

Sympathetic skin response in obstructive sleep apnea syndrome

**Beata Zakrzewska-Pniewska¹, Tadeusz Przybyłowski²,
Krzysztof Byśkiniewicz², Anna Kostera-Pruszczyk¹, Wacław
Droszcz² and Barbara Emeryk-Szajewska¹**

¹Department of Neurology and ²Department of Pneumonology, Medical Academy, 1a Banach St., 02-097 Warsaw, Poland

Abstract. Examination of the sympathetic skin response (SSR), a non-invasive method of studying conduction in the sympathetic nervous system was performed in 15 male patients with obstructive sleep apnea syndrome (OSAS) evaluated by polysomnography who were compared with 7 non-apneic snorers and 26 controls. The aim of the study was to assess sympathetic nervous system function in OSAS, to compare the results with those found in non-apneic heavy snorers, to define the pattern of abnormalities and to study the correlations between SSR results and polysomnographic parameters. In the OSAS group the mean hand latency was significantly longer than in non-apneic snorers and healthy subjects. The most characteristic pattern of abnormalities was an absence of a foot response found in 12 of 15 OSAS patients. There were no correlations between SSR abnormalities and polysomnographic parameters. The SSR method seems to be useful in assessment of the sympathetic nervous system, especially of those parts related to sudomotor function, in OSAS.

Key words: autonomic nervous system, obstructive sleep apnea, sympathetic skin response

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterized by an abnormal sleep-related breathing pattern with apneic or hypopneic episodes, repetitive oxygen desaturation and short arousals. Recent investigations (Soliven et al. 1987, Gould et al. 1988, Martin 1989, Stoohs et al. 1990, Young et al. 1993) have emphasized an abnormal upper airway resistance accompanied by noisy breathing (snoring) in OSAS patients.

Autonomic nervous system activity changes are observed in this syndrome. Parasympathetic tone is increased during sleep (Bonsignore et al. 1994) but the sympathetic system may be activated during apnea (Cullen Hardy et al. 1994). Recent work points out the role of the activity of the autonomic system during apnea and inter-apneic phase of sleep (Macefield et al. 1995, 1995a). Evaluation of sympathetic activity in humans by electrophysiological means was, until the last decade, difficult to perform and was based mainly upon indirect testing, such as recording from effector organs (e.g., blood pressure responses to postural changes, the cold pressor test, semiquantitative sweating examination, and tests of pupillary response).

Recording of electrical potentials from the skin following various stimuli have been used for a long time (to our knowledge the first description was by Tarchanoff in 1890), but the physiological explanation of these responses remained unknown. Later, with the understanding that they depend upon activity of sweat glands, this technique has been extensively used in psychological and psychophysiological research. The essential development in our understanding of these skin potentials came from the introduction of microneurographic recording techniques in sympathetic nerve fibers by Hagbarth (1972). Later work using this technique helped to clarify the function of the afferent and efferent reflex pathways. It was shown that sympathetic outflow in human extremity nerves consists of two main types of activity: muscle sympathetic nerve activity (MSNA) and skin sympathetic nerve activity (SSNA). MSNA mainly causes vasoconstrictor responses engaged in blood flow control, whereas SSNA contains vasoconstrictor and sudomotor impulses, engaged in thermoregulation. The technique of microneurography is invasive. The introduction of the microelectrode into a nerve is painful, clear records of sympathetic outflows are not obtained from every, even normal, subject. The investigated discharges are taken from a limited number of nerve fibers.

The method is also time-consuming, which makes it impractical for wider clinical use.

A slow reflex depolarization of the skin, the so-called galvanic skin response (GSR) or sympathetic skin response (SSR), is known to occur following a deep breath, or an unexpected or arousing stimulus. It originates from synchronized activation of sweat glands as a response to a volley discharge in efferent sympathetic nerve fibers. The experimental data show that the afferent pathway of the SSR consists of large myelinated fibers. This was demonstrated by inducing tourniquet ischemia in an arm and recording the SSR from hand and foot: it was not recordable in both hand and foot after median nerve stimulation, but was present in both following tibial nerve stimulation (Uncini et al. 1988). Ischemia induces conduction block in large-diameter fibers, but does not affect significantly unmyelinated ones. The central segment of the SSR is polysynaptic and influenced by a variety of facilitatory and inhibitory factors. The central control of sudomotor responses probably reaches cortical levels; an excitatory influence of the limbic cortex has been shown in animals. Animal experiments have shown the importance of the medullary reticular formation as well as the powerful regulatory influences from the midbrain, hypothalamic or limbic structures (Isanat 1961, Willcott 1969).

Mental stress and emotional excitation have been shown to increase the sympathetic activity (McLeod et al. 1987) and to have a facilitating effect on the SSR. The efferent side of the reflex is made up by sympathetic nerve fibers emerging from cells of the intermediolateral nucleus which extends from T1 to L2. The axons of these white rami communicantes are myelinated and short; they end in the sympathetic paravertebral ganglia. Post-ganglionic fibers are unmyelinated (C) and innervate sweat glands in the skin. Sympathetic fibers (sudomotor as well as vasomotor) for the upper limb leave the spinal cord at T2-T6 level; fibers that reach the lower limb leave the cord at T12-L2 level and the sudomotor outflow probably leaves the spinal cord earlier than the vasomotor one. The SSR is probably mediated mostly by sweat gland activation. The most obvious demonstration for that is that atropine, locally applied, inhibits the SSR (Knezevic and Bajada 1985). Since the eccrine glands are the only structures in the skin that are cholinergically innervated, the influence of the SSR on sweat gland function seems obvious. The response was shown to correlate well with the sweat response evoked by acetylcholine iontophoresis, a direct measure of sudomotor activity.

The greatest density of eccrine sweat glands is in the palms and soles and emotional, in contrast to the thermoregulatory, sweating is also most prominent at these sites. This correlates with the ease of recording the SSR from palms and soles compared to other skin areas.

Therefore we used this non-invasive technique for studying the autonomic sympathetic sudomotor function in obstructive sleep apnea patients and in non-apneic heavy snorers.

The present work was carried out to evaluate the usefulness of the non-invasive test SSR in assessing the autonomic sympathetic sudomotor function in patients with OSAS. The aim of the study was also to compare the results found in healthy controls, in non-apneic heavy snorers and in OSAS patients. We wanted to define the

pattern of SSR abnormalities and to study the correlations between SSR and polysomnographic parameters.

METHODS

OSAS was diagnosed with the use of a computerized polysomnograph SOMNOSTAR produced by Sensor Medics (Sensor Medics Corporation, 22705 Savi Ranch Parkway, Yorba Linda, California).

Sleep studies included routine parameters: EEG (C3-A2, O1-A2), electrooculography (EOG) and EMG for monitoring sleep stages, measurement of airway flow, movements of thorax and abdomen and pulsoximetry for diagnosis of disturbances of respiration during sleep (Martin 1989). Sleep stages were analyzed according to

P.H.
SSR: stim r. med.

4/68, 8/195, 89.04.06

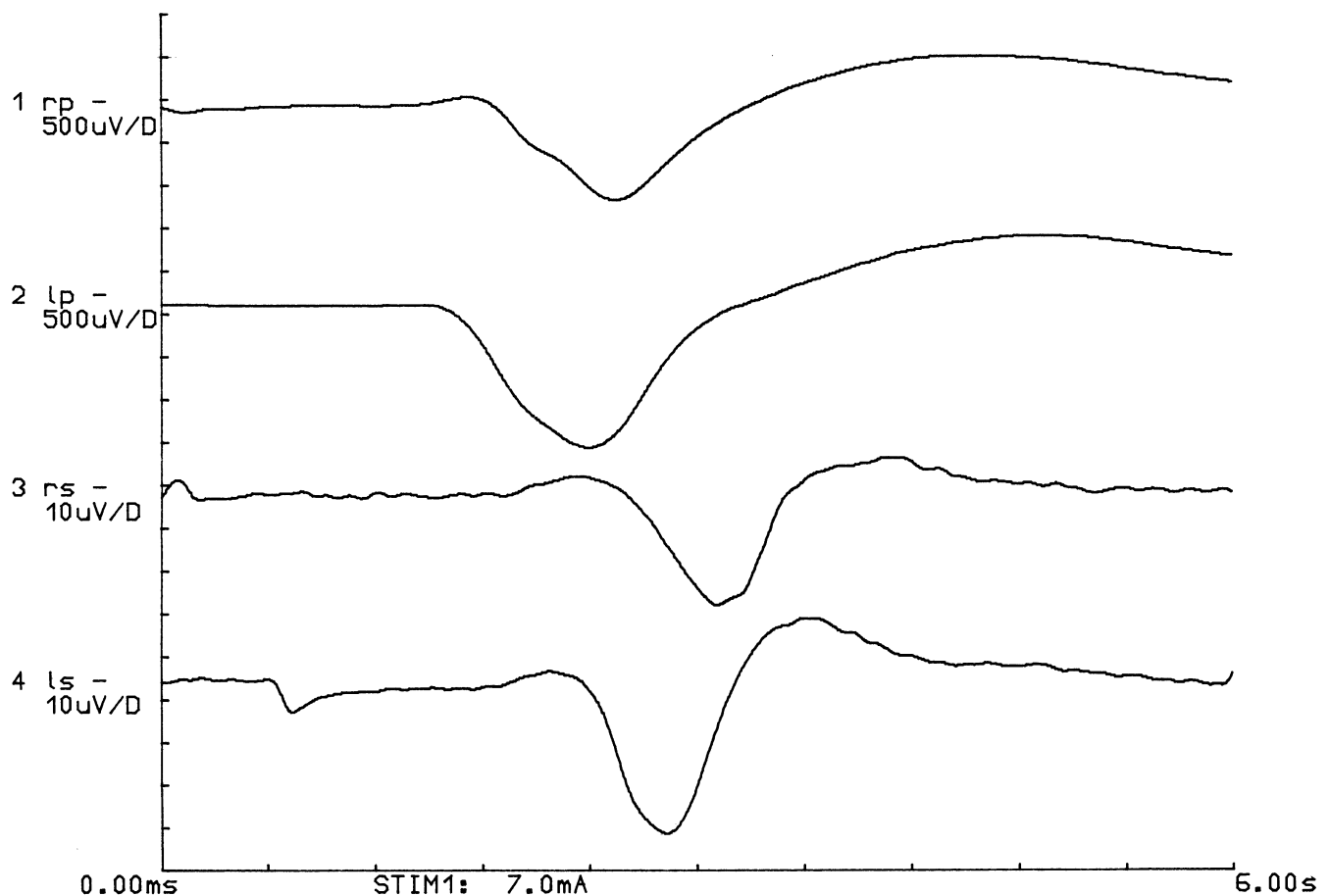


Fig. 1. Normal SSR response recorded in healthy control after right median nerve stimulation: rp, right palm; lp, left palm; rs, right sole and ls, left sole responses. Voltage is given for each recording in μV per division ($\mu\text{V}/\text{D}$)

criteria given by Rechtschaffen and Kales (1968). Sleep studies were conducted between 23.00 p.m. and 6.00 a.m. next morning. Apnea was defined as cessation of respiratory air flow for longer than 10 s. Hypopnea was diagnosed when a decrease of flow amplitude by more than 50% was observed for longer than 10 s with a parallel desaturation and arousal. An apnea and hypopnea index (AHI) was calculated as the number of apneic and hypopneic episodes per hour of sleep. SaO_2 min indicates minimal oxygen saturation reading recorded during sleep study. SaO_2 mean indicates averaged oxygen saturation reading recorded during sleep study.

The sympathetic skin response was recorded in subjects lying supine in a semi-darkened room, with ambient temperature of 22–26 °C, after relaxing for 10 min. The SSR was recorded at the same time during the 24 h cycle (between 10.00 a.m. and 11.00 a.m.). Mean pO_2 found in the conditions of examination was: -80.78 ± 13.08 mm Hg in the non-apneic heavy snorers and 77.14 ± 8.00 mm Hg in the OSAS patients. Standard EMG disc electrodes were placed in the center of the right and left palms as well as in the center of the right and left soles with reference electrodes on the dorsal surface of hands and feet. Five consecutive electrical stimuli with 10–12 mA intensity and of 0.2 ms duration were applied to the right median nerve at the wrist. The stimuli were delivered at irregular intervals of more than 30 s to assure reproducibility. Recordings were made simultaneously from four limbs with EVOMATIC Disa System using a band pass of 2–5,000 Hz for upper limbs and of 2–2,000 Hz for lower limbs. The input sensitivity was from 50 to 500 μV depending on the amplitude.

TABLE I

Sympathetic skin response scores	
0	normal
1	increase in latency in one limb
2	absence of response from lower limbs
3	increase in latency and decrease in amplitude from upper and lower limbs
4	increase in latency and decrease in amplitude from upper limbs, absence of response from the lower limbs
5	increase in latency and decrease in amplitude from one upper and absence of response from the other limbs
6	absence of response

The latency and amplitude (from negative to positive peak) of the largest response were measured. An example of an SSR response in a control subject is shown in Fig. 1. The SSR was considered abnormal if the latency deviation was more than 2 SD compared with the control group. The degree of abnormality was quantified using our laboratory scores defined in Table I - grading responses from 0 (normal) to 6 points (absent). The correlations between SSR abnormalities (hand and foot latency values as well as scores) and body mass index (BMI), apnea/hypopnea index (AHI), SaO_2 mean and SaO_2 min were studied using Pearson's correlation coefficients test. For group comparisons Wilcoxon rank-sum test was used. Statistical significance was defined as $P < 0.05$. Values are presented as means \pm SD.

Subjects

Obstructive sleep apnea syndrome was diagnosed in 15 male patients with a mean age of 45.8 ± 7.2 years. All of them were obese with mean BMI of 36.9 ± 6.2 kg/m^2 . There was no clinical evidence of peripheral neuropathy on neurological examination. Most of the patients had severe sleep apnea syndrome: mean apnea/hypopnea index (AHI) was 51.4 ± 18.3 . Mean minimal SaO_2 observed during sleep was $63 \pm 20\%$, mean value of averaged O_2 saturation was $85.4 \pm 8.5\%$. The results obtained in the OSAS group were compared with those from 7 non-apneic heavy snorers whose mean age was 48.0 ± 8.6 years, mean BMI- 29.8 ± 5.5 kg/m^2 , AHI did not exceed 10 (mean AHI- 2.6 ± 2.3). In non-apneic snorers the mean SaO_2 value was $93.7 \pm 1.3\%$ and mean minimal SaO_2 value was 89.6 ± 1.5 . The results of SSR studies in those two groups were compared with SSR findings in the control group of 26 healthy subjects without breathing abnormalities during sleep with a mean age of 37.7 ± 10.6 years.

RESULTS

In control subjects hand SSR had a latency of 1.32 ± 0.10 s (right hand), 1.30 ± 0.11 s (left hand). The mean latency from lower limbs was 1.77 ± 0.20 s (right and left foot).

In the OSAS group the mean right hand latency was 1.56 ± 0.19 s, the mean left hand latency was 1.54 ± 0.18 s and it differed significantly from control group values ($P < 0.05$, Wilcoxon rank-sum test). The mean right and left foot latency in OSAS patients was 2.08 ± 0.42 s. There was no significant difference between OSAS group and normal controls for mean foot latency because

TABLE II

Mean SSR latencies in patients and controls. The foot response was absent in 12 of 15 OSAS patients and in two of 7 non-apneic snorers. Because of a small number of measurements the means of foot latency could not be statistically compared

Recording place	OSAS group (<i>n</i> = 15)	Non-apneic group (<i>n</i> = 7)	Control group (<i>n</i> = 26)
Right hand ($\bar{x} \pm \text{SD}$)	$1.56 \pm 0.19 \text{ s}^*$	$1.50 \pm 0.14 \text{ s}^*$	$1.32 \pm 0.10 \text{ s}$
Left hand ($\bar{x} \pm \text{SD}$)	$1.54 \pm 0.18 \text{ s}^*$	$1.48 \pm 0.13 \text{ s}^*$	$1.30 \pm 0.10 \text{ s}$
Right foot ($\bar{x} \pm \text{SD}$)	$2.08 \pm 0.42 \text{ s}$	$2.00 \pm 0.14 \text{ s}$	$1.77 \pm 0.20 \text{ s}$
Left foot ($\bar{x} \pm \text{SD}$)	$2.08 \pm 0.42 \text{ s}$	$2.07 \pm 0.15 \text{ s}$	$1.77 \pm 0.20 \text{ s}$

* $P < 0.05$.

J.W. 46y.
SSR: stim r. med.

3/203,

93.11.25

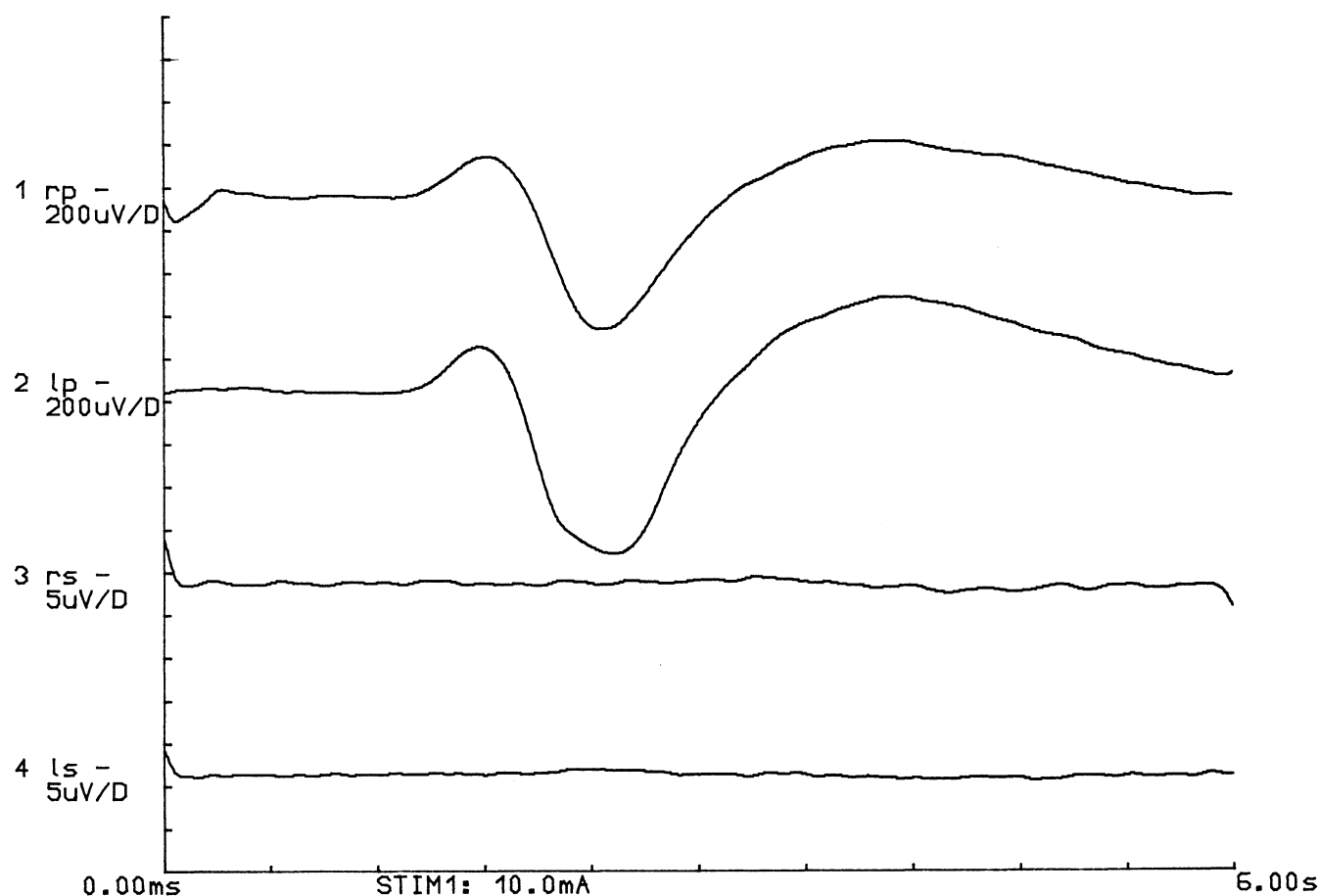


Fig. 2. Abnormal SSR response recorded in patient with OSAS after right median nerve stimulation: the responses from upper limbs are normal, absence of the response from lower limbs. Other explanation as in Fig. 1.

TABLE III

SSR abnormalities in scores		
Score	OSAS patients (n = 15)	Non-apneic snorers (n = 7)
0	2 (13%)	3 (43%)
1	1 (7%)	2 (28%)
2	6 (40%)	2 (28%)
3	1 (7%)	0
4	3 (20%)	0
5	1 (7%)	0
6	1 (7%)	0
Total (abnormal SSR)	13 (86%)	4 (56%)

of the small number of responses obtained from lower limbs ($n = 4$) in OSAS patients (Table II).

The main finding was an absence of foot response found in 12 of 15 OSAS patients (80%) - see example in Fig. 2.). A delay in hand latency was observed in 5 (33%) of patients, whereas in 5 others the SSR recorded simultaneously from upper limbs was normal. In 3 patients (20%) the SSR from upper and lower limbs was normal. In one patient (6%) a response from one hand only was

found and there was no SSR from others limbs. In one patient there was no response from hands and feet. In two patients (13%) SSR was normal from all four limbs.

In non-apneic heavy snorers group the mean right hand latency was 1.50 ± 0.14 s and left hand latency was 1.48 ± 0.13 s, these mean latencies from upper limbs differed significantly from these obtained in control group ($P < 0.05$). The mean right foot latency in non-apneic snorers was 2.00 ± 0.14 s, on the left 2.07 ± 0.15 s. There was no difference between these values and the results in the control group (Table II) but the number of SSR obtained was small ($n = 5$).

In 5 cases (71%) all responses were present. In two of them (28%) an abnormal SSR pattern was observed consisting of delay of hand latency and in 3 of 7 (43%) hand and foot latencies were normal. In 2 of 7 patients there was no response from lower limbs.

The quantitative SSR analysis in both non-normal groups and in controls was performed using the score system defined in our laboratory.

Table III and Fig. 3 show the scores found in the 3 groups.

The score analysis showed that in OSAS group SSR changes were more pronounced than in non-apneic group.

There was no correlation between SSR abnormalities (latencies and scores) and BMI, AHI, SaO_2 min and SaO_2 mean in OSAS and non-apneic group.

SSR ABNORMALITIES

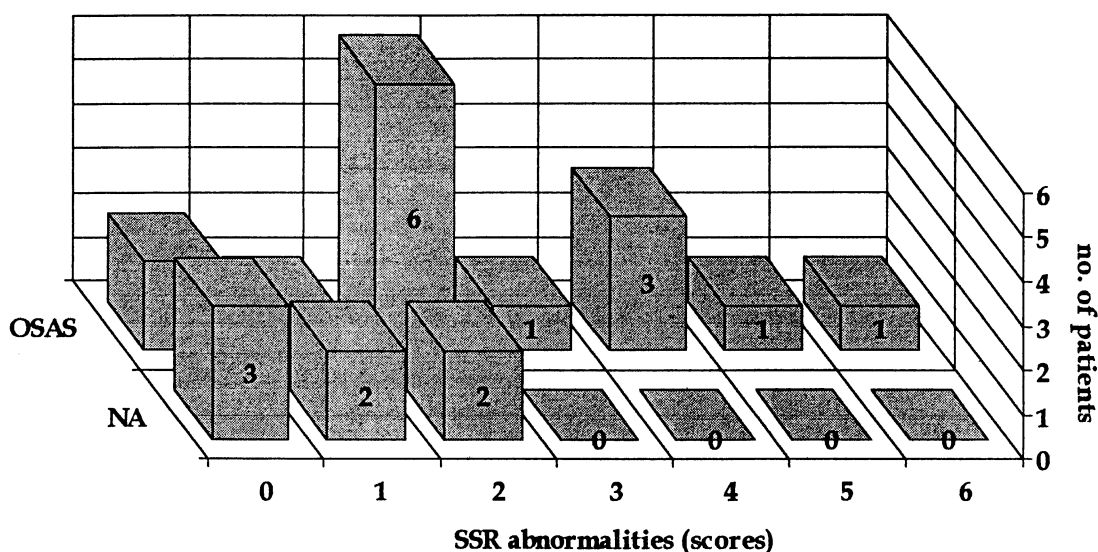


Fig. 3. SSR abnormalities distribution (in scores) in OSAS and non-apneic group.

DISCUSSION

The results of our study showed that sympathetic skin response was very often absent or delayed in patients with obstructive sleep apnea syndrome (87%). In non-apneic heavy snorers group such disturbances were less frequent (present in 57%), whereas in healthy subjects the SSR was always present.

The delay of latency or the absence of the SSR may reveal an autonomic sympathetic sudomotor activity defect (Tarchanoff 1890, Shahani et al. 1984, Knezevic and Bajada 1985, Baba et al. 1988, Niakan et al. 1988, Uncini et al. 1988, Watahiki et al. 1989, Elie et al. 1995).

The delay in latency or the absence of the SSR may depend on the functional lesion at different sympathetic levels: at the afferent side of the SSR reflex arc represented by cutaneous nerves, at the central part, still incompletely known, or on the efferent side of the reflex pathways consisting of sudomotor sympathetic fibers. Therefore the SSR delay or absence may not represent only a peripheral effect due to altered responsiveness of sweat glands.

Hoeldtke et al. (1992) observed greatly diminished or absent autonomic surface potentials on the soles in patients with pure autonomic failure and in patients with multiple system atrophy. These authors proposed the SSR as a sensitive index of sympathetic dysfunction and not only peripheral gland dysfunction. The sympathetic skin response test is indicated for assessing the integrity of peripheral sympathetic cholinergic function and in progressive autonomic failure syndromes (Ravits 1997).

Electrodermal activity reflects sympathetic cholinergic sudomotor function which induces changes in resistance of the skin to electric conduction (Knezevic and Bajada 1985, Uncini et al. 1988, Hoeldtke et al. 1992, Gutrecht 1994). The changes are regulated by activity in the sweat glands but may be generated by presecretory activity (Ravits 1997).

The sympathetic system was studied in apneic syndromes by several authors (Hagbarth et al. 1972, Bonsignore et al. 1994, Takeuchi et al. 1994, Macefield et al. 1995, 1995a) using microneuronography. It has been well established (Bonsignore et al. 1994, Macefield et al. 1995) that the autonomic nervous system plays a crucial role during the post-apneic phase of apneic syndromes. Altered autonomic responses are very common in OSAS patients (Bonsignore et al. 1994) supporting the hypothesis that OSAS may reset the threshold of autonomic adaptation through chronic sympathetic overstimulation.

It is quite probable that during post-apnea the autonomic nervous system is simultaneously affected by different factors such as hypoxia, arousal and lung inflation. The data obtained during obstructive sleep apnea indicated that MSNA increased progressively during apneas and fell abruptly at resumption of ventilation (Macefield et al. 1995, 1995a).

Sympathetic skin nerve activity evaluated by microneuronography reveals increase of SSNA in response to mental stress, to sensory stimuli, to deep breathing and apnea. Under resting conditions SSNA consists of irregular bursts of impulses varying in strength and duration in relation to the respiratory rhythm. Deep breathing following sleep apnea induces a strong burst of SSNA.

The breathing disorder represented by sleep apnea may be accompanied by sympathetic skin overactivity revealed by microneuronography. Contrary to the microneurographic data our results showed a permanent defect of sympathetic sudomotor system activity in OSAS patients using the non-invasive technique of SSR. We postulate that overstimulation and hyperfunction of sympathetic skin fibers accompanying apneic events proved by Macefield et al. (1995, 1995a) may be followed by the failure of the sympathetic skin activity. A similar mechanism for SSR abnormalities was proposed by Dettmers et al. (1993) in patients with amyotrophic lateral sclerosis. Sympathetic system hyperactivity may be responsible for development of arterial hypertension in obese patients with sleep-disordered breathing as suggested by Coy et al. (1996). Carlson et al. (1993) demonstrated that resting muscle sympathetic outflow was higher in sleep apnea patients than controls. As noted by Ferguson (1993), sympathetic outflow to muscle is regulated primarily by afferent information from cardiopulmonary and arterial chemoreceptors. Increased sympathetic activity might result from decreased inhibition, increased excitation, altered central neural processing of afferent information, or a combination of these mechanisms. Hedner et al. (1992) recently reported an abnormal pressor response to hypoxia in sleep apnea patients, suggesting that chemoreflex function might be abnormal in this disease. A link between intermittent hypoxia and sustained sympathetic hyperactivity was recently suggested in humans by Morgan et al. (1995), who demonstrated that sympathetic activation could persist even after removal of an hypoxic stimulus. A similar activation of the sympathetic nervous system by episodic hypoxia is suggested by the work of Fletcher et al. (1992) in rats. In these studies hypertension, which fol-

lows exposure of rats to repetitive, non-apneic hypoxia, can be prevented by chemical sympathectomy. In all these situations the overactivity of sympathetic system may be evaluated by microneuronography. But alternatively, central neural processing of sympathetic activity may be altered by chronic sleep disruption and sleep deprivation. Therefore in OSAS patients we postulate that chronic sleep disruption due to the apneic episodes during sleep alters central mechanisms of sympathetic sudomotor control and induces SSR changes. These changes are less frequent in non-apneic snorers as compared with OSAS group because in those subjects apneic episodes activating the sympathetic system more rarely appear.

The most characteristic pattern of SSR abnormalities consisted of the absence of the foot response. It may be explained by the fact that the longest sympathetic fibers (innervating the lower limbs) are more prone to damage.

The intensity of breathing disturbances (hypoxemia) may influence the degree of SSR abnormalities. Therefore the SSR changes are more pronounced in OSAS than in non-apneic snorers. Similar results were found by Cullen Hardy et al. (1994).

There were no correlations between SSR parameters and polysomnographic parameters in both groups—OSAS and non-apneic patients. It may be due to the fact that during apneic and post-apneic episodes the sympathetic sudomotor system is simultaneously affected by many different factors and autonomic involvement in OSAS is the result of a number of different factors.

Concluding, we propose the SSR as a useful non-invasive technique for assessment of sympathetic sudomotor system involvement in OSAS and other apneic syndromes.

A further study is planned to confirm the results of our pilot study in a larger group of OSAS and non-apneic heavy snorers. As the method of SSR is easy to perform and reproducible, we plan also to determine the influence of continuous positive airways pressure (CPAP) treatment on sympathetic sudomotor function in OSAS patients.

ABBREVIATIONS

SSR	- sympathetic skin response
OSAS	- obstructive sleep apnea syndrome
MSNA	- muscle sympathetic nerve activity
SSNA	- skin sympathetic nerve activity
EOG	- electroculography

AHI	- apnea and hypopnea index
SaO ₂ min	- minimal oxygen saturation during sleep
SaO ₂ mean	- averaged oxygen saturation during sleep
pO ₂ mean	- partial oxygen pressure
BMI	- body mass index
CPAP	- continuous positive airways pressure

REFERENCES

- Baba M., Watahiki J., Matsunaga M., Takebe K. (1988) Sympathetic skin response in healthy man. *Electromyogr. Clin. Neurophysiol.* 28: 277-283.
- Bonsignore M.R., Marrone O., Insalaco G., Bonsignore G. (1994) The cardiovascular effects of obstructive sleep apnoeas: analysis of pathogenic mechanisms. *Eur. Resp. J.* 7: 786-805.
- Carlson J.T., Hedner J., Elam M., Ejnell H., Sellgren J., Wallin B.G. (1993) Augmented resting sympathetic activity in awake patients with obstructive sleep apnea. *Chest* 103: 1763-1768.
- Coy T.V., Dismale J.E., Ancoli-Israel S., Clausen J.L. (1996) The role of sleep-disordered breathing in essential hypertension. *Chest* 108: 890-895.
- Cullen Hardy J., Gray K., Whisler S., Lenenberg U. (1994) Sympathetic and blood pressure responses to voluntary apnea are augmented by hypoxemia. *J. Appl. Physiol.* 77: 2360-2365.
- Dettmers C., Fatepour D., Faust H., Jerusalem D. (1993) Sympathetic skin response abnormalities in amyotrophic lateral sclerosis. *Muscle and Nerve* 16: 930-934.
- Elie B., Louboutin J.P. (1995) Sympathetic skin response (SSR) is abnormal in multiple sclerosis. *Muscle and Nerve* 18: 185-189.
- Ferguson D.W. (1993) Sympathetic mechanisms in heart failure. *Circulation* 87: (Suppl. VII) VII68-75.
- Fletcher E.C., Lesske J., Behm R., Miller C.C.3rd, Strauss H., Unger T. (1992) Carotid chemoreceptors, systemic blood pressure, and chronic episodic hypoxia mimicking sleep apnea. *J. Appl. Physiol.* 72: 1978-1984.
- Gould G.A., Whyte K.F., Rhind G.B., Airlie M.A.A., Catterall J.R., Shapiro C.M., Douglas N.J. (1988) The sleep hypopnea syndrome. *Am. Rev. Resp. Dis.* 137: 895-898.
- Guilleminault C. (1989) Clinical features and evaluation of obstructive sleep apnea. In: *Principles and practice of sleep medicine* (Eds. M.H. Kryger, T. Roth and H. C. Dement). W.B. Saunders Company, Philadelphia, p. 552-558.
- Gutrecht J.A. (1994) Sympathetic skin response. *J. Clin. Neurophysiol.* 11: 519-524.
- Hagbarth K.E., Hallin R.G., Hongell A., Torebjork H.E., Wallin B.G. (1972) General characteristics of sympathetic activity in human skin nerves. *Acta Physiol. Scand.* 84: 164-176.

- Hedner J.A., Wilcox I., Laks L., Grunstein R.R., Sullivan C.E. (1992) A specific and potent pressor effect of hypoxia in patients with sleep apnea. *Am. Rev. Resp. Dis.* 146: 1240-1245.
- Hoeldtke R.D., Davis K.M., Hshien P.B., Gaspar S.R., Dworkin R.E. (1992) Autonomic surface potential analysis: assessment of reproducibility and sensitivity. *Muscle and Nerve* 15: 926-931.
- Isanat F. (1961) Galvanic skin responses from stimulation of limbic cortex. *J. Neurophysiol.* 24: 176-181.
- Knezevic W., Bajada S. (1985) Peripheral autonomic surface potentials: a quantitative technique for recording sympathetic conduction in man. *J. Neurol. Sci.* 67: 239-251.
- Macefield V.G., Wallin B.G. (1995) Effects of static lung inflation on sympathetic activity in human muscle nerve at rest and during asphyxia. *J. Auton. Nerv. Syst.* 53: 148-156.
- Macefield V.G., Wallin B.G. (1995a) Modulation of muscle sympathetic activity during spontaneous and artificial ventilation and apnoea in humans. *J. Auton. Nerv. Syst.* 53: 137-147.
- McLeod J.C., Tuck R.R. (1987) Disorders of the autonomic nervous system: part 2. Investigation and treatment. *Ann. Neurol.* 21: 519-529.
- Martin R.J. (1989) Indications and standards for cardiopulmonary sleep studies. In: *Principles and practice of sleep medicine* (Eds. M.H. Krygier, T. Roth and W. C. Dement). W.B. Saunders Company, Philadelphia, p. 708-716.
- Morgan B.J., Crabtree D.C., Palta M., Skatrud J.B. (1995) Combined hypoxia and hypercapnia evokes long-lasting sympathetic activation in humans. *J. Appl. Physiol.* 79: 205-213.
- Niakan E., Harati Y. (1988) SSR in diabetic peripheral neuropathy. *Muscle and Nerve* 11: 261-264.
- Ravits J.M. (1997) AAEM minimonograph # 48: autonomic nervous system testing. *Muscle and Nerve* 20: 919-937.
- Rechtschaffen A., Kales A. (1968) A manual of standardised terminology, techniques and scoring for sleep stages of human subjects. US Government Printing Office, NIH Publication No 204, Washington DC.
- Shahani B., Halperin J.J., Boulu Ph., Cohen J. (1984) Sympathetic skin response - a method of assessing unmyelinated axons dysfunction in peripheral neuropathies. *J. Neurol. Neurosurg. Psychiatr.* 47: 536-542.
- Soliven B., Maselli R., Jaspán A., Green A., Graziano H., Petersen M., Spire J.P. (1987) Sympathetic skin response in diabetic neuropathy. *Muscle and Nerve* 10: 711-716.
- Stoohs R., Guilleminault C. (1990) Obstructive sleep apnea syndrome or abnormal upper airway resistance during sleep. *J. Clin. Neurophysiol.* 7: 83-92.
- Takeuchi S., Iwase S., Mano T., Okada H., Sugiyama Y., Watanabe T. (1994) Sleep-related changes in human muscle and skin sympathetic nerve activities. *J. Auton. Nerv. Syst.* 47: 121-129.
- Tarchanoff J. (1890) Über die galvanischen Erscheinungen auf der Haut des Menschen bei Reizung der Sinnesorgane und bei verschiedenen Formen der physischen Tätigkeit. *Pflüger's Arch. Ges. Physiol.* 46: 46.
- Uncini A., Pullman S.L., Lovelace R.E., Gambi D. (1988) The sympathetic skin response: normal values, elucidation of afferent components and application limits. *J. Neurol. Sci.* 87: 299-306.
- Watahiki J., Baba M., Matsunaga M., Takebe K., Onuma T. (1989) Sympathetic skin response in diabetic neuropathy. *Electromyogr. Clin. Neurophysiol.* 29: 155-159.
- Willcott R.C. (1969) Electrical stimulation of the anterior cortex and skin potential response in the cat. *J. Comp. Physiol. Psychol.* 69: 465-472.
- Young T., Palta M., Dempsey J., Skatrud J., Weber S., Badr S. (1993) The occurrence of sleep-disordered breathing among middle aged adults. *N. Engl. J. Med.* 328: 1230-1235.

Received 20 December 1996, accepted 9 March 1998