Simultaneous heart rate variability and polysomnographic analyses in fibromyalgia

Sirs,

Dysautonomia is frequent in fibromyalgia (FM). Several groups of investigators using heart rate variability (HRV) analysis have shown that patients with FM have changes consistent with relentless sympathetic hyperactivity accompanied with sympathetic hypo-reactivity to stress (1-3). It has been proposed that such dysautonomia explains the multisystemic features of FM (4). The majority of FM patients have sleep problems manifested as light,unrefreshing sleep followed by stiffness, aching and fatigue upon awakening in the morning. The seminal electroencephalographic studies by Moldofsky and co-workers demonstrated that FM patients have a pattern of alpha wave intrusion into the deep sleep stages (5). The objective of this pilot investigation was to perform simultaneous HRV and polysomnography analyses in FM patients.

We studied 11 patients with FM (ACR criteria) and 10 age/sex matched healthy persons. All subjects were free from any medication that could affect the autonomic nervous system. All participants gave their informed consent. The institution's ethics and human research committees approved the protocol. All subjects spent one night in a sleep research laboratory. Polysomnography was analyzed following the recommendations of Rechtschaffen and Kales (6) using Sleepscan, Bio-logic equipment.

A Hewlett-Packard ambulatory electrocardiographic recorder (model 43400B) was used for the heart rate variability analysis. Standard time and frequency domain analyses were done according to accepted guidelines (7). The nocturnal sympatho-vagal balance was calculated as the ratio of the spectral power of the low-frequency ("sympathetic") band to the high frequency ("parasympathetic") band in the first 5 minutes of each hour from 11 pm to 6 am. Student's T test was used to compare the polysomnography and HRV values between patients and controls.

One patient was found to have multiple ventricular premature beats during the study, thus making heart rate variability analysis unrealizable. She was later diagnosed as having mitral valve prolapse. This case is not included in the analysis. Table I outlines the outstanding results. Patients with FM displayed significantly higher arousal/awakening episodes as well as a significantly higher sympatho/vagal balance.

Our method did not allow definition of the time sequence between the sympathetic surge and arousal/awakening episodes. Nevertheless concurrent analysis of HRV and polysomnography variables in normal people has shown that during non-rapid eye movement (N-REM) sleep there is a predominance of the high frequency band power, suggestive of parasympathetic activity. In contrast low frequency band oscillations predominate during REM sleep and wakefulness. Furthermore, a specific time domain method demonstrated that heart rate acceleration preceded electroencephalographic changes, suggesting that sympathetic surge is the cause of arousal/awakening episodes (8).

We recognize that there are certain limitations to our investigation. Polysomnographic and heart rate variability analyses were performed during the first night in a sleep research center, not allowing subjects to spend a previous night in the same laboratory to get accustomed to a foreign environment. The sample size was small, possibly concealing other significant differences between patients and control subjects.

There is mounting evidence that dysautonomia is frequent in fibromyalgia. Sympathetic hyperactivity may explain such diverse symptoms as pseudo-Raynaud's phenomenon, sicca complex, irritable bowel and anxiety. Concurrent sympathetic hypo-reactivity explains the constant fatigue and morning stiffness (4). FM defining features (chronic widespread pain and tenderness at palpation on specific anatomic points) can be explained through the pathogenesis known as "sympathetically maintained pain" (9). This pathogenesis is supported on the study showing that FM subjects have norepinephrine-evoked pain (10). Results of the present investigation propose that the constant arousal/awakening episodes that FM subjects have, may also be caused by sympathetic hyperactivity.

Table I. Outstanding polysomnographic and electrocardiographic results in 10 patients with fibromyalgia and 10 normal controls (± SD).

Variable	(units)	Fibromyalgia group		Control group		P value
No. of patients		10		10		NS
No. of female pts.		10		10		NS
Age	(years)	33.4	(11.3)	33.5	(10.0)	NS
Heart rate variability analysis						
Mean	(msecs.)	935.7	(129.7)	925.3	(173.5)	NS
RR-StD	(msecs.)	88.15	(30.17)	81.89	(41.72)	NS
CoVr	(%)	9.29	(2.40)	8.83	(2.72)	NS
MSSD	(msecs.)	47.17	(31.76)	50.7	(34.36)	NS
PNN5	(%)	21.22	(22.79)	21.2	(18.73)	NS
SDANN	(msecs.)	56.4	(20.69)	50.8	(25.57)	NS
HR	(beats x min.)	64.61	(9.83)	66.85	(12.19)	NS
Nocturnal sympatho-vagal balance		3.41	(0.66)	1.59	(0.36)	0.0001
Polysomnography						
Arousal/awakening index		33.05	(14.9)	18.65	(7.62)	0.007
Sleep efficiency	(%)	0.85	(0.09)	0.87	(0.07)	NS
Stage 1	(%)	8.18	(3.86)	5.60	(1.74)	NS
Stage 2	(%)	62.32	(9.02)	65.28	(9.02)	NS
Slow wave sleep	(%)	11.2	(6.06)	12.72	(6.99)	NS
REM sleep	(%)	18.31	(4.76)	17.63	(4.43	NS
Apnea/hr index		1.11	(1.17)	2-02	(3.63)	NS
Periodic leg movement/hr		3.16	(6.73)	1.83	(2.16)	NS

Mean:mean R-R interval duration; RR-StD:standard deviation of all R-R intervals; CoVr:coefficient of variation; MSSD:square root of the mean of the sum of the squares of differences between adjacent R-R intervals; PNN50: number of pairs of adjacent R-R intervals differing by > 50 msecs divided by the total number of R-R intervals; SDANN: standard deviation of the averages of R-R intervals in all 5-minute segments of the entire recording; HR: mean heart rate. Arousal + awakening index: number of arousals + awakening/hr.

M. KOOH, C. PINEDA, M. MARTÍNEZ-LAVÍN, A. NAVA, S. MEZA, M.-C. AMIGO, A. MARTÍN-DEL-CAMPO, R. DRUCKER-COLÍN, A.G. HERMOSILLO

Instituto Nacional de Cardiología and Universidad Nacional Autónoma Mexico.

Address correspondence to: Manuel Martínez-Lavín, MD. Chief Rheumatology Department, Instituto Nacional de Cardiología Ignacio Chávez, Juan Badiano 1, 14080 México DF, Mexico.
E-mail: mmlavin@infosel.net.mx

References

1. MARTINEZ-LAVIN M, HERMOSILLO AG, ROSAS M, SOTO ME: Circadian studies of autonomic nervous balance in patients with fibromyalgia. A heart rate variability analysis. *Arthritis Rheum* 1998; 42: 1966-71.
2. COHEN H,NEUMANN L, SHORE M,AMIR M, CASSUTO Y, BUSKILA D: Autonomic dysfunction in patients with fibromyalgia: Application of power spectral analysis of heart rate variability. *Semin Arthritis Rheum* 2000; 29:

217-27.

3. RAJ RR,BROUILLARD D, SIMPSOM CS, HOPMAN WM,ABDOLLAH H: Dysautonomia among patients with fibromyalgia: A non-invasive assessment. *J Rheumatol* 2000; 27: 2660-5.
4. MARTINEZ-LAVIN M, HERMOSILLO AG: Autonomic nervous system dysfunction may explain the multisystem features of fibromyalgia. *Semin Arthritis Rheum* 2000; 29: 197-9.
5. MOLDOFSKY H, SCARISBRICK P, ENGLAND R, SMYTHE H: Musculoskeletal symptoms and non-REM sleep disturbance in patients with "fibrosistis"syndrome and healthy subjects. *Psychosom Med* 1975; 37: 341-51.
6. RECHTSCHAFFEN A, KALES A: *A Manual of Standardized Terminology, Techniques, and Scoring System for Sleep Stages in Hu - man Subjects.* UCLA Brain Information Service/Brain Research Institute, Los Angeles, 1968.
7. TASK FORCE OF THE EUROPEAN SOCIETY OF CARDIOLOGYAND THE NORTH AMERICAN SOCIETY OF PACING AND ELECTROPHYSIOLOGY: Heart rate variability standars of measurement, physiological interpretation, and clinical use. *Circulation* 1996; 93: 1043-65.
8. OTZENBERGER H, SIMON C, GRONFIER C, BRANDENBERGER G: Temporal relationship between dynamic heart rate variability and electroencephalographic activity during sleep in man. *Neuroscience Lett* 1997; 229: 173-6.
9. MARTÍNEZ-LAVIN M: Is fibromyalgia a generalized reflex sympathetic dystrophy. *Clin Exp Rheumatol* 2001; 19: 1-3
10. MARTÍNEZ-LAVÍN M, VIDAL M, BARBOSA RE,PINEDA C,CASANOVA JM, NAVA A: Norepinephrine-evoked pain in fibromyalgia. A randomized pilot study (ISRCTN 70707830). *BMC Musculoskeletal Disord* 2002; 3: 2.