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Original Article

Effect of Hyperventilation on Excitability of The Human Cortex and Cardiac Autonomic Variability

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Abstract

Hyperventilation (HV) enhances cortical excitability in widely distributed networks including motor, auditory and visual cortices. The depth and frequency of respiration also affects cardiac autonomic nervous system (ANS) activity. The aim of the present study was to evaluate the effect of hyperventilation on cortical excitability and cardiac autonomic activity. The excitability of the human cortex was recorded in terms of visual (VRT) and auditory reaction times (ART). Cardiac ANS activity was recorded and analysed in terms of heart rate variability (HRV) before, during and after hyperventilation, in control and study group. This study involved 50 first MBBS students, who were divided into control group and study group (25 each). Anthropometric characteristics were noted. HRV and auditory and visual reaction times were recorded using polygraph (AD instruments) before, during and after HV for 5 minutes. The results were analysed statistically using SPSS software. ART and VRT were significantly reduced after hyperventilation (p=0.001) as compared to the values before and during HV. There was also alteration in HRV before, during and after HV. Hyperventilation alters the excitability of the human cortex by varying cardiac autonomic activity and hence should be borne in mind during extreme physiological conditions and also certain pathological states.

Introduction

Hyperventilation (HV), producing hypocapnia, increases the excitability of the human cortex, which could be evidenced in the motor and visual cortices. A hyperventilation induced increase in excitability within the central nervous system may account for clinical phenomena such as facilitation of spike-wave discharges. EEG studies and magneto-encephalographic studies demonstrate that HV enhances cortical excitability in widely distributed networks (1).

Heart rate variability (HRV) is a measure of the extent of modulation of the cardiac sympathetic and parasympathetic tones and increased HRV is a marker of healthy cardiac autonomic activity (2). Different physiological factors may influence HRV such as gender, age, circadian rhythm, respiration and body position (3). Respiration modulates the autonomic flow to the heart as evidenced by respiratory sinus arrhythmia and contributes to HRV (4).

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In general, in HRV frequency domain parameters, the low-frequency component (LF) has been thought to reflect mainly the sympathetic nervous activity both at the cardiac (with vagal influences) and vascular level (5, 6), while the high frequency component (HF) reflects vagal activity on the heart together with nonneural changes, which follow inspiration induced increases in venous return (7, 8) and LF/HF ratio suggests sympathovagal balance (6, 9).

It is also documented that different breathing patterns, including hyperventilation, have major impact on cardiac autonomic nervous system (ANS) activity. HRV analysis is a widely employed method to assess cardiac ANS activity (10). Owing to its non-invasive nature, HRV and especially short-term HRV recordings (5 min), are easily obtainable from patients or healthy volunteers (10, 11).

A few researchers have reported the effect of various types of breathing patterns on HRV parameters and excitability of cortex, but to the best of our knowledge no investigation has been done to study the changes during hyperventilation and its immediate effects.

The aim of the present study was to evaluate the effect of hyperventilation on cortical excitability and cardiac autonomic activity. The excitability of the human cortex was recorded in terms of visual (VRT) and auditory reaction times (ART). Cardiac ANS activity was recorded and analysed in terms of heart rate variability (HRV) before, during and after hyperventilation, in control and study group.

Materials and Methods

Subjects and methods

This study was done on 50 first year medical students aged 17-20 years. Ethical clearance from the institute and informed consent from the subjects were obtained. Subjects with past or present history of any neuro-psychiatric or respiratory disorders, systemic illnesses like diabetes, cardiac disease and hypertension were excluded. Anthropometric characteristics like height (cm), weight (kg), and body mass index (kg/m^2) were recorded. The findings of the physical examinations, electrocardiography on all the volunteers before the start of the experiment showed normal results.

Experimental set up

Subjects were made to relax in sitting position for 15 min. Subjects were sufficiently familiarized with the procedure. Then using powerlab (AD Instruments), a data acquisition system, visual and auditory reaction times and Heart rate variability was calculated by recording ECG in Lead II for 5 minutes in a relaxed spontaneously breathing state. Recordings with artefacts such as extrasystolic or supraventricular beats or other arrhythmias comprising more than 5% of the total epoch were discarded. Baseline respiratory rate, heart rate, blood pressure and short-term HRV indices in the supine resting state were measured in the morning following 15 minutes of supine rest, 2-4 hours after a light breakfast. The subjects were asked to refrain from heavy physical activity for 24 hours and from consumption of alcohol and caffeinated beverages for 12 hours, prior to the measurements. The frequency domain parameters studied were low frequency in normalized units (LF nu), high frequency in normalized units (HFnu) and the ratio of LF to HF (LF/HF ratio). Low frequency and high frequency spectral powers were determined by integrating the power spectrum between 0.04 and 0.15 Hz and between 0.15 and 0.4 Hz respectively.

Experimental protocol

50 students were selected for study and they were divided into 2 groups i.e. study and control group, 25 in each using lot method. In study group, heart rate variability, visual and auditory reaction times were recorded before, during and after hyperventilation. The first recording was taken during normal breathing for 5 minutes. After this, subjects were instructed to hyperventilate to their maximum capacity and recordings were taken during the event (for a maximum of 5 min) and third reading was taken immediately after hyperventilation, again for 5 minutes. In control group, heart rate variability readings and reaction time were taken 3 times with normal breathing of 5 minutes each.

Statistical analysis

ANOVA and t test were applied in order to analyze the differences of the mean values of visual and auditory reaction time, HRV parameters before, during and after hyperventilation. Statistical analysis was performed using the SPSS (v. 15.0, SPSS Inc., Chicago, IL, USA). A p value < 0.05 was considered statistically significant.

Results

The present study involved 50 subjects, 25 each in study and control group. There was no significant difference in age, weight and BMI between two groups. All the values in the tables are expressed in terms of mean±standard deviation (SD). The mean values of, auditory and visual reaction time before, during and after hyperventilation in study group are tabulated in Table I. The auditory and visual reaction time have increased significantly (p=0.001) during hyperventilation as compared to resting state and auditory and visual reaction time have significantly decreased immediately after hyperventilation and also there is significant difference (p=0.001) between before and after hyperventilation.

Table II shows the mean values of ART and VRT in control group, there are no significant changes during normal breathing.

The mean values of LFnu, HFnu, LF/HF ratio before, during and after hyperventilation in study group are tabulated in Table III. LF has slightly increased from 65.02±10.87 to 68.96±7.30 during hyperventilation and reached near to resting state after hyperventilation. HF decreased during hyperventilation from 23.70±5.31 to 20.78±4.02 compared to resting state, but there was slight increase in HF i.e. 24.61±7.92 after hyperventilation and also LF/HF increased during hyperventilation as compared to resting state. Although there were changes in parameters of HRV

TABLE I: Reaction times in the study group.

	Basal values normal breathing for 5 minutes (1)	*During hyperventilation (2)*	*After hyperventilation for 5 minutes (3)*	*p value (1 and 2)*	*p value (2 and 3)*	*p value (1 and 3)*
VRT (ms)	506.38±145.82	594.94±174.43	474.33±146.69	.001*	.001*	.001*
ART (ms)	223.66±56.06	351.33±70.38	210.05±55.12	.001*	.001*	.001*

Where VRT - visual reaction time, ART - auditory reaction time, * = p value < 0.05 statistically significant.

TABLE II: Reaction time in control group.

	Basal values normal breathing for 5 minutes (1)	*During normal breathing for next 5 minutes (2)*	*After normal breathing for 5 minutes (3)*	*p value (1 and 2)*	*p value (2 and 3)*	*p value (1 and 3)*
VRT (ms)	408.13±127.85	409.46±126.33	408.13±125.68	.342	.727	.601
ART (ms)	226.40±58.49	227.80±57.53	228.86±58.75	.082	.316	.240

Where VRT - visual reaction time, ART - auditory reaction time.

TABLE III: Frequency domain parameters of HRV in the study group.

	Basal values normal breathing for 5 minutes (1)	*During hyperventilation (2)*	*After hyperventilation for 5 minutes (3)*	*p value (1 and 2)*	*p value (2 and 3)*	*p value (1 and 3)*
LF(nu)	65.02±10.87	68.96±7.30	64.48±11.15	0.235	0.209	0.778
HF(nu)	23.70±5.31	20.78±4.02	24.61±7.92	0.589	0.084	0.490
LF/HF	3.17±1.73	3.47±.94	2.93±1.19	0.455	0.151	0.307

Where LF - low frequency, HF - high frequency, nu - normalised units.

TABLE IV: Frequency domain parameters of HRV in control group.

	Basal values normal breathing for 5 minutes (1)	*During normal breathing for next 5 minutes (2)*	*After normal breathing for 5 minutes (3)*	*p value (1 and 2)*	*p value (2 and 3)*	*p value (1 and 3)*
LF(nu)	66.19±8.69	64.84±9.11	66.44±8.76	0.659	0.448	0.938
HF(nu)	22.46±4.87	22.95±5.24	21.77±4.42	0.886	0.206	0.128
LF/HF	2.98±1.02	2.99±.94	3.20±.97	0.975	0.290	0.294

Where LF - low frequency, HF - high frequency, nu - normalised units.

during hyperventilation but they were not statistically significant.

Table IV shows mean values of HRV parameters in control group, there were no significant variations in recording of LF, HF and LF/HF ratio in all the 3 readings.

Table V shows the comparison of mean values of HRV parameters in control and study group before, during and after hyperventilation. Certainly, there is a difference between study and control groups, but it is not statistically significant. The statistics in Table VI shows the comparison of ART and VRT in study and control group. There is highly statistically significant difference in ART and VRT during the hyperventilation.

TABLE V: Comparison of HRV parameters in study and control group.

HRV parameters		*Study group*	*Control group*	*p value*
LF/HF	Before	3.17±1.37	2.98±1.02	0.123
	During	3.47±.95	2.99±.94	0.811
	After	2.93±1.19	3.20±.97	0.239
LF	Before	65.02±10.87	66.19±8.69	0.162
	During	68.96±7.30	64.84±9.11	0.708
	After	64.48±11.15	66.44±8.76	0.081
HF	Before	23.62±8.26	23.70±5.31	0.09
	During	20.78±4.02	22.95±5.24	0.164
	After	24.61±7.92	21.77±4.42	0.09

Where LF - low frequency, HF - high frequency.

TABLE VI: Comparison of Reaction time parameters in study and control group.

HRV parameters		*Study group*	*Control group*	*p value*
VRT (ms)	Before	506.38±145.85	408.13±127.85	0.786
	During	594.94±174.43	409.46±126.33	0.036*
	After	474.33±146.69	408.13±125.68	0.248
ART (ms)	Before	223.66±56.06	226.40±58.49	0.301
	During	351.33±70.38	227.80±57.53	0.00*
	After	210.05±55.12	228.88±58.75	.140

Where VRT - visual reaction time, ART - auditory reaction time; * p value <0.05 statistically significant.

Discussion

The results of the present study indicate increased excitability of the cortex, especially the auditory and visual cortices, as evidenced by a significant decrease in the ART and VRT, after hyperventilation. The HV-induced physiological changes are thought to be a consequence of increased neuronal excitability resulting from the hypocapnia-induced alkalosis and altered synaptic transmission as demonstrated by several studies (12-16).

A recent *in vitro* study in the rat hippocampus showed that stability of spontaneous gamma activity (20–80 Hz) increases during hypocapnia as a result of enhanced GABAergic transmission (17). Extensive theoretical and experimental work on the rat hippocampus suggests that networks of interneurons coupled with GABAergic connections are responsible for rhythmogenesis and neuronal synchronization underlying gamma oscillations (18-24).

Recently, the possible role of gap junctions on interneuronal synchronization has received a lot of attention. Since the conductivity of gap junctions increases with intracellular pH, it is possible that respiratory alkalosis could affect the gap junctions and thus the properties of the interneuronal network (25).

Thus hyperventilation, by inducing alkalosis and decreasing calcium concentration, interact with inhibitory GABA and excitatory glutaminergic

transmission in the CNS, thereby increasing the excitability.

The results of the present study were similar to a study by Mogyoros et al., 1997 (26), which showed that there was a decrease in motor evoked potential (MEP) onset latency after hyperventilation, which provides support for the notion of hyperventilation-induced increase in central excitability as hyperventilation does not alter peripheral conduction velocity (1).

In general, the LF component of HRV has been thought to reflect mainly the sympathetic nervous activity both at the cardiac (with vagal influences) and vascular level (5, 6), while the HF component reflects vagal activity on the heart together with nonneural changes, which follow inspiration induced increases in venous return (7, 8), and LF/HF ratio suggests sympathovagal balance (6, 9).

The HRV analysis after HV shows increase in HF and decrease in the LF/HF ratio, indicating a parasympathetic dominance, which may also favor faster reaction times, as reported in the literature.

During hyperventilation, an increase in the reaction times was seen, and this could be due to the distraction caused by HV itself, and also due to an increase in, LF, LF/HF ratio and decreased HF, which signifies sympathetic predominance, which may delay the reaction times.

In contrary to the present study, Brown et al showed increased respiratory rate has been linked to a reduction in LF and HF power which could be due to different breathing frequencies and depths which distribute vagal firing within the respiratory cycle but do not alter the net level of vagal outflow (27).

Similar to present study, Guzik et al reported increased HF and reduced LF power with increased breathing rate has also been reported (28), Pal GK et al (29) reported that fast breathing exercise increased sympathetic tone and decreased parasympathetic tone in healthy adults.

Metronome-guided (paced) breathing appears to result in increased HF and reduced LF power compared with spontaneous breathing in some (30, 31), but not all (32) studies. In addition, paced breathing may (30, 33) or may not (34, 35) increase HRV analysis reproducibility.

The effects of present study i.e., shift of sympathovagal balance towards sympathetic side during hyperventilation could be due to a well known concept of pulmonary stretch receptor inputs and chemoreceptor inputs feed back to the medullary respiratory centres (36). It may be postulated that during the deep breathing exercise these two inputs get exaggerated due to the increased tidal volume and the larger than normal oscillations in the arterial PO_2 and PCO_2, leading to entrainment of the central respiratory neurons and a re- setting of the respiratory rhythm. Similarly, the mechanisms producing sinus arrhythmia would have been operating at an exaggerated level during the deep breathing exercises. This would have resulted in increased modulation of the cardiac autonomic tones leading to increased HRV (37).

So after an episode of hyperventilation HRV analysis showed decrease in the LF/HF ratio, indicating a parasympathetic dominance, which also favors faster reaction time as reported in the literature.

Limitations of the study

Smaller sample size, limited age group, uncontrolled HV are some of the limitations of the study.

Conclusion

It can be concluded that increased cortical excitability in the form of faster reaction times; and a shift towards parasympathetic dominance in HRV may be achieved by hyperventilation. This could be utilized in improving the performance / skills of the subjects/students. It should also be borne in mind during extreme physiological conditions and also certain pathological states.

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