

Evaluation of abnormalities of orthostatic postural control in systemic sclerosis

P.G. Giacomini, A. Zoli¹, S. Ferraro, A.V. Raffaldi, F. Bartolozzi², S. Di Girolamo

Otorhinolaryngology Division, University of Rome "Tor Vergata", Rome;

¹Rheumatology Division, Institute of Internal Medicine and Geriatrics, and

²Institute of Hygiene, Catholic University of the Sacred Heart, Rome, Italy.

Abstract

Objective

Systemic sclerosis (SSc) is a multi-systemic disease of unknown etiology characterized by damage to the small arteries, arterioles and capillaries. The documented occurrence of various neuropathies in SSc patients led us to hypothesize that there is a potential for postural control impairments in such disease. This study was aimed at evaluating the orthostatic postural control of SSc patients who do not manifest balance or hearing symptoms.

Methods

Postural stability was assessed in 36 female SSc patients by means of a static computerized posturography technique. Their immunological and microvascular condition were evaluated by means of blood tests and microcapillaroscopy of the digital vessels. Posturography and microcapillaroscopy were performed before and after treating the patients with Iloprost. In order to compare results, posturography was also carried out on a control group composed of 10 healthy women of similar age. Both groups were studied in two different sensory conditions, i.e. with eyes opened and with eyes closed.

Results

Posturography results showed relevant differences in body sway between patients and control subjects. Fourier spectral analysis of body sway showed that, independently from visual control, SSc patients exhibit a higher level of low/middle frequency oscillations (both on the lateral and the anteroposterior axis). No relationship was established between disease stage and postural performance.

Conclusion

This study seems to indicate a subtle neurophysiological dysfunction in the orthostatic postural control of female SSc patients. Further tests on the somatosensory neurological function of SSc patients may help support the above mentioned findings.

Key words

Systemic sclerosis, posturography, postural alterations.

Pier Giorgio Giacomini, MD; Angelo Zoli, MD; Simona Ferraro, MD; Arianna Valeria Raffaldi, MD; Francesco Bartolozzi, MD; Stefano Di Girolamo, MD.

Please address correspondence to:

Dr. P.G. Giacomini, ENT Division, PTVViale Oxford, 81 00133 Rome, Italy.

E-mail address: digirolamo@med.uniroma2.it

Received on March 3, 2003; accepted in revised form on January 21, 2005.

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Introduction

Otoneurological disturbances are often linked to autoimmune alterations. For instance, sensorineural hearing losses, tinnitus or dizziness are often caused by damage to the inner ear and/or the neural structures of the central nervous system (CNS). The above-reported immune-mediated symptoms may result from systemic as well as local pathologies (1). In previous studies dealing with systemic diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), we have been able to demonstrate subtle and widespread alterations of the auditory and balance systems in asymptomatic patients. Neurophysiological auditory alterations as well as voluntary oculomotricity and orthostatic postural control impairments were detected (2-4).

This work prompted us to investigate the postural performance of patients affected by systemic sclerosis (SSc). This is a multi-systemic disease of unknown etiology characterized by damage to the small arteries, arterioles, and capillaries with increased collagen production and deposition in different areas. SSc can affect the skin, heart, lungs, kidneys, joints, muscles, and gastroenteric system, eventually leading to diffuse fibrosis (5,6). The documented occurrence of various neuropathies in SSc patients led us to hypothesize a potential for postural control impairments in the disease (7-15). A review of the literature showed that SSc is often associated with autonomic dysfunctions and postural impairments due to significant myopathy (8, 16). Postural control is the final result of several centrally integrated functions that depend on sensory inputs coming from:

- i. the posterior labyrinth of the inner ear (which perceives linear and angular accelerations)
- ii. fusiform receptors (that carry information about muscles, legs and spine stretching/contraction)
- iii. the eyes, which enable us to perceive the surrounding environment through vision.

After receiving the above listed inputs, the CNS sends out anticipatory or compensatory responses in order to maintain postural balance. The aim of this

study was to evaluate the orthostatic postural control of SSc patients without obvious balance or hearing symptoms. To do so, postural control was tested in 36 SSc patients by means of a staticomputerized posturography device that records body sway. At the same time, blood tests and digital vessel microcapillaroscopy were carried out in order to provide a complete evaluation of the immunological and microvascular condition of the patients.

Materials and methods

Thirty-six female patients who fulfilled the criteria for the classification of systemic sclerosis (17) with a mean age of 50.5 ± 8.2 years and a mean disease duration of 3 ± 1.5 years constituted the study group. The control group comprised 10 healthy female volunteers with a mean age of 48 ± 9.2 years. Informed consent was obtained from the subjects before each test. Patients and controls were selected after being thoroughly interviewed in order to ensure the absence of possible confounding neurological conditions (alcohol addiction, thyroid disease, lumbar root disease, etc.). They had a corrected visual acuity of 10/10 and did not manifest any labyrinthine symptoms. All subjects who displayed symptoms or showed clinical evidence of postural instability or hypotension were excluded from the study.

Sera from all the patients were tested for antinuclear (ANA) and anticentromere antibodies (ACA) by immunofluorescence, for anti-DNA antibodies by ELISA and for anti-ENA and anti-SCL70 antibodies by double immunodiffusion.

Nailfold microcirculation study was performed both in the scleroderma patients and in normal controls using Computerized Videocapillary Microscopy (Videocap-Dietosystem, Scalar Co. Ltd, Italy). This device consists of a fiberopic illuminator equipped with an image digitalization software program designed to perform morphometric and densitometric analyses. First, the nailfold epidermis was made transparent to light by applying a droplet of immersion oil. Then a fiber optic cold light illuminator was placed on the pa-

tient's finger and the nailfold was observed magnified by 200. All fingers of both hands were examined excluding the thumbs, where the capillaries are less visible.

Analysis of the capillaroscopic pictures was based on qualitative as well as quantitative parameters. The main qualitative aspects were the general architectural arrangement, the presence of oedema, the presence/absence of extravasations, the presence of tortuous loops and the visibility of the subpapillary venous plexus (SVP).

Static posturography was performed using a normalized computerized static posturography platform (S.Ve.P. – Amplaid, Bologna, Italy). Detailed information about this device has already been published (18). Briefly, it consists of a computer controlled platform that records body sway by means of three pressure-sensitive strain gauges. The gauges are located on the vertexes of an equilateral triangle whose image is drawn on the platform. From information provided by the sensors, a computer records the position of the pressure centers of the feet and plots a figure called a statokinesigram (Fig. 1). During the test the subjects were asked to stand as still as possible, first with their eyes open and then with their eyes closed. Quantitative posturography parameters were calculated from the statokinesigram:

- i. Trace length (mm), i.e. the length of the trace made by the center of pressure during the examination.
- ii. Trace surface (mm²), i.e. the surface perimeter that includes 90% of the area covered by the trace.
- iii. Mean velocity of body sway (mm/sec), i.e. the mean velocity of the center of pressure during examination. In order to quantify variations in velocity, the standard deviation (SD) of velocity was measured as well.
- iv. Fourier Fast Transformation (FFT) on both X and Y axes: FFT calculates the frequency composition of body sway by means of a mathematical model.

FFT records:

1. Fundamental frequency (referred to as "Fmax" in Fig. 2), i.e. the fre-

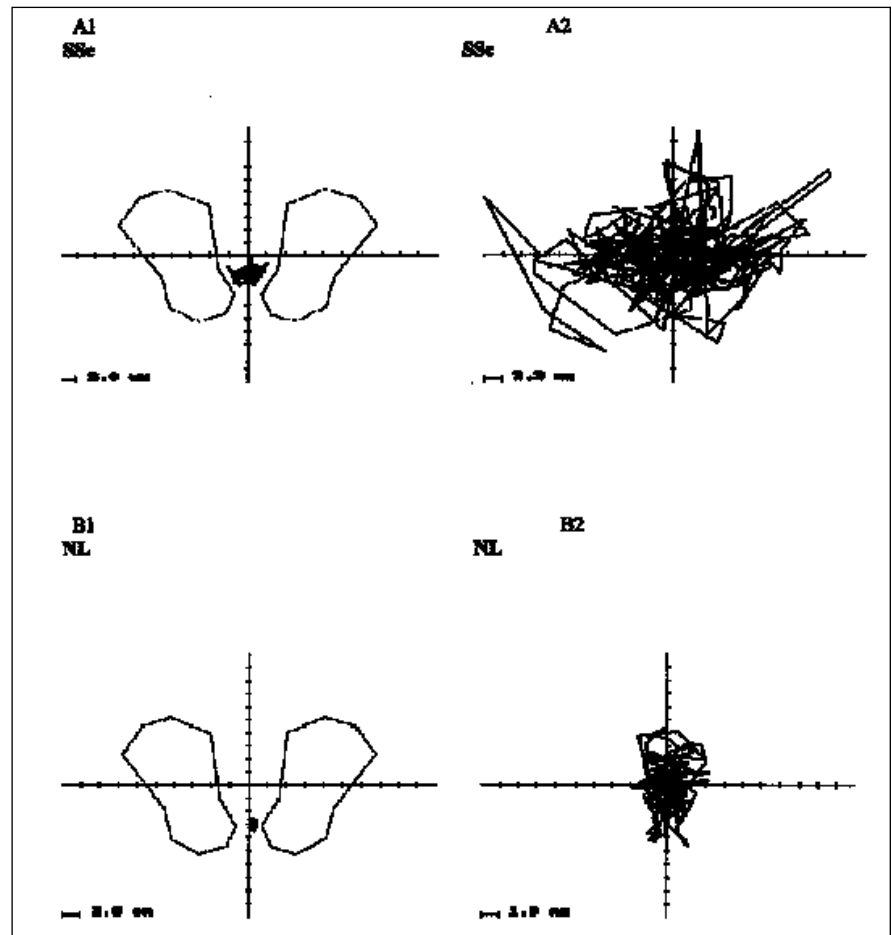


Fig. 1. Statokinesigram. Center of gravity (CoG) position during examination referred to:
A1: surface of posturography platform in a SSc patient with eyes opened;
A2: mean position of CoG in a SSc patient with eyes opened;
B1: surface of posturography platform in a normal control with eyes opened;
B2: mean position of CoG in a normal control with eyes opened.

- quency of oscillations, measured in Hz, represented by the maximum power (energy) normalized to 100 (Fig. 2).
2. Frequency power spectra, i.e. the means \pm SD of the energies of oscillations (defined hereby: intensity of oscillation) within pre-established ranges of frequency. The oscillations were quantified by measuring the length (in mm) of the bars reported on FFT graphs (Fig. 2). The energy distribution was then divided in three frequency bands: low (0.01-0.5 Hz), middle (0.5-1 Hz), and high (> 1 Hz).

All parameters were recorded at a frequency of 10 Hz and in two different sensory conditions, namely with eyes open and with eyes closed.

Critical limits for the normal values of spectral composition being unavaila-

ble, we analyzed the mean differences between the two groups. Posturography and capillaroscopy were performed both before and after treating SSc patients with Iloprost. Iloprost is a synthetic prostacyclin which provides prolonged vasodilatation, reduces platelet aggregation and promotes endothelial lining function repair. For one week, all SSc patients were treated with 0.5–2 ng/Kg/min of Iloprost 6 hours a day.

Statistical analysis

Normal distribution of continuous variables was assessed by Shapiro-Francia test. Continuous variables were compared by Student's t-test. Categorical variables were compared by the χ^2 test or Fisher exact test when required. Statistical analysis was performed using Stata 6.0 software (Texas Station University College).

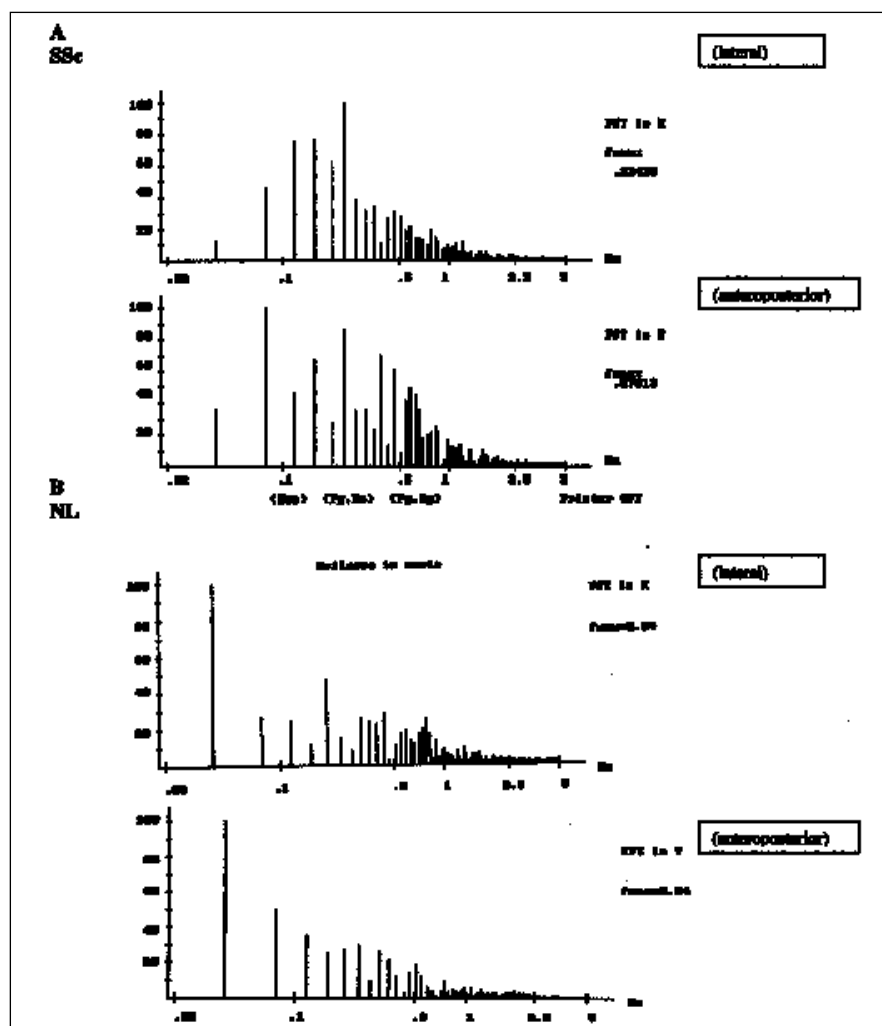


Fig. 2. FFTgraphs. When examined with their eyes open, one of the differences between patients and controls is that patients show an increase in low-middle frequency oscillations on both axes (X & Y). Horizontal axis: frequency range (Hz); Vertical axis: arbitrary units of intensity of oscillation; Vertical bars: intensity of oscillations at different frequency; Upper display: oscillations on lateral plane (X); Lower display: oscillations on anteroposterior plane (Y); F max: fundamental frequency of oscillation (the tallest vertical bar of each panel).

Results

Posturography reveals that SSc patients exhibit a pattern of body oscillation which is different from normal subjects. Fourier spectral analysis of body

sway shows that, independently from visual control, SSc patients exhibit a higher level of low/middle frequency oscillations (both on the lateral and the anteroposterior axes) (Tables I and II).

Table I. Posturographic spectral analysis with eyes open. The reported data show significant differences in body oscillation frequencies between cases and controls (mean \pm SD).

Parameter	Patients	Controls
LFX	20.3 \pm 2.9	14.6 \pm 0.7 #
MFY	8.3 \pm 5.3	4.3 \pm 0.7 §
MFY	5.0 \pm 1.2	3.5 \pm 0.7 *

§ $p < 0.05$; * $p < 0.01$; # $p < 0.001$

LFX: low frequency body oscillation on the lateral axis (X); MFY: middle frequency body oscillation on the lateral axis (X); MFY: middle frequency body oscillation on the anteroposterior axis (Y).

When examined with their eyes open SSc patients show a remarkable increase in low frequency oscillations along the X axis (lateral displacements) and in middle frequency oscillations along both the X and Y (anteroposterior displacements) axes.

The results in Table I can be summarized as follows:

- low frequency body oscillation (0.01 – 0.5 Hz) on X axis is 20.3 ± 2.9 in SSc patients vs. 14.6 ± 0.7 in normal subjects ($p < 0.001$)
- middle frequency body oscillation (0.5–1.0 Hz) on X axis is 8.3 ± 5.3 in SSc patients vs. 4.3 ± 0.7 in controls ($p < 0.05$); on Y axis is 5.0 ± 1.2 in SSc vs. 3.5 ± 0.7 in normal subjects ($p < 0.01$).

When examined with their eyes closed patients showed a remarkable increase of low and middle frequency oscillations on the Yaxis.

The results in Table II can be summarized as follows:

- low frequency body oscillation on Y axis is 23.1 ± 3.4 in SSc patients vs. 12.8 ± 2.3 in normal subjects ($p < 0.001$)
- middle frequency body oscillation on Y axis is 10.8 ± 4.6 in SSc patients vs. 3.6 ± 1.5 in controls ($p < 0.001$).

Such a multi-planar/pluri-frequency pattern of oscillation, being also independent from visual control, seems to suggest a non-labyrinthine etiology of this phenomenon.

Table III also shows a statistically irrelevant increase in trace length, trace surface, velocity, and standard deviation of velocity, both with eyes opened and with eyes closed. As for the disease stage, 18 patients showed a scleroderma active pattern, which is characterized by capillary destruction, large avascular areas and branched capillaries. All of them presented anti-SCL70 antibodies. On the other hand, the remaining 18 patients showed a scleroderma slow pattern, which is characterized by giant capillaries with no avascular areas and few or no branched capillaries, 14 out of them showed anticentromere antibodies, the remaining 4 anti-SCL70 antibodies. No relationship has been found between disease stage

Table II. Posturographic spectral analysis with eyes closed. The reported data show significant differences in body oscillation frequencies between cases and controls (mean \pm SD).

Parameter	Patients	Controls
LFY	23.1 \pm 3.4	12.8 \pm 2.3 #
MFY	10.8 \pm 4.6	3.6 \pm 1.5 #

$p < 0.001$

LFY: low frequency body oscillation on the anteroposterior axis (Y); MFY: middle frequency body oscillation on the anteroposterior axis (Y).

Table III. Primary summary variables in the posturography (mean \pm SD): cases vs controls with open eyes (OE) and closed eyes (CE).

		Patients	Controls
Trace length (mm.)	OE	202 \pm 53	192 \pm 27
	CE	338 \pm 130	302 \pm 53
Trace surface (mm ²)	OE	160 \pm 64	130 \pm 51
	CE	295 \pm 118	252 \pm 63
Mean velocity (mm/sec) (\pm SD)*	OE	8 \pm 2	7 \pm 1
	CE	13 \pm 5	13 \pm 2.8
Standard deviation of velocity **	OE	5 \pm 2	4 \pm 0.7
	CE	8 \pm 3	8 \pm 1.6

Primary summary variables in the posturography (mean \pm SD): cases vs controls with open eyes (OE) and closed eyes (CE).

OE: open eyes; CE: closed eyes.

*Standard deviation of the mean of the velocity; **mean of the standard deviations of velocity.

(active vs slow pattern) and postural performance in our patients.

Capillaroscopic quantitative parameters show a statistically significant change in the mean venular diameter before (75.35 μ m) and after (58.64 μ m; $p = 0.007$) the Iloprost treatment. Conversely, the treatment did not produce any changes in posturographic parameters.

Discussion

Similarly to other autoimmune diseases, SSc is likely to trigger vestibulo-spinal reflex malfunctionings (2). However, there is seems to be no specific medical literature on this topic. The CNS maintains the upright stance at the level of the brainstem, cerebellum, basal ganglia, and the thalamus. There are three sources of input to the CNS (mainly the vestibular nuclei in the brainstem) that allow it to function properly: the visual, proprioceptive and posterior labyrinthine systems. The vestibulo-spinal reflex, directed from the CNS to the lower limbs, enables the subject to exert compensatory and anti-

gravity muscular activities aimed at keeping the upright stance. The final result of such a reflex activity is a continuous slow-paced/long-length oscillation of the body to and from its center of gravity, in the fashion of an inverted pendulum. Whenever the sensory input or motor output are disturbed, an abnormality of the postural sway is expected to occur (19). As a consequence, A compensatory mechanism elicits a fast-paced/short-length body sway (20).

The frequency composition of the body sway may selectively indicate the control mechanism employed in each case: labyrinthine control affects mainly low frequency sway, mixed labyrinthine/proprioceptive control affects higher frequency oscillations (21-23).

In this paper, the pattern of body oscillations on both planar axes, independently from visual control, suggests a perturbed postural control in SSc patients, thus confirming preliminary hypotheses (24).

A detailed evaluation of results indicates that in SSc patients, the overall

control of the postural system (as depicted by primary summary posturographic variables) is almost normal. From a physical point of view these findings may be described as a difficultly maintained standing position.

A more in depth analysis of postural balance (i.e. spectral evaluation of the body sway) reveals that SSc patients maintain their upright stance by increasing the number and frequency of body oscillations as expected when posture is challenged (20,25). Balance is therefore conserved, but a greater effort must be exerted to achieve this goal.

The effects of non-specific chronic illnesses on the abnormalities observed in SSc patients remain undefined. We therefore recommend further controlled tests on SSc patients matched with other chronic reumatic diseases, not involving microvasculature.

The increase (about two-fold) of the standard deviation of parameters recorded in SSc vs. NL subjects may indicate a heterogeneity in the amount of "compensatory" body oscillations exerted by each SSc patient to maintain the upright stance. The degree of the etiologic dysfunction may explain the differences between patients. Since visual control didn't influence whatsoever SSc patients' postural performance, we can therefore confirm the non-labyrinthine nature of the phenomenon.

The described subclinical postural abnormalities in SSc patients seem to confirm the initial hypothesis of this paper. The precise etiology of such a postural disturbance cannot be defined on the basis of this paper only. Even though SSc patients showed an alteration in their finger capillaries, this was not related to posturography results. Postural alterations may result from compromised functioning of peripheral somatosensory neural structures (22, 25,26). Since scleroderma may possibly affect some of these structure (such as peripheral nerves and the paraortosystem) there is reason to suppose a potential for postural impairment in SSc patients (7, 8).

Further evaluations of SSc patients by posturography and neurophysiological

tests may confirm our findings and clarify the relationship between postural abnormalities and subclinical peripheral neuropathies.

In summary, this study provides evidence for a subtle neurophysiological dysfunction of the orthostatic postural control in female SSc patients. Further controlled assessment by somatosensory testing of neural function may be useful to complete the above mentioned results.

References

1. BERRETTINI S, RAVECCA F, BRUSCHINI L, URSINO F, SELLARI-FRANCESCHINI S: Progressive sensorineural hearing loss: immunologic etiology. *Acta Otorhinolaryngol Ital* 1998; 18 (Suppl. 59): 33-41.
2. GIACOMINI PG, ZOLI A, BRUNO E, DI GIROLAMO S, CARICCHIO R, ALTOMONTE L: Posture in systemic lupus erythematosus. *Clin Exp Rheumatol* 1995; 13: 357-60.
3. GIACOMINI PG, ZOLI A, BRUNO E *et al.*: Voluntary oculomotricity in systemic lupus erythematosus. *Clin Exp Rheumatol* 1997; 15: 579-80.
4. MAGARÒ M, ZOLI A, ALTOMONTE L *et al.*: Sensorineural hearing loss in rheumatoid arthritis. *Clin Exp Rheumatol* 1990; 8: 487-90.
5. MARICQ HR, SPENCER-GREEN G, LEROY EC: Skin capillary abnormalities as indicators of organ involvement in scleroderma. *Am J Med* 1976; 61: 862-70.
6. RODNAN GP, MYEROWITZ RL, JUST GO: Morphologic changes in the digital arteries of patients with progressive systemic sclerosis and Raynaud's phenomenon. *Medicine* 1980; 59: 393-408.
7. CORBO M, NEMNI R, IANNACCONE S *et al.*: Peripheral neuropathy in scleroderma. *Acta Neurol Scand* 1993; 87: 382-729.
8. DESSEIN PH, JOFFE BI, METZ RM, MILLAR DL, LAWSON M, STANWIX AE: Autonomic dysfunction in systemic sclerosis: sympathetic overactivity and instability. *Ann J Med* 1992; 93: 143-50.
9. DYCK PJ, HUNTER GG: A case-control and nerve biopsy study of CREST multiple mononeuropathy. *Neurology* 1997; 49: 1641-5.
10. KNUPP-OLIVEIRA S, CERINIC MM: Polyneuropathy as initial manifestation of systemic sclerosis. *Scand J Rheumatol* 1999; 28: 260-1.
11. LOPEZ DOMINGUEZ JM, BLANCO OLLERO A: Peripheral neuropathy in progressive systemic sclerosis. *Neurologia* 1995; 10:178-80.
12. LORI S, MATUCCI-CERINIC M, CASALE R *et al.*: Peripheral nervous system involvement in systemic sclerosis: the medial nerve as target structure. *Curr Opin Rheumatol* 1996; 8: 569-75.
13. NITTA Y, SOBUE G: Progressive systemic sclerosis associated with multiple mononeuropathy. *Dermatology* 1996; 193: 22-6.
14. OLNEY RK: Neuropathies associated with connective tissue disease. *Semin Neurol* 1998; 18: 63-72.
15. SCHADY W, SHEARD A, HASSELL A, HOLT L, JAYSON MI, KLIMIUK P: Peripheral nerve dysfunction in scleroderma. *Q J Med* 1991; 80: 661-75.
16. BARREA P, DEN BROEDER AA, VAN DEN HOOGEN FH, VAN ENGELN BG, VAN DE PUTTE LB: Postural changes, dysphagia and systemic sclerosis. *Ann Rheum Dis* 1998; 57: 331-8.
17. SUBCOMMITTEE FOR SCLERODERMA CRITERIA of the American Rheumatism Association Diagnostic and Therapeutic Criteria Committee: Preliminary criteria for the classification of systemic sclerosis (scleroderma). *Arthritis Rheum* 1980; 23: 581-90.
18. BIZZO G, GUILLET N, PATA A, CAGEY PM: Specification for building a vertical force platform designed for clinical stabilometry. *Med Biol Eng Comput* 1985; 23: 474-6.
19. NORRÈ ME: Sensory interaction testing in platform posturography. *J Laryngol Otol* 1993; 107: 496-501.
20. NASHER LM: Adapting reflexes controlling the human posture. *Exp Brain Res* 1976; 26: 59-72.
21. YONEDA S, TOKUMASU K: Frequency analysis of body sway in the upright posture. *Acta Otorhinolaryngol (Stockh)* 1986; 102: 87-92.
22. GIACOMINI PG, SORACE F, MAGRINI A, ALESSANDRINI M: Spectral analysis in stabilometry for alterations in postural control. *Acta Otorhinolaryngol Ital* 1998; 18: 83-7.
23. ALESSANDRINI M, GIACOMINI PG, SORACE F, BRUNO E: Postural stabilization after otolithic repositioning for posterior semicircular canal canalolithiasis. *Acta Otorhinolaryngol Ital* 1998; 18: 368-72.
24. GIACOMINI PG, ALESSANDRINI M, ZOLI A: Posturographic alterations in systemic sclerosis: preliminary results. *Acta Otorhinolaryngol Ital* 2001; 21: 237-42.
25. GIACOMINI PG, BRUNO E, MONTICONE G *et al.*: Postural re-arrangement in IDDM patients with peripheral neuropathy. *Diabetes Care* 1996; 19: 372-4.
26. UCCIOLI L, GIACOMINI PG, PASQUALETTI P *et al.*: Contribution of central neuropathy to postural instability in IDDM patients with peripheral neuropathy. *Diabetes Care* 1997; 20: 929-34.