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AN ANALYSIS COMPARING THE VARIABILITY OF HEART RATE IN PATIENTS DIAGNOSED WITH SCHIZOPHRENIA AND MAJOR DEPRESSIVE DISORDER

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ABSTRACT:

Background: Heart rate variability (HRV) is a metric that quantifies the fluctuations in heart rate (HR) from one beat to the next, as measured using electrocardiography. It is widely regarded as a practical and non-invasive indicator of autonomic nervous system (ANS) function. Researchers have recorded abnormalities in the autonomic nervous system (ANS) and the consequent reduction in heart rate variability (HRV) in several psychiatric diseases. However, there is a significant deficiency in Indian literature when it comes to comparative examinations of these autonomic nervous system (ANS) and heart rate variability (HRV) anomalies in relation to mental health disorders.

Aim: This study is intended to fill the gap by examining and contrasting heart rate variability (HRV) in two cohorts: those diagnosed with schizophrenia and those with major depressive disorder (MDD).

Results: The mean age of the patients with schizophrenia was 36.3 (± 8.42) years; patients with depression was 39.9 (± 11.20) years; and healthy controls were 38.9 (± 9.09) years. The mean heart rate of the patients with schizophrenia was 90.2 (± 7.32) beats per minute (bpm); in patients with depression, it was 86.7 (± 12.33) bpm; and in healthy controls, it was 90.7 (± 10.22) bpm.

Conclusion: This study provides insight into the distinct HRV patterns linked to these particular psychiatric disorders, enhancing our comprehension of their fundamental physiological basis and potential implications for clinical treatment.

Key words: heart rate variability, major depressive disorder, schizophrenia, psychiatric.

INTRODUCTION:

The optimal heart rate variability (HRV) inside an organism signifies a robust physiological state and an inherent capacity to self-regulate, adjust, and promptly recuperate (1-2). To maintain this balance, the parasympathetic system needs to demonstrate a heightened level of awareness and

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respond swiftly to any alterations in the external or internal surroundings. The heart rate variability (HRV) can be used to measure this balance (3–4). Prior research has established a connection between reduced heart rate variability (HRV) and many factors that increase the risk of cardiovascular disease and psychophysiological stress (5-7).

Stress induces adverse feelings and an increased heart rate. Furthermore, it appears to exert a substantial influence on the fundamental mechanisms underlying the majority of psychiatric disorders. Individuals with schizophrenia exhibit cardiac autonomic dysregulation, resulting in deficits in affective and cognitive functioning (9) and decreased heart rate variability (10–11). Previous studies have indicated that some psychological characteristics can act as indications of the autonomic function's capacity to adjust and react to changes in the environment and psychological stress (12).

The presence of psychopathology and dysregulated unpleasant emotions is characterised by dysregulation in the autonomic nervous system and reduced heart rate variability (HRV) caused by increased sympathetic activity and decreased vagal tone (13). Research has investigated the correlation between heart rate variability (HRV) and psychological stress as a means of evaluating the autonomic function of individuals with mental and physical health conditions (12).

The aim of this study was to assess and compare the heart rate variability (HRV) parameters in people diagnosed with schizophrenia and those diagnosed with serious depression. The study also examined the use of HRV measurement as a quantitative indicator to differentiate between different psychiatric diseases.

MATERIAL AND METHODS:

Study design: A Cross-sectional study with 30 subjects in each group chosen by convenient sampling technique was taken up for a period of three months in the department of Physiology in collaboration with department of Psychiatry, at Government Medical College and Hospital, Ananthapuram, Andhra Pradesh, India.

Study tools: Hamilton Depression Rating Scale (HDRS) was used for Major Depressive disorder (A score of 0–7 is within the normal and score of 20 or higher (indicating at least moderate severity)

Brief psychiatric rating scale (BPRS) used for Schizophrenia (BPRS total score of 31, ‘moderately ill’ to a BPRS score of 41 and ‘markedly ill’ to a BPRS score of 53)

Materials: Spandan smartphone-based portable ECG device developed by Sunfox Technologies Pvt. Ltd-India was used for recording the lead II-based HRV test for duration of a minimum of 5 minutes, as recommended by the American Heart Association. Spandan ECG provides the HRV parameters in both the time domain and the frequency domain.

Inclusion Criteria: All patients fulfilled the criteria for Axis I diagnosis as outlined in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5). Healthy control participants were selected from the surrounding population, specifically relatives of patients and workers employed at Government Medical College, Anantapuramu.

Exclusion criteria: patients with a history of cardiovascular disease, neurological disorder, substance abuse, mental retardation, and brain trauma.

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Study Procedure: Following the explanation of the study's necessity and objectives, signed informed consent was obtained from all patients and healthy subjects. Demographic data was collected from both patients and healthy volunteers, and HRV measurements were taken after completing HDRS and BPRS assessment forms.HRV measures were obtained during the morning period for both patients and healthy individuals. Prior to measurement, smoking and coffee drinking were strictly forbidden for a minimum of 6 hours. Following a period of approximately 10 minutes, during which each participant was given the opportunity to adjust to the experimental settings. A portable ECG device was linked using a three-lead connection with electrodes placed on the right arm, left arm, and left foot of the subject in a seated position. This setup was used to record a 5-minute Lead II HRV.

RESULTS:

The mean age of the patients with schizophrenia was 36.3 (± 8.42) years, patients with depression was 39.9 (± 11.20) years and healthy controls was 38.9 (± 9.09) years. There is no significant difference in mean age between patients with schizophrenia, depression and healthy controls.

Proportion of males and females in schizophrenia group was 60% and 40% respectively, depression group was 46.7% and 53.3% respectively and healthy controls group was 60% and 40% respectively. Gender distribution of patients in schizophrenia, depression and healthy controls group was not significant statistically.

Median duration of illness of patients with schizophrenia was 6.0 years with interquartile range of 4.0 years to 8.0 years and patients with depression were 3.5 years with interquartile range of 2.0 years to 10.0 years. This difference in median duration of illness between schizophrenia and depression was not significant.

Mean BPRS score of patients with schizophrenia was 32.1 (± 6.10) and mean HDRS score of patients with depression was 12.5 (± 4.77)

Table 1: Comparison of patient information and disease characteristics

Variable	**Schizophrenia (N=30)**	**Depression (N=30)**	**Healthy Control (N=30)**	**p-value**
Age (Mean ± SD)	36.3 ± 8.42	39.9 ± 11.20	38.9 ± 9.09	0.338[#]; NS
Gender				
Male	18 (60%)	14 (46.7%)	18 (60%)	0.487[$]; NS
Female	12 (40%)	16 (53.3%)	12 (40%)	
Duration of disease (Median with IQR)	6.0(4.0 – 8.0)	3.5 (2.0 – 10.0)	-	0.077[€]; NS
BPRS score (Mean ± SD)	32.1 ± 6.10	-	-	-
HDRS score (Mean ± SD)	-	12.5 ± 4.77	-	-

SD = Standard deviation; IQR = Inter-quartile range; NS = Not Significant # = ANOVA test p-value; $ = Chi-square test p-value; € = Mann-Whitney U test p-value

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Table 2: Comparison of HRV items

Variable	Schizophrenia (N=30)	Depression (N=30)	Healthy Control (N=30)	p-value
HR (Mean ± SD)	90.8 ± 6.56	87.1 ± 12.27	91.5 ± 9.78	0.183; NS
LF (Mean ± SD)	439317 ± 174728	399095 ± 162604	553859 ± 189124	0.003¥; S
HF (Mean ± SD)	376478 ± 146808	356840 ± 105837	597599 ± 178305	<0.001¥; S
LF/HF (Mean ± SD)	1.18 ± 0.22	1.17 ± 0.41	0.93 ± 0.13	<0.001¥; S
SDANN (Median with IQR)	8.66 (7.74 – 11.9)	8.54 (5.92 – 14.3)	19.8 (14.9 – 29.6)	<0.001Q; S
SDNN (Mean ± SD)	17.2 ± 5.73	18.7 ± 9.45	33.4 ± 15.05	<0.001¥; S
RMSDNN (Median with IQR)	13.1 (8.27 – 22.8)	12.2 (7.87 – 26.2)	18.8 (16.2 – 34.1)	0.011Q; S

¥ = Tukey's post-hoc test shows significance exists between depression and healthy control group, and also between schizophrenia and healthy controls, but not between schizophrenia and depression

Q = Dwass-Steel-Critchlow-Fligner (DSCF) pairwise comparison after Kruskal-Wallis test shows significance exists between depression and healthy control group, and also between schizophrenia and healthy controls, but not between schizophrenia and depression

The mean heart rate of the patients with schizophrenia was 90.2 (± 7.32) bpm, in patients with depression was 86.7 (± 12.33) bpm and healthy controls was 90.7 (± 10.22) bpm. There is no significant difference in mean heart rate between patients with schizophrenia, depression and healthy controls. HRV parameters such as LF, HF, LF/HF, SDANN, SDNN and RMSDNN shows overall significant difference between schizophrenia, depression and healthy controls groups. On pair wise comparisons, LF and RMSDNN have significantly reduced only in patients with depression compared to healthy controls. But, HF, LF/HF, SDANN and SDNN have significantly reduced in both patients with schizophrenia and depression compared to healthy controls.

Time domain:

SDNN units -ms (Standard deviation of the normal R−R intervals (N−N intervals)

SDANN units -ms Standard deviation of R−R intervals in successive five-minutes.

RMSDNN units ms square root of the mean sum of squares of successive R−R differences ***(Used as index of vagal cardiac control***)

Frequency domain:

LF - ms2 Power of low-frequency range (0.04−0.15 Hz)

(Modulated by sympathetic activity of heart rate)

HF -ms2 Power of high-frequency range (0.15−0.4 Hz)

(A marker of vagal modulation)

LF/HF-ms2 Ratio of LF to HF ***(Reflects the global sympatho-vagal balance***

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DISCUSSION:

In the current study, we have investigated the difference in HRV parameters in patients suffering from schizophrenia, MDD, and normal healthy controls. Psychiatric illness, which occurs in the brain, is neither visible nor clearly understood. There is an intimate connection between the heart and the brain, and HRV is considered to indirectly reflect complex patterns of brain activation and provide information about the central nervous system's (CNS) functional organisation and bidirectional interaction between the CNS and the ANS.

HRV is known to be regulated by the prefrontal cortex region of the brain, which is pivotal in the regulation of ANS. HRV can be investigated as a promising physiological biomarker for psychiatric illnesses, with potential application in diagnosing and treating them (14). While the identification of psychiatric disorders is based on specific criteria established by the DSM V, there are still variations and uncertainty concerning the severity of the illness and its prognosis. Considering that supplementary data and detailed patient histories significantly influence a psychiatrist's evaluation of a patient's condition, incorporating additional objective measures like vital signs or laboratory values could assist a psychiatrist in both diagnosing patients and tailoring their treatment plans. Integrating HRV monitoring into existing standards can enhance the accuracy of forecasting psychiatric patients' prognoses and treatment outcomes.

Researchers have documented dysfunctions in the autonomic nervous system (ANS) and the resulting decrease in heart rate variability (HRV) across a spectrum of psychiatric disorders. The known physiology between the limbic system and the autonomic nervous system does suggest the possibility that the emotional symptoms and lowered HRV seen in psychiatric conditions may be due to limbic outputs as a common cause. If so, then limbic dysregulation may be responsible for the lowered HRV seen in mentally ill patients as well (Hum Brain Mapp 30:47–58, 2009).

This study compared the HRV of patients' psychiatric disorders (i.e., schizophrenia and MDD) with that of healthy controls. HF, which is a marker of vagal modulation, was significantly reduced in individuals with MDD compared with healthy controls. The present results are not consistent with the previous study of Moon E et al. (15). However, another study by Rush AJ et al. (16) reported that vagal nerve stimulation (VNS) successfully improves depressive symptoms in treatment-resistant depression, suggesting a strong relationship between sympatho-vagal dysregulation and depressive symptoms.

RMSDNN is supposedly related to parasympathetic activity and the index of vagal cardiac control, providing another measure of vagal tone. It was significantly reduced in patients with schizophrenia compared with healthy controls. The present results are consistent with previous studies by Bär et al. (5) and Valkonen-Korhonen et al. (17). Therefore, decreased RMSSD in patients with schizophrenia suggests that this disorder is characterised by dysfunctional parasympathetic activity.

Prospects for the future: Despite the obstacles, the HRV study has considerable potential for enhancing our comprehension of mental health issues. Future research should prioritise the development of more advanced HRV measures, the integration of HRV with other biomarkers and clinical assessments, and the evaluation of the effectiveness of HRV-based therapies in large-scale clinical trials.

Medical Uses: The examination of heart rate variability (HRV) has the capacity to profoundly transform the diagnosis and treatment of mental health conditions. It can aid in the identification,

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anticipation of treatment responses, and direction of tailored therapies. HRV biofeedback and other therapies that specifically address autonomic dysfunction may also enhance mental health results.

CONCLUSION:

The study deduced that psychiatric diseases, such as schizophrenia and MDD, had varying effects on HRV indices. Different HRV indices (LF, HF, LF/HF, SDANN, SDNN, and RMSDNN) were significantly lower in people with depression and schizophrenia compared to healthy controls. This shows that these conditions had a noticeable effect on these measures.

LIMITATIONS OF THIS STUDY:

Although HRV research has yielded promising outcomes, it is important to acknowledge many inherent constraints. These factors encompass measurement inaccuracy, individual characteristics, and confounding variables. Prudent deliberation of these constraints is crucial when interpreting HRV studies. The small sample size and inability to enroll an equal number of male and female participants in this study are its limitations. These limitations were unavoidable due to the voluntary nature of participation. Furthermore, smartphone-based HRV tests solely provide analysis in the time domain and frequency domain, without the capability to do non-linear complexity analysis. It is important to note that this device cannot serve as a substitute for a regular HRV device. Standardisation of HRV measurement and analysis is necessary to guarantee consistency and reliability across investigations.

CONFLICT OF INTEREST: NONE
FINANCIAL RESOURCES: NIL

AUTHOR CONTRIBUTIONS:

Dr. Ezra Paul and Dr. K. Sarala have conceptualised the study. Data was acquired by Dr. Ezra Paul, Dr.Varadarajulu Boya, Dr. Shahanka Vunnam, and Dr. Shaik Arif. The data was analysed by all the authors. The study was supervised by Dr. K. Sarala. The original manuscript was drafted, reviewed, and edited by all the authors.

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