin, or calcitonin [12].

The present study was performed to determine the extent to which current, communitybased treatment for older FM patients is 1) in accord with published guidelines, and 2)

effective in reducing symptoms. The study was part of a longitudinal clinicopathological study of FM in persons 50 years and older established in 2005 at Banner Sun Health Research Institute in Sun City, AZ. The aim of that study was to investigate the relationship of glial cytokine expression in spinal cord with local and regional pain and tenderness. The data from clinical evaluations performed on this cohort of subjects from 2005 through 2011 were summarized and are reported here, along with information about past and current treatments. Demographic data, body mass index, alcohol use, smoking, medical comorbidity, and cognitive function were compared to that of a control population studied during the same period.

MATERIALS AND METHODS

The research was in full compliance with the ethical rules for human experimentation stated in the Declaration of Helsinki. FM and control subjects were independently recruited from the community through lectures, radio and newspaper advertisements, and referrals from physicians for enrollment in the Brain and Body Donation Program (BBDP) at Banner Sun Health Research Institute (BSHRI). Written informed consent, approved by the BSHRI Institutional Review Board, was obtained from subjects in both groups.

FM subjects met the American College of Rheumatology (ACR) 1990 criteria for FM [1] as confirmed by a board-certified rheumatologist. Control subjects were identified by database query as being female and evaluated during the target interval. Subjects in both groups were examined at least every 2 years, and no subject was lost to follow-up. Each visit included a medical history, review of medications, physical and neurological examination, tender point examination, and neuropsychological testing. Tender point examination was performed by a physician trained in its administration. A dolorimeter was not used; the "blanching nail" test was used to gauge correct pressure in palpating tender points.

The neuropsychological test battery used was in conformance with the National Alzheimer's Coordinating Center (NACC) protocol, with domains and tests listed in Table 1. Other scales included the Geriatric Depression Scale [13], Clinical Dementia Rating Scale [14], Neuropsychiatric Inventory Questionnaire [15], and Functional Activities Questionnaire [16], which were administered at each visit by personnel trained and certified in their administration. All tests and scales have demonstrated reliability and validity. This battery provides a complete characterization of the subject's cognitive performance, functional status, and any confounding psychiatric problems at the time of evaluation.

FM subjects were asked to complete a BSHRI FM Clinic Questionnaire, with responses reviewed in an interview with study staff. The questionnaire included questions about the onset of illness, family history, current symptoms, marital status, current and past exercise, current and past habits, treatments for FM, sleep, work status, and life stressors. Impairment in large muscle activities was self-rated using question 1 of the Physical Function Subscale from the Fibromyalgia Impact Questionnaire (FIQ) [17], which lists 11 items such as shopping, laundry, and meal preparation, and asks respondents to indicate how they functioned in that task – *always able (0), mostly able (1), occasionally able (2), or never able (3)* – over the past week. The total point score was divided by the number of activities

scored, as proposed by Bennett [17]. Subjects were then asked to pick from a list of 15 causes of impaired physical function, or to write in what they perceived as the cause of impairment. An outline drawing of a human figure was provided for subjects to shade usual pain areas. The study team then interpreted the shadings as corresponding to muscle groups or body regions. A visual analog scale was provided for subjects to indicate current "best pain" and "worst pain" (0–10) on an unruled line. Measurement of the line segment yielded a quantitative estimate of pain.

Data were entered to an Excel file, and analyzed using the software program STATA-12 (StataCorp LP, College Station, Texas). The initial visit was selected as the index visit, unless neuropsychological testing was not obtained until the second visit. For longitudinal observations, data from all visits was used. Mean, median, and range were used to summarize continuous variables, and proportion was used to summarize binary variables. Median values were reported in lieu of means for continuous variables with skewed distribution. Confidence intervals were given to indicate the precision of estimated parameters. To compare continuous variables between the FM and control groups, the Wilcoxon rank-sum test was used. In the group comparisons, for a normal variable with equal standard deviation (SD) in FM and control groups, the power was 80% to detect a difference in the means of 0.53 SD, and 90% to detect a difference of 0.61 SD using a 2-sided, two-sample t-test with p<.05 level of significance. To compare binary variables between groups, the Fisher's exact test was used. To correlate two continuous variables with age as a covariate, Spearman's rank order correlation coefficient was used. Correlations between each assessment and age were determined using linear and logistic regression.

RESULTS

Demographics

51 subjects with FM and 81 control subjects were studied. All subjects were Caucasian, and all female except for one male in the FM group. In the FM group, 90% of subjects were 65 years of age or older, but as shown in Table 2, the FM group overall was significantly younger than the control group. The FM subjects were more likely to be married, whereas the control subjects were more likely to be widowed. There was no difference between the groups in mean years of education.

Age at Onset and Diagnosis

The mean age at onset of FM symptoms was 51.6 years (range 21–88), and the mean age at diagnosis was 58.2 years (range 36–90). It took a mean of 7 years for the diagnosis to be made (range 0.5–28). There was a strong inverse correlation between the age at symptom onset and the number of years to diagnosis (ρ =–0.607, p<0.001).

Pain and Tenderness

On the 0 to 10 scale, the "best pain" average for FM subjects was 3.36 (SE=0.15; 95% CI: 3.07–3.66) and "worst pain" 8.25 (SE=0.13; 95% CI: 8.00–8.50). Usual pain areas reported most frequently among 48 FM subjects included upper back in 36 (76%; 95% CI 65–90%), neck in 31 (65%; 51–79%), lower back in 23 (47%; 32–61%), gluteal muscles in 18 (37%;

23–51%), and "all over" in 6 (12%; 3–22%). On tender point examination, the mean number of positive tender points was 13 (SE=0.64; 95% CI: 12–15), the median was 14, and the range was 0 to 18. (Note that a patient could have met criteria for FM at visit #1, then started treatment so that by visit #2 when neuropsychological testing was performed – the "index visit" – the number of tender points could be 0.) Within this sample, age was independent of pain level as determined by Spearman's rank order correlation coefficient (for *best pain*, ρ =0.238, *p*=0.129; for *worst pain*, ρ =0.081, *p*=0.611).

FM Symptoms

Table 3 shows the frequency with which FM symptoms were reported for the index evaluations. The most common symptoms reported were muscle pain, stiffness, and awakening tired and in pain. Poor sleep also was common. FM subjects indicated that they "felt good" a mean of 3 days out of the last 7 (SE=0.31; 95% CI: 2–4 days), and that they missed doing housework because of FM a mean of 1.5 days out of the last week (SE=0.29; 95% CI: 1–2 days). Only one of the FM subjects was employed, on a part-time basis.

Physical Impairment

On the first question of the Physical Function Subscale of the Fibromyalgia Impact Questionnaire, FM subjects registered a mean score of 0.90 (SE=0.08; 95% CI: 0.73–1.06), which they correlated to a mild degree of impairment ("always" to "mostly" able to perform physical activities); the range of scores was 0 to 2.18. Subjects attributed impairment primarily to stiffness, lack of energy, and pain. Within this sample, age was independent of FIQ score, as determined by Spearman's rank order correlation coefficient (ρ =–0.062, p>0.673).

Sleep

Median total sleep time for the FM subjects was 7.5 hours (range 4.5–12), the median number of nocturnal awakenings was 2.5 (range 1–7), and the median number of days feeling refreshed upon awakening was 4 (range 0–30) in the last 30 days. Within this sample, age was independent of these sleep parameters, as determined by Spearman's rank order correlation coefficient: for total sleep time, ρ =–0.275, *p*=0.138; for awakenings, ρ =0.217, *p*=0.138; and for number of days refreshed on awakening, ρ =0.167, *p*=0.255. Overall, 63% of subjects reported non-restorative sleep (95% CI: 49–77%). Other sleep phenomena reported included restless legs in 53% (95% CI: 39–67%), snoring in 35% (95% CI: 21–49%), bruxism in 31% (95% CI: 17–44%), and apneas in 21% (95% CI: 9–33%).

Medical Comorbidities

The frequency of various medical conditions was compared in FM and control groups, as shown in Table 4. The following conditions were found to be significantly more common in the FM group: asthma, chronic fatigue, COPD, depression, GERD, irritable bowel syndrome, osteoarthritis, obstructive sleep apnea, rheumatoid arthritis, and restless legs syndrome. Although not the focus of this study, it was interesting to note that certain comorbidities that would be expected to be more frequent in the older control group – osteoarthritis, for example – were significantly more frequent in the FM group.

Treatment

As shown in Table 5, subjects indicated that they had tried a variety of treatments for FM, but treatments they judged to be helpful were few; massage and NSAIDs topped that list, followed by exercise and dual-acting antidepressants. As discussed in an earlier section, neither massage nor NSAIDs are recommended treatments. Not tried were pregabalin and cognitive-behavior therapy (CBT), both strongly recommended treatments. Several subjects indicated that pregabalin had been offered to them, but was refused because of the potential for weight gain and cognitive side effects. For most subjects, CBT had not been offered. Although some subjects had tried amitriptyline or cyclobenzaprine, these medications are generally not recommended as safe in geriatrics [18].

Table 6 lists current pharmacologic treatments for FM in our cohort, which also conformed poorly to published guidelines [10–12]. More than half of our subjects were currently taking NSAIDs, almost one-quarter were taking opioids, and one-quarter were taking estrogen, and not one of these treatments is recommended. Only a small number were taking dual-acting antidepressants. Although our subjects themselves indicated that exercise was beneficial, many noted that they were unable to optimize this treatment because of limitations from stiffness and lack of energy. Almost uniformly, they reported their exercise programs as self-directed and informal rather than part of a structured program. No relationships were found between any current medications and current pain ratings or activity levels using the Wilcoxon rank-sum test.

Habits

No difference was found between the FM and control groups in current smoking habits (very few subjects in both groups) or past smoking habits (about half of subjects in both groups). Current drinking was more likely in the control group as determined by Fisher's exact test (p<0.03; 95% CI: 27–37%).

Of FM subjects, 72% reported that they were currently exercising (95% CI: 57–84%), although most indicated this was "light" exercise that was not a prescribed or formal program. Similarly, 78% reported past exercise (95% CI: 66–91%) of the same description. Within this sample, age was independent of current exercise, as determined by the Wilcoxon rank-sum test (p>0.174). Of FM subjects, 23% stated that they were currently dieting (95% CI: 11–35%), while 53% had dieted in the past (95% CI: 38–68%). Current caffeine use was reported by 63% (95% CI: 49–77%) and past caffeine use by 78% (95% CI: 65–90%).

Body Mass Index

Mean BMI for the FM group was 26.2 kg/m² (SE=0.80; 95% CI: 24.6–27.8 kg/m²) and for the control group 24.2 kg/m² (SE=0.43; 95% CI: 23.4–25.1 kg/m²); the difference was statistically significant by 2-group t-test (p=0.019). Adjustment for age did not change the results. The FM group had two extreme outliers, one at a BMI of 45 kg/m² and the other at a BMI of 13.7 kg/m². Whether the outliers were included or excluded from the analysis, the results were unchanged.

Stress and Mood

Some degree of current life stress was reported by 45/48 (94%) of FM subjects (95% CI: 87–100%), but the stress was rated as "mild" by most respondents. On the 30-item Geriatric Depression Scale (GDS), the FM subjects had a mean score of 6.84 (SE=0.65; 95% CI:5.53–8.15) and the control subjects 3.24 (SE=0.48; 95% CI: 2.29–4.19). Although these mean scores did not approach any recognized threshold for clinical depression, the difference between the means was significant (p<0.001) as determined by the Wilcoxon rank-sum test.

Cognition

The battery of neuropsychological tests used in the BBDP is optimized to detect incident cognitive impairment in Alzheimer's disease and other neurodegenerative diseases. Using this battery, 5 subjects (10%) in the FM program were diagnosed with mild cognitive impairment and 1 subject with mixed vascular dementia during the study. Forty-five subjects (90%) with FM showed no evidence of cognitive impairment. All control subjects were unimpaired at baseline, in accord with BBDP enrollment criteria, and remained unimpaired on follow-up. The FM and control subject groups were indistinguishable on cognitive tests at the index visit, as shown in Table 7. This remained true after adjusting for the age difference between the groups.

Longitudinal Analyses

The mean number of evaluations performed on FM subjects during the study period was 2.75 (SE=0.19; 95% CI: 2.34–3.11), spanning a mean of 3.42 years (SE=0.27; 95% CI: 2.87–3.97). Across years, a total of 132 visits were captured for this group. The mean change in pain severity over time was very small, only -0.16 on the 0-10 pain scale (SE=0.47, 95% CI: -1.11-0.80). This was not significantly different from zero (p<0.91). The mean change in number of pain areas was not *statistically* significant at +3.12 (SE=0.19, 95% CI: 2.74-3.50, p>0.11), but could well have represented detectable worsening to the subject. Tender point changes (positive to negative, or the reverse) showed no particular trend. The median change in hours of sleep (+0.5) and median change in number of nocturnal awakenings (+1) were small. In general, other FM symptoms were also stable across epochs, either present or absent in a given individual. Least likely to change were the symptoms found to be most common overall: muscle pain, stiffness, and awakening tired. Most likely to change were joint swelling, excess fatigue, pain on awakening, urination problems, bloating, and exertional fatigue.

DISCUSSION

This cohort of elders with FM reported and manifested a substantial burden of pain and tenderness over time. In the majority of subjects, pain mostly affected the neck and back, whereas tenderness was more or less equally distributed across tender points. Subjects consistently reported that pain significantly affected physical activity level, sleep, and mood.

Current treatments for FM in our cohort did not conform to published guidelines [10–12]. As noted in an earlier section, current recommendations emphasize a multi-pronged approach to treatment, including aerobic exercise, cognitive-behavioral therapy, and specific

medications. The effectiveness of exercise as a component of FM treatment has been demonstrated [19,20], and exercise is universally recommended in current treatment guidelines [1,10,11,21]. Our subjects endorsed exercise as beneficial, but were engaged only in "light" exercise (e.g., casual walking) that was not part of a graded or supervised program. Similarly, our subjects had little to no experience with cognitive-behavioral therapy. Our subjects also endorsed massage as an effective treatment, in line with findings from the Yunus study [6]. Massage is not currently recommended for non-age selected patients, as there is no evidence to support this mode of therapy [21]. In fact, few of our own subjects were engaged in regular massage, mostly because of cost.

Specific medications used by our subjects to treat FM also diverged from treatment guidelines. More than half of our subjects were currently taking NSAIDs, even though these drugs are not a recommended treatment [12,21], and in spite of safety concerns about their chronic use in elders [18]. Almost one-quarter were taking opioids, and one-quarter estrogen, and neither of these treatments have been found effective in treating FM [21]. Only a small number of our subjects were currently taking dual-acting antidepressants, which are recommended treatments. It should be noted that two recommended medications for FM in non-age selected patients – amitriptyline and cyclobenzaprine – are considered inappropriate for use in the geriatric population [18].

Cognitively, the FM group could not be distinguished from the healthy control group on traditional tests designed to detect incident cognitive impairment. Both groups showed normal cognitive profiles, with exceptions in the FM group noted above. Like their younger counterparts, all of our FM subjects self-reported cognitive problems relating to attention and the ability to "multi-task." It has been suggested that traditional neuropsychological tests may be insensitive to deficits in fibromyalgia because they are attention-directed tasks that are free of distraction [22]. Leavitt and Katz found that fibromyalgia patients demonstrated less impairment on memory tasks free of stimulus competition (e.g., WMS-R Logical Memory) than on tasks with stimulus competition (e.g., Paced Auditory Serial Addition Task, Letter-Number Sequencing, and Auditory Consonant Trigrams [23]. It may be true that the cognitive tests used in our battery – the NACC protocol described above – are not optimized to detect cognitive problems in the FM population.

A weakness of this study that could impact the validity of certain results is the significant difference in mean age between the FM and control groups. This may confound the group comparisons of BMI, medical comorbidity, and neuropsychological testing, in spite of adjustments made for age using regression models. In addition, group comparisons were not possible on variables of pain, sleep, and tender points, as these data were not collected for the control population.

Strengths of the study include the standardized BBDP evaluation of subjects, confirmation of the diagnosis of FM by a board-certified rheumatologist using the ACR 1990 criteria, the scope and detail of information specific to FM collected, the longitudinal study design with serial evaluations, the fact that no patient was lost to follow-up, and the corroboration of subject reports by an informant and by a study physician who interviewed each subject and performed a physical and tender point examination.

In summary, this cohort of older subjects reported significant ongoing morbidity from undertreated FM. Few of our subjects were engaged in an adequate exercise or weight management program, and few had experience with CBT. These represent important missed opportunities for treatment. In addition, pharmacological treatment in this cohort was far from optimized. One goal of treatment for FM in older patients would be to eliminate ineffective and potentially harmful treatments such as opioids, chronic use of NSAIDs, and steroid medications. Age-appropriate pharmacological interventions could include the use of dual-acting antidepressants, provided these drugs are started at appropriately low doses and titrated slowly in accord with geriatric prescribing guidelines.

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Cognitive Tests and Rating Scales

Domain	Tests
Attention	WMS-R Digit Span, Trail Making Test A/B, Stroop
Memory	Rey AVLT, WMS-R Logical Memory Subtest (Story A), BVMT-R
Language	COWAT, Category Fluency, Boston Naming Test
Visuospatial	Clock Drawing Test, Benton Judgment of Line Orientation
Executive	Trail Making Test B, Stroop Interference, COWAT, Category Fluency, Clock Drawing Test

Scale	Description		
Geriatric Depression Scale	30-item self-report assessment for depression. (Yesavage, 1982)		
Clinical Dementia Rating Scale (CDR)	Structured interview yielding scores in 3 cognitive and 3 functional domains; used to stage dementia. (Morris, 1993)		
Neuropsychiatric Inventory Questionnaire (NPI-Q)	Instrument to assess 12 areas of psychopathology in patients with dementia. (Cummings, 1994)		
Functional Activities Questionnaire	10-item scale to assess independence in instrumental activities of daily living. (Pfeffer, 1982)		

WMS-R=Wechsler Memory Scale-Revised, AVLT=Auditory Verbal Learning Test, BVMT-R=Blessed Visual Memory Test-Revised, COWAT=Controlled Auditory Word Association Test.

Demographic Data

	Fibromyalgia (n=51)	Control (n=81)	<i>p</i> -value
age (mean, range)	73 (55–95)	82 (58–95)	<.001
education (mean, SE, 95% CI)	14.6 (.29; 14–15)	15.1 (.36; 14–16)	.297
Marital status:			
married	32 (63%)	39 (48%)	
widowed	9 (18%)	32 (40%)	
divorced	7 (14%) 9 (11%)		.029
single	3 (6%)	1 (1%)	

Frequency of Reported Symptoms of FM

Symptom	No. Subjects (%; 95% CI) (n=51)		
Muscle pain	49 (96; 90–100)		
Stiffness	44 (86; 76–96)		
Awaken tired	44 (86; 76–96)		
Pain on awakening	42 (82; 70–93)		
Poor sleep	41 (80; 69–91)		
Muscle weakness	39 (76; 63–88)		
Pain with exertion	37 (73; 61–86)		
Excess fatigue	37 (72; 59–85)		
Bloating	31 (61; 47–75)		
Joint swelling	30 (58; 44–73)		
Exertional fatigue	28 (55; 41–69)		
Restless legs	27 (53; 39–67)		
Urination problems	26 (51; 37–66)		
Dizziness	25 (49; 35–63)		
Memory loss	25 (49; 34–63)		
Constipation	24 (47; 32–61)		
Loose stools	24 (47; 32–61)		
Anxiety	14 (27; 15–40)		
Premenstrual syndrome history	16 (31; 17–44)		
Swallowing problems	14 (27; 14–39)		
Logical reasoning impaired	10 (20; 9–32)		
Panic attacks	7 (14; 4–24)		

Comorbid Medical Conditions: FM versus Control Subjects

	FM Subjects Frequency (%) (n=51)	Control Subjects Frequency (%) (n=81)	Age-adjusted <i>p</i> -value [#]
Atrial fibrillation	6 (12%)	5 (6%)	0.131
Alcoholism	2 (4%)	2 (2%)	0.684
Anxiety	14 (27%)	7 (9%)	0.071
Asthma	11 (22%)	6 (7%)	0.030*
Back surgery	7 (14%)	5 (6%)	0.088
Carpal tunnel syndrome	7 (14%)	3 (4%)	0.070
Chronic fatigue	8 (16%)	3 (4%)	0.025*
COPD	9 (18%)	4 (5%)	0.006**
Depression	28 (55%)	16 (20%)	0.001**
GERD	21 (41%)	22 (27%)	0.017*
Hypertension	31 (61%)	49 (60%)	0.307
Irritable bowel	15 (29%)	4 (5%)	0.001**
Osteoarthritis	47 (92%)	29 (36%)	<0.001***
Urinary problems	11 (22%)	11 (14%)	0.114
Insomnia	7 (14%)	6 (7%)	0.934
Obstructive sleep apnea	8 (16%)	1 (1%)	0.015*
Peripheral neuropathy	7 (14%)	15 (19%)	0.815
PTSD	3 (6%)	0	0.056
Rheumatoid arthritis	4 (8%)	0	0.021*
Restless legs	22 (43%)	4 (5%)	<0.001***
Thyroid disease	22 (43%)	31 (38%)	0.085

[#]Age-adjusted *p*-values were calculated using logistic regression with age included as a confounder, except for PTSD and rheumatoid arthritis, where, *p*-values were calculated using Fisher's exact test without adjustment for age because the frequencies for the control group were "0".

Past FM Treatments

Treatment	Treatments Tried No. Subjects (%; 95% CI) (n=51)	Treatments Found Helpful No. Subjects (%; 95% CI) (n=32 respondents)	
Exercise	34 (66; 51–80)	9 (28; 23–45)	
Massage	31 (61; 46–76)	15 (47; 29–65)	
NSAIDs	28 (55; 39–70)	14 (44; 26–62)	
Muscle relaxants	28 (55; 39–70)	6 (19; 4–33)	
Antidamanata	18 (26, 22, 51)	Dual-acting: 7 (22; 7–37)	
Anudepressants	18 (30; 22–31)	SSRI: 1 (3; 0–9)	
Chiropractic manipulation	17 (34; 20–49)	5 (16; 2–29)	
Acupuncture	17 (34; 20–49)	3 (9; 0–20)	
Steroid injections	14 (27; 14–41)	2 (6; 0–15)	
Hypnotics	14 (27; 14–41)	2 (6; 0–15)	
Oral steroids	9 (18; 6–30)	2 (6; 0–15)	
Anxiolytics	6 (11; 2–21)	1 (3; 0–9)	
Opioids	4 (7; 0–15)	5 (16; 2–29)	

Current Pharmacologic Treatments for Fibromyalgia

Treatment	No. Subjects (%; 95% CI) (n=49 respondents)		
NSAIDs	21 (57; 43–72)		
Estrogen	12 (24; 12–37)		
Opioids	11 (22; 10–35)		
Anxiolytics	10 (20; 9–32)		
Hypnotics	9 (18; 7–30)		
Muscle relaxants	8 (16; 6–27)		
SSRIs	8 (16; 6–27)		
Duloxetine	7 (14; 4–24)		
TCAs	4 (8; 0–16)		
Bupropion	1 (2; 0–6)		
Mirtazapine	1 (2; 0–6)		
Milnacipran	1 (2; 0–6)		
Pregabalin	1 (2; 0–6)		
Tramadol	1 (2; 0–6)		
Venlafaxine	1 (2; 0–6)		

Cognitive Test Results: Fibromyalgia vs Control Subjects

	FM Group mean (SE)	Control Group mean (SE)	Age-adjusted <i>p</i> -value [*]
Auditory-Verbal Learning Test (AVLT): Total Learning	45.3 (1.5)	45.5 (1.14)	0.945
AVLT long-term recall	9.22 (0.42)	9.18 (0.39)	0.984
AVLT % recall	78.8 (2.34)	77.7 (2.46)	0.700
Digit Span Total	15.3 (0.39)	15.7 (0.65)	0.607
Clock	9.41 (0.12)	9.47 (0.17)	0.901
Stroop Color/Number	62.8 (1.78)	63.6 (12.5)	0.608
Stroop Word/Color/Number	33.5 (1.35)	33.2 (1.05)	0.914
Stroop Interference	-2.88 (1.06)	-3.87 (0.63)	0.923
Trailmaking Test A	36.4 (1.68)	38.6 (2.61)	0.679
Trailmaking Test B	97.1 (6.85)	107 (12.8)	0.702
Letter Fluency (COWAT)	37.5 (1.81)	41.2 (1.41)	0.300
Animal naming	17.2 (0.80)	16.6 (0.48)	0.584
Judgment Line Orientation	22.7 (0.59)	22.4 (0.53)	0.882
MMSE	28.8 (0.18)	28.7 (0.14)	0.507

*Age-adjusted p-values were determined by linear regression with age included as a confounder.