

## Assessment of gender differences in autonomic nervous control of the cardiovascular system

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### Abstract

**Objective:** To determine the differences in the control of the cardiovascular system by the autonomic nervous system between young males and females.

**Methods:** The cross-sectional study was conducted at the Khyber Medical College, Peshawar, Pakistan, from June 2017 to April 2018, and comprised physically healthy medical students of both genders studying in first and second year of their academic studies. The subjects were made to perform the hand grip test and the Valsalva manoeuvre. Their electrocardiogram was recorded during and after the Valsalva manoeuvre. Blood pressure and heart rate were monitored before, during and after both the manoeuvres. Parasympathetic activity was assessed by calculating the Valsalva ratio. Sympathetic activity was measured by observing the increase in diastolic blood pressure during hand grip manoeuvre, and decrease in systolic blood pressure during the Valsalva manoeuvre. Data was analysed using SPSS 20.

**Results:** Of the 140 subjects, 70(50%) each were males and females. There was no significant difference between the parasympathetic system and sympathetic system working of the two genders ( $p>0.05$ ). There was significant difference between the two groups in sympathetic system when checked on the basis of the hand grip test ( $p<0.05$ ).

**Conclusions:** Sympathetic system was found to be acting more efficiently in young males compared to their female counterparts.

**Keywords:** Autonomic nervous system, Cardiovascular system, Valsalva manoeuvre, Hand grip.  
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### Introduction

Among the body system modulation processes, autonomic nervous system (ANS) is one of the top players. Its two subdivisions, sympathetic nervous system (SNS) and parasympathetic nervous system (PNS), often have antagonistic actions. Generally, the "fight and flight" responses are illustrated by the sympathetic system. The parasympathetic system is responsible for the "rest and digest" situations.<sup>1</sup> Stress reactivity is an individual's ability to react to a stress which maybe external or internal. The three main systems, which are top responders to stress, are the central nervous system (CNS), cardiovascular system (CVS) and the endocrine system (ES). Different individuals respond differently to stress.<sup>2,3</sup> Epinephrine and norepinephrine are called the stress hormones. They are mediators of the sympathetic nervous system and are released during rest to maintain base tone as well as during stressful conditions.<sup>4</sup> By artificially exposing the body to stress, its response can be quantified. That is the principal behind ANS testing. These responses can be elicited in various systems, such as ES or CVS. Various tests have been devised for this purpose including Valsalva manoeuvre (VM), tilt testing, sudomotor testing and hand grip test (HGT). One way of quantifying the SNS is by measuring the changes in heart rate (HR) and blood pressure (BP) during

these manoeuvres, i.e by checking the response of the CVS to stress.<sup>5</sup>

The testing of PNS is more technical, and is based on judging the baroreceptor responses. One way of doing that is via measuring the R-R interval in the electrocardiogram (ECG) during and after VM. The ratio of HR during and after VM is then determined and is called the Valsalva ratio (VR), which can be used for PNS response assessment.<sup>5,6</sup>

Various differences exist with respect to gender. Those that involve CVS modulation by ANS include males having a lower baseline HR, and a smaller QT interval than females.<sup>7</sup> When the body is exposed to stress, such as isometric exercise, males have a rise in total peripheral resistance, and, hence, an increase in the diastolic blood pressure (DBP), whereas, in females the HR increases and the DBP response is not clearly observed.<sup>8</sup> Some other studies suggest that females have a higher PNS and lower SNS activity during both basal and active situations.<sup>9-11</sup>

Looking at the theoretical background of ANS physiology, there is a possibility that gender-related differences exist in beat-to-beat dynamics in healthy adult population.<sup>11</sup> It is realised that these have not been explored in research properly.

Moreover, there are no local studies on this topic, and epidemiological data obtained from international studies

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indicate that resting HR, a measure of vagal function, predicts cardiovascular mortality. The higher the vagus nerve (parasympathetic) activity, the slower will be the HR, which will, in turn, lead to better health. This implies that there is a relation between cardiovascular pathology and increased HR.<sup>12</sup> Females show greater vagal tone than males.<sup>13</sup>

The current study was planned to determine the differences in the control of CVS by ANS between young males and females.

## Subjects and Methods

The cross-sectional study was conducted in the Physiology Department of Khyber Medical College, Peshawar, Pakistan, from June 2017 to April 2018, and comprised medical students of first and second year.

The sample size was calculated using the formula:

$$\text{Patients per group} = f(\alpha, \beta) \times 2 \times \text{SD}^2 / (d)^2^{14,15}$$

The value used for  $f(\alpha, \beta)$  targeting 90% power was 10.5; (d) was the effect size, which is the smallest detectable difference in mean for the parameter of interest, which, in this case, was VR, and was taken as 0.12.<sup>11</sup> SD was the standard deviation for VR, which was taken as 0.223.<sup>11</sup>

The sample was raised using simple random sampling from among students who were mentally and physically healthy. Those on medications modifying CVS function were excluded and so were those having medical illness such as diabetes mellitus (DM), hypertension (HTN), thyroid, cardiac, respiratory or major psychiatric disorders. Also excluded were those who smoked or had tea/coffee more than six cups per day.

After taking informed consent, each subject was asked to perform VM for 15 seconds by blowing into the disposable mouthpiece of the oral manometer and maintaining a pressure of 40mmHg. During the procedure, nose-clip was applied. A continuous ECG was recorded in lead II during the manoeuvre (15 seconds) and 1 minute after the procedure. HR was also recorded. VR was then calculated using the formula:

Valsalva Ratio = Longest R-R interval immediately after the manoeuvre / shortest R-R interval during the manoeuvre. (16)(10) Value <1.21 was considered abnormal and as showing PNS derangement.<sup>6,16,17</sup>

Baseline SBP was noted before the manoeuvre and during the procedure to determine SNS function. Its fall at the beginning of phase II was not to exceed 21mmHg from the baseline value, and had to return to normal at the end of phase II.<sup>18</sup>

Table-1: Baseline parameters (n=140).

Parameters	Gender	Range	Minimum	Maximum	Mean±SD
Baseline SBP	Male	49	113	162	132.25±11.20
	Female	450	93	138	112.88±10.41
Baseline DBP	Male	44	59	103	82.70±8.99
	Female	47	54	101	77.78±9.75
Baseline Heart rate	Male	63	54	117	83.85±14.29
	Female	66	64	130	92.94±14.33

For HGT, first the maximum voluntary contraction (MVC) was determined by asking the subject to apply maximum possible pressure to a dynamometer and then to apply 30% of MVC and maintain it for 5 minutes with the right hand. DBP was measured in the left arm at rest and during (4 min into the test) the handgrip. BP and HR were recorded using Omron M2 Basic, which fulfilled the 2010 European Society of Hypertension (ESH) international protocol.<sup>19</sup>

SNS activity was assessed by measuring DBP response (rise) to sustained handgrip, which was calculated as DBP during the test minus baseline DBP (11) DBP response to sustained handgrip if >16mmHg showed severe rise. DBP response 11-15mmHg showed moderate rise, and <10 showed mild rise.<sup>20</sup>

Data was analysed using SPSS 20. Mann-Whitney U test was performed While keeping significance level at 5% ( $p < 0.05$ ).

## Results

Of the 140 subjects, 70(50%) each were males and females. The majority of subjects, 46 (32.9%) were aged 19 years; 43 (30.7%) 18 years; and 39 (27.9%) 20 years.

Mean VR in males was 1.48±0.28 and in females it was 1.49±0.25 ( $p=0.745$ ).

There was no difference between the mean SBP fall between the two groups ( $p=0.48$ ) as shown in figure 1. There was no difference between the mean SBP rise between the two groups ( $p=0.928$ ). There was significant difference between the mean DBP rise between the two groups ( $p=0.009$ ) as shown in figure 2. There was no difference between the mean DBP fall between the groups ( $p=0.682$ ).

## Discussion

Gender difference is one of the most researched topics in medical science. Yet some aspects still need to be explored and validated.<sup>21</sup> One such aspect is gender difference in ANS's control of the CVS. The ANS is a silent force and maintainer of the homeostasis. It subconsciously controls a battery of viscera, including the heart, eyes, gut, glands, urinary bladder etc.<sup>1</sup>

In the present study there was no significant difference in mean VR between the two genders. Since VR is an indicator

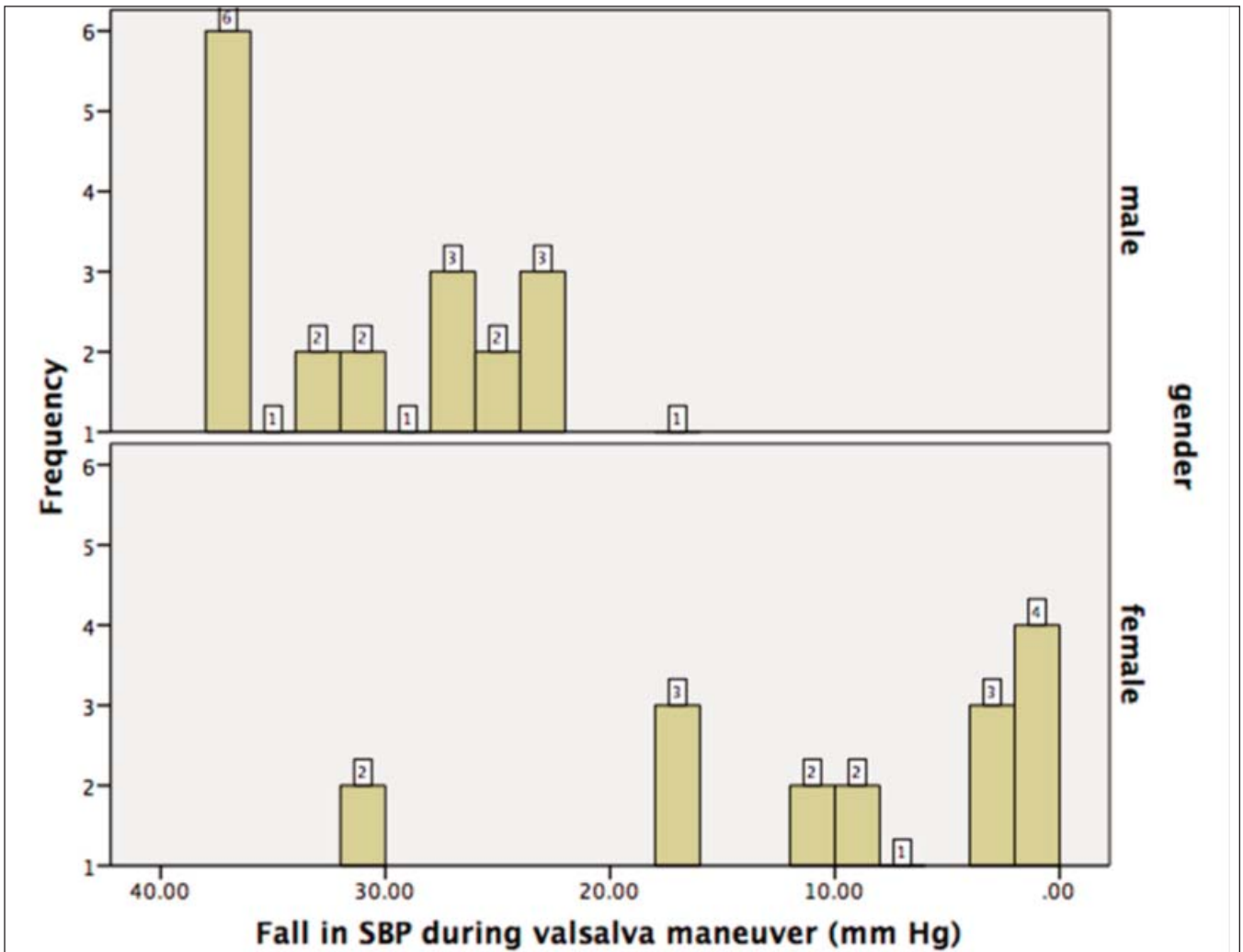


Figure-1: Fall in systolic blood pressure (SBP) during Valsalva manoeuvre.

of PNS function, this shows that there was no difference in PNS stimulation between the genders. A study in India presented similar results.<sup>16</sup> According to the cut-off value for normal VR, which is 1.21 or higher, there were 58 (82.9%) normal males and 59 (84.3%) normal females as shown in table 2. According to a study, the normal VR values for males aged 10-29 years is 0.38-2.53, and for females of the same age range, it is 0.1-1.39.<sup>5</sup> In our study, the mean VR in males ranged 1.2-1.76 and in females 1.24-1.74.

According to a study, a rise in DBP of more than 16mmHg was affiliated with good SNS function.<sup>20</sup> A study conducted

Table-2: Valsalva Ratio of participants.

Gender	Normal n (%)	Abnormal n (%)	Total n (%)
Male	58 (82.9)	12 (17.1)	70 (100)
Female	59 (84.3)	11 (15.7)	70 (100)
Total	117 (83.6)	23 (16.4)	140 (100)

on 52 male HTN patients showed that both SBP and DBP rose during HGT.<sup>22</sup> Another study showed that DBP rose during HGT from a mean value of 72.88±1.83 to 83.00±1.83 mmHg.<sup>23</sup> With consistent isometric exercise training, the resting DBP decreases.<sup>24</sup>

While checking SNS function via HGT in our study, three patterns were observed; there was rise in DBP, fall in DBP, and no change in DBP in various cases. A study conducted on young adult African-American female university students showed a DBP rise from 77±2 to 112±5 mmHg.<sup>25</sup>

The present study however, revealed diverse outcomes with regards to DBP. In majority of the subjects, there was a fall in DBP during HGT exercise (26.42% males and 30% females). In 6.43% males and 3.57% females, there was no change in DBP, while rise was seen only in 17.14% males and 16.42% females. A study depicted that DBP was not altered by HGT exercise.<sup>26</sup>

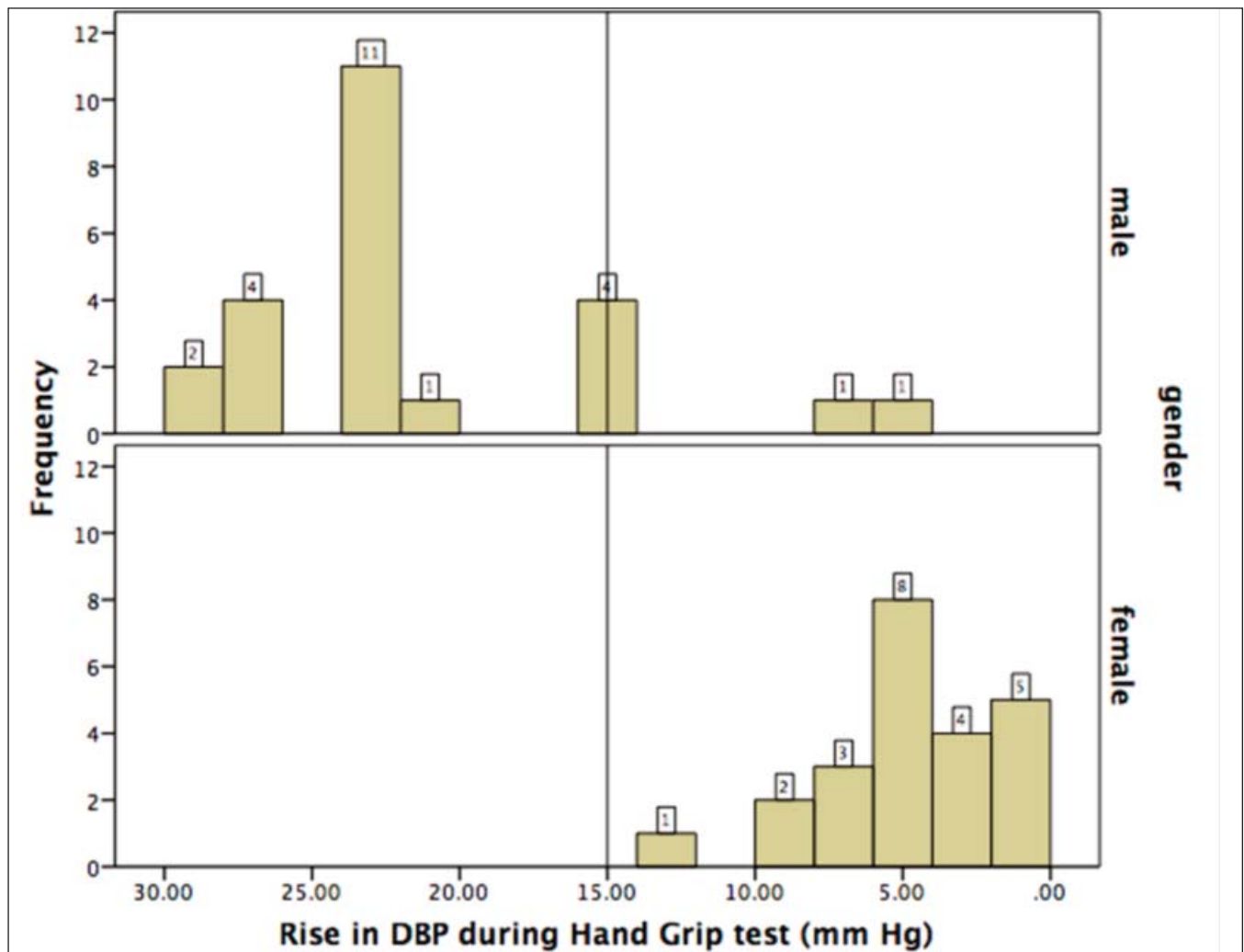


Figure-2: Rise in diastolic blood pressure (DBP) during hand grip test.

The SBP change during VM also showed three patterns; rise, fall and no change in both genders. The criteria for optimum SNS function is that the fall in SBP shouldn't be more than 21 mmHg.<sup>18</sup> When SNS was judged on the basis of VM, no difference was noted between males and females.

The limitations of the current study are that the results are affected by the manner in which VM was performed. Some subjects might have performed it by raising the mouth pressure only, rather than the intrathoracic pressure. We tried to minimise this by educating each subject to the optimum level. Another limitation is that neurotransmitter levels could not be measured in blood and compared with the results. This happened because their half-life was too short.

Further studies need to be done on the topic of gender differences in ANS control of CVS in order to elaborate the

complexities related to the two genders.

**Conclusion**

There was no significant difference in PNS between the two genders. However, when it came to SNS, the males showed predominant activity.

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**Conflict of Interest:** None.

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