Published in final edited form as:

Clin Auton Res. 2013 April ; 23(2): 113–116. doi:10.1007/s10286-012-0180-8.

Autonomic testing in healthy subjects – preliminary observations

Gisela Chelimsky, MD¹, Sarah Ialacci², and Thomas C. Chelimsky, MD³

¹Medical College of Wisconsin, Dept. of Pediatrics, Milwaukee WI

²Case Western Reserve University, Cleveland OH

³Medical College of Wisconsin, Dept. of Neurology, Milwaukee WI

Abstract

Autonomic testing is used clinically. Yet, the prevalence of “abnormal” variants in the healthy population have not been reported. We report the results of autonomic testing in healthy females > 18 years, in whom we found decrease or absent sudomotor function in 1–2 locations. These findings should caution physicians in the interpretation of autonomic testing. This report underscores the need of larger studies to determine the prevalence of these findings

Keywords

Sudomotor test; healthy controls; autonomic testing

Background

Autonomic testing is commonly used clinically. Apart from the Mayo Clinic [1, 2], few groups have published their experience with normal values [3, 4]. In particular, norms for sudomotor function are scarce. As part of a study evaluating autonomic dysfunction in pelvic pain, we enrolled healthy control subjects. These subjects are exceptionally well screened by history and detailed neurologic examination to have no evidence of any neurologic or autonomic disorder. We had expected to find only syncope and an occasional low axon reflex response. We therefore felt it important to report the abnormalities detected in this population at this early stage before we have recruited our full complement of 38 healthy subjects.

Methods

This Case Medical Center IRB approved prospective study from 2/2011 to 2/2012 was part of the larger ICEPAC project (Interstitial Cystitis Evaluation of Psychophysiologic and Autonomic Characteristics) that evaluates the phenotype of interstitial cystitis/bladder pain (IC/BPS) syndrome and myofascial pelvic pain syndrome compared to healthy control subjects (females > 17 years). We report the autonomic testing results of the healthy

controls. Exclusions included BMI ≥ 35 , diabetes, prior or current: IC/BPS, chronic pelvic pain, irritable bowel syndrome, cyclic vomiting syndrome, complex regional pain syndrome, chronic fatigue, functional abdominal pain, functional dyspepsia, migraine headaches, Raynaud syndrome, postural tachycardia syndrome, reflex syncope, fibromyalgia, myofascial pelvic pain syndrome, temporo-mandibular joint disorders, panic disorder, post-traumatic stress disorder, periodic limb movement in sleep, multiple chemical sensitivity, dysmenorrhea, were breastfeeding, were within 180 days of giving birth or had major surgeries or pregnancy in the past 180 days prior to enrollment. The subject underwent a neurological and tender point examination for fibromyalgia. Subjects were excluded if they had any neurologic abnormality, pin sensation less than 8/10 in any extremity (10 = forehead) or $> 8/18$ fibromyalgia tender point sites rated $> 3/10$.

Subjects were instructed to stop all caffeinated beverages and chocolate 24 hour prior to autonomic testing, all autonomically active medications 5 half-lives before, and eat a routine light meal. The testing battery has been published previously, including the cardiac response to deep breathing testing cardiac parasympathetic function, sympathetic cardiac and vasomotor functions assessed by the cardiovascular responses to a 15 second Valsalva maneuver at 40 mmHg and the 70 degree tilt table test for 30 minutes, utilizing a beat-to-beat non-invasive photoplethysmographic blood pressure monitor.

We looked for 3 patterns on upright tilt: (i) postural tachycardia (> 30 bpm heart rate rise in the first 10 minutes of the upright portion of the study); (ii) orthostatic hypotension (> 20 mmHg drop in systolic pressure or > 10 mmHg drop in diastolic pressure within the first 3 minutes of the study); and (iii) reflex syncope (sudden drop in blood pressure often accompanied by a drop in heart rate with symptoms of fainting or near-fainting at anytime during the study). Quantitation includes total drop in systolic pressure, diastolic pressure, rise in heart rate, and timing of syncope, if any.

The post-ganglionic quantitative sudomotor axon reflex test (QSART) provides a specific measure of cholinergic sympathetic efferent small fiber function and is performed in standard fashion [1] using Q-Sweat technology (WR Medical Electronics Co, Maplewood, MN).

Results

Fourteen females participated (mean 31 years, range 20–55 years), BMI Mean of 22.9 ± 3.3 . The medications stopped before testing are added to table 2. Three subjects were on oral contraception. Some were taking multivitamins, fish oil, vitamin D and non-steroidal anti-inflammatory medications at time of testing. The cardiac response to deep breathing was normal in all subjects. One subject showed a decreased cardiac response to the Valsalva maneuver of 1.21. None of the subjects reported any orthostatic symptoms during the tilt test. One subject had a heart rate increase of 35 from baseline in the first 10 minutes (age 24) and five had a heart rate increase of greater than 30 bpm from baseline after the initial 10 minutes upright (table 1). One subject had a syncopal episode without postural tachycardia or orthostatic hypotension. Table 1 summarizes the cardiovascular autonomic testing. Nine of 13 had decreased or absent axon reflex sweating in the forearm, and many had reduced

sweating in other locations with one subject demonstrating decreased or absent sweating in all locations evaluated.

Discussion

This study evaluates the results of autonomic testing in a healthy group of females specifically pre-screened to exclude all disorders associated with autonomic dysfunction, including diabetes, obesity and other functional disorders increasingly associated with an autonomic dysfunction, like chronic fatigue [5], fibromyalgia [6], etc. The main findings of this study included: 1) The cardiac responses are generally normal in normal subjects (with a single reduced Valsalva ratio in one subject); 2) In young adult females, the asymptomatic heart rate increase during the upright portion of the tilt may be > 30 bpm, similar to the data described by Singer et al. (2011) [7] in subjects < 18 years of age; 3) Healthy subjects without any clear medical condition may have decreased or absent sweat output when evaluated by quantitative sudomotor axon reflex test (QSART). The forearm was most commonly decreased or absent (11/14 subjects), which is of unclear clinical significance given the normal findings in the hand. Six of the 14 had 2 or more abnormal values.

This study is critically important in the interpretation of autonomic testing results. The cardiac responses to deep breathing and Valsalva maneuver are robust in this population as in other studies [2]. However, as has also been reported by others, the quantitative sudomotor axon reflex may not be as clear-cut. Our results suggest that a reduced sweat response may be a common finding in healthy population. Due to a clinical suspicion of such a phenomenon, we had heretofore come to regard a single abnormal value as reflecting no clinical significance. However the current findings suggest that even 2 reduced values may not be that uncommon. Furthermore, sweat output in the forearm, a more proximal site was consistently lower than sweat output in the hand, a more distal site. This cause for this finding is unclear, and deserves further evaluation in the future.

The current study is not powered to establish norms, but only to determine their validity. At this point, until we have accumulated a larger number of healthy subjects, we are only recommending: 1) caution when interpreting sudomotor testing and place it in the context of the results of the complete battery of autonomic testing and clinical presentation; 2) abnormal values may or may not truly reflect a clinically significant abnormality; 3) measurement of sudomotor function in a larger series of carefully screened healthy adults to determine the prevalence of abnormal sudomotor and be able to make clear recommendations on the interpretations of these results; 4) consideration of a prospective study following these normal subjects to determine if an abnormal sudomotor response is an early marker of disease.; 5) caution when measuring sweat output in the forearm, since in all of our subjects the values in the forearm were smaller than in the distal hand; 6) reassessment of normal tilt heart rate values, 1 subject exceeded 30 bpm in the first 10 minutes, and 5 more in the full 30 minute tilt. If postural tachycardia syndrome is defined as a heart rate in excess of some quantity bpm in combination with orthostatic symptoms, none of the healthy subjects would have met this set of criteria since none had symptoms. However the presence of symptoms seems to be the more critical diagnostic element, putting into question the exact role of the heart rate change norm.

This study is a preliminary communication and has the obvious limitations of having been conducted in healthy women only, and of having inadequate subject number for meaningful statistical analysis. Furthermore, at this time there are no reports of normal sweat values utilizing Q-sweat technique. Despite this, our findings demonstrating extremely decreased or absent sweat output as well the discrepancy between the hand and the forehead are significant even in the absence of normative values. A full report is intended to follow powered for norm determination. However, its strength is the very rigorous determination of neurologic health by both history and examination, and the careful conduct of the autonomic studies.

Acknowledgments

This research was supported in part by a grant from the National Institutes of Health – National Institution of Diabetes Digestive and Kidney Diseases R01-DK-083538.

References

1. Low PA, Caskey PE, Tuck RR, Fealey RD, Dyck PJ. Quantitative sudomotor axon reflex test in normal and neuropathic subjects. *Ann Neurol*. 1983; 14:573–580. [PubMed: 6316835]
2. Low PA, Denq JC, Opfer-Gehrking TL, Dyck PJ, O'Brien PC, Slezak JM. Effect of age and gender on sudomotor and cardiovagal function and blood pressure response to tilt in normal subjects. *Muscle Nerve*. 1997; 20:1561–1568. [PubMed: 9390669]
3. Straub RH, Lang B, Palitzsch KD, Scholmerich J. Estimation of the cut-off value in cardiovascular autonomic nervous function tests: not-age-related criteria or the age-related 5th percentile. *J Diabetes Complications*. 1997; 11:145–150. [PubMed: 9174894]
4. Vita G, Princi P, Calabro R, Toscano A, Manna L, Messina C. Cardiovascular reflex tests. Assessment of age-adjusted normal range. *J Neurol Sci*. 1986; 75:263–274. [PubMed: 3772389]
5. Okamoto LE, Raj SR, Peltier A, Gamboa A, Shibao C, Diedrich A, Black BK, Robertson D, Biaggioni I. Neurohumoral and haemodynamic profile in postural tachycardia and chronic fatigue syndromes. *Clin Sci (Lond)*. 2011; 122:183–192. [PubMed: 21906029]
6. Staud R. Autonomic dysfunction in fibromyalgia syndrome: postural orthostatic tachycardia. *Curr Rheumatol Rep*. 2008; 10:463–466. [PubMed: 19007537]
7. Singer W, Sletten DM, Opfer-Gehrking TL, Brands CK, Fischer PR, Low PA. Postural Tachycardia in Children and Adolescents: What is Abnormal? *J Pediatr*.

Summary of demographic data and cardiovascular testing (values in bold/italic are abnormal for age in our lab)

Table 1

Subject	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	S11	S12	S13	S14
Age	20	37	20	41	20	24	52	21	20	32	55	28	20	41
Race	C	C	Af	C	C	C	C	C	As	C	C	C	C	As
BMI	23	19	28	27	24	22	21	26	27	20	26	22	20	19
DB	26	18	38	23	43	30	17	30	38	24	25	21	23	22
Normal DB	18	16	18	16	18	18	16	18	18	18	12	18	18	16
V Ratio	1.21	1.69	2.31	1.50	1.77	1.98	2.67	1.59	1.76	2.55	2.4	2.37	1.71	2.09
Normal VR	1.50	1.45	1.50	1.45	1.50	1.50	1.35	1.50	1.50	1.50	1.3	1.5	1.5	1.5
Orthostatic symptoms	No	No	No	No	No	No	No	No	No	No	No	No	No	No
HR >30 <10'	No	No	No	No	No	35	No	No	No	No	No	No	No	No
HR >30 >10'	No	No	No	No	33	42	No	No	34	32	32	40	No	No
Syncopal	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes

DB= deep breathing; VM= Valsalva ratio; C=Caucasian; Af=African American; O=other; As=Asian; HR>30= HR increase > 30 bpm during tilt; Time HR >30= describes if HR increase was before or after 10 minutes of tilt

Summary of sudomotor function for all subjects (Values in bold/italic are abnormal for our laboratory . Sweat output in nl/cm2-mm)

Table 2

	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	S11	S12	S13	S14
L foot	2	I4		55	20	20	24	46	68	8	75	27	35	7
L calf	51	36	45	36	34	58	50	113	64	I4	82	75	23	8
L hand	31	57	I3	23	23	24	I4	I4	21	0	45	158	61	I3
L forearm	0	21	0	7	0	7	5	0	0	0	34	I2	0	28
Total Abnormal	2	1	2	1	1	1	2	2	1	4	0	1	1	3
Meds	N	1	N	N	N	2	N	N	N	3	4	5	6	N

Legend for meds: N= no meds. (1) Citalpam, stopped 7 days before; (2) Sertaline 50 mg stopped 5 days before; (3) montelukast; (4) Levodihydroxine, stopped 1 day before; (5) Levodihydroxine; (6) Sertaline 100mg stopped 5 days before; on Lipitor.