Short Report

Influence of age and gender on the function of postganglionic sympathetic sudomotor axons

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ABSTRACT

Background. The quantitative sudomotor axon reflex test (QSART) is an autonomic function test to evaluate the function of postganglionic sympathetic sudomotor axons. The QSART is used for research and in clinical assessment of various neurological diseases, but few studies have assessed the influence of age, gender and reported a normative range. We assessed the influence of age and gender on QSART parameters.

Methods. We recruited 61 healthy volunteers (41 men and 20 women) after obtaining written informed consent. The QSART was recorded as per standard protocol after iontophoretic stimulation (using acetylcholine) for 5 minutes. We analysed the sweat response to obtain total sweat production, rate of sweat production and latency time from the start of stimulation to sweat response. We assessed these parameters in the right medial forearm, right proximal leg, right distal leg and right proximal foot.

Results. Men had significantly higher evoked sweat volume and sweat latency period compared to women. A positive correlation was observed between age and evoked total sweat volume. An inverse correlation was noted between age and evoked sweat latency period.

Conclusion. Postganglionic sudomotor function increased significantly with age. Men had significantly higher sweat volume suggesting sympathetic predominance. These results might help establish normative data for the Indian population.

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INTRODUCTION

The quantitative sudomotor axon reflex test (QSART) is an autonomic function test to evaluate the function of postganglionic sympathetic sudomotor axons.¹ It is characterized by the evoked sweat response which is based on iontophoresis of acetylcholine.

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Application of small amount of current helps acetylcholine in one compartment of the multicompartmental sweat cell/capsule (a component of Q-sweat apparatus) to stimulate postganglionic sudomotor fibres. Iontophoresed acetylcholine stimulates axonal nicotinic receptors and produces an axon reflex of sudomotor fibres. The neural impulse produced as a result of the activated axon terminal travels antidromically to a branch-point initially, and then travels orthodromically to other nerve terminals leading to release of acetylcholine. Acetylcholine released at the nerve terminals in the neuro-glandular junction binds to M_3 muscarinic receptor of the sweat glands and evokes sweat response.² Functional integrity of the postganglionic sympathetic sudomotor fibres results in evoked sweat response. This is modulated by the central neural drive for sweating.³

The QSART is used for research and clinical purposes. In particular, studies assessed the QSART in neuropathy,^{4,5} diabetes mellitus,⁶⁻⁸ postural tachycardia syndrome,⁹ Parkinson disease¹⁰⁻¹² and familial dysautonomia.¹³ However, few studies assessed the influence of age and gender, and reported a normative range.^{14,15} Addressing normal physiological variations helps in better understanding of the aberrant values in the diseased state. We, therefore, assessed the influence of age and gender on QSART parameters.

METHODS

We did this study at the Autonomic Laboratory, Department of Neurophysiology, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru. We recruited 61 healthy volunteers after obtaining written informed consent. Those with any medical or psychiatric illness, receiving any medication were excluded. They were asked to refrain from taking stimulants such as tea, coffee and smoking for 24 hours. General physical examination was done and anthropometric measurements were taken before the recording. The room temperature was maintained at 23 °C. Volunteers were advised to relax for 15 minutes in the supine position. Sudomotor function was evaluated by the QSART using Q-Sweat device (WR Medical Electronics). The skin surfaces of the recording sites were cleaned with absolute alcohol. Then, meridian electrodes were attached to four sites. These included the right medial forearm (75% distance from the ulnar epicondyle to the pisiform bone, innervated by ulnar nerve), right proximal leg (5 cm distal to the fibular head laterally, innervated by the peroneal nerve), right distal leg (5 cm proximal to the medial malleolus medially, innervated by the saphenous nerve) and right proximal foot (over the extensor digitorum brevis muscle, innervated by the sural nerve). Meridian electrodes were then filled with 10% acetylcholine solution. Then, the components were attached to constant current stimulator Iontophor II (Model 6111PM/DX). Ground electrodes were fixed to the skin at about 5 cm from the recording meridian electrodes.

Once all the components were assembled, the recording of QSART was done using WR Test Works software. The Q-Sweat device uses room air through a desiccant to pick up moisture from the skin. For measurement, this moisture is evaporated inside a capsule where it is transported by airflow to temperature and humidity sensors. Initially, resting sweat was recorded for 10 minutes until the baseline sweat response stabilized. Once baseline sweat response was stabilized, iontophoretic stimulation (using acetylcholine) was done with a current strength of 2 mA for 5 minutes. After iontophoretic stimulation, sweat response was recorded for another 5 minutes. The sweat response was then analysed offline to obtain total sweat production, rate of sweat production and latency time from start of stimulation to sweat response for all four recording sites.

Statistical analysis

The *t*-test was used to analyse continuous variables and chi-square test to assess discrete variables. Spearman's correlation was done to assess the relationship between age and QSART parameters. A p value of <0.05 was considered statistically significant.

RESULTS

The men and women were comparable with respect to age and body mass index (p=0.94 and 0.29, respectively; Table I). Men had significantly higher evoked sweat volume and latency period compared to women (Table II). Evoked sweat volume was significantly higher in the distal leg in men. Although other sites had greater evoked sweat volume in men compared to women, it was not statistically significant. A similar observation was seen in evoked sweat latency time—it was higher in men but statistically significant only at the proximal leg and foot (Table III).

A positive correlation was seen between age and total sweat volume, while an inverse correlation was observed between age and sweat latency time (Table IV; Fig. 1).

TABLE I. Demographic details of the study population (n=61)

Total (n=61)	Women (n=20)	Men (<i>n</i> =41)
33.97 (8.49)	33.85 (9.36)	34.02 (8.16)
163.03 (8.22)	155.20 (5.31)	166.85 (6.51)
65.61 (9.43)	61.10 (9.50)	67.80 (8.69)
24.74 (3.83)	25.50 (4.63)	24.38 (3.38)
	Total (n=61) 33.97 (8.49) 163.03 (8.22) 65.61 (9.43) 24.74 (3.83)	Total (n=61) Women (n=20) 33.97 (8.49) 33.85 (9.36) 163.03 (8.22) 155.20 (5.31) 65.61 (9.43) 61.10 (9.50) 24.74 (3.83) 25.50 (4.63)

Data are presented as mean (SD)

TABLE II. Mean (SD) quantitative sudomotor axon reflex test (QSART) measured over four skin sites (n=61)

Site of recording	Sweat latency	Total sweat volume
	(minutes)	(µl) (<i>n</i> =61)
Forearm	2.70 (1.85)	0.39 (0.49)
Proximal leg	1.99 (0.88)	0.66 (0.54)
Distal leg	2.39 (1.08)	0.60 (0.53)
Foot	2.44 (1.05)	0.47 (0.39)

TABLE III. Differences in sweat volume and latency measures between men and women

QSART measures and	Men (<i>n</i> =41)	Women (n=20)	p value
site of recording			
Sweat latency (minutes)			
Forearm	2.97 (2.15)	2.16 (0.74)	0.06
Proximal leg	2.14 (0.86)	1.70 (0.88)	0.03*
Distal leg	2.52 (1.22)	2.13 (0.68)	0.19
Foot	2.64 (1.01)	2.01 (1.03)	0.05*
Total sweat volume (µl)			
Forearm	0.42 (0.57)	0.32 (0.30)	0.79
Proximal leg	0.70 (0.58)	0.56 (0.42)	0.54
Distal leg	0.71 (0.58)	0.38 (0.30)	0.05*
Foot	0.49 (0.44)	0.41 (0.24)	0.87

TABLE IV.	Correlation	between	sweat	output	and	age
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Spearman's correlation	Age		
	r	p value	
Latency (minutes)			
Forearm	-0.353	0.005*	
Proximal leg	-0.241	0.062	
Distal leg	-0.251	0.051	
Foot	-0.275	0.032*	
Volume (µl)			
Forearm	0.267	0.038*	
Proximal leg	0.189	0.145	
Distal leg	0.076	0.561	
Foot	0.306	0.017*	

DISCUSSION

Our results suggest that the evoked sweat volume is higher in men than in women; this is consistent with previous studies.^{14,15} Interestingly, the sweat gland density of men and women is comparable. However, differential rate of sweat production exists between genders. Investigations on different branches of the autonomic nervous system have shown a higher sympathetic tone in men. In particular, cardiac autonomic function studies have shown a greater sympathetic tone in men compared with women.¹⁶ Our data show similar findings in sudomotor function too.

We observed a positive correlation between ageing and sudomotor function, though some studies have reported decreasing sweat volume with ageing.^{14,15} The possible discrepancy in our study can be attributed to our younger study population (age range 21–50 years; mean [SD] 33.97 [8.49]).

This is probably the first study among Indian volunteers reporting a normative range. This data might be helpful in the early detection of neuropathy.

In conclusion, postganglionic sudomotor function significantly increased with age in our study population. Men had significantly higher sweat volume suggesting sympathetic predominance compared with women.

REFERENCES

- Freeman R, Chapleau MW. Testing the autonomic nervous system. Handb Clin Neurol 2013;115:115–36.
- 2 Riedel A, Braune S, Kerum G, Schulte-Mönting J, Lücking CH. Quantitative sudomotor axon reflex test (QSART): A new approach for testing distal sites. *Muscle Nerve* 1999;22:1257–64.
- 3 Illigens BM, Gibbons CH. Sweat testing to evaluate autonomic function. *Clin Auton Res* 2009;**19**:79–87.
- 4 Namer B, Pfeffer S, Handwerker HO, Schmelz M, Bickel A. Axon reflex flare and quantitative sudomotor axon reflex contribute in the diagnosis of small fiber neuropathy. *Muscle Nerve* 2013;47:357–63.
- 5 Thaisetthawatkul P, Fernandes Filho JA, Herrmann DN. Contribution of QSART to the diagnosis of small fiber neuropathy. *Muscle Nerve* 2013;**48**:883–8.
- 6 Itoh H, Uebori S, Asai M, Kashiwaya T, Atoh K, Makino I. Early detection of orthostatic hypotension by quantitative sudomotor axon reflex test (QSART) in type 2 diabetic patients. *Intern Med* 2003;42:560–4.
- 7 Peltier A, Smith AG, Russell JW, Sheikh K, Bixby B, Howard J, et al. Reliability of quantitative sudomotor axon reflex testing and quantitative sensory testing in neuropathy of impaired glucose regulation. *Muscle Nerve* 2009;**39**:529–35.
- 8 Shimada H, Kihara M, Kosaka S, Ikeda H, Kawabata K, Tsutada T, et al. Comparison of SSR and QSART in early diabetic neuropathy—the value of length-dependent pattern in QSART. Auton Neurosci 2001;92:72–5.
- 9 Peltier AC, Garland E, Raj SR, Sato K, Black B, Song Y, et al. Distal sudomotor findings in postural tachycardia syndrome. *Clin Auton Res* 2010;20:93–9.
- 10 Asahina M, Mathias CJ, Katagiri A, Low DA, Vichayanrat E, Fujinuma Y, et al. Sudomotor and cardiovascular dysfunction in patients with early untreated Parkinson's disease. J Parkinsons Dis 2014;4:385–93.
- 11 Kawada M, Tamada Y, Simizu H, Yanagishita T, Yamashita N, Ishida N, et al. Reduction in QSART and vasoactive intestinal polypeptide expression in the skin of



Fig 1. Scatter plot showing relation between age and total sweat volume at various sites. X-axis represents age in years; Y-axis denotes total sweat volume at various sites expressed in μ l/cm².

Parkinson's disease patients and its relation to dyshidrosis. J Cutan Pathol 2009; 36:517-21.

- 12 Oh ES, Lee JH, Seo JG, Sohn EH, Lee AY. Autonomic and cognitive functions in Parkinson's disease (PD). Arch Gerontol Geriatr 2011;**52**:84–8.
- 13 Bickel A, Axelrod FB, Marthol H, Schmelz M, Hilz MJ. Sudomotor function in familial dysautonomia. J Neurol Neurosurg Psychiatry 2004;75:275–9.
- 14 Lee JB, Lee IH, Shin YO, Min YK, Yang HM. Age- and sex-related differences in

sudomotor function evaluated by the quantitative sudomotor axon reflex test (QSART) in healthy humans. *Clin Exp Pharmacol Physiol* 2014;**41**:392–9.

- 15 Tavee JO, Polston D, Zhou L, Shields RW, Butler RS, Levin KH. Sural sensory nerve action potential, epidermal nerve fiber density, and quantitative sudomotor axon reflex in the healthy elderly. *Muscle Nerve* 2014;**49**:564–9.
- 16 Abhishekh HA, Nisarga P, Kisan R, Meghana A, Chandran S, Trichur Raju, et al. Influence of age and gender on autonomic regulation of heart. J Clin Monit Comput 2013;27:259–64.