Sympathetic skin response test in essential hypertensive patients

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Background
Essential hypertension is the most prevalent type of hypertension, affecting 90–95% of hypertensive patients. Although no direct cause has been identified, there are many factors such as overactivity of the sympathetic nervous system.
Objectives
To study the predictive value of the sympathetic skin response (SSR) test to determine the role of sympathetic overactivity in essential hypertensive patients.
Methods
The study was carried out on 30 essential hypertensive patients and 15 normal controls who were similar in terms of age and sex. Thorough history taking, neurological and cardiological examination, and the neurophysiological technique (SSR) test were performed in both the groups.
Results
Three patients were found to have an upper limb latency less than 1.2 ms, which was faster than the fastest upper limb SSR in the controls, and two patients were found to have a lower limb latency less than 1.9 ms, which was faster than the fastest lower limb SSR in the controls. However, there was no statistically significant difference between the patient and the control groups in terms of the mean SSR latencies and amplitudes in the upper and lower limbs.
Conclusion
Although SSR has a low diagnostic value in patients with essential hypertension, it might be a good diagnostic test particularly in the presence of signs and symptoms of sympathetic overactivity such as tachycardia and sweating.

Keywords:
essential hypertension, sympathetic overactivity, sympathetic skin response test

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Introduction

Essential hypertension is the most common type of hypertension, affecting 90–95% of hypertensive patients [1]. Although no direct cause has been identified, there are many factors such as overactivity of the sympathetic nervous system. The autonomic nervous system plays a central role in maintaining cardiovascular homeostasis through pressure, volume, and chemoreceptor signals by altering the peripheral vasculature and kidneys, causing increased cardiac output, increased vascular resistance, and fluid retention. Disorder of the system, as in the case of overactivity of the sympathetic nervous system, increases blood pressure and contributes toward the development and maintenance of hypertension [2].

The primary, well-known role of the sympathetic nervous system in cardiovascular control is the maintenance of blood pressure and the regulation of blood flow for seconds to minutes through the arterial baroreflex (short-term regulation). However, this aspect of the sympathetic nervous system is evolving as new evidence emerges about its additional role in the long-term regulation of blood pressure. The mechanisms of increased sympathetic nervous system activity in hypertension are complex and involve alterations in baroreflex pathways at both peripheral and central levels. Arterial baroceptors are reset to a higher pressure in hypertensive patients and this peripheral resetting reverts to normal when the arterial pressure normalizes [3].

Aim of the work

To examine the value of the sympathetic skin response (SSR) test in patients already diagnosed with essential hypertension for a better understanding of the sympathetic neural mechanism in cardiovascular disease.

Participants and methods

Participants

Our study included 45 patients, who were divided into two groups. Group A included 15 control individuals of both sexes (eight women and seven men), ranging in age between 31 and 52 years, mean age 41.80 years. They were matched in terms of age and sex with the patient group. Group B included 30 diagnosed and treated essential hypertensive patients, 15 women (50%) and 15

men (50%), ranging between 32 and 52 years, mean age 42.73 years. The patients were selected from our outpatient clinic of the Internal Medicine Kasr El Aini Hospital Cairo University, and from the Internal Medicine and Cardiovascular Departments, Cairo University.

Inclusion criteria:

(1) Male and female patients, ranging in age from 30 to 55 years, already diagnosed clinically with essential hypertension for at least 1 year and on treatment, whether controlled with medication or not.

Exclusion criteria:

(1) Patients with any psychiatric, degenerative, or systemic diseases that cause dysautonomic functions as diabetes mellitus, renal, or liver dysfunction.
(2) Patients on any treatment other than antihypertension drugs that may affect the sympathetic tone such as selective serotonin reuptake inhibitors.

Methods

All the participants included were subjected to the following.

History taking

Careful history taking, especially for autonomic symptoms and signs such as sweating, bowel disturbances such as constipation, urinary disturbance, palpitation, flushing, and dry mouth.

Clinical examination

A general examination (including blood pressure measurements in supine and standing positions), neurological examination, and cardiac examination were performed.

Application of neurophysiological techniques

The SSR test was carried out in a semidark room. The patient lay flat and was asked to relax for 20 min before the test. The machine used was a Nihon Kohden neuropack EMG-based (Nishochiai Shinjuku-ku, Tokyo, Japan) evoked potential system. A bipolar stimulator surface electrode was used so that the cathode was directed proximally over the wrist point of the contralateral upper limb and to the planter surface at the midfoot of the contralateral lower limb. Surface disk electrodes 1 cm in diameter, stainless steel, were applied with an adhesive paste after thorough cleaning with alcohol. In the upper limb, the active electrode was placed over the second palmer interspace 3 cm proximal to the web space, with the reference electrode over the pulp of the middle finger. In the lower limb, the active electrode was placed over the second planter interspace in the midfoot, with the reference electrode over the pulp of the second toe. The ground electrode was positioned between the recording electrodes and the stimulating electrode. The recording was performed from the right side and stimulation over the left side either at the upper or the lower limb. The intensity of the stimulation was 20 mA, with a duration of 0.2 ms and a rate of stimulation of 0.1 s. The low filter was set to 0.5 Hz, the high filter was set to 5 kHz, and the interstimulus interval was 1 min. The latency and amplitude were measured. The latency is the time between the stimulus artifact and the beginning of the response and the amplitude is the peak-to-peak difference. After 1 min, another response is elicited to ensure the consistency of the first one.

Statistical analysis

Data were coded and analyzed using the statistical package SPSS (SPSS software, International Business Machines Corp., New York, USA) version 15. Data were summarized as mean, SD, minimal and maximal value (range) for quantitative variables, and the number and percent for qualitative variables. Comparisons between groups were carried out using the χ^2-test for quantitative variables, whereas an independent-sample *t*-test and analysis of variables were used for normally distributed quantitative variables. Parametrical Mann–Whitney test and the Kruskal–Wallis test were used for qualitative variables that were not normally distributed. Correlations were assessed to test for a linear relation between variables.

A *P*-value less than or equal to 0.05 was considered to be statistically significant.

Results

There was no statistically significant difference between the patient and the control groups in the SSR latencies and amplitudes in the upper and lower limbs (Tables 1 and 2 and Fig. 1).

(1) The value of 1.2 s, which represents the shortest upper limb latency of SSR in the control group, was considered as the cut-off point. Individual evaluation of cases showed three cases (10%) with faster upper limb SSR latency ($\leq$1.2 s). The value of 1.9 s, which represents the shortest lower limb latency of SSR in the control group, was considered as the cut-off point. Individual evaluation of cases showed two cases (6.7%) with faster lower limb SSR latency ($<$1.9 s). Four patients had heart rate more than 100 beats/min; three of these patients had faster upper limb latency of SSR and two patients had faster lower limb latency.
(2) In addition, two patients had excessive sweating with faster upper limb latency of SSR and one patient had a faster lower limb latency. There was a statistically significant difference between patients receiving different types of antihypertensives and upper limb latency of SSR ($P = 0.019$). The highest percent of a faster SSR response was found in patients on diuretics, followed by those on angiotensin-converting enzyme inhibitors, whereas patients on calcium channel and β-blockers did not show any deviation from the normal range. There was no significant correlation between the presence of sweating, the duration of illness, or the stage of hypertension in the patient group and upper or lower limb latency and amplitude of the SSR (Fig. 2).

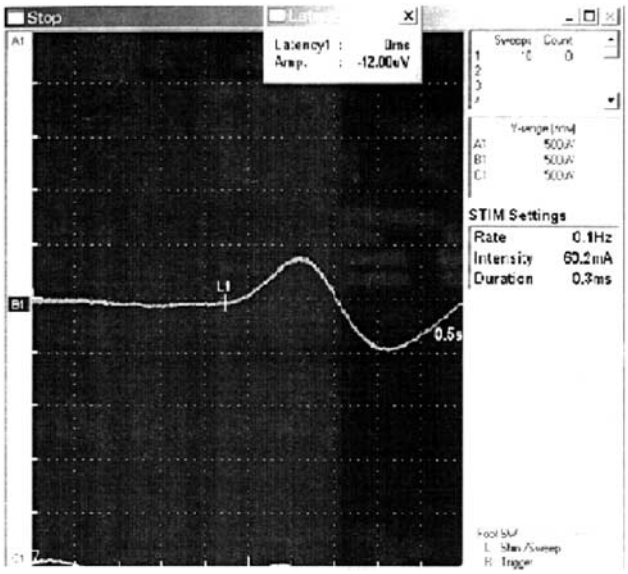
Table 1 Comparison between the mean latencies of upper and lower limbs sympathetic skin response in the control and the patient groups

Latencies (s)	Control group	Essential hypertensive group	*P*-value
Upper limb			
Mean ± SD	1.51 ± 0.13	1.43 ± 0.17	0.164
Range	1.22–1.74	0.76–1.60	NS
Lower limb			
Mean ± SD	2.13 ± 0.30	2.00 ± 0.11	0.114
Range	1.90–2.78	1.74–2.20	NS

Table 2 Comparison between the mean amplitudes of upper and lower limbs sympathetic skin response in the control and the patient groups

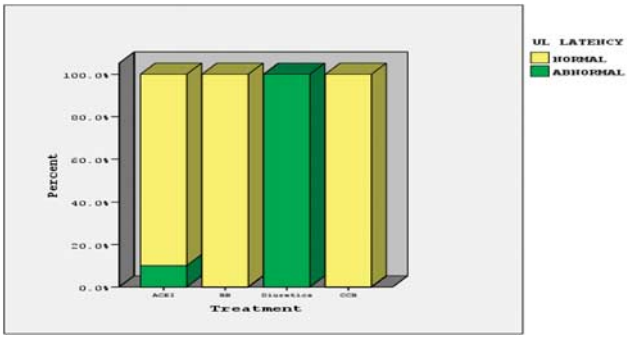
Amplitude (mV)	Control group	Essential hypertensive group	*P*-value
Upper limb			
Mean	1.07 ± 0.66	0.99 ± 0.48	0.894
Range	0.56–2.50	0.40–2.00	NS
Lower limb			
Mean	0.46 ± 0.31	0.57 ± 0.27	0.111
Range	0.10–1.20	0.13–1.20	NS

Figure 1



Normal sympathetic skin response of the lower limb (control group).

Figure 2



Percentage of faster upper limb (UL) sympathetic skin response in patients receiving different types of therapy.

Discussion

Sympathetic activation has been implicated in the pathogenesis of hypertension, coronary artery disease, cardiac arrhythmias, and heart failure [2]. One of the methods for the assessment of sympathetic system is the evaluation of the SSR.

In our study, 30 patients with already diagnosed essential hypertension on treatment, whether controlled or not, were subjected to an SSR test, and it was found that there was no statistically significant difference between the normal controls and the essential hypertensive patients in terms of the latency and amplitude of SSR recorded from the upper and lower limbs. These results are in agreement with those of Grassi *et al.* [4], Esler *et al.* [5], and Hagbarth *et al.* [6]. These findings were confirmed by Vissing *et al.* [7], who reported that the sympathetic activation spares the skin in essential hypertensive patients and the mechanism could be the reflex originating from baroceptors, which were impaired in several patients with chronic blood pressure elevation, restraining muscle sympathetic nerve activity without influencing skin sympathetic nerve activity.

Although the number of patients was not sufficient for a statistical evaluation, we could find a significant negative correlation between the presence of tachycardia in our patients and latency of upper limb SSR ($P = 0.001$). Sinski *et al.* [8] reported that tachycardia is the simplest and probably the most reliable marker of sympathetic overactivity in humans with hypertension. This may explain our findings in these patients.

Supporting the theory that sympathetic hyperactivity is important in the pathology of reflex sympathetic dystrophy, Clinchot and Lorch [9] found a shorter latency SSR in a patient with reflex sympathetic dystrophy in the upper limb where excessive sweating was found. This is in agreement with our findings in two patients with excessive sweating; both had a faster upper limb latency.

Our study found a statistically significant difference between patients with different types of antihypertensive therapy and upper limb latency. The highest percent of SSR abnormality was among patients on diuretic therapy, followed by patients under angiotensin-converting enzyme inhibitor therapy, whereas those on calcium channel and β-blockers did not show any SSR abnormality. Our data might indicate the impact of various drugs and their effect on the sympathetic nervous system.

Although SSR had a low diagnostic value in patients with essential hypertension, sympathetic overactivity is involved in the pathogenesis of patients with essential hypertension. SSR might be a good diagnostic test particularly in the presence of signs and symptoms of sympathetic overactivity such as tachycardia and sweating.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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الملخص

أثبتت الدراسات أن زيادة نشاط الجهاز العصبى السمبثاوى الذاتى يلعب دورا هاما فى نشأة وتطورمرض فرط ضغط الدم الأساسى. تهدف هذه االدراسة إلى معرفة مدى حساسية الإختبار المعروف بالجهدالطرفى للجهاز السمبثاوى فى مرضى فرط ضغط الدم الأساسى وهل سيكون هناك دور لهذا الاختبار فى اكتشاف زيادة نشاط الجهاز العصبى السمبثاوى الذاتى. أجريت االدراسة على ثلاثين مريضا يعانون من فرط ضغط الدم الأساسى و خمسة عشرمن الأصحاء بحيث تعرض كل منهم لإختبار الجهدالطرفى للجهازالسمبثاوى الذاتى للطرفين العلويين والسفليين. أظهرت االدراسة ثلاث مرضى كان إختبار الجهدالطرفى للجهازالسمبثاوى الذاتى للطرف العلوي أقل من 1.2 ثانية والتي تمثل أسرع قيمة في الأصحاء و أظهرت الرساله اثنين من المرضي إختبار الجهدالطرفى للجهازالسمبثاوى الذاتى للطرف والسفلي أقل من 1.9 ثانية والتي تمثل أسرع قيمة في الأصحاء

ومن هذه النتائج نستخلص أن إختبار الجهدالطرفى للجهاز السمبثاوى الذاتى قد يكون وسيله ناجحة لتشخيص زيادة نشاط الجهاز العصبى السمبثاوى الذاتى إذا صحب ذلك بأعراض مثل زيادة عدد ضربات القلب أو التعرق .

الكلمات الدالة :

فرط ضغط الدم الأساسى

الجهدالطرفى للجهاز العصبى السمبثاوى

زيادة نشاط الجهاز العصبى السمبثاوى