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Neurological Signs and Symptoms in Fibromyalgia

Nathaniel F. Watson, MD[1], **Dedra Buchwald, MD**[2], **Jack Goldberg, PhD**[3], **Carolyn Noonan, MS**[2], and **Richard G. Ellenbogen, MD**[4]

[1]Department of Neurology, University of Washington, Seattle, USA

[2]Department of Medicine, University of Washington, Seattle, USA

[3]Department of Epidemiology, University of Washington, Seattle, USA

[4]Department of Neurological Surgery, University of Washington, Seattle, USA

Abstract

Objective—To determine the type and frequency of neurological signs and symptoms in individuals with fibromyalgia (FM).

Methods—Persons with FM (*n=166*) and pain-free controls (*n=66*) underwent systematic neurological examination by a neurologist blinded to disease status. Neurological symptoms present over the preceding 3 months were assessed with a standard questionnaire. We used logistic regression to evaluate the association of neurological symptoms and examination findings with FM status. Within the FM group we examined the correlation between self-reported symptoms and physical examination findings.

Results—Compared to the control group, age and gender adjusted estimates revealed the FM group had significantly more neurological abnormalities in multiple categories including: cranial nerves IX and X (42% vs. 8%), sensory (65% vs. 25%), motor (33% vs. 3%), and gait (28% vs. 7%). Similarly, the FM group endorsed significantly more neurological symptoms than the control group in 27 of 29 categories with the biggest differences observed for photophobia (70% vs. 6%), poor balance (63% vs. 4%), and weakness (58% vs. 2%) and tingling (54% vs. 4%) in the arms and legs. Poor balance, coordination, tingling, weakness in the arms and legs, and numbness in any part of body correlated with appropriate neurological exam findings in the FM group.

Conclusions—This blinded, controlled study demonstrated neurological physical examination findings in persons with FM. The FM group had more neurological symptoms than controls, with moderate correlation between symptoms and signs. These findings have implications for the medical work-up of patients with FM.

Keywords

Fibromyalgia; signs; symptoms; pain; neurological

Introduction

Fibromyalgia (FM) is a condition of unknown etiology characterized by widespread muscle pain, sleep disturbances, fatigue, and various neurological complaints (1). Despite considerable speculation and research, the etiology of FM remains uncertain. Although a

Address correspondence and reprint requests to Nathaniel F Watson, MD, MS, University of Washington Sleep Disorders Center at Harborview, Box 359803, 325 Ninth Avenue, Seattle, WA 98104-2499; Tel: 206 744-4999;Fax 206 744-5657; nwatson@u.washington.edu.

wide range of abnormalities and causes have been proposed (2,3), none have gained widespread acceptance or withstood the rigors of repeated scientific inquiries.

Fibromyalgia patients frequently report an onset of illness following a motor vehicle accident, surgery, or other trauma (4), often in the craniocervical region. Indeed, FM is 13 times more common following neck than lower extremity injuries (5,6). Neurological symptoms such as paresthesias, blurred vision, numbness, and weakness are commonly reported by FM patients, with numbness present in up to 84% of individuals (1,4,7–9). These symptoms, along with head and neck pain and difficulty walking (10,11), overlap with symptoms experienced by patients with neuroanatomic abnormalities such as Chiari I malformations, spinal canal stenosis, and positional cervical compression (5,12). Although highly controversial, it has been suggested that Chiari I malformation and FM are comorbidities and some practitioners have recommended decompressive craniotomy and cervical laminectomy as treatments for FM (13), particularly in those manifesting signs of cervical myelopathy (14). However, to our knowledge, no blinded, controlled studies have systematically assessed objective neurological findings in patients with FM.

The goals of this study were to conduct blinded neurological examinations and assess recent symptoms in FM patients and pain-free controls. We also correlated signs and appropriate symptoms in the FM group. An excess of objective findings, in tandem with correlating symptoms, would suggest the need to perform detailed neurological examinations in all FM patients, as well as a possible neuroanatomical origin for FM (5,14).

Materials and Methods

Participants

All individuals in the present study were participating in a study of Chiari I malformation and FM. Individuals with FM were identified either through an academic referral clinic devoted to the evaluation of chronic pain and fatigue or local advertising in the greater Seattle, Washington metropolitan area. The FM group was required to be: 1) ≥ 18 years of age; 2) if female, non-pregnant and; 3) have FM by self-report or by review of the medical records. A Research Coordinator trained by one of our team (DB) verified the diagnosis of FM according to the 1990 American College of Rheumatology guidelines by confirming the presence of chronic, widespread pain and ≥ 11 of 18 tender points on examination (1).

Control participants, recruited through advertising at 3 medical institutions, were required to be: 1) ≥ 18 years of age; 2) if female, non-pregnant and; 3) deny chronic, widespread pain or chronic fatigue. The Research Coordinator screened controls on the telephone for pain and FM related symptoms using the validated London Fibromyalgia Epidemiology Study Screening Questionnaire (15). This research was reviewed and approved by the University of Washington Institutional Review Board.

Symptoms

A self-report questionnaire inquired about past and current health status including symptoms characteristic of FM, headaches, and neurological functioning, including visual, auditory, balance, coordination, motor, sensory and gait.

Signs

A neurological exam was performed by a board certified neurologist (NFW) blinded to participant status. Neurological findings were recorded on a standardized form indicating the presence or absence of abnormalities. Examination of cranial nerves I-XII assessed smell, visual acuity, extraocular muscle palsy, papilledema, visual field cuts, pupillary shape,

symmetry and reactivity, facial sensation, masseter strength, facial symmetry, hearing, nystagmus, gag reflex, hoarseness, shoulder shrug, and tongue bulk and displacement. The cerebellar examination assessed the presence of tremor, dysdiadochokinesia, and dysmetria. To determine sensory deficits, participants were evaluated for analgesia or anesthesia, dissociated sensory loss, and impaired proprioception, vibration, temperature, or pinprick sensation. Dorsal columns were assessed with the Romberg sign. Motor examination ascertained weakness, impaired fine motor control, decreased or increased tone, and atrophy. Reflex testing evaluated patients for hyper- or hyporeflexia, Babinski sign, clonus, and trophic joint changes. Gait was assessed for ataxia and tested formally with tandem maneuvers and stance addressed the presence or absence of scoliosis or kyphosis.

Correlation of Signs and Symptoms

To better understand the relationship of symptoms and signs, specific symptoms were linked *a priori* with neurological signs in the FM group as follows: 1) difficulty swallowing linked to abnormal gag reflex; 2) tingling in arms or legs and numbness in any part of body each linked to analgesia/anesthesia or impairments in vibration, temperature, or pinprick sensation; 3) weakness in arms or legs was correlated with the presence of weakness or atrophy; and 4) poor balance, poor coordination, or abnormal clumsiness linked to positive Romberg sign, ataxia, impaired proprioception, or abnormal tandem gait. We also linked poor coordination with dysdiadochokinesis and abnormal clumsiness with impaired fine motor control on examination.

Statistical Analysis

Participants missing ≥ 1 key analysis variable (n=24; 9%) were excluded from all analyses. Descriptive statistics were reported as means with ranges for continuous variables and percents for categorical variables. We used logistic regression to evaluate the association of neurological symptoms and examination findings with FM status. A series of models was fit where symptoms and signs were the outcome variables and the independent variables included an indicator of FM, gender, and age. We present age and gender-adjusted prevalence estimates and 95% confidence intervals. Wald tests from the age and gender-adjusted models were used to test for a statistically significant difference between the FM and control groups. For the objective findings, we limited statistical testing to overall abnormality of ≥ 1 condition in each symptom category; however, for completeness, we report prevalence estimates and 95% confidence intervals for each condition. In some instances, odds ratios were not obtainable due to the absence of controls with neurological symptoms or signs. In this case, statistical testing was performed with Fisher's exact test. We examined the association between self-reported symptoms and signs in the FM group using tetrachoric correlations which provide an estimate of the underlying correlation when examining the relationship between two dichotomous variables (16). Analyses were completed using Stata/SE 10.1 for Windows (StataCorp LP, College Station TX, 2008).

Results

Demographics

There were 166 subjects in the FM group and 66 subjects in the control group. The FM group was older (50 vs. 41 years) and comprised of many more women (94% vs. 50%) than the control group. The majority of participants in both groups were white, including 89% of the FM group and 71% of the control group.

Symptoms

The FM group endorsed more neurological symptoms than the control group in 27 of 29 categories investigated (Table 1). These symptoms encompassed a large range of neurological functioning including the visual and auditory systems, cerebellum, cranial nerves, respiration, and sensory and motor systems. The biggest differences were observed for “bright lights bother eyes” (70% vs. 6%; $p<0.01$), “poor balance” (63% vs. 4%; $p<0.01$), and “weakness” (58% vs. 2%; $p<0.01$) and “tingling” (54% vs. 4%; $p<0.01$) in the “arms and legs.”

Signs

The detailed neurological examination revealed multiple differences between the FM group and the pain-free controls. Compared to the control group, the FM group was characterized by more hoarseness suggesting greater dysfunction in cranial nerves IX and X (42% vs. 8%; $p<0.01$). The FM group also had more sensory findings than controls (65% vs. 25%; $p<0.01$) consisting of diverse abnormalities including pinprick, temperature, and vibratory sensation as well as analgesia/anesthesia. Specific dermatomal distributions were not identified. The FM group also had more abnormal findings on the motor examination than controls (33% vs. 3%; $p<0.01$), due primarily to weakness on strength testing and impaired fine motor control. Involvement of specific muscle groups was not noted. The FM group also had more gait problems than their pain free counterparts (28% vs. 7%; $p<0.01$), particularly on tandem gait. Table 2 provides further details, including other aspects of the neurological examination that did not differ between the 2 groups.

Correlation of Signs and Symptoms

Significant correlations were observed between several signs and symptoms in the FM group. Complaints of both numbness in any location (rho=0.29; p=0.03) and tingling in arms or legs (rho=0.26; p=0.05) correlated with corresponding examination findings. Likewise, poor balance (rho=0.33; p=0.01), poor coordination (rho=0.31; p=0.01), and weakness in arms or legs (rho=0.31; p=0.03) were associated with appropriate objective findings. Lesser correlations were observed for the symptom abnormal clumsiness (ρ=0.23; p=0.08).

Discussion

To our knowledge, this is the first blinded, controlled study to demonstrate objective findings on detailed neurological examination in FM. Specifically, we found that individuals with FM exhibited abnormalities of cranial nerves IX and X, sensation, strength, and gait as compared to pain-free controls. As expected, symptoms affecting all neurological systems were more common in the FM group, with correlations observed between many of these symptoms and objective examination findings. These neurological signs support the possibility of a craniocervical neuroanatomic cause for the FM symptom complex, such as Chairi I malformation, spinal canal stenosis, or positional (flexion/extension) cervical compression (5,12,14).

In this regard, our results are consistent with the findings of 2 recent case series that assessed symptoms and performed detailed neurological examinations and neuroimaging in FM patients (5,12). In one study of 270 patients with FM, detailed neurological examinations were consistent with cervical myelopathy (5). Reported findings included upper thoracic spinothalamic sensory level (83%), hyperreflexia (64%), inversion of the radial periosteal reflex (57%), positive Romberg sign (28%), ankle clonus (25%), positive Hoffman sign (26%), impaired tandem walk (23%), dysmetria (15%), and dysdiadochokinesia (13%). Neuroimaging revealed 20% of participants had cerebellar tonsillar ectopia > 5 mm and 46% experienced clinically important spinal canal stenosis with the neck positioned in mild

extension. In another study (12), 49 FM patients with signs such as positional cervical pain, abnormal grip, positive Romberg or gait dysfunction, and symptoms of dizziness and unsteadiness underwent flexion/extension midline sagittal magnetic resonance imaging with transaxial measurement of cervical spinal canal diameter. Details of the neurological examination were not presented, but almost 4% of these highly selected patients had Chiari I malformation. As well, 71% showed evidence of intermittent cervical spinal cord compression, usually in extension, but neutral sagittal cervical spine views only documented cervical spine abutment in 29%. Taken together, these studies suggest neurological findings are common in FM and may, in some cases, have a neuroanatomical basis.

We also found significant correlations between objective neurological examination findings and symptoms in the FM group across multiple neurological systems. This observation underscores the need to perform careful neurological examinations in all FM patients, particularly those with neurological complaints. These findings are congruent with possible neuroanatomical causes for FM in some patients (5,14). Of note, no study has reported the results of neurological examinations, radiological, and neuroimaging data that would permit recommendations to be made regarding which patients should be evaluated for neuroanatomical conditions. Even so, the potential importance of indentifying and treating underlying causes of the symptoms of the FM complex was suggested by a recent non-randomized study of surgical vs. non-surgical treatment of cervical myelopathy (14). The surgical group experienced reductions in number of body regions with pain, and improvements in neurological signs and physical and mental quality of life (14). Although the non-randomized nature of the intervention raises the prospect of confounding by indication, it highlights the need for carefully designed, rigorously blinded and controlled studies of craniocervical neuroanatomy in FM.

This study has several limitations. First, there is a concern about subject referral and the highly selected sample of patients with FM. Second, our samples were different with respect to gender and age. We addressed this issue by adjusting for age and gender in our logistic regression analysis whenever possible for the primary examination and symptom endpoints. In the instances when no participants in the control group experienced a sign or symptom we could not perform an adjusted analysis. Third, a higher than expected percentage of controls was indicated to have asymmetric reflexes or hyporeflexia, possibly due to the dichotomous nature of the examination data. Although this could have overwhelmed and obscured any subtle reflex differences between the two groups, the fact that the same blinded neurologist performed all examinations obviates any general bias in these estimates. Lastly, findings on the neurological examination can be influenced by factors such as patient effort, pain, and the patients understanding of the exam, and in some cases such as hoarseness, may have alternative explanations. In cases where the effort was variable, or the subject appeared to be confused by the examination, the examining neurologist paused to re-explain the exam, and reminded the patient to concentrate and give their best effort.

In conclusion, we documented that selected abnormalities in cranial nerves and sensory, motor, and gait functions were more common in FM than pain-free controls. Neurological symptoms were also common, and importantly, correlated with examination findings in many instances. Future investigations of the underlying neuroanatomy of FM could advance our understanding of diagnosis and treatment.

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Table 1

Prevalence of neurological symptoms for participants with and without fibromyalgia

	Fibromyalgia (n = 166)		No Fibromyalgia (n = 66)	
Symptom	**%**	**(95% CI)**	**%**	**(95% CI)**
Blurred vision[1]	46	(38 – 54)	6	(2 – 15)
Bright lights bother eyes[1]	70	(62 – 78)	6	(2 – 17)
Double vision[2]	15	(10 – 23)	1	(0 – 8)
Loss of peripheral vision[2]	10	(6 – 17)	1	(0 – 8)
Floaters, wavy lines, flashing lights	42	(34 – 50)	25	(15 – 39)
Dizziness[1]	53	(45 – 62)	4	(1 – 13)
Poor balance[1]	63	(54 – 71)	4	(1 – 13)
Ringing in ears[1]	46	(38 – 55)	13	(6 – 25)
Ear pressure[1]	35	(27 – 44)	2	(0 – 8)
Decreased hearing[2]	25	(18 – 33)	7	(2 – 18)
Vertigo[1]	30	(23 – 39)	1	(0 – 10)
Noises or talking that hurts ears[1]	45	(36 – 54)	1	(0 – 10)
Difficulty swallowing[1]	29	(23 – 37)	0	--
Sleep apnea[1]	32	(24 – 41)	3	(1 – 12)
Tremors[2]	16	(11 – 23)	3	(1 – 13)
Palpitations[1]	28	(21 – 36)	3	(1 – 12)
Poor coordination[1]	45	(38 – 53)	0	--
Constant throat pain or sore throat[1]	35	(27 – 43)	1	(0 – 9)
Lightheadedness[1]	52	(45 – 60)	0	--
Shortness of breath[1]	39	(31 – 49)	1	(0 – 9)
High blood pressure[1]	23	(16 – 32)	4	(1 – 13)
Tingling in arms or legs[1]	54	(46 – 63)	4	(1 – 14)
Numbness in any part of body[1]	50	(41 – 58)	3	(1 – 10)
Burning feeling in arms, legs, face, or torso[1]	38	(30 – 47)	2	(0 – 11)
Cannot feel hot objects in hands	3	(1 – 8)	0	--
Weakness in arms or legs[1]	58	(49 – 66)	2	(1 – 10)
Abnormal clumsiness[1]	38	(31 – 46)	0	--
Loss of muscle mass[1]	13	(9 – 19)	0	--
Incontinence of urine[2]	25	(18 – 33)	7	(3 – 19)

Prevalence estimates and p-values are age- and sex-adjusted when possible based on sample composition, otherwise estimates are unadjusted and p-values from Fisher's exact test

[1] $p<0.01$

^{2} $p<0.05$

CI = confidence interval

Table 2

Prevalence of neurological findings in participants with and without fibromyalgia

	Fibromyalgia (n = 166)		No Fibromyalgia (n = 66)	
Sign	**%**	**(95% CI)**	**%**	**(95% CI)**
Cranial nerve I				
Impaired sense of smell	2	(1 – 7)	1	(0 – 8)
Cranial nerve II, III, IV, VI				
Visual acuity	72	(62 – 80)	66	(48 – 79)
Abnormal for ≥ 1 condition below	14	(9 – 20)	10	(4 – 21)
Extraocular muscle palsy	3	(1 – 8)	1	(0 – 8)
Papilledema	0	--	0	--
Field cut	1	(0 – 4)	3	(0 – 11)
Pupils equal, round reactive to light/accommodation	11	(7 – 18)	5	(1 – 14)
Cranial nerve V				
Abnormal for ≥ 1 condition below	12	(7 – 18)	2	(0 – 11)
Facial sensation decreased	11	(7 – 17)	2	(0 – 10)
Chewing decreased	1	(0 – 4)	0	--
Cranial nerve VII				
Facial musculature asymmetric	1	(0 – 5)	0	--
Cranial nerve VIII				
Abnormal for ≥ 1 condition below	7	(3 – 13)	7	(2 – 21)
Hearing abnormal	5	(3 – 11)	7	(2 – 21)
Nystagmus abnormal	1	(0 – 5)	0	--
Cranial nerve IX, X				
Abnormal for ≥ 1 condition below[1]	42	(34 – 51)	8	(3 – 19)
Gag reflex abnormal	6	(3 – 11)	2	(1 – 10)
Hoarseness	38	(30 – 47)	5	(2 – 16)
Cranial nerve XI				
Shoulder shrug asymmetrical	0	--	0	--
Cranial nerve XII				
Abnormal for ≥ 1 condition below	1	(0 – 4)	0	--
Tongue atrophy	1	(0 – 4)	0	--
Tongue displacement	0	--	0	--
Cerebellar				
Abnormal for ≥ 1 condition below	16	(10 – 23)	4	(1 – 16)
Tremor	7	(4 – 12)	2	(0 – 10)
Dysdiadochokinesia	7	(3 – 13)	2	(0 – 12)
Dysmetria on finger nose test	1	(0 – 4)	0	--
Romberg present	7	(4 – 12)	0	--
Sensory				

	Fibromyalgia (n = 166)		No Fibromyalgia (n = 66)	
Sign	**%**	**(95% CI)**	**%**	**(95% CI)**
Abnormal for ≥ 1 condition below[1]	65	(56 – 72)	25	(14 – 39)
Analgesia or anesthesia	22	(16 – 30)	2	(0 – 8)
Dissociated sensory loss	8	(5 – 13)	0	--
Impaired proprioception	4	(2 – 9)	0	--
Impaired vibratory sensation	38	(30 – 47)	20	(11 – 35)
Impaired temperature sensation	40	(32 – 49)	6	(2 – 17)
Impaired pinprick sensation	47	(39 – 56)	7	(3 – 18)
Motor				
Abnormal for ≥ 1 condition below[1]	33	(25 – 41)	3	(1 – 11)
Weakness	21	(14 – 29)	2	(0 – 13)
Impaired fine motor control	11	(7 – 17)	1	(0 – 8)
Decreased tone	0	--	0	--
Increased tone	1	(0 – 5)	0	--
Atrophy	4	(2 – 9)	0	--
Reflexes				
Abnormal for ≥ 1 condition below	57	(49 – 65)	45	(31 – 60)
Not symmetric or physiologic	52	(43 – 60)	35	(22 – 50)
Hyperreflexia	14	(10 – 21)	5	(1 – 13)
Hyporeflexia	39	(31 – 48)	32	(20 – 47)
Joint abnormalities – trophic	4	(2 – 10)	1	(0 – 11)
Positive Babinski	1	(0 – 4)	0	--
Clonus	2	(1 – 6)	2	(0 – 10)
Stance				
Abnormal for ≥ 1 condition below	18	(12 – 26)	11	(5 – 25)
Scoliosis	2	(1 – 5)	0	--
Kyphosis	17	(11 – 25)	11	(5 – 25)
Gait				
Abnormal for ≥ 1 condition below[1]	28	(21 – 38)	7	(3 – 18)
Tandem abnormal	26	(18 – 35)	6	(3 – 18)
Ataxia	6	(3 – 11)	0	--

Prevalence estimates and p-values are age- and sex-adjusted when possible based on sample composition, otherwise prevalence estimates are unadjusted and p-values from Fisher's exact test, significance testing for overall abnormality of ≥ 1 sign in each symptom category only

[1] $p<0.01$

CI = confidence interval