

Sympathetic skin response test in essential hypertensive patients

Thesis

Submitted in the partial fulfillment of the master degree in clinical Neurophysiology

Presented by:

Khalid Mohammad Abd-Allah Taher
M.B.,B.CH
Faculty of Medicine
Cairo University

Supervised by:

Prof.Dr. Ann Ali Abdalkader
Professor of Clinical Neurophysiology
Head of Clinical Neurophysiology Unit
Faculty of Medicine
Cairo University

Ass. Prof.Dr.Shereen Fathy Sheir
Professor of Neurology
Faculty of Medicine
Cairo University

Ass. Prof.Dr. Ayat Allah Farouk
Professor of Clinical Neurophysiology
Faculty of Medicine
Cairo University

Faculty of Medicine
Cairo University
2011

Abstract

Background: Essential hypertension is the most prevalent hypertension type affecting 90-95% of hypertensive patients. Although no direct cause has identified itself, but there are many factors such as sympathetic nervous system over activity.

Objectives: To Study the predictive value of sympathetic skin response (SSR) test to detect the role of sympathetic over activity in essential hypertensive patients.

Methods: The study was conducted on 30 essential hypertensive patients and 15 normal controls of similar age and sex. Through history taking, neurological and cardiological examination and neurophysiological technique (SSR) test were done to both groups.

Results: No statistically significant difference between both controls and patients groups regarding the upper and lower limbs latency or amplitude of the (SSR) test.

Conclusion: We conclude that the SSR test had a low diagnostic value in essential hypertensive patients. As if the sympathetic over activity is involved in pathogenesis of these patients, this leads to alteration in arterial baroreceptors sensitivity to blood pressure changes which affect the blood vessels of muscle and relatively sparing the skin blood vessels.

Recommendation: Several electrophysiological techniques providing evidence that sympathetic over activity is present in patients with essential hypertension should be done such as muscle sympathetic nerve activity, plasma noradrenalin measurement and baroreceptors sensitivity assessment.

Key words:

Essential hypertension.

Sympathetic skin response test (SSR).

Sympathetic over activity.

Arterial baroreceptors.

Acknowledgment

First and foremost thanks to Allah, the most kind and the most merciful, for helping me to achieve this work.

I would like express my deep appreciation and profound gratitude to **Professor. Dr. Ann Ali Abdalkader**, Professor of Clinical Neurophysiology and Head of Neurophysiology unit, Faculty of Medicine, Cairo University, for her precious time and effort to give me helpful advice, generous cooperation and excellent supervision. Working under her supervision is a great honor. I shall always remain grateful.

It's a great pleasure to express my sincere thanks and deepest gratitude to **Dr. Shereen Fathy Sheir**, Ass. Professor of Neurology, Cairo University for her encouragement and valuable advice that guide me throughout this thesis.

I would like to express my deepest thanks to **Dr. Ayat Allah Farouk**, Ass. Professor of Clinical Neurophysiology, Cairo University, for her inspiring supervision and continuous support throughout every step in this work.

Also I would like to express my deepest thanks to all staff members of Clinical Neurophysiology Unit and Neurology Department, Cairo University, for their help.

All my thanks and loves are offered to my family, especially my father, mother and my wife, who were always loving, encouraging and supporting.

Content	Page
List of abbreviations	I
List of Figures	II
List of Tables	IV
Introduction	1
Review of Literature • Autonomic nervous system anatomy and physiology • Autonomic regulation of cardiovascular function • Essential hypertension • Role of sympathetic over activity in essential hypertension • Baroreflex device therapy in treatment of hypertension • Methods for measuring sympathetic nervous system activity in cardiovascular diseases • Evaluation of autonomic nervous system • Sympathetic skin response test	4 24 30 37 42 47 55 79
Subjects & Methods	93
Results	98
Discussion	118
Summary & Conclusion	125
Recommendations	127
References	128
Appendices	-
Arabic Summary	-

LIST OF ABBREVIATIONS

ABP	Arterial blood pressure
ANS	Autonomic nervous system
BAT	Baroreflex activation therapy
BRS	Baroreflex sensitivity
CNS	Central nervous system
CVP	Central venous pressure
DHPG	Dihydroxyphenylglycol
DOPAC	Dihydroxyphenylacetic acid
ECG	Electrocardiogram
EMG	Electromyogram
HR	Heart rate
HRV	Heart rate variability
HTN	Hypertension
MIBG	Metaiodobenzylguanidine
nTS	Nucleus of solitary tract
PNS	Peripheral nervous system
QSART	Quantitative sudomotor axon reflex test
REM	Rapid eye movement
SA node	Sinoatrial node
SD	Standard deviation
SNS	Sympathetic nervous system
SPECT	Single photon emission computed tomography
SSR	Sympathetic skin response
TPR	Total peripheral resistant
TST	Thermoregulatory sweat test

LIST OF FIGURES

Figure No.	Description	Page No.
1	Organization of somatic and autonomic nervous system	6
2	Innervations of organ by autonomic nervous system	12
3	Location of autonomic nervous system receptors	20
4	Influence of higher parts of the brain on autonomic functions	23
5	Autonomic reflex	29
6	Indications that an increase sympathetic outflow may be key factor in Primary hypertension.	41
7	The Rheos hypertension system.	45
8	Normal planter and palmer SSR shape	86
9	Sympathetic skin response technique from upper limb	97
10	Sympathetic skin response technique from lower limb	97
11	Normal SSR of the upper limb(control group)	100
12	Normal SSR of the lower limb(control group)	100
13	Correlation between age of control group and latency of SSR recorded from upper limb.	102
14	Correlation between age of control group and latency of SSR recorded from lower limb.	102

15	Correlation between age of control group and amplitude of SSR recorded from upper limb.	103
16	Correlation between age of control group and amplitude of SSR recorded from lower limb.	103
17	Comparison between the mean latency of upper limb SSR in control and patients groups.	108
18	Comparison between the mean latency of lower limb SSR in the control and patients groups.	109
19	Comparison between the mean amplitude of upper limb SSR in the control and patients groups.	110
20	Fast palmer SSR response.(case no.4)	112
21	Fast palmer SSR response (case no.8)	112
22	Percentage of faster upper limb latency of SSR in patients with heart rate>100 beat/minute and patients with heart rate <100 beat/minute.	115
23	Correlation between heart rate of patients group and upper limb latency of SSR.	115
24	Comparison between patients with excessive sweating regards the upper limb latency of SSR.	116
25	Percentage of faster upper limb SSR in patients with different types of therapy.	117

LIST OF TABLES

Figure No.	Description	Page No.
1	Classification of hypertension.	30
2	Laboratory tests can be performed to identify possible causes of hypertension.	34
3	Normal values of SSR latency and amplitude in healthy subjects.	87
4	The mean latencies and amplitudes of the SSR recorded from upper and lower limbs in normal control group.	99
5	Comparison between the mean latencies of SSR recorded from upper and lower limbs in male and female control group.	101
6	Comparison between the mean amplitudes of SSR recorded from upper and lower limbs in male and female control group.	104
7	The mean latencies and amplitude of SSR recorded from both upper and lower limbs in patients group.	105
8	Comparison between the mean latency of SSR recorded from both upper and lower limbs in male and female patients group.	106

9	Comparison between the mean amplitudes of SSR recorded from upper and lower limbs in male and female patients group.	107
10	Comparison between the mean latencies of SSR recorded from both upper and lower limbs in the control and patients groups.	108
11	Comparison between the mean amplitudes of SSR recorded from both upper and lower limbs in the control and patients groups.	110
12	Percentage of faster latency of SSR recorded from upper limb in both groups.	111
13	Clinical data of hypertensive patients	113
14	Percentage of faster upper limb latency in patients with heart rate >100 beat/minute versus patients with heart rate <100 beat/minute.	114
15	Percentage of faster upper limb SSR regards the type of therapy in patients group.	118

INTRODUCTION

The human internal environment is regulated in large measure by the integrated activity of the autonomic nervous system and endocrine glands. The autonomic nervous system is the part of the nervous system concerned with the innervations of involuntary unstriated muscles and many of the secretory glands (*Guyton and Hall, 2006*).

Autonomic function can be evaluated by a large number of tests, both invasive and non-invasive. Non –invasive tests may be used to confirm a clinical diagnosis of autonomic neuropathy and assess the relative involvement of sympathetic and parasympathetic pathways. To localize the site of the lesion more precisely, complex and often investigations may be required (*Aminoff, 2005*).

The sympathetic skin response (SSR) is a polysynaptic reflex generated in deep layers of the skin by activation of sweat glands via sudomotor sympathetic efferent fibers (*Claus and Schordorf., 1999*).

The efferent part of the SSR reflex arch consists of myelinated sympathetic fibers of neurons from intermediolateral nucleus in thoracolumbar(T1-L2) part of the spinal cord that terminate in paravertebral sympathetic ganglia. Post ganglionic fibers are unmyelinated (type c)fibers and innervate the eccrine sweat glands. The central part of the reflex arch is not fully understood. It is presumably polysynaptic with a connection to the structures of hypothalamus, ventrolateral part of the brain stem, medial and basal parts of the frontal lobe and medial part of the temporal lobe (*Linden and Berlitz.,1995*).

Essential hypertension is the most prevalent hypertension type, affecting 90-95% of hypertensive patients (**Caretero and Oparil,2000**).

Although no direct cause has identified itself, there are many factors such as sympathetic nervous system over activity (**Takahshi, 2008**).

The autonomic nervous system plays a central role in maintaining the cardiovascular homeostasis via pressure, volume, and chemoreceptor signals. Done by altering peripheral vasculature and kidneys, causing increased cardiac output, increased vascular resistance, and fluid retention. Disorder of the system, as in case of sympathetic nervous system over activity, increases blood pressure and contributes to the development and maintenance of hypertension (**Takahashi, 2008**).

The primary recognized 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 via the arterial baroreflex (short term regulation). However, this view of the sympathetic nervous system is evolving as new evidence emerges about its additional role in the long-term regulation of blood pressure (**Joyner et al, 2008**).

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 baroreceptors are reset to a higher pressure in hypertensive patients and this peripheral resetting reverts to normal when arterial pressure normalize (**Joyner et al, 2008**).

AIM OF THE WORK

To study the value of sympathetic skin response test in already diagnosed patients with essential hypertension hoping for better understanding of sympathetic neural mechanism in cardiovascular disease and ultimately lead to remarkable improvements in clinical managements.

AUTONOMIC NERVOUS SYSTEM

The human nervous system is divided into the central nervous system (CNS), comprising the brain and spinal cord, and the peripheral nervous system (PNS), consisting of all the nerves and neurons that reside or extend outside the central nervous system, such as to serve the limbs and organs (*Sherwood,2008*).

The peripheral nervous system, in turn, is commonly divided into two subsystems, the somatic nervous system and the autonomic nervous system (*Sherwood, 2008*).

The autonomic nervous system (ANS) is that part of the peripheral nervous system(PNS) that largely acts independent of conscious control (involuntarily) and consists of nerves in cardiac muscle, smooth muscle, and exocrine and endocrine glands. It is responsible for maintenance functions (metabolism, cardiovascular activity, temperature regulation, digestion) that have a reputation for being outside of conscious control. The other main subdivision of the peripheral nervous system, the somatic nervous system, consists of cranial and spinal nerves that innervate skeletal muscle tissue and are more under voluntary control (Figure 1) (*Sherwood, 2008*).

The autonomic nervous system is typically divided into two main subsystems, the sympathetic nervous system and the parasympathetic nervous system. These tend to balance each other, offering opposite and yet complementary effects .The sympathetic nervous system deals with the response to stress and danger, releasing epinephrines (adrenaline), and in general increasing activity and metabolic rate(fight or flight reaction). The parasympathetic nervous system counters this, and is central during rest, sleeping, and digesting food and, in general, lowers metabolic rate,

slows activity, and restores blood pressure and resting heartbeat, and so forth (*Furness, 2006*).

A third subsystem, the enteric nervous system, is classified as a division of the autonomic nervous system as well. This subsystem has nerves around the intestines, pancreas, and gall bladder. In terms of numbers of neurons, the enteric is the largest autonomic division. In humans, it contains 200–600 million neurons (*Furness, 2006*).

Sensory and motor neurons

Neurons active in the autonomic nervous system (and the PNS in general) can be divided into sensory neurons and motor neuron. A more comprehensive definition is that the reflex arcs of the ANS comprises both a sensory (or afferent) arm, and a motor (or efferent, or effector) arm (*Guyton and Hall, 2006*).

Sensory neurons

The sensory arm is made of “primary visceral sensory neurons” found in the peripheral nervous system (PNS) and in “cranial sensory ganglia:” the geniculate, petrosal, and nodose ganglia, appended respectively to cranial nerves VII, IX, and X. Primary sensory neuron project (synapse) onto “second order” or relay in the medulla oblongata, forming the nucleus of the solitary tract (nTS), which integrates all visceral information (*Fox, 2006*).

Motor neurons

Motor neurons of the ANS are also located in ganglia of the PNS, called “autonomic ganglia (*Furness, 2006*).

Figure (1) Organization of Somatic and Autonomic Nervous System Neurons

- (a) The cell body of the somatic neuron is in the CNS, and its axon extends to the skeletal muscle.
- (b) The cell body of the preganglionic neuron is in the CNS, and its axon extends to the autonomic ganglion and synapses with the postganglionic neuron. The postganglionic neuron extends to and synapses with its effector organ (**Seeley et al ., 2004**).

