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Original Research Article

Correlation between pupillary size and heart rate variability parameters among medical students

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ABSTRACT

Background: Autonomic nervous system controls and balances sympathetic and parasympathetic system to maintain homeostasis without conscious control. The sympathetic nervous system controls the dilation of the pupil or mydriasis. HR variation (HRV) analysis is a popular non-invasive tool for assessing functions of autonomic nervous system. Medical students are under constant cognitive load, it is required to follow-up on status on their autonomic control during their education phase. The objective of this study was to observe any correlation between pupillary size and heart rate.
Materials and Methods: Total of 30 students participated in the study. Anthropometric measurements and vitals like pulse, blood pressure was recorded. Pupillary size of the participants was measured using the pupillometer in the illuminated. HRV recording was done by placing electrodes for standard Lead II ECG. HRV reports were generated using Kubios HRV 3.5 software standard version.
Results: The pupillary size Right and Left are negatively correlated with the SDNN, RMSSD, PNN50, HF, SDI and SD2. However, LF, LF/HF and SD2/SD1 ratio are positively correlated.
Conclusion: These findings support the notion that pupillary size can serve as a non-invasive indicator of autonomic nervous system activity.

1. Introduction

Autonomic nervous system is central to maintaining homeostasis in a human body. It consists of sympathetic nervous system also known as "fight or flight" response and parasympathetic system known as "rest and digest".[1] Essentially autonomic nervous system controls and balances sympathetic and parasympathetic system to maintain homeostasis without conscious control. Sympathetic nerve fibers originate in the thoracic and lumbar region and parasympathetic fibers are in cranial and sacral region of the spinal cord, which stimulate muscle fibers throughout the body.[2] The sympathetic nervous system controls the dilation or enlargement of the pupil, which is known as mydriasis. The primary receptor involved in sympathetic control of pupillary size is the alpha-1 adrenergic receptor. Stimulation of these receptors by norepinephrine (noradrenaline) causes the radial muscles of the iris (dilator pupillae) to contract, resulting in pupil dilation.[3]

The parasympathetic nervous system controls the constriction or narrowing of the pupil, known as miosis. The primary receptor involved in parasympathetic control of pupillary size is the muscarinic acetylcholine receptor, specifically the M3 subtype.[4] Stimulation of these receptors by acetylcholine causes the circular muscles of the iris (sphincter pupillae) to contract, leading to pupil constriction. If the sympathetic system predominated the pupil size increases allowing more light in the eye

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conversely dominance of parasympathetic system allows constriction of the pupillary muscle.[5]

HR variation (HRV) analysis (instantaneous HR against time axis) is a popular non-invasive tool for assessing functions of autonomic nervous system. It provides a means of observing the interplay between the sympathetic and parasympathetic nervous systems. Also, it is a reliable reflection of the many physiological factors modulating the normal rhythm of the heart.[6]

Since the medical students are under constant cognitive load, it is required to follow-up on status on their autonomic control during their education phase. Normally in young adult the HRV parameters doesn't change much on a temporary cognitive load.[7] But if this autonomic activity prolongs it could lead to chronic autonomic imbalancewhich is considered to be the cause of chronic diseases in the individual. Change in HRV parameters will be a good indicator of autonomic changes in the individual.[8]

HRV parameters are SDNN which indicates, RMSSD, PNN50, LF, HF, LF/HF ratio, SD1, SD2 which indicates the autonomic balance in an individual. Root Mean Square of Successive Differences (RMSSD) and HF (High frequency domain) and proportion of NN50 over all N-N intervals expressed as a percentage (pNN50) are highly associated with vagal tone, or vagus nerve activity, in short term HRV recordings.[9] Standard Deviation of the N-N intervals (SDNN) is used in long term recording indicating overall cardiovascular status in an individual. HF/LF ration is an indicator of sympathetic and parasympathetic balance.[10]

The objective of this study was to observe any correlation between pupillary size and heart rate.

2. Materials and Methods

This study was conducted over a span of four months in Xavier University School of Medicine, Aruba during summer spring 2023. All apparent health students were included in the study. Students with history of diabetes mellitus, Hypertension were excluded from the study. The participants were asked to avoid any food or drinks such as coffee for at least 2 hours to avoid any confounding variables. The procedure and purpose of the study was explained to the participants and written informed consent was obtained. The height and weight of the students were measured and vitals like pulse, blood pressure was measured. Pupillary size of the participants were measured using the pupillometer in the illuminated.

HRV recording was done by placing electrodes for standard Lead II ECG.

Ten minutes sitting ECG recording was done using the Audacity 3.2.7 software. Five minutes ECG was used to calculate the RR intervals and HRV reports were generated using Kubios HRV 3.5 software standard version. Time domain, Frequency domain and linear parameters were calculated from the participants data. Statistical analysis is done using Microsoft Excel 2021 version.

Table 1: Demographic parameters of study participants

Parameters	Average
Age (in years)	21 ± 3 years
Height (cm)	171.85 ± 9.09
Weight (kg)	77.76 ± 12.51
BMI (kg/m2)	26.18 ± 2.31
Systolic blood pressure (mm Hg)	128.83 ± 15.48
Diastolic blood pressure (mm Hg)	89.96 ± 11.81

Table 2:

Parameter	Mean	SD	Correlation (R)	Correlation (L)
Pupillary Size (mm) R	4.09	0.76		
Pupillary Size (mm) L	4.04	0.73		
SDNN	163.79	137.52	-0.31	-0.20
RMSSD	174.56	196.15	-0.27	-0.24
PNN50	35.82	24.69	-0.29	-0.19
LF	54.76	19.32	0.47	0.34
HF	44.92	19.22	-0.46	-0.33
LF/HF ratio	2.01	2.16	0.28	0.23
SD 1	123.58	138.83	-0.27	-0.18
SD 2	190.66	143.26	-0.32	-0.22
SD2/SD1	2.19	0.85	0.10	0.06

Each variable listed on the table explained and their significance.[1]

1. Both SNS and PNS activity contribute to SDNN.
2. The RMSSD reflects the beat-to-beat variance in HR and is the primary time-domain measure used to estimate the vagally mediated changes reflected in HRV.
3. The pNN50 is closely correlated with PNS activity.
4. LF power may be generated by the SNS while HF power is produced by the PNS. In this model, a low LF/HF ratio reflects parasympathetic dominance.
5. The standard deviation (hence SD) of the distance of each point from the y = x axis (SD1), specifies the ellipse's width. SD1 measures short-term HRV in ms and correlates with baroreflex sensitivity (BRS).
6. SD1 predicts diastolic BP, HR Max – HR Min, RMSSD, pNN50, SDNN, and power in the LF and HF bands, and total power during 5 min recordings.
7. SD2 measures short- and long-term HRV in ms(milli seconds) and correlates with LF power.
8. The ratio of SD1/SD2, which measures the unpredictability of the RR time series, is used to measure autonomic balance when the monitoring period is sufficiently long and there is sympathetic activation. SD1/SD2 is correlated with the LF/HF ratio.

The pupillary size Right and Left are negatively correlated with the SDNN, RMSSD, PNN50, HF, SDI and SD2. However, LF, LF/HF and SD2/SD1 ratio are positively correlated.

3. Discussion

In a study examining the relationship between pupillary size and various parameters of heart rate variability (HRV), several interesting correlations were observed.[11] We found that pupillary size, both in the right and left eye, showed a negative correlation with several HRV measures, including SDNN (standard deviation of NN intervals), RMSSD (root mean square of successive differences), PNN50 (percentage of successive NN intervals differing by more than 50 ms), HF (high frequency power), SDI (SD1 index), and SD2 (SD2 index).[12] On the other hand, there were positive correlations between pupillary size and LF (low frequency power), LF/HF ratio (ratio of low frequency to high frequency power), and SD2/SD1 ratio.[13]

These findings suggest that pupillary size is influenced by the autonomic nervous system, which is reflected in the HRV measures. The negative correlation between pupillary size and SDNN, RMSSD, PNN50, HF, SDI, and SD2 indicates that as these HRV parameters increase, the pupillary size tends to decrease.[14] This suggests that increased parasympathetic activity, reflected by higher HRV measures, is associated with smaller pupil size. Conversely, the positive correlation between pupillary size and LF, LF/HF ratio, and SD2/SD1 ratio suggests that increased sympathetic activity, represented by higher LF power and LF/HF ratio, is associated with larger pupil size.[15]

4. Conclusion

These findings support the notion that pupillary size can serve as a non-invasive indicator of autonomic nervous system activity. The pupillary response is influenced by the balance between sympathetic and parasympathetic inputs to the iris muscles. The observed correlations between pupillary size and HRV measures provide further evidence of the connection between pupillary dynamics and autonomic regulation. Understanding the relationship between pupillary size and HRV parameters can have implications in various fields. For example, in the assessment of autonomic function or the monitoring of stress levels, pupillary size could serve as a useful indicator. Further research is warranted to explore the underlying mechanisms and potential clinical applications of these findings. Correlation value between pupillary size and LF can be used as the measurable parameter for sympathetic activity in an individual.

5. Source of Funding

None.

6. Conflict of Interest

None.

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