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## Nerve conduction tests in patients with fibromyalgia: comparison with normal controls

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**Abstract** The purpose of this study was to evaluate nerve conduction in fibromyalgia (FM) patients and normal subjects. Testing of F waves and motor, sensory, and mixed nerve conduction was performed in 33 consecutive female FM patients complaining of paresthesias in the extremities and in 17 age- and sex-matched healthy volunteers. The nerve conduction results in FM patients were no different from those of normal subjects except for prolonged peroneal distal motor latency ( $P=0.048$ ) and decreased peroneal motor conduction velocity ( $P=0.030$ ). Five of the 33 patients (15%) showed abnormalities in peroneal nerve conduction, five (15%) had carpal tunnel syndrome (CTS), and overall nine (27%) had electrophysiologic findings of focal entrapment, which indicated that focal neuropathies were common in this patient group. There was no evidence of generalized polyneuropathy in the FM patients.

**Keywords** Fibromyalgia · Paresthesia · Nerve conduction tests · Entrapment neuropathy

### Introduction

Fibromyalgia (FM) is a chronic disorder characterized by widespread pain and tenderness at multiple sites [1]. The exact mechanism underlying FM remains obscure. A generalized pain modulation and perception disorder, which may involve sensitization of peripheral pain

pathways, central pathways, or both has been put forward as a pathophysiological explanation [2, 3, 4]. Many studies have investigated the nervous system in FM. Lower pain thresholds have been reported in FM patients [2, 5], and this phenomenon was more prominent in sites with underlying nerves than in bony and pure muscle sites [6]. Laser evoked potential studies were compatible with the presence of peripheral C fiber sensitization, probably combined with a dysfunction in central pain pathways [2, 4]. Brainstem dysfunction in auditory brainstem response studies [7, 8], motor cortical dysfunction in magnetic stimulation [9], and the inability to relax between contractions in surface electromyography [10] have been reported. In needle electromyography, no electrodiagnostic evidence of ongoing denervation or focal spasm were found in tender points [11]. Autonomic nervous system dysfunction has also been demonstrated in FM patients [12, 13, 14]. However, there is no comparative nerve conduction study, which may have implications for understanding the underlying pathophysiological basis of FM.

Paresthesia in the extremities is a common complaint in FM patients. The frequency of paresthesias has been reported at between 67.1% and 84% in different studies [1, 15]. The role of the peripheral nervous system in paresthesias in FM patients is not known. Paresthesias in the extremities are frequently seen in neurologic disorders as well, especially in focal and generalized neuropathies [16]. For this reason, these neuropathies may be overlooked or misdiagnosed in FM patients. A high prevalence of undetected carpal tunnel syndrome (CTS) in patients with FM has been reported [17], and a similar phenomenon may exist for various neuropathic conditions in FM patients. Additionally, a possible association between FM and CTS was suggested because of the higher prevalence of CTS in FM than of CTS alone [18, 19].

Adequate data on electroneurophysiologic examination of the peripheral nervous system in patients with FM have not been published. Only one retrospective study described that 94% of cases had normal

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electrodiagnostic test results, but the tests performed and the methodology were not defined [15].

The purpose of this study was a prospective and detailed electroneurophysiologic evaluation of peripheral nerves in FM patients compared with normal controls, to improve understanding of the pathophysiologic mechanism and detection of the focal and generalized neuropathies that might be overlooked or misdiagnosed in this patient group. A possible role of the peripheral nervous system in paresthesias in FM patients was also investigated.

## Patients and methods

Thirty-three consecutive female patients fulfilling the 1990 American College of Rheumatology criteria for FM [1] and complaining of paresthesias in the extremities were enrolled in the study. The patients were selected at a single physical medicine and rehabilitation outpatient clinic. Seventeen age- and sex-matched healthy volunteers served as the control group. The control subjects were the carepersons of the inpatient subjects in the same hospital, and none of them had any known neurological disease or complaint. All subjects agreed to participate in the study after receiving information about the test procedure. Age (years), height (cm), and body weight (kg) were recorded in all subjects.

### Nerve conduction studies

All subjects were tested by a single author (M.E.) using an electroneuromyogram instrument (Medelec Synergy, Oxford, UK). Tests were performed on the side where paresthetic complaints were prominent in FM patients and on the dominant side in control subjects. Nerve conduction tests were performed in standard fashion using surface stimulation and recording techniques. Motor, mixed, and sensory tests were performed orthodromically, except for sural sensory nerve conduction, which was tested antidromically.

Median, ulnar, peroneal, and tibial motor studies were performed by recording the compound muscle action potential (CMAP) from the respective muscle, with the recording electrode placed on the muscle belly and the reference electrode over the tendinous insertion. Stimulations were supramaximal. The CMAPs were recorded from the abductor pollicis brevis muscle by stimulating the median nerve at the wrist (5 cm proximal to the active recording electrode) and at the antecubital fossa. They were also obtained by stimulating the ulnar nerve at the wrist (5 cm proximal to the recording electrode placed on the abductor digiti minimi) and at the ulnar sulcus. The peroneal nerve was stimulated at the ankle (8 cm proximal to the active recording electrode placed on the extensor digitorum brevis) and at the fibular head. Recordings were obtained from the abductor hallucis muscle by stimulating the tibial nerve at the ankle (just behind the medial malleolus) 10 cm proximal to the recording electrode and at the knee crease. Distal motor latency (DL) was measured from the beginning of the stimulus artifact to the onset of the action potential. Motor conduction velocity ( $V_{mot}$ ) was calculated from the difference between the latencies of the two stimulation sites. The CMAP amplitude was measured from baseline to the first negative peak. F wave studies were performed for the median, ulnar, tibial, and peroneal nerves by recording from the same muscles and with the same electrode placement. The active stimulating electrode was located proximally. At least ten supramaximal stimulations were applied in a random fashion. Minimum F wave latencies ( $F_{min}$ ) were recorded. Median, ulnar sensory, and mixed conduction studies were performed orthodromically as previously described [20]. In median sensory conduction studies, the digit2-wrist segment, in ulnar sensory studies the digit5-wrist segment, and in mixed nerve

studies of both median and ulnar nerves the wrist-elbow segment were tested. Sural sensory conduction was tested antidromically by recording just behind the lateral malleolus and stimulating 14 cm proximally [20]. Sensory and mixed conduction velocities ( $V_{sens}$ ,  $V_{mix}$ ) were calculated from the beginning of the stimulus artifact to the peak of the sensory or mixed nerve action potential (SNAP, MNAP), and amplitudes were measured from peak to peak. Latencies were expressed in milliseconds (ms), amplitudes in millivolts (mV) for CMAPs, and in microvolts ( $\mu$ V) for SNAPs and MNAPs. Nerve conduction velocities were calculated as meters per second (m/s). Standard instrument settings were used for motor, mixed, and sensory conduction and F wave tests. The filter settings were 3–10,000 Hz for motor nerve conduction, 20–2,000 Hz for sensory and mixed nerve conduction, and 30–10,000 Hz for F waves.

### Statistical analysis

For data analysis, version 8.0 SPSS software was used. The data were expressed as mean  $\pm$  standard deviation (SD). Student's *t*-test for independent samples was used for comparing the groups. A *P* value of  $<0.05$  was used as a cutoff level for statistical significance.

### Normative data

When the values obtained from FM patients varied by more than 2SD from the mean values of normal subjects, they were considered abnormal in the tests of distal latency, minimum F wave latency, and nerve conduction velocity. For the amplitude of CMAP, SNAP, and MNAP, values below the lowest normal value were considered to be abnormal.

## Results

The mean age was  $39.2 \pm 5.9$  years (range 24–48) for patients with FM and  $39.7 \pm 6.9$  years (range 28–49) for control subjects. The demographic characteristics of the groups are summarized in Table 1. There was no statistically significant difference between the groups with respect to age, height, or weight ( $P > 0.05$ ). The average duration of FM reported by the patients was  $8.0 \pm 6.9$  years.

The sensory and mixed nerve conduction results are presented in Table 2, the motor nerve conduction results are presented in Table 3, and the  $F_{min}$  results are listed in Table 4. The sensory and mixed nerve conduction values and F wave values did not differ between the two groups. There was no statistically significant difference between the groups in motor nerve conduction, except for peroneal distal motor latency and peroneal motor conduction velocity: the former was prolonged ( $P = 0.048$ ), and the latter was decreased ( $P = 0.030$ ) in FM patients. When the patients were evaluated

**Table 1** Demographic characteristics of FM patients and normal control subjects

	FM ( <i>n</i> = 33)	Control ( <i>n</i> = 17)	<i>P</i> value
Age (years)	$39.2 \pm 5.9$	$39.7 \pm 6.9$	0.792
Height (cm)	$158 \pm 6.5$	$157 \pm 4.6$	0.844
Weight (kg)	$67.5 \pm 10.1$	$69.2 \pm 13.1$	0.636

**Table 2** Mean values of sensory and mixed nerve conduction studies in FM and normal control subjects, and normal limits. *V<sub>sens</sub>* sensory nerve conduction velocity, *SNAPamp* sensory nerve action potential amplitude, *V<sub>mixed</sub>* mixed nerve conduction velocity, *MNAPamp* mixed nerve action potential amplitude

		FM mean ± SD (n = 33)	Control mean ± SD (n = 17)	P value	Normal limit	
Median nerve	Digit2-wrist	<i>V<sub>sens</sub></i> (m/s)	40.75 ± 4.9	42.42 ± 3.3	0.214	35.83
		<i>SNAPamp</i> (μV)	22.4 ± 9.7	24.2 ± 8.9	0.544	9.3
	Wrist-elbow	<i>V<sub>mixed</sub></i> (m/s)	50.4 ± 2.4	50.5 ± 2.3	0.955	45.9
		<i>MNAPamp</i> (μV)	43.9 ± 20.8	40.0 ± 17.5	0.520	23.9
Ulnar nerve	Digit5-wrist	<i>V<sub>sens</sub></i> (m/s)	40.91 ± 3.3	41.15 ± 2.7	0.791	35.8
		<i>SNAPamp</i> (μV)	19.6 ± 7.2	19.3 ± 9.6	0.896	8.2
	Wrist-elbow	<i>V<sub>mixed</sub></i> (m/s)	53.4 ± 2.8	52.8 ± 2.8	0.464	47.2
		<i>MNAPamp</i> (μV)	52.0 ± 23.1	46.9 ± 19.1	0.431	18.6
Sural nerve	<i>V<sub>sens</sub></i> (m/s)	38.06 ± 2.8	39.00 ± 2.5	0.249	33.9	
	<i>SNAPamp</i> (μV)	15.7 ± 8.4	14.3 ± 9.0	0.592	3.0	

**Table 3** Mean values of motor nerve conduction studies in FM and normal control subjects, and normal limits. *DL* distal motor latency, *V<sub>motor</sub>* motor nerve conduction velocity, *CMAmp* compound muscle action potential amplitude

		FM (n = 33) mean ± SD	Control (n = 17) mean ± SD	P value	Normal limit
Median nerve	DL (ms)	3.15 ± 0.59	3.11 ± 0.23	0.777	3.57
	<i>V<sub>motor</sub></i> (m/s)	58.1 ± 4.9	57.9 ± 3.7	0.894	50.6
	<i>CMAmp</i> (mV)	8.6 ± 2.9	8.1 ± 2.6	0.596	4.5
Ulnar nerve	DL (ms)	2.47 ± 0.24	2.36 ± 0.17	0.086	2.70
	<i>V<sub>motor</sub></i> (m/s)	62.9 ± 4.3	64.1 ± 4.3	0.337	55.6
	<i>CMAmp</i> (mV)	9.4 ± 1.9	9.3 ± 1.7	0.900	6.9
Peroneal nerve	DL (ms)	4.55 ± 0.80	4.11 ± 0.52	0.048*	5.15
	<i>V<sub>motor</sub></i> (m/s)	50.6 ± 3.3	53.0 ± 4.0	0.030*	45.0
	<i>CMAmp</i> (mV)	5.0 ± 2.1	5.3 ± 1.9	0.583	2.1
Tibial nerve	DL (ms)	4.53 ± 0.73	4.62 ± 0.76	0.683	6.14
	<i>V<sub>motor</sub></i> (m/s)	47.8 ± 4.6	49.8 ± 4.3	0.137	41.2
	<i>CMAmp</i> (mV)	11.4 ± 4.7	8.9 ± 3.0	0.053	4.1

\**P* < 0.05

**Table 4** Shortest F wave latencies (*F<sub>min</sub>*) in FM patients and normal control subjects, and normal limits

	<i>F<sub>min</sub></i> in ms (mean ± SD)		<i>P</i> value	Normal limit
	FM (n = 33)	Control (n = 17)		
Median	24.3 ± 2.0	23.8 ± 1.3	0.434	26.4
Ulnar	24.3 ± 1.6	24.1 ± 1.4	0.589	26.9
Peroneal	44.5 ± 3.8	43.2 ± 3.7	0.260	50.6
Tibial	45.7 ± 3.5	44.7 ± 3.0	0.312	50.6

individually, the following abnormalities were identified: five patients (15%) had median mononeuropathy at the wrist (all had decreased *V<sub>sens</sub>* at the digit2-wrist segment and prolonged median motor DL), five (15%) had abnormal findings in peroneal nerve conduction (two had prolonged motor DL and prolonged F wave latencies, one had prolonged motor DL and decreased CMAP amplitude, one had decreased *V<sub>mot</sub>*, and one had prolonged motor DL), and one showed findings suggesting S1 radiculopathy (prolonged tibial F wave latency, normal peroneal nerve conduction, normal peroneal F wave and decreased sural SNAP amplitude). One patient had both CTS and peroneal abnormalities. There was no

evidence of generalized polyneuropathy in the FM patients.

When the 17 normal control subjects were evaluated individually, the following abnormalities were identified: one (5.9%) had median mononeuropathy at the wrist (decreased *V<sub>sens</sub>* at the digit2-wrist segment and prolonged median motor DL), one (5.9%) had abnormal findings in peroneal nerve conduction (prolonged motor DL), and one had findings suggesting lumbar radiculopathy (prolonged peroneal F wave latency, normal tibial, peroneal, and sural nerve conduction, and normal tibial F wave latency).

## Discussion

The evaluation of peripheral nerves by nerve conduction tests and the proximal segments of the nerves by F wave latencies revealed no difference between the study groups except prolonged peroneal distal motor latency and decreased peroneal motor conduction velocity in the FM group. When the subjects were assessed individually, abnormalities in peroneal nerve conduction were found in five patients (15%) and one control (5.9%).

Distal motor latency was increased in four patients, coupled with prolonged  $F_{\min}$  in two and with decreased CMAP amplitude in one. These findings were in agreement with peroneal nerve entrapment at the ankle, which is called anterior tarsal tunnel syndrome. In this syndrome, compression of the peroneal nerve may be due to local trauma or tight shoes and gives rise to pain on the dorsum of the foot, sensory deficits in the small web area between the first and second toes, and atrophy of the extensor digitorum brevis [21, 22]. The fifth patient with abnormal peroneal nerve conduction had decreased  $V_{\text{mot}}$  and a CMAP amplitude value at the lower limit of the normal group in stimulation of the peroneal nerve at the fibular head. The DL and  $F_{\min}$  latencies were normal. Although additional popliteal peroneal nerve stimulation and an inching study would be helpful for better determination of the entrapment site, the above findings suggested peroneal nerve entrapment at the fibular head. The peroneal nerve at this point is superficial, covered only by skin and subcutaneous tissue, and is exceptionally vulnerable to external compression. Habitual leg crossing is the classic cause of peroneal nerve entrapment at the fibular head [23, 24].

In the FM group, five of the 33 patients (15%) had median mononeuropathy at the wrist (all had decreased  $V_{\text{sens}}$  at the digit2-wrist segment and prolonged median motor DL). In the control group, only one subject (5.9%) had median mononeuropathy at the wrist. Higher prevalences of CTS in FM patients and a possible association between these two conditions have been reported previously [18, 19]. In a recent study, the prevalence of CTS was reported to be 10% in FM patients and 4% in normal control subjects, but the difference was not statistically significant [25]. A high prevalence of undetected CTS in patients with FM (16%) has also been reported [17]. None of the patients had multiple nerve involvement, except one with both CTS and peroneal abnormalities. There was no evidence of generalized polyneuropathy in FM patients.

The findings in this study indicate that focal neuropathies in FM patients are common. Overall, nine of the 33 patients (27%) had electrophysiologic findings of a focal entrapment neuropathy. This percentage may increase when extensive and detailed studies are performed for entrapment neuropathies. The etiology of such entrapments is most likely multifactorial. Simple nerve compression secondary to weight loss, prolonged periods of immobilization, incorrect positioning of body parts, and repetitive motion are likely to be important. The possible association between FM and entrapment neuropathies needs further investigation.

In this study, no evidence of a generalized abnormality of the peripheral nervous system was found which would play a role in the pathogenesis of FM. However, entrapment neuropathies appear to be common in this patient group. In FM patients complaining of paresthesias, detailed neurologic examination and appropriate electrodiagnostic tests may be helpful for detecting undiagnosed entrapment neuropathies. Appropriate

therapeutic measures (ergonomic instructions, splints, corticosteroid injections) for these entrapment neuropathies can be offered to improve the patients' quality of life.

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