The Effect of Varied Temperatures at Different Times of The Day On The Duration of Voluntary Apnea In Healthy Young Male Adult Subjects

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Abstract
Background/Objective: Apnea is the temporary stoppage of breathing, most often in reference to transient blockage of atmospheric oxygen. Apnea during temperature change has been linked to a number of disorders including hypertension, stroke, arrhythmias, cardiomyopathy, heart failure, diabetes, obesity and heart attacks. This study was aimed at investigating the effect of varied temperature at different times of the day on the duration of voluntary apnea in healthy young male subjects. **Materials and Methods:** A total of 60 apparently healthy young male subjects with a mean age of 23 ± 1 years, body weight of 63.2 ± 1.8 kg, and height of 169.9 ± 1.8cm who were non-smokers and not on any medication were recruited for this study. Informed consent was obtained from each participant after proper notification and information on the nature of the research, risk involved, benefits as well as confidentiality. The experimental period lasted for 4 weeks after which the data was analyzed. Measurements were recorded in the morning, afternoon and night. **Results:** Voluntary apnea in the morning 26.70 ± 1.30, was significantly (p=0.016) higher when compared to the afternoon period 22.43 ± 1.16. It was also observed that voluntary apnea was significantly (p=0.020) higher in the night 26.82 ± 1.44, when compared to the afternoon 22.43 ± 1.16. These results clearly show that the duration of voluntary apnea increases when temperature falls in the morning and night times of the day. This knowledge may be useful in the management of patients with sleep apnea.

Keywords: Voluntary apnea, Environmental temperature, Breathing, Oxygen, Times of the Day.

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Introduction

Apnea is defined as a temporary cessation of gas exchange between the lungs and the atmosphere (1). Apnea can be involuntary for example, drug-induced such as by opiate toxicity (2) or a consequence of neurological disease or trauma as seen in sleep apnea, in which the most prominent subtype is obstructive sleep apnea (3). Apnea can also be voluntary and this is called Voluntary apnea, also known as breath holding. The physiology of breath-holding is complex, and voluntary breath-hold duration varies from subject to subject and is affected by many factors, including practice, psychology, respiratory chemo-reflexes, and lung stretch (4). When a voluntary apnea is initiated, it begins with a phase without respiratory movements and with no subjective urge to breathe, this is also called the "easy going phase" (EP) (5); but when partial pressure for carbon dioxide ($PaCO_2$) rises, the onset of involuntary breathing movements (physiological break-point) is triggered, where the drive-to-breath is no longer suppressed and diaphragmatic contractions unconsciously occur. Both phases occur prior to the resumption of breathing (volitional break-point), where the individual is no longer able to volitionally maintain a closed airway (6, 4). During voluntary apnea, a series of cardiovascular reflexes collectively called the "diving response" is initiated to prevent hypoxia of oxygen-dependent organs. This response, is protective during voluntary apneas in healthy humans, and includes conservations of oxygen (O_2) and prevention of the development of hypoxia, leading to prolonged apneas (7) or less arterial desaturation in a given apneic time (8). The mechanisms responsible for oxygen conservation are both vasoconstriction, directing the blood mainly to the brain and heart, while other organs may rely on anaerobic metabolism (9) and the reduced work of the myocardium during bradycardia with subsequent reduction in its metabolism (10).

Thermoregulation is a mechanism by which mammals maintain body temperature with tightly controlled self-regulation independent of external temperatures. Human beings have a normal core internal temperature of around 37 degrees Celsius (98.6 degrees Fahrenheit) measured most accurately via a rectal probe thermometer. This is the optimal temperature at which the human body's systems function (11). A healthy body copes with both moderately high and low environmental temperatures by sensing changing skin and core temperatures. For example, the heat in a warm environment triggers blood vessel vasodilation, an increase in the rate at which blood is pumped (cardiac output), and sweating. This brings heat to the body's surface to dissipate, in part by sweat evaporation and ultimately causes a drop in warm temperatures (13). On the other hand, exposure to cold temperatures causes vasoconstriction to slow down the transfer of heat to the body's surface (12), in other to conserve heat for the body. When behavioural adaptations, such as moving to warm locations or wearing more clothing, have failed and core temperature drops, shivering initiates to generate heat. As the core temperature drops further, hypothermia occurs and may involve confusion and drowsiness (13). Cold temperatures have been associated with exacerbation of respiratory conditions, including chronic obstructive pulmonary disease and asthma (14). Studies have shown that the apnea-hypopnea index during obstructive sleep apnea was higher in a cold temperature, because a low room temperature could have an influence on the nasal and pharyngeal mucosa of patients with obstructive sleep apnea and therefore lead to increased neuropathy in the upper airway (15). This study compared the effect of varied temperatures at different periods of the day on the duration of voluntary apnea in healthy young male adult subjects.

Materials and Methods

Ethics Statement: Informed consent was obtained from each participant after proper notification and information on the nature of the research, risk involved, benefits as well as confidentiality. The experiment was performed according to the University of Benin Research Ethics protocol.

Study Area and Subject Recruitment: This research was conducted in Benin City, Edo State, Nigeria.

Inclusion Criteria: All of the participants were healthy non-smokers not on any medication and history of pulmonary or cardiac disease. Also, participants were able to exercise without discomfort, and reported no pulmonary defect by X-ray or physical examination.

Exclusion Criteria: Subjects with known medical history, drug addiction, smokers and persons with recent thoraco-abdominal surgery were excluded from this study.

Study Population: A total of 60 young subjects were recruited for this study with a mean age of 23 ± 1 years, body weight of 63.2 ± 1.8 kg, and height of 169.9 ± 1.8 cm. All participants were instructed to refrain from caffeine and alcohol for at least 24 hours before the study. The voluntary breath-holding duration was assessed three times, with 10-min intervals of normal resting breathing.

Temperature measurement: The temperature of subjects was measured in three different periods of the day, in order to capture different environmental temperatures associated with these periods of the day as follows: Period A: morning temperature between 8am – 10am. Period B: Afternoon temperature between 12pm - 2pm. Period C: Night period between 8pm – 10pm. The temperature was recorded using manual and digital thermometers. The subjects were allowed to hold their breath, which was timed to determine the duration with a stop watch.

Statistical Analysis: Data were subjected to statistical analysis using the IBM SPSS statistics software (Statistical Package for Social Sciences) (Version 25) and relevant statistical values were obtained. One-way analysis of variance (ANOVA) was carried out and all results were presented as means ± SEM (standard error of means). P values less than 0.05 ($p<0.05$) were considered statistically significant.

Results

Table 1 shows the mean temperature across different time durations that is, morning, afternoon and night. It was observed that afternoon had the highest temperature (36.61 ± 0.08) followed closely by night (35.88 ± 0.11). The lowest temperature was in the morning (35.67 ± 0.10).

Table 2-4 shows the effect of varied temperatures on Voluntary apnea. Voluntary apnea in the morning (26.70 ± 1.30) was significantly ($p=0.016$; Table 2) higher when compared to the afternoon period (22.43 ± 1.16). It was also observed that voluntary apnea was significantly (0.020; Table 3) higher in the night (26.82 ± 1.44) when compared to the afternoon (22.43 ± 1.16). There was no significant difference between the voluntary apnea in the morning and night (Table 4).

Table 1: Temperatures across different time durations

Morning (ºC)	Afternoon (ºC)	Night (ºC)
35.67 ± 0.10	36.61 ± 0.08	35.88 ± 0.11

Values are shown in mean±SEM, $p<0.05$ was considered significant

Table 2: Differences observed in Voluntary Apnea between Morning and Afternoon Participants

Variable	Morning	Afternoon	Test statistics	p-value
Voluntary Apnea	26.70 ± 1.30	22.70 ± 1.24	-2.446	0.016

Values are shown in mean±SEM, p<0.05 was considered significant

Table 3: Differences observed in Voluntary Apnea between Afternoon and Night Participants

Variable	Afternoon	Night	Test statistics	p value
Voluntary Apnea	22.70 ± 1.16	26.82 ± 1.44	-2.371	0.020

Values are shown in mean±SEM, p<0.05 was considered significant

Table 4: Differences observed in Voluntary Apnea between Morning and Night Participants

Variable	Morning	Night	Test statistics	p value
Voluntary Apnea	26.70 ± 1.30	26.82 ± 1.44	-0.066	0.947

Values are shown in mean±SEM

Discussion

During a temporary stoppage of breathing or apnea, the continuation of metabolic activities causes gradual changes in alveolar gases that result in the rise of carbon dioxide and a fall in oxygen. These gases ultimately become unique stressors, eliciting incremental hypoxia, hypercapnia, and sympathetic nervous system activation (16). These concomitant blood gas chemostimuli accumulate at the metabolic rate, to stimulate both central and peripheral chemoreceptors, which continuously increases the drive to breathe and likely reduces the duration of voluntary apnea (17). The incremental increase in CO_2 during voluntary apnea likely stimulates the central respiratory chemoreceptors, increasing the drive to breathe and likely shortening the duration of voluntary apnea (18). The associated hypercapnia during the period of voluntary apnea also plays a role in stimulating peripheral chemoreceptors, especially as oxygen levels decrease during apnea, because the peripheral chemoreceptors have been established to detect changes in oxygen (19).

Results from this study showed that there was a significant decrease in the duration of mean voluntary apnea in the afternoon subjects compared to the morning subjects. This difference may be the direct result of the variation in temperature between the morning and afternoon periods. Temperature has been established to increase with increasing day light and the physical and body composition of an individual will ultimately determine the physiological vitals at any given time (20). As the temperature increases, oxygen needed by vital organs increases and subsequently this decreases the duration of voluntary apnea. It has been known since early in the 20th century that a rise in temperature is associated with an increase in metabolic rate, such that each degree rise in temperature is associated with a 10–13% increment in oxygen consumption. This elevation in temperature itself is responsible for speeding up metabolism (21). Haugen *et al.,* found that the resting metabolic rate was 6% higher at noon than in the morning hours (22). The most important byproduct of metabolism that triggers the breaking point for voluntary apnea is CO_2 (21). Furthermore, it is believed that during normal sleep the metabolic rate reduces by around 15% and reaches a minimum in the morning in a standard circadian pattern (23). There are also some evidences to support that total energy expenditure follows a circadian rhythm, as observed in constant routine studies suggesting that the human body burns fewer calories during the

biological night (24, 25). The points highlighted above contribute to lower production of carbon dioxide and slow generation of hypoxia in the morning time compared to the afternoon. Thus, the slow generation of CO_2 ensures that the duration of apnea is increased in the morning. But when the metabolic rate increases, due to an increase in temperature as seen in the afternoon, there is an increase in metabolic activities in the body resulting in a shorter duration of voluntary apnea as observed in this study, as more CO_2 will be built up faster in the body and subsequently recruited to produce hydrogen ions (H^+) and more O_2 is consumed faster by body cells for the chemical reaction during metabolism leading to hypoxia. Both chemicals (that is the CO_2 and H^+) and hypoxia stimulates the peripheral receptors and central chemoreceptors, from where impulses are sent to the medullary respiratory centres (26), triggering the breaking point phase of voluntary apnea, by overriding the cerebral cortex which is the centre for voluntary breath control and signalling the diaphragm and external intercostal muscles to initiate respiration (17, 27). This relationship between the duration of voluntary apnea and metabolic rate is in line with the works of Nikita and Igor, 2017 (28).

There was no statistical difference when voluntary apnea was studied in the morning participants and compared to the night participants. This could be because the morning and night temperature does not differ significantly. Hence, the metabolic rate may have followed a slightly similar pattern, which involves a mechanism of reducing the rate of utilization of O_2 and lowering the production of CO_2.

There was a significant difference observed when the duration of voluntary apnea was studied in the afternoon participants compared to the night participants. This difference could be due to a decrease in the state of alertness in preparation for sleepiness which can be stimulated by a decrease in the environmental temperature associated with night time, a deviation from the higher afternoon temperature. There is clear data to support the fact that temperature is colder at night and body temperature drops before and during sleep at night time, due to the flow of cold air (29). It has also been observed that in the cooler night hours of the day when the body prepares for sleep, there is dilation of blood vessels in the skin to facilitate heat loss, in order to produce the signal for the onset of sleep, this ultimately results in a decrease in core body temperature. Once core body temperature drops to produce sleep onset, it remains low throughout the night and rises again shortly before awakening (30). Again, this fall in night time temperature may result in reduced chemosensitivity of the Peripheral and central chemoreceptors which is known to occur during the night hours (31, 32), as a result of the fall in body temperature, an effect observed in a study by Bosco *et al.,* (33) in preparation of the body for sleep. It is well documented that ventilatory and central sensitivity to CO_2 is proportional to the temperature. Thus sensitivity by peripheral and central chemoreceptors decreases with decreasing temperature (34, 35), this effect may have reduced the ability of these receptors to effectively detect the presence of CO_2, H^+ and hypoxia in the body, resulting in a slower response of receptors and increased duration of voluntary apnea. This statement is supported by the study of Santin *et al.*, which concluded that cooling reduced chemosensitive responses of locus coeruleus (chemoreceptive brain stem region in anuran amphibians that contains neurons sensitive to physiological changes in $C0_2$/pH) neurons as temperature decreased until the elimination of CO_2/pH sensitivity at 10°C, while warming which increases the temperature as seen in the afternoon would increase, normocapnic firing rates of locus coeruleus neurons (34). A similar study in cats by Paintal, showed that reduction of metabolism by lowering the temperature greatly slowed the development of

excitation of aortic chemoreceptors and pulmonary stretch receptors after circulatory arrest, and reduced the excitatory effect of hypoxia (35).

In conclusion, this study showed that there was a significant increase in the duration of voluntary apnea in the morning subjects compared to the afternoon subjects and night subjects compared to the afternoon subjects. This effect of varied temperature on the duration of apnea in the morning may be due to the decrease in metabolism associated with a low temperature in the morning time, which results in low production of CO_2, slower utilization of O_2 and slower attainment of a hypoxic state. The increased duration of apnea at night in comparison to afternoon, may be the result of decreased sensitivity of the peripheral and chemoreceptors triggered by low body temperature, which is a direct effect of a fall in environmental temperature observed at night. These findings demonstrate that the duration of voluntary apnea increases with a decrease in environmental temperature associated with the morning and night times of the day. This knowledge may be useful in the management of patients with sleep apnea.

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