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Effect of Gender and Age on Autonomic Functions in Healthy Adults

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ABSTRACT
Sympathovagal balance plays vital role in maintaining homeostasis. The autonomic function differences between males and females are worth analysis and thus the present study was designed. The autonomic function differences between young and elderly healthy subjects of both sexes (males and females) were compared in the present study. The study subjects (both males and females) were recruited in the present study and were further divided into two group on the basis of age(greater and less than 55 years). To assess sympathetic tone, hand grip test and blood pressure response tolying to standing and for the parasympathetic deep breathing test, the heart rate response to lying to standing, and the Valsalva maneuver were conducted using the standard protocol. In age group <55 years , HGT and OHT of males were 18.12±3.05 and 9.125±2.52 respectively, while in females it were 14.13±2.97 and 12.13±2.66. The difference was significant. Parasympathetic tests, namely DBT, 30:15 Ratio and Valsalva Ratio, were 1.37±.103, 1.06±.042 and 1.32±.079 respectively in males as compared to 1.47±.113, 1.10±.05 and 1.38 in females. The parasympathetic tone was found to be significantly higher in females than in males. In age group greater than 55years,the sympa the ticdoma in were significantly higher in males as compared to females. The results of parasympathetic tests (DBT, 30:15 Ratio of heart rate response to standing and Valsalva ratio) showed parasympathetic dominance in females. However, the difference between males and females were found to be non-significant. Sympathetic tone is predominant in males below the age of 55 years whereas in femalesparasympathetictoneisdominant.Thedifferencebetweenthetwo issignificant. With advancing age, the difference in parasympathetic tone is insignificant, whereas the sympathetic difference remains significant.

INTRODUCTION

The autonomic nervous system is an integral part of the nervous system. The somatic nervous system plays a role in voluntary activities like walking, running, grasping an object, speaking and chewing. At the same time, the autonomic nervous systemis involved in involuntary activities like cardiac functions, intestinal peristalsis and other involuntary routine activities like defecation, micturition and ejaculation. Whereas most of its actions are involuntary, some, suchasbreathing, work in tandem with the consciousmind[1]. The autonomic nervous system plays a crucial role in maintaining homeostasis. In fact autonomic control of hemodynamic is crucial to maintaining cardiovascular homeostasis after orthostasis[2] It has been postulated, that in the pathophysiology of most lifestyle diseases, there may be a role in the deterioration of the autonomic nervous system[3]. The autonomic nervous system's functional capacity changes with different life phases. It has been found that it changes in different phases of the menstrual cycle[4]. Similarly, many studies have observed that the balance between the sympathetic and parasympathetic domains of the autonomic nervous system modulates with increasing age. It also changes with different kinds of emotions. In some emotional conditions like anger, fear and grief, the sympathetic limb of the autonomic nervous system predominates and in other states like happiness, sleep, and rest conditions, the parasympathetic domain is more active[5].

Variation of autonomic function has been studied in various physiological conditions like pregnancy, in obese and nonobese person[6], various phases of the menstrual cycle, etc and pathological conditions like diabetes, hypertension and thyroid disease.

Here, we have studied differences in autonomic functions in healthy males and females of different age groups. Very few studies have been carried out on autonomic function changes in males and females. It is a topic that remains unexplored. The studies done in the past about autonomic function changes in males and females resulted in conflicting opinions. Some previous studies show both sympathetic and parasympathetic dominance in males, while others show vice versa. Some other studies show sympathetic dominance in males and more parasympathetic activity in females. The present study was, hence, carried out to determine the same and to correlate any gender-specific predominance of sympathetic and parasympathetic nervous systems on sympathovagal functioning, if any. The differences in autonomic functions in males and females, if any, may be attributed to developmental differences or physiological effects of male and female sex hormones, respectively. There are many tools to determine autonomic functions in a subject. There are several clinical tests to determine autonomic functions, like the deep breathing test, the Valsalva test for the parasympathetic limb and the hand grip test for the sympathetic[7]. Heart rate variability, i.e., beat-to-beat variation in the heart rate, which is influenced by both sympathetic and parasympathetic nervous activity, is an excellent tool to assess the functional status of the sympathetic and parasympathetic nervous system and sympathovagal balance[8].

MATERIALS AND METHODS

The study was conducted in the autonomic function as of the Department of Physiology of L.L.R.M. Medical College Meerut, in collaboration with the Department of Medicine of associated S.V.B.P. hospital Meerut over 24 months following approval from the institutional ethical committee. A total of 59 healthy volunteers were recruited for the study and were further divided into two groups:

- **Age group <55:** males (n=16) and females (n=15)
- **Age group ≥55 year:** males (n=17) and females (n=11)

Selection Criteria:

Inclusion Criterion: Healthy subjects willing to participate in the study and giving consent were included with no history of smoking or alcohol intake. The Menstruating femalesubjects who participated were recruited during the follicular phase of their menstrual cycle[9].

Exclusion Criterion: Subjects taking medications or suffering from diseases affecting the autonomic system like diabetes, hypertension, or those with autonomic dysfunction and orthostatic hypotension were excluded.

Assessment of Autonomic Function: After obtaining consent by filling out a consent form, a detailed history and clinical examination of volunteers were done to rule out any other cause of autonomic dysfunction in the subjects. Before starting the examination, the subjects were allowed to acclimate themselves to the laboratory's experimental and environmental conditions and procedures were explained to them before starting autonomic function tests. The following parameters were takeninall subjects: Body mass in dex (Kg/m^2)was calculated after measurement of weight and height of subjects. Blood pressure (mm Hg) was measured in sitting posture using a mercury sphygmomanometer under resting conditions and Pulse (beats/min) was recorded clinically for a full minute.

The Following Autonomic Function Tests were Conducted:

Parasympathetic Function Tests:

- **H.R. Variation (H.R.V.) with Deep Breathing:** Subjects were asked to breathe deeply and evenly

at six breaths/min in the supine position. The E.C.G. was recorded during the procedure. The mean difference of the maximum-minimum H.R. was calculated[10,11,12].

- **HR Response to Valsalva Maneuver:** Subjects were asked to strain forat least 15 seconds. The E.C.G. was continuously recorded during the procedure and for the following 60s. The Valsalvaratio was calculated during straining astheratio between the mos text ended mean R.R. intervals to the shortest mean R.R. interval[10,11,12].
- **30:15 Ratio of H.R. Response to Standing:** The subjects were made to stand up immediately after lying down for 5-7 minutes. E.C.G. was recorded immediately and continued throughout 60 s. The 30:15 ratios (the mean ratio between the R.R. interval of the 30th beat and the fifth beat) were estimated[10,11,12].

Sympathetic Function Tests:

- **Blood Pressure response to Standing:** Blood pressure was mea sure dusing an automatic B.P. machine calibrated against a standard mercury sphygmomanometer. Subjects were made to stand from alying position after a relaxation of 5 minutes. B.P. was measured immediately after the patient stood up and at 1, 2 and 3 min intervals after the average of the three readings were taken, the difference between the average of systolic and diastolic readings at rest and after standing was measured[10,11,12].
- **Isometric Handgrip Test (HGT):** The baseline B.P. was recorded before starting the maneuver. The subjects were asked to exercise isometric by pressing the handgrip dynamometer (Inco) at 30% of maximum voluntary contraction for 2 minutes. The blood pressure was recorded simultaneously from the non-exercising arm at the 1st and 2nd minute and measured after grip release and recording continued till the 4th minute. The highest increase in diastolic blood pressure was taken as a test response[10,11,12].

Statistical Analysis: Descriptive statistics of collected variables were estimated and mean and standard deviation values represented these. All variables were analyzed based on Age. They were categorized by dividing all individuals as <55 and greater than or equal to 55 years of Age. The normality of the variables was assessed by using the Shapiro-Wilk test. Independent samples t-test and Mann-Whitney tests were applied based on the normality of the variables to analyze the difference between the genders of the anthropometric and clinical parameters. The level of significance was set at 5%. IBM SPSS version 20software was used for all statistical analysis.

RESULTS AND DISCUSSIONS

The sympathetic domain assessed by the Hand Grip Test (HGT) and Orthostatic Hypotension Test (O.H.T.) were significantly higher in males than in females ($P \leq 0.05$). In contrast, Parasympathetic status assessed by the Deep Breathing Test (D.B.T.), ValsalvaRatio and Heart rate response to lying to standing (30:15 ratio) was significantly higher in females than males. ($P \leq 0.05$) (Table 1). Sympathetic tone was significantly higher in males than females, similar to a group aged 55 years. However, unlike the younger age group (age 55), Parasympathetic function (D.B.T., Valsalva and 30:15 ratio) showed no significant difference between males and females of the older age group (Age $\geq$55 years) (Table 2).

Several studies have been done to assess autonomic function in various pathological conditions like diabetes and hypertension. However, there is a limited need to be more involved in assessing autonomic functions in healthy subjects. In this study, we have compared autonomic status between healthy adult males and females. For the assessment of autonomic functions, we used different autonomic function tests. Viz. A deep breathing test considers heart rate variability with a cyclical deep breath, a Valsalva test measures heart rate variability with the Valsalva maneuver and a hand grip test involves blood pressure response to isometric muscle contraction.

In 55 years age group, test results reveal sympatheticdom inance in males and in creased parasympathetic tone in females compared to males. Both the changes are statistically significant. The above findings between healthy adult males and females of the age group 55 years can be explained by the fact that males have higher levels of testosterone and adrenaline hormones and females show higher estrogen activity.

The effects of sex hormones are suggested to be present at the CNS (i.e., brain andspinal cord) level, at the peripheral neuron level, both sympathetic and parasympathetic postganglionic neuron and effector organ level, i.e., cardiac muscle[13]. Apart from endocrine differences, some other factors may also contribute to differences in autonomic functions, like structural differences between different organs and physiological differences.

In the Age group =55 years, sympathetic dominanceo fmalesis main tainedas in the younger age group (55 years), but as the age advances, female parasympathetic dominance is blunted. However, the blunting of parasympathetic dominance in females can be explainedby the fact that, after menopause, the level of female sex hormones declines. Other factors may also contribute.

Previous studies on this topic haveshown inconclusive results. In a study by Anthony M. Dar *et al.* in 2001, it was concluded that there is a preponderance of

Table 1: Comparison of Autonomic Function (Both Sympathetic and Parasympathetic) and Baseline Parameters Between Males and Females (< 55 years)

Variable	(Group III) (MALE, Age <55 Years)		(Group IV) (Female, Age <55 Years)		Independent-Samples t- test
	Mean	SD	Mean	SD	p-value
Age	44.06	8.22	42.33	7.76	0.606
BMI	22.10	2.80	22.76	2.67	0.509
Pulse	87.62	6.59	81.67	6.32	0.016*
SBP	123.37	6.91	117.86	6.43	0.030*
DBP	82.62	4.48	78.26	4.83	0.014*
SYM-HGT	18.12	3.05	14.13	2.97	0.001*
SYM-OHT	9.125	2.52	12.13	2.66	0.003*
PSYM-DBT	1.37	.103	1.47	.113	0.017*
PSYM-30:15 Ratio	1.06	.042	1.10	.05	0.049*
PSYM-Valssal VA	1.32	.079	1.38	.087	0.034*

P≤0.05 considere dassignificant,* Means significant difference between male and female.

Table 2: Comparison of Autonomic Function (Both Sympathetic and Parasympathetic) and Baseline Parameters Between Males and Females (Greater than Equal to 55 Years)

Variable	(Group I) (Male, Age ≥55 Years)		(Group II) (Female , Age ≥55 Years)		Independent-Samples t- test
	Mean	SD	Mean	SD	p-value
Age	65.52	5.65	66.63	5.33	0.629
BMI	22.03	2.07	22.27	2.16	0.458
Pulse	90.05	5.84	88.45	5.79	0.482
SBP	135.05	5.15	133.09	5.24	0.329
DBP	90.12	4.77	87.37	4.65	0.111
SYM-HGT	14.24	1.99	12.18	2.08	0.014*
SYM-OHT	18.12	2.78	22.18	2.84	<0.01*
PSYM-DBT	1.17	.09	1.19	.103	0.853
PSYM-30:15 Ratio	1.03	.06	1.05	.030	.486
PSYM-Valsalva	1.20	.10	1.23	.09	0.395

sympathetically mediated responses in males and parasympathetic in females. These results are similar to our study. Another study done on the same topic by Shailaja Moodithaya *et al.* in 2011 shows that gender differences in autonomic function exist and males show sympathetic predominance and females show parasympathetic[14], but this difference disappears post-menopause in females, which may be explained by the drastic reduction of estrogen level after menopause. Bageshree Nilkanth Pande *et al.* in 2019 concluded a relative sympathetic dominance in males, and vice versa in females. Thus studies mentioned above coincide with our study, but other studies done previously do not match our results. A study byBhowmick et al. found parasympathetic responses showed that maximum responses were more in case of males, whereas sympathetic responses showed that maximum responses were more in males and in some cases more in females[15]. In another study by Zachariah and Joseph *et al.,* no statistically significant difference was observed between males and females in both sympathetic and parasympathetic domains. But during mental stress, males show relative sympathetic dominance[16].

Thus, most of the studies show relative sympathetic predominance in males. This could bethe reason that in young and middle age, males are more prone to suffer from adverse cardiovascular events like myocardial infarction, stroke, peripheral vascular disease, etc., whereas females are relatively protected. Thus, it can be postulated that young males are more prone to cardiovascular adverse events, which can be prevented by decreasing cardiovascular sympathetic tone. Different techniques like yoga, meditation, and light exercise, such as jogging, may decrease sympathetic tone and prevent or postpone adverse cardiovascular events[17].

Limitations: The study has been done with a small sample size. It can be done on a larger sample size. Instead of the autonomic function test, the Heart Rate Variability Test (HRV)can be used to assess autonomic function Status. HRV is considered to be a better tool for measuring sympathovagal status.

CONCLUSION

The above study concluded that there are differences in autonomic function based on gender. Male subjects in the younger age group (55 years) show significant sympathetic dominance, whereas females show higher parasympathetic status than males. However, this difference becomes insignificant as the age advances from the younger to the older age group (≥55 years) in parasympathetic function, while significant

sympathetic dominance of male subjects is maintained in the older age group (≥55 years) too.

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