EFFECT OF GRADED HEAD-UP TILT ON PARASYMPATHETIC REACTIVITY

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Abstract: Thirteen healthy subjects were tested for parasympathetic reactivity during head-up tilt and reversal of the tilt. Head-up tilt (70°) resulted in significant increase in baseline heart rate and diastolic blood pressure. Headup tilt also led to increased parasympathetic reactivity as measured by Valsalva manoeuvre and hand grip test. Heart rate response to deep breathing test did not change. The reversal of the tilt led to returning of heart responses to original values. Responses indicate towards enhanced parasympathetic reactivity during head-up tilt position.

Key words:	head-up tilt parasympathetic	Valsalva
isome	tric autonomic functions	reverse tilt

INTRODUCTION

The assessment and quantification of the cardiovascular responses to head-up tilt are particularly important as postural hypotension is a cardinal manifestation of autonomic failure. A head-up tilt leads to pooling of the blood in lower parts of the body and low pressure in carotid sinus (1). This stimulates baroreceptors that mediates immediate increase in heart rate through withdrawal of vagal tone and presumably a slight sympathetic nerve activity promotes the acceleration (2, 3). Van Brederode et al (4)observed a gradual heart rate increase starting after 1.5 sec elicited by 70° tilt in healthy subjects and tilt down (head-down) resulted in an abrupt heart rate (HR) decrease after 3.5 sec and heart rate reached pretilt level within 8 sec. A sharp biphasic, immediate heart rate response was observed with more intense acceleration after 90° tilt than after 70° tilt and they suggested that tilt angle determines the extent of immediate acceleration (5). They further added that

faster tilts, as those of 2 sec and 5 sec augment the hemodynamic consequences of the 90° tilt and thereby the nervous cardiac response. Others (6) compared 70° head-up tilt (HUT) in 1.5 sec and 3 sec and 90° head-up tilt in 3 sec and found that the initial heart rate and blood pressure responses induced by the three tilt manoeuvres were almost identical in time course and amplitude. Van Brederode et al (4) suggested that the immediate heart rate changes after active change of posture are due to 'muscle-heart reflex' that instantaneously inhibits cardiac vagal tone. The initial heart rate increase on standing is almost exclusively mediated by withdrawal of vagal tone, since it is blocked by atropine. Whereas, sustained tachycardia of later phases depends predominantly on sympathetic stimulation (2). This was later supported by the finding that the plasma norepinephrine level increased progressively as the tilt angle increased from $0-80^{\circ}$ (7). Others have found that during low level passive tilt, there is an increased sympathetic activity and during

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high level tilt, there is change in both sympathetic and parasympathetic tone (8). Thus it is clear that postural change leads to sustained change in autonomic tone(8). The question how these change influence 'autonomic reactivity' has been addressed in the recent past. Many researchers have attempted to find out the effect of body positions on parasympathetic reactivity by using various tests (9). Rossberg and Martinez (10) reported that the heart rate increase following a 70° head-up tilt in 1.6 sec was more pronounced during expiration than during inspiration. As the intensity of cardiovascular responses to the Valsalva manoeuvre are partially dependent on cardiac preload and venous return prior to and on release of the strain, purposeful manipulation of body position and extremities could differently affect by trapping venous flow in the periphery. Indeed the heart rate and pulse pressure changes were observed greater when Valsalva manoeuvre was performed in the sitting than supine position (1). In the light of present review, it is clear that the physiological relationship between certain parasympathetic test responses and head-up tilt induced autonomic responses remains to be elucidated. So, purpose of this study was to observe the effect of different degrees of tilting on certain parasympathetic test responses. We hypothesized that the degree of head-up tilt will determine the magnitude of reflex heart rate change in response to test situations. The objectives of the study were :

1. To study heart rate responses in different degree of head-up tilting and the reverse tilting.

2. To study cardiac responses induced by deep breathing test, Valsalva manoeuvre and isometric exercise in different degrees of tilt position.

METHODS

The study was conducted on thirteen subjects $(24-36 \text{ yrs}; \text{ mean } \pm \text{SD} : 29 \pm 4)$ with

no history of hypertension, renal diseases, diabetes or other diseases that could affect the autonomic functions. The subjects were sedentary and were drawn from the Department of Physiology, All India Institute of Medical Sciences. None of the subjects were smoker or alcoholic. Every subject was investigated at Autonomic Function Lab in the Department of Physiology, All India Institute of Medical Sciences. All tests were performed in a temperature controlled (22±1°C) room between 10 a.m. to 12 noon after two hours of food intake. An informed consent was obtained from the subjects after explaining the procedure in detail. For the test the subject was made to lie down on the tilt table. ECG electrodes were placed and connected to the Polyrite (INCO, Ambala, India). The ECG (lead III) and respiration (through stethograph) were recorded throughout tests. From lying position (0°) subjects were tilted to 30°, 50°, 70° head-up tilt positions and also in reverse sequences i.e. 50° R, 30° R, 0° R, (suffix R indicates reverse position). The speed of tilting was 5° / sec. Baseline heart rate was calculated from ECG strip of thirty seconds, which was doubled to find out per min heart rate. After 5 min rest period in 0° position and after 2 min rest in each tilting position the following non-invasive tests were carried out.

1. Deep breathing test: The subjects were instructed to take 4 deep breaths each of 10 sec (12). The E : I ratio (13) and difference in heart rate during inspiration and expiration were calculated.

 $E: I ratio = \frac{Maximum R-R interval during expiration}{Minimum R-R interval during inspiration}$

2. Valsalva manoeuvre : Valsalva manoeuvre was carried out by the subject by expiring forcefully in a closed tube to raise and to maintain a pressure of 40 mm Hg for 15 sec. Due care was taken to prevent deep breathing before and after the release of strain (1).

Valsalva ratio (14) was calculated using the following formula:-

Valsalva ratio= Shortest R-R interval after manoeuvre (Phase IV)

In order to understand the dynamics of Valsalva ratio (which is based on maximum and minimum heart rate changes during test), we analysed component responses of Valsalva manoeuvre namely bradycardia ratio [minimum heart rate (beats/min) (Phase IV) / Resting heart rate (beat/min) and tachycardia ratio [maximum heart rate (beats/min)) (Phase II)/Resting heart rate (beats/min)].

3. Hand grip test (Isometric exercise): The subject pressed the hand grip dynamometer for one min at 50% of his/her maximal voluntary effort. Adequate effort by all subjects was ensured. Heart rate was monitored by ECG. We did not do pressure measurement during hand grip test since it could have influenced heart rate.

For statistical comparison of multiple values (7 in number) for head-up tilts and reversal of tilts a non-parametric Friedman test was applied. The chi-square, probability level and multiple comparison value at 0.05 level of significance were calculated to find out significant changes among individual parameters.

RESULTS

Table I provides descriptive data for baseline parameters and the results of three tests. Mean values of baseline heart rate and diastolic blood pressure showed a gradual rise with the increasing head-up tilt. Baseline heart rate (measured after five min of rest) significantly increased from a mean value of 72.46 ± 9.56 to 79.07 ± 8.02 (P < 0.05) from supine position i.e. 0° to 70° head-up position. On reversal of tilt from 70° to 0°, the heart rate signi- ficantly decreased (P < 0.05) from 79.07 ± 8.02 to 69.38 ± 8.73 . Other tilt positions those showed significant changes for heart rate were 30° to 70°, 30° to 50°, 50° to 70° in head-up tilt direction. Reverse tilt from 50° to 0° also showed significant changes in heart rate (76.3 \pm 8.63 to 69.38 \pm 8.73, P < 0.05).

Second important baseline parameter which showed significant changes during head-up tilt was diastolic blood pressure. The diastolic pressure showed significant rise for tilt from 0° to 70° and from 30° to 70°. The reversal of tilt did not show any significant change. However, during reversal of tilt, there was a trend showing decline in diastolic blood pressure (Table I). Baseline systolic blood pressure did not show any significant change both in head-up tilt and reversal of the tilt.

The Valsalva ratio showed significant rise from $1.79 \pm .37$ to $2.25 \pm .43$ between 0° and 50° reversal. From 0° to 30° Valsalva ratio showed sharp but insignificant rise which attained a plateau for next two tilt positions i.e. 50° and 70°. Reversal of tilt did not show any significant change.

During the head-up tilt the bradycardia and tachycardia ratios showed significant changes at the same tilt position i.e. at 0° to 50° positions. The lowest values of bradycardia ratio were seen at 50° R and 30° R positions.

The value of bradycardia ratio of reverse tilt positions i.e. between 50° R and 0° R was found significant increased; whereas, 30° R and 0° R showed significant decrement. The tachycardia ratio did not change significantly between any of the positions. However, tachycardia ratio values showed trend towards biphasic response. The value of tachycardia ratio at 70° had tendency to come back near to its original value. Similar tendency was seen on complete reversal of tilt (restoration of 0°).

The phase II R-R interval of Valsalva manoeuvre showed trends of changes similar to bradycardia ratio (Fig. 1). The phase II

Parameters —	Magnitude of head-up tilt							
	0°	30°	50°	70°	50°R	30°R	0°R	
BHR (per min)	72.46 ± 9.56	68.38 ± 8.07	72.15 ± 9.14	79.07 ± 8.02	76.30 ± 8.63	72.76 ± 8.50	69.38 ± 8.7	
BSP (mmHg)	117.77 ± 7.77	117.66 ± 9.61	117.77 ±10.46	115.77 ± 10.83	115.77 ± 14.47	118.44 ± 13.00	114.66 ± 9.53	
BDP (mmHg)	73.77 ± 5.14	75.55 ± 8.98	77.77 ± 9.45	83.11 ± 6.41	81.77 ± 9.18	81.77 ± 7.10	77.00 ± 7.7	
Pulse pressure(mmHg) 45.11 ± 5.30	44.33 ±10.48	42.22 ± 8.50	33.77 ± 7.57	35.11 ± 10.72	37.77 ± 9.71	37.66 ± 5.3	
Mean presure	88.80 ± 6.07	90.32 ± 8.64	91.84 ± 8.55	95.77 ± 7.40	92.36 ± 8.80	94.36 ± 8.61	89.55 ± 7.9	
BRR (per min)	20.50 ± 3.96	17.25 ± 3.99	18.00 ± 2.82	19.00 ± 2.82	18.50 ± 4.37	19.50 ± 3.90	20.00 ± 5.3	
Baseline R–R Int (sec)	0.84 ± 0.10	0.89 ± 0.11	0.84 ± 0.09	0.76 ± 0.07	0.80 ± 0.08	0.84 ± 0.08	0.87 ± 0.03	
E:I ratio	1.45 ± 0.15	1.37 ± 0.13	1.38 ± 0.11	1.38 ± 0.08	1.34 ± 0.11	1.38 ± 0.14	1.45 ± 0.1	
HR dif (per min)	27.65 ± 6.72	22.86 ± 5.43	25.66 ± 7.45	25.69 ± 5.97	25.08 ± 4.83	24.67 ± 7.14	26.34 ± 6.6	
VR	1.79 ± 0.37	2.05 ± 0.38	2.01 ± 0.43	2.01 ± 0.36	2.25 ± 0.43	2.17 ± 0.52	1.85 ± 0.2	
BR	0.84 ± 0.08	0.82 ± 0.08	0.81 ± 0.08	0.77 ± 0.08	0.74 ± 0.07	0.74 ± 0.09	0.84 ± 0.0	
TR	1.51 ± 0.25	1.70 ± 0.26	1.61 ± 0.28	1.53 ± 0.28	1.67 ± 0.18	1.63 ± 0.25	1.60 ± 0.2	
Phase II								
R–R Int (sec)	0.54 ± 0.06	0.49 ± 0.03	0.49 ± 0.04	0.47 ± 0.05	0.45 ± 0.03	0.48 ± 0.04	0.54 ± 0.0	
Phase IV								
R-R Int (sec)	0.98 ± 0.12	1.05 ± 0.14	1.03 ± 0.14	0.99 ± 0.13	1.06 ± 0.15	1.11 ± 0.15	1.04 ± 0.1	
BHR - Baseline H	leart Rate		BSP - Ba	seline Systolic	Pressure			
BDP - Baseline I	Diastolic Press	ure	BRR - Ba	seline Respirate	ory Rate			
R-R Int - R-R Interv	val		E:I ratio - Ex	piration/Inspira	tion Ratio			
HR dif - Heart Rat	e Difference		VR - Va	lsalva Ratio				
BR - Bradycard	ia Ratio		TR - Ta	chycardia Ratio				
DBT - Deep Brea	thing Test		VM - Va	lsalva Manoeuv	re			

TABLE I: Baseline parameters and results of DBT and VM (Men ± SD) at different degrees of head-up tilt and the reverse tilt.

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R-R interval showed gradual decline from 0.54 ± 0.06 sec at 0° position to 0.47 ± 0.05 sec at 70° position. This value further declined to 0.45 ± 0.03 sec on reversal to 50° position. On further reversal of head-up tilt (30°R to 0°R) the value tends to rise. Phase IV bradycardia and tachycardia ratio showed reverse trends on comparisons (Fig. 1).

1,2 1. R R ١ n .8 e ٧ 8 .6 .4 2.5 2 R a ti 1.5 1 0.5 0 30 60 70 50'R 30'R 0 R Degree of tilt

Fig. 1 : Effect of different degrees of head-up tilt (0° to 70°) and reverse tilt (50°R, 30°R and 0°R) on the various parameters derived from ECG taken during Valsalva manoeuvre. From above downwards : Phase IV R-R interval (-*-), baseline R-R interval (-0-), Phase II R-R interval (-0-), Valsalva ratio (-*-), tachycardia ratio (+), and bradycardia ratio (-•-).

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In deep breathing test the E:I ratio showed tendency to decline during head-up tilt. The lowest value was seen at 50°R position. On full reversal to 0° the E:I ratio returned back to original value. Changes in heart rate differences during deep breathing test did not follow any pattern.

During hand grip test the initial comparison of R-R intervals showed significant changes for $0^{\circ}-70^{\circ}$ and $30^{\circ}-70^{\circ}$ comparisons (Fig. 2). The measurement of R-R interval at

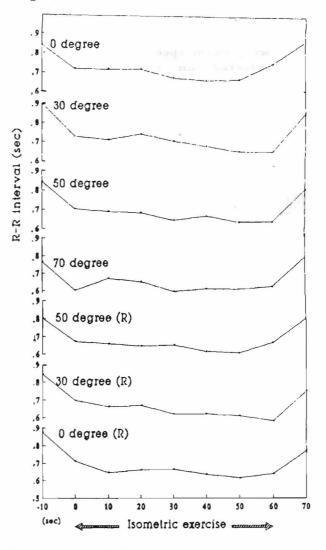


Fig. 2: Trends of R-R interval changes during isometric exercise. R' indicates reverse of head-up tilt to 0°.

tenth sec did not show any significant change at any position. The R-R interval at 20th sec showed significant changes for 3 comparisons i.e. significant decline in values at $30^{\circ}-50^{\circ}$ R, $30^{\circ}-30^{\circ}$ R and $30^{\circ}-0^{\circ}$ comparisons. Further the R-R interval at 30th sec of hand grip test showed significant falls for 2 comparisons namely between $30^{\circ}-70^{\circ}$ and between $30^{\circ}-30^{\circ}$ R positions.

DISCUSSION

In the present study we have attempted to find out the effect of graded head-up tilt on parasympathetic reactivity in human. For tilting we used the speed of 5°/sec. The speed was selected on the basis of two considerations; first, the speed was close to most commonly used tilt speeds (5) and secondly this speed was convenient for manual tilting. Since the tilt differences were multiples of 5°, it was easy to count seconds and tilt the subject to a desired position. Various tilt positions (30°, 50°, 70°, 50°R, 30°R, 0°R) used were the positions which could possibly influence the parasympathetic reactivity (5, 8). We used reverse tilt after 70° in exactly opposite way and with the same speed, so as to enable us to compare similar positions with head-up tilt. To our knowledge this is the first report documenting reverse tilt.

Graded head-up tilt resulted in significant increase in baseline heart rate. Such findings have been reported by many workers (15, 16). During head-up tilt, there is increase in sympathetic tone and decrease in parasympathetic tone (2). The reverse headup tilt has shown in the reversal of heart rate to its original value. Initial tilts from 0° to 30° and 30° to 50° did not appear significant stimulus for change in heart rate. Similar findings also have been observed by Mukai and Hyano (5). Head-up tilt from 50° to 70° was an adequate stimulus to cause increase in heart rate. During reverse tilt heart rate

showed significant reversal only at $0^{\circ}R$ (as measured from $70^{\circ}R$ or $50^{\circ}R$) suggesting that head-up tilt is more potent stimulus than reversal of tilt.

The head-up tilt has resulted in significant increase in diastolic blood pressure as measured after 2 min stay in that position. Like heart rate the differences for diastolic blood pressure were significant only between 0° and 70°; and between 30° and 70° of tilt. Also the reversal of tilt did not show any significant restoration of diastolic blood pressure. Two points emerge from findings of changes in heart rate and diastolic blood pressure. First, head-up tilt is a strong stimulus for changes in diastolic blood pressure and heart rate but not the reversal of tilt; secondly, during reversal of tilted positions, the diastolic blood pressure did not change, however the heart rate returned to supine resting level. In conclusion, the headup tilt is a stronger stimulus than reverse head-up tilt. Also the reverse head-up tilt influences heart rate and diastolic pressure differentially.

During different degrees of tilt the heart rate reactivity was measured by three tests namely, deep breathing, Valsalva manoeuvre and isometric exercise. These tests were selected because each of the test requires different stimulus for causing heart rate changes. The deep breathing requires no afferent stimulus (sinus arrhythmia). Valsalva manoeuvre involves passive changes in blood pressure leading to reflex heart rate changes and heart rate changes during isometric exercise could be centrally determined or/and due to reflex from muscles afferent (17, 18, 19). Deep breathing test did not show any significant changes in E:I ratio and variation in heart rate. Thus the present speed and range of tilt did not influence the status of respiration induced parasympathetic cardiac reactivity.

The responses to Valsalva manoeuvre were interesting. There was significant rise in Valsalva ratio from 0° position to 50°R. This rise in Valsalva ratio has returned to its near original value on complete reversal of headup tilt. From 0° to 70° head-up tilt the Valsalva ratio has shown gradual rise from 1.79 ± 0.37 to 2.01 ± 0.36 . A value of Valsalva ratio of 1.92 ± 0.34 for healthy controls was reported from our Lab earlier (20). This value was recorded in sitting posture, and two values of 0° and 70° positions justifiably lie on either side of it.

The Valsalva response is essentially consists of tachycardia and bradycardia. Analysis of tachycardia and bradycardia responses revealed that tachycardia ratio remained almost unchanged while bradycardia ratio showed changes parallel to Valsalva ratio although in opposite direction. Thus, it appears that this is the bradycardia which is responsible for significant changes in Valsalva ratio. It may be that during head-up tilt, the parasympathetic system banks more upon inducing bradycardia than inducing tachycardia. The bradycardia ratio declined between 50°R and 0°R. The reversal in Valsalva ratio was delayed and seen only in 30°R to 0°R positions. Perhaps, this delay in bradycardia ratio was responsible for delayed changes in Valsalva ratio. Surprisingly, bradycardia ratio and phase II tachycardia showed inverse relationship. Another inverse relationship was seen in tachycardia ratio and in phase IV bradycardia. Phase IV bradycardia has shown a parallelism with baseline heart rate (Fig. 3). It implies that there may be a common mechanism operating for the two.

Heart rate changes during isometric exercise were most pronounced at the beginning, 20th sec and 30th sec. The initial response suggests that tilt has resulted in increase in heart rate. Responses at 20th and

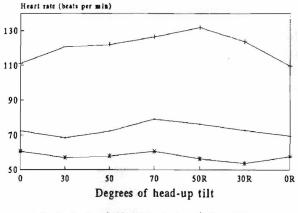




Fig. 3 : Effect of different degrees of head-up tilt (0° to 70°) and reverse tilt (50° R, 30° R and 0° R) on the heart rate responses during Valsalva manoeuver. This shows that during tilted positions the difference between bradycardia and tachycardia widens with maximum value at 50°R.

30th sec suggest that at these time points, heart rate during reverse head-up tilt was significantly higher than the same position (30°) after head-up tilt. It indicates that these time points are significant in determining heart rate reactivity. Earlier Vaz et al (21) reported these time points for heart rate responses after head-up tilt. Fig. 2 suggests that maximum increase in heart rate was seen when the subject attained 70° head-up tilt. This indicates that effect of isometric exercise and head-up tilt on heart rate were additive. Similar effect of pre-existing isometric exercise was seen on response to Valsalva manoeuvre, where tachycardia achieved during Valsalva manoeuvre was more in presence of isometric exercise (22). Analysis of recovery of heart rate after hand grip exercise suggests that it was steeper in tilted positions when compared to horizontal positions (Fig. 2).

In conclusion, this study suggests that graded head-up tilt results in significant changes in heart rate responses secondary to

blood pressure changes and isometric exercise. Therefore, it is possible that tilt results in alteration of stimulus bound changes in parasympathetic reactivity. This conclusion is further confirmed bv reversal of parasympathetic reactivity when horizontal position was resumed after the tilt. The mechanism of alteration in parasympathetic responsivity during tilt position appears due to decrement in parasympathetic tone rather than enhancement in sympathetic tone. In our earlier study (22), we have shown that enhanced sympathetic activity secondary to isometric exercise does not alter Valsalva ratio, it may shift values of both tachycardia and bradycardia upwards, thus keeping the same ratio. Lower parasympathetic tone during head-up tilt may result in relative increase in heart rate, thus providing scope for greater bradycardia during Valsalva manoeuvre.

Considering absence of changes in parasympathetic reactivity at low level tilts, it is not possible to work out the quantitative relationship between degree of head-up tilt and magnitude of response for the given tilt speed. Nevertheless, Fig. 1 and Fig. 2 suggest that there are trends towards gradual increase in parasympathetic reactivity which returns back on reversal to horizontal. To further quantify such responses, beat to beat variability during different test situations needs to be done along with simultaneous measurement of autonomic tone at faster tilt speeds.

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