Differential Analysis of Heart Rate Variability in School Going Adolescents: Comparing Healthy Individuals with Those Experiencing Depression and Anxiety

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ABSTRACT

Background

Adolescents often struggle with depression and anxiety, which can greatly affect their well-being and functioning. Early detection is crucial for timely intervention and long-term health.

Objective

The objective of this study is to compare heart rate variability between depressed and anxious adolescents and their healthy peers.

Method

In this cross-sectional study, adolescents aged between 13-18 years were randomly selected from various schools. Participants were assessed for depression and anxiety using the Revised Child Anxiety and Depression Scale-25 (RCADS-25). Heart Rate Variability was measured using Power lab, with recorded variables including Median normal to normal interval (NN), Standard deviation of the normal-to-normal interval (SDNN), Root Mean Square of the Successive Differences (RMSSD), Percentage of successive normal to normal interval differing by more than 50 milliseconds (pNN50), Low frequency power % (LF), High frequency power % (HF), and the LF:HF ratio.

Result

Reduction in certain time domain HRV parameters was observed among the subset of depressed students in Classes XI and XII, such as NN interval (p=0.019), SDNN (p=0.024), and RMSSD (p=0.034). Anxious adolescents showed a significant reduction in HRV compared to their healthy counterparts [(NN, p<.001), (SDNN, p=0.011), (RMSSD, p=0.017), (pNN50, p=0.016). Students with symptoms of both depression and anxiety demonstrated significantly reduced HRV parameters compared to the healthy group, affecting NN, (p<.001), SDNN, (p=0.003), RMSSD, (p<.001), pNN50, (p< .001), HFP %, (p< .001) and LF: HF (p=.005). This association was observed in both males and females.

Conclusion

Adolescents with depression and anxiety have lower HRV than their healthy peers. Monitoring HRV may help to objectively detect these conditions.

KEY WORDS

Adolescents, Anxiety, Depression, Heart rate variability

INTRODUCTION

Depression is a major public health concern and is projected to become the leading cause of global disease burden by 2030.[1] Between 2001 and 2010, the worldwide prevalence of elevated depressive symptoms among adolescents was 24% This figure increased to 37% between 2011 and 2020.[2] In India, approximately 5% of the population suffers from depression, and an additional 15% contends with various other mental health disorders.[3] Notably, a robust correlation exists between depression and suicide, encompassing ideation and attempts, underscoring the need for a focused research agenda to assess and prevent suicidal outcomes.[4]

Adolescence is a critical developmental phase, marked by substantial cognitive, emotional, and social transformations. In this context, understanding physiological markers related to mental health challenges is imperative. The interplay between depression, anxiety, and the autonomic nervous system highlights the importance of Heart Rate Variability (HRV) as a metric. Heart Rate Variability, indicating the variation in time intervals between heartbeats, reflects the balance between sympathetic and parasympathetic influences, with higher variability suggesting better adaptability and resilience. Studies have shown a reduction in HRV in both clinical and subclinical depression and anxiety.[5]

Inaccurate assessment of mental disorders hinders effective care.[3] Enhancing subjective diagnoses with objective evidence, such as HRV, could improve accuracy. Research indicates that depression in adults is preceded by a reduction in HF-HRV, but there is a gap in understanding this association in children and adolescents. Hence this gap can be filled by research in younger age group to study the pathway of its development.[5]

Investigating HRV in adolescents is crucial for understanding its pathophysiology during early developmental phases.[6] This study aims to bridge these gaps, exploring HRV's potential in monitoring mental health assessments among adolescents.

METHODS

This cross-sectional study was conducted in East Sikkim, India, from June 2021 to August 2023. The research took place in 5 randomly selected Higher Secondary schools out of 31 schools, by a lottery system.

The sample size was determined based on a previous study, which reported a 40% prevalence of depression in adolescents, with a relative error of 10%.[7] The study aimed to maintain a type 1 error rate of 5% (95% confidence interval). Accounting for an anticipated attrition rate of 10%, the calculated sample size was 660.

To ensure a representative sample, the total number of eligible students in each class, spanning from class VIII to Class XII in each of the chosen schools, were tallied. Following this, 25 students were randomly chosen from each class using a simple lottery method. Adapting the sampling strategy to rural schools with smaller student populations, we employed the probability proportional to size (PPS) technique by taking 25% of the total strength of each class to ensure that the selected students reflect the overall population size, thus preserving representativeness.

Both male and female students between 13-18 years of age, willing to participate in the study.

Absentees on HRV recording day, BMI > 30, smokers, students with cardiorespiratory diseases, hypothyroidism, hyperthyroidism, or on beta-blockers were reasons for exclusion from the study.

Depression and Anxiety Assessment Tool

The Revised Children's Anxiety and Depression Scale (RCADS-25) is a validated self-administered questionnaire consisting of 25 items in two subsets, assessing anxiety and depressive symptoms in children. Each item is rated on a 4-point Likert scale, and total scores indicate the severity of symptoms, converted to T-scores using gender- and grade-specific equations. T-scores categorize severity levels, with ≥ 65 indicating medium severity and > 70 representing high severity. Students with Depression scale scores ≥ 65 were categorized as depressed, excluding those with high anxiety scale scores to mitigate confounding. Similarly, those with high anxiety scores but < 65 on the Depression scale were classified as Anxious, and those scoring ≥ 65 on both scales were categorized as Depressed & Anxious. Questionnaires with more than 3 unanswered questions were excluded during analysis.

Revised Child Anxiety and Depression Scale-25 has acceptable reliability in school-based samples. It demonstrates very good internal consistency and good test-retest reliability.[8,9] The test retest stability of the RCADS-25 has been found to be acceptable with all intraclass correlation coefficient value of > 0.79.[10] It also has cross cultural validity.[11-14]

HRV Recording

Heart Rate Variability was recorded using an automated instrument, the MLS510/8 Power Lab (AD Instruments), and its paired software for Windows, MLU260/8 Lab Chart Pro V 8.

Recording was conducted in the school lab, classroom, or auditorium, provided by the school from 10:00 am to 12:00 noon. Guidelines of "Task Force for Pacing and Electrophysiology" were followed.[14] Participants were advised to refrain from drinking coffee the previous day. They were comfortably seated and metal jewelry, watches, and mobile phones were removed. Participants were instructed to relax and remain still during the recording

to minimize interference. Silence was maintained in the recording room. Skin cleanliness was ensured, and pre-gelled electrodes were securely fixed. ECG was recorded in a standard Lead-II configuration for 5 minutes using the Power lab Data acquisition system. Data was saved for offline analysis.

Heart Rate Variability module was used, and the recording was done at a range of 500uV, Low Pass 10 Hz, High Pass 10 Hz, with Mains filter and Anti-alias on. As ectopic beats can introduce irregularities in the NN interval, an automated setting for removing ectopic beats was applied. This helped to provide a consistent and reliable assessment of HRV and maintain the integrity of the analysis. In the HRV module, settings for beat detection and beat classifier spectrum was set between NN interval of 800 and 1200ms at a complexity of 1-1.5. Any beat beyond this spectrum was considered as artifact. R waves were sensed by a separately adjusted Histogram at a bin width of 10 ms, pNN threshold of 50ms and SDNN averaging at 300s.

The following indices were obtained from the recording:

Time domain indices: These include Median NN (normal to normal interval), SDNN (Standard deviation of the NN), that measures overall heart rate variability, RMSSD (square root of the mean squared difference of successive NNs) which reflects parasympathetic modulation of the autonomic system and pNN50 (Percentage of successive NN intervals differing by more than 50 milliseconds).

Frequency domain indices: These included Total power, Low frequency power % (LF band: 0.04-0.15 Hz), reflecting sympathetic function, High frequency power % (HF band: 0.15-0.45Hz) associated with the parasympathetic or vagal tone and the LF:HF ratio that shows the sympathovagal balance.

Questionnaires were filled by the students on the first day and HRV recordings were performed on the second and third days of school visits.

The study was approved by the Institutional Ethics Committee at Sikkim Manipal Institute of Medical Sciences. Permission was obtained from the authors of RCADS-25. Written informed consent was acquired from students aged 18 years, while consent from teachers and parents and assent from students was obtained for those below18 years, ensuring confidentiality and anonymity of the participants.

Demographic data were summarized using descriptive statistics. Normality was assessed with the Shapiro-Wilk test and histograms. Parametric independent t-test and non-parametric Wilcoxon test were used to compare healthy individuals to groups affected by depression, anxiety, or both. Parametric tests of comparison were used in subgroup analyses if the minimum group size was 30, following the Central Limit Theorem. A p-value ≤ 0.05 indicated significance, with a 95% confidence interval. Participants scoring 65 or above in Depression, Anxiety, or both on the RCADS assessment were considered affected. Analyses were stratified by gender and academic class. HRV parameters in both time and frequency domains were examined using SPSS software version 27.0.

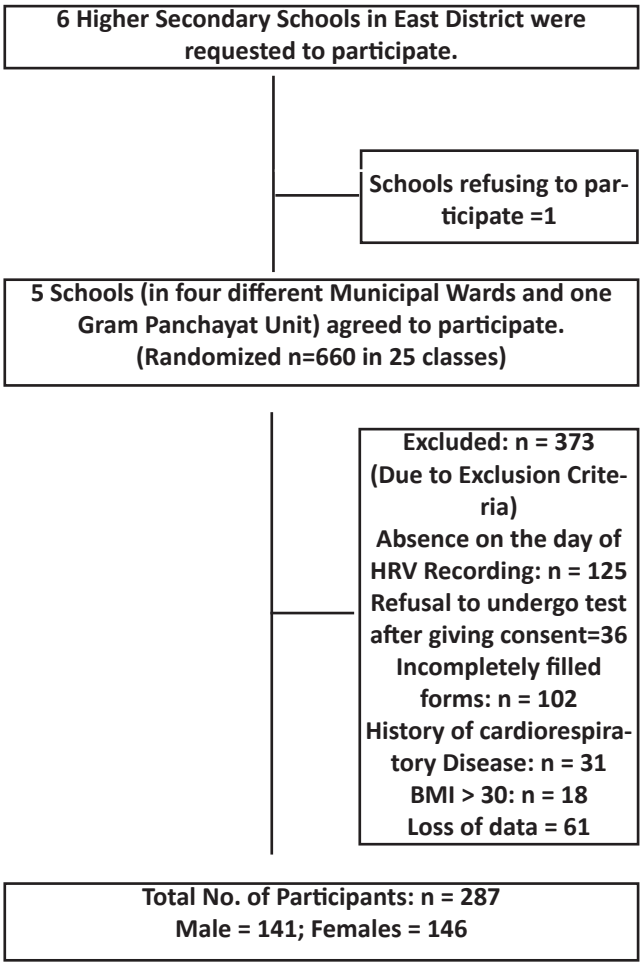

Figure 1. Flow of participants through the study period

RESULTS

A total of 660 students participated in the study, with only 287 undergoing HRV recording due to various exclusion criteria outlined in figure. 1. Among the participants, 145 (50.53%) were girls. The mean age of the total population was 15.4 years, with a standard deviation of ±1.8, as indicated in table 1. Of the 287 students, 25 exhibited solely depressive symptoms, 52 displayed only symptoms of anxiety, and 50 exhibited symptoms of both depression and anxiety, indicating a significant proportion experiencing the co-occurrence of depression and anxiety.

A significant difference in HRV was not achieved between the depressed and healthy subjects. However, upon conducting a more detailed analysis, it was observed that there was a statistically significant decrease in time domain HRV parameters, such as Median NN interval (p=0.019), SDNN (p=0.024), and RMSSD (p=0.034), among the subset of depressed students of Classes XI and XII, compared to their healthy counterparts (Table 2).

Table 1. Descriptives of demographic data of the participants

		Total (n= 287)	Male (n=142)	Female (n=145)	p
		(Mean ± SD)			
Age (years)	Class VIII (n=49)	13.57 ± 1.34	13.22 ± 0.94	13.77 ± 1.20	0.102
	Class IX (n=63)	14.54 ± 1.32	14.69 ± 1.59	14.37 ± 0.93	0.324
	Class X (n=83)	15.52 ± 1.24	15.48 ± 1.39	15.42 ± 1.11	0.624
	Class XI (n=34)	16.47 ± 0.66	16.52 ± 0.68	16.39 ± 0.65	0.560
	Class XII (n=58)	17.50 ± 1.14	17.68 ± 0.98	17.29 ± 1.29	0.208
	Total	15.48 ± 1.76	15.67 ± 1.87	15.29 ± 1.64	0.069
Height (cms)	160.72 ± 10.22	160.72 ± 10.22	166.97 ± 7.79	154.59 ± 8.47	<0.001
Weight (kg)	50.65 ± 9.52	50.65 ± 9.52	53.96 ± 9.96	47.41 ± 7.86	<0.001
Body Mass Index (kg/m^2)	19.60 ± 3.19	19.60 ± 3.19	19.31 ± 3.04	19.89 ± 3.32	0.124
		n (% of total population)			
Grade	Class VIII to Class X	195 (67.94)	90 (63.38)	105 (72.41)	
	Class XI to Class XII	92 (32.05)	52 (36.61)	40 (27.58)	
De-pressed	Class VIII to X	15 (5.23)	4 (2.81)	11 (7.58)	
	Class XI to XII	10 (3.48)	7 (4.92)	3 (2.1)	
Anxious	Class VIII to IX	33 (11.49)	20 (14.08)	13 (8.96)	
	Class XI to XII	19 (6.62)	10 (7.04)	9 (6.20)	
De-pressed as well as Anxious	Class VIII to X	30 (10.45)	12 (8.45)	18 (12.41)	
	Class XI to XII	20 (6.96)	4 (2.81)	16 (11.03)	

In anxious adolescents, there was a significant reduction in time domain HRV parameters [(NN, p<0.001), (SDNN, p=0.011), (RMSSD, p=0.017), (pNN50, p=0.016)] compared to their healthy counterparts (Table 3). Nearly all HRV parameters were significantly reduced in students exhibiting symptoms of both depression and anxiety compared to the healthy group [(NN, p<0.001), (SDNN, p=0.003), (RMSSD, p<0.001), (pNN50, p<0.001), (HFP%, p<0.001), (LF: HF, p=0.005)] (Table 4).

The total sample was further stratified by gender, and an analysis was conducted. The results revealed that both time and frequency domain indices were diminished in males experiencing both depression and anxiety [(NN, p<0.001), (SDNN, p=0.009), (RMSSD, p=<0.001), (pNN50, p=0.001), (HFP%, p=0.006), (LF: HF, p=0.016)] compared to healthy males (Table 5). However, in females, a reduction was observed only in time domain indices [(NN, p<.001),

Table 2. Comparison of Heart Rate Variability parameters between healthy and depressed students in class XI & XII class

Parameters	Healthy (n=45)	Pure Depression (n=10)	z	p
NN	775.10 (721.20 - 847.60)	687.10 (618.42-747.95)	-2.342	0.019
SDNN	82.79 (62.85 -218.50)	58.87 (40.25-112.07)	-2.251	0.024
RMSSD	79.54 (51.95 -323.00)	39.24 (25.55-144.20)	-2.114	0.034
PNN50	44.09 (24.53 - 87.23)	15.44 (5.69-85.02)	-1.819	0.069
TP	5942.00 (3653.00 - 61500.00)	3085.50 (2048.00-24667.25)	-1.773	0.076
HFP (%)	40.17 (24.51 - 59.10)	29.60 (18.59-53.21)	-1.387	0.166
LFP (%)	26.92 (22.02 - 37.70)	28.32 (24.51-42.22)	-0.557	0.578
LF: HF	0.65 (0.43 - 1.40)	1.09 (0.49-1.89)	-1.239	0.215

Note: all values are in median and inter-quartile range unless stated otherwise; NN (normal to normal interval), SDNN (Standard deviation of the NN interval), RMSSD (square root of the mean squared difference of successive NNs), pnn50 (Percentage of successive NN differing by more than 50 milliseconds), HFP (High frequency power), LFP (Low frequency power).

Table 3. Comparison of Heart Rate Variability parameters between healthy and anxious students from all classes

Parameters	Healthy (n=160)	Anxious (n=52)	U	p
NN	745.80 (683.55 - 816.50)	684.85(630.37-722.35)	-4.74	<0.001
SD NN	61.24 (42.25 - 79.61)	49.20 (38.04-66.85)	-2.53	0.011
RMSSD	50.53 (33.93 - 77.05)	39.09 (30.31-63.01)	-2.38	0.017
pNN50	27.30 (10.88 - 49.73)	13.92 (7.98-30.59)	-2.41	0.016
TP	3652.00 (1767.00 - 5942.00)	2477 (1270.25-6421.50)	-1.48	0.137
HFP (%)	37.13 (24.69 - 54.72)	31.37 (21.96-52.52)	-1.13	0.258
LFP (%)	30.61 (23.67 - 40.62)	33.89 (24.35-44.95)	-1.13	0.257
LF: HF	0.92 (0.47 - 1.53)	1.23 (0.45-1.99)	-1.34	0.180

Note: all values are in median and inter-quartile range unless stated otherwise; NN (normal to normal interval), SDNN (Standard deviation of the NN interval), RMSSD (square root of the mean squared difference of successive NNs), pnn50 (Percentage of uccessive NN differing by more than 50 milliseconds), HFP (High frequency power), LFP (Low frequency power).

(RMSSD, p=.003), (pNN50, p=.001), (HFP%, p=0.019)] compared to healthy females (Table 6).

DISCUSSION

The main aim of this study was to investigate potential associations between depression and HRV, as well as between anxiety and HRV, among adolescents attending

Table 4. Comparison of Heart Rate Variability parameters between healthy and both depressed and anxious students from all classes

Parameters	Healthy (n=160)	Depressed and Anxious (n=50)	U	p
NN	745.80 (683.55 - 816.50)	632.20 (573.63 - 691.28)	-6.551	<0.001
SDNN	61.24 (42.25 - 79.61)	45.95 (36.27 - 65.09)	-2.969	0.003
RMSSD	50.53 (33.93 - 77.05)	30.60 (20.41 - 47.31)	-4.783	<0.001
pNN50	27.30 (10.88 - 49.73)	9.90 (1.31 - 25.05)	-4.661	<0.001
TP	3652.00 (1767.00 - 5942.00)	2200.50 (1428.75 - 4322.50)	-2.275	0.023
HFP (%)	37.13 (24.69 - 54.72)	28.06 (17.13 - 38.82)	-3.308	<0.001
LFP (%)	30.61 (23.67 - 40.62)	23.82 (33.51 - 46.09)	-.967	0.334
LF: HF	0.92 (0.47 - 1.53)	0.83 (1.10 - 2.38)	-2.784	0.005

Note: all values are in median and inter-quartile range unless stated otherwise; NN (normal to normal interval), SDNN (Standard deviation of the NN interval), RMSSD (square root of the mean squared difference of successive NNs), pNN50 (Percentage of successive NN differing by more than 50 milliseconds), HFP (High frequency power), LFP (Low frequency power).

Table 5. Comparison of Heart Rate Variability parameters between healthy and both depressed and anxious male students from all classes

Parameters	Healthy (n=85)	Depressed and Anxious (n=16)	U	p
NN	756.90 (697.45 - 843.85)	647.40 (598.45 - 717.95)	-3.93	<0.001
SDNN	66.58 (49.66 - 91.39)	46.68 (37.69 - 65.25)	-2.62	0.009
RMSSD	54.61 (37.23 - 88.45)	30.04 (24.25 - 43.07)	-3.61	<0.001
Pnn50	27.42 (13.92 - 49.73)	8.67 (3.46 - 23.79)	-3.27	0.001
TP	3937.00 (2186.50 - 9338.00)	2080.50 (1492.00 - 4363.50)	-2.23	0.026
HFP (%)	35.42 (23.58 - 54.43)	20.22 (14.47 - 35.55)	-2.74	0.006
LFP (%)	30.77 (22.71 - 41.70)	32.99 (23.41 - 46.62)	-0.44	0.662
LF: HF	0.95 (0.49 - 1.61)	1.99 (0.79 - 2.86)	-2.4	0.016

Note: all values are in median and inter-quartile range unless stated otherwise; NN (normal to normal interval), SDNN (Standard deviation of the NN interval), RMSSD (square root of the mean squared difference of successive NNs), pNN50 (Percentage of successive NN differing by more than 50 milliseconds), HFP (High frequency power), LFP (Low frequency power).

school. In this study, there was a notable reduction in HRV parameters in students experiencing depression and anxiety as compared to their healthy counterparts.

Chalmers et al. and Koch et al. conducted a meta-analyses and reported that adults with depressive disorders

Table 6. Comparison of heart variability parameters between healthy and both depressed and anxious female students from all classes

Parameters	Healthy (n=75)	Depression & Anxious (n=34)	U	p
NN	728.60 (652.00 - 786.70)	616.70 (547.90 - 685.05)	-4.804	<0.001
SDNN	56.60 (36.98 - 70.08)	44.13 (32.47 - 65.16)	-1.210	0.226
RMSSD	48.16 (30.25 - 70.70)	31.29 (20.41 - 50.11)	-2.956	0.003
pNN50	27.18 (8.23 - 49.73)	11.26 (1.14 - 31.47)	-3.195	0.001
TP	2797.50 (1460.75 - 4831.50)	2279.50 (1282.25 - 4586.25)	-0.625	0.532
HFP (%)	38.71 (28.68 - 55.02)	32.78 (21.11 - 40.15)	-2.348	0.019
LFP (%)	30.21 (23.93 - 38.35)	33.69 (23.82 - 45.05)	-0.958	0.338
LF: HF	1.91 (0.45 - 1.39)	0.96 (0.83 - 2.32)	-1.891	0.059

Note: all values are in median and inter-quartile range unless stated otherwise; NN (normal to normal interval), SDNN (Standard deviation of the NN interval), RMSSD (square root of the mean squared difference of successive NNs), pnn50 (Percentage of successive NN differing by more than 50 milliseconds), HFP (High frequency power), LFP (Low frequency power).

exhibited a reduction in both Low-Frequency (LF) and High-Frequency (HF) components, along with an increased LF:HF ratio when compared to healthy controls.[15,16] Additionally,. Koenig et al. observed a decrease in RMSSD and SDNN in individuals with depressive disorders.[5] Vân der Kooy et al. reported a similar finding in elderly individuals with depression.[17] The study emphasized a similar relation irrespective of age. Jans et al. suggested a relationship between depression and changes in autonomic cardiac regulation, potentially affecting minors.[18] Blooda et al. found a negative association between frequency domain parameters of HRV and depression in adolescents.[19] However, it is important to note that not all studies support this observation. Yeragani et al. found no significant disparities in HRV indices between individuals with depressive disorders and control groups.[20]

In our study, although the mean values of both time and frequency domain parameters exhibited a reduction in the depressed group, statistical significance was not attained. This lack of significance could be attributed to the relatively small sample size within the depressed group, consisting of only 25 students who met the criteria for pure depression without concurrent symptoms of anxiety, aligning with the prevalence rates.

However, upon conducting a more detailed analysis, we sought to determine if the alterations in HRV were statistically significant within specific age groups. This exploration showed a notable and statistically significant decrease in time domain HRV parameters such as Median NN, SDNN, and RMSSD among depressed children in Classes

XI and XII, in comparison to their healthy counterparts. Despite the relatively small number of depressed students in this subgroup (n=10), the findings may indicate a significant association between HRV and depression that becomes more pronounced with increasing age.

Among participants exhibiting symptoms of anxiety, numerous studies have consistently reported reduced HRV in comparison to healthy controls and Cheng et al. in their systematic review and meta-analysis, reported a significant decrease in HRV among individuals with anxiety disorders, with an effect size of 0.39, when compared to healthy individuals.[21,22] Moreover, a study conducted by Theyer et al. also identified a similar finding in participants experiencing anxiety.[23] Numerous studies have demonstrated a negative association between various HRV parameters and anxiety across different anxiety disorders.[24-27]

Heart Rate Variability Biofeedback (HRVB) training has emerged as a promising treatment option for various mental health disorders. Kees et al. provides substantial evidence in supporting the association of vagal dysregulation with mental health disorders such as depression and anxiety.[28]

Our study, focused on adolescent participants, found significant reductions in time domain HRV parameters (NN, SDNN, RMSSD, pnn50) among anxious adolescents compared to healthy peers, aligning with previous findings in adult populations. However, no significant differences were observed in frequency domain parameters. This contrasts with some studies, such as Hammel et al., which did not identify associations in HRV parameters between individuals with generalized anxiety disorder and healthy subjects.[29] This could be because of the small sample size in their study. Longitudinal studies in children suggest that anxiety disorders are relatively stable over time and can predict anxiety and depressive disorders in adolescence and adulthood. Thus, early diagnostic tools like HRV assessment may prove beneficial in this regard.

The coexistence of anxiety disorders with other psychiatric conditions, especially mood disorders, has been recognized and acknowledged for many decades. In our study, out of the 127 students who had either Depression or anxiety, 50 (17.42%) students demonstrated symptoms associated with both anxiety and depression.

It was observed that nearly all HRV parameters were significantly reduced in students exhibiting symptoms of both depression and anxiety compared to the healthy group this supports the existing literature and emphasizes the potential impact of concurrent depression and anxiety on HRV in the adolescent population. In the present study, both time and frequency domain indices reduced in males experiencing both depression and anxiety. However, in females, a reduction was noted only in time domain indices compared to healthy counterparts. These results are concordant with the reports of Henje Blom et al. that mentions a decrease in HRV parameters in adolescent females with anxiety disorders and/or major depressive disorder compared to healthy controls.[30]

Strength of the study

Given the coexistence of depression and anxiety in a substantial majority of participants, utilization of RCADS, a validated assessment tool specifically designed to differentiate between depression and anxiety symptoms, has helped in mitigating the confounding effect of each other on HRV. Investigating the neurophysiological aspects of depression and anxiety in young individuals marks an initial step in understanding the correlation between physiological flexibility, particularly HRV, and psychological flexibility.

Limitation of the study

Symptoms of depression and anxiety were assessed solely through questionnaires, without clinical assessment by a psychiatrist. Additionally, due to the coexistence of both conditions, the number of students solely experiencing depression or anxiety was limited for analysis.

Recommendation:

- Future studies could incorporate clinical assessments by psychiatrists in addition to questionnaires.
- A hospital based study with a larger sample size may strengthen the reliability of the result by improving statistical power.
- Conducting longitudinal studies could provide a deeper understanding of the trajectory of these mental health conditions.

CONCLUSION

Adolescent students displaying symptoms of both depression and anxiety showed significant decreases in both time and frequency domain parameters of Heart Rate Variability compared to healthy peers. Similarly, those with symptoms of anxiety alone exhibited a notable reduction in HRV, particularly in time domain parameters. Though no significant differences in HRV parameters were found in individuals experiencing depression alone in younger age group, depressed students in higher classes showed reduced HRV in time domain parameters. This decline in HRV was consistent across genders. Utilizing HRV as a physiological biomarker in depressed and anxious adolescents could aid in diagnosis and timely intervention, potentially improving mental health outcomes during adolescence and adulthood.

REFERENCES

1. Won E, Kim YK. Stress, the autonomic nervous system, and the immune-kynurenine pathway in the etiology of depression. *Curr Neuropharmacol*. 2016;14(7):665-73.
2. Shorey S, Ng ED, Wong CHJ. Global prevalence of depression and elevated depressive symptoms among adolescents: A systematic review and meta-analysis. *Br J Clin Psychol.* 2022;61(2):287-305.
3. World Health Organization, Depression. SEARO [Internet]. 2017 [cited 2020 Jul 28]; Available from: http://www.searo.who.int/india/topics/depression/about_depression/en/
4. Brådvik L. Suicide Risk and Mental Disorders. *J Environ Res Public Health*. 2018;15(9):2028
5. Koenig J, Kemp AH, Beauchaine TP, Thayer JF, Kaess M. Depression and resting state heart rate variability in children and adolescents -A systematic review and meta-analysis. *Clin Psychol Rev.* 2016;46:136-50.
6. Spitzer C, Gläser S, Grabe HJ, Ewert R, Barnow S, Felix SB, et al. Mental health problems, obstructive lung disease and lung function: Findings from the general population. *J Psychosom Res*. 2011;71(3):174-9.
7. Klaufus L, Verlinden E, Van Der Wal M, Kösters M, Cuijpers P, Chinapaw M. Psychometric evaluation of two short versions of the Revised Child Anxiety and Depression Scale. *BMC Psychiatry* [Internet]. 2020 Feb 5 [cited 2023 Sep 11];20:1. [about 12 p.] Available from: https://bmcpsychiatry.biomedcentral.com/articles/10.1186/s12888-020-2444-5
8. Ebesutani C, Korathu-Larson P, Nakamura BJ, Higa-McMillan C, Chorpita B. The Revised Child Anxiety and Depression Scale 25-Parent Version: Scale Development and Validation in a School-Based and Clinical Sample. *Assessment*. 2017;24(6):712-28.
9. Muris P, Meesters C, Schouten E. A brief questionnaire of DSM-IV-defined anxiety and depression symptoms among children. *Clin Psychol Psychother*. 2002;9(6):430-42.
10. Young J, Ramachandran S, Stewart R, Orengo-Aguayo R, Chorpita BF. Psychometric Properties of the Spanish Revised Child Anxiety and Depression Scale 25-Item Version in El Salvador. J *Psychopathol Behav Assess.* 2021;43(2):271-80.
11. Carvajal-Velez L, Ottman K, Ahs JW, Li GN, Simmons J, Chorpita B, et al. Translation and Adaptation of the Revised Children's Anxiety and Depression Scale: A Qualitative Study in Belize. *J Adolesc Health*. 2023;72(1S):S34-S39
12. Perkins JD, Alós J. Rapid mental health screening in conflict zones: a translation and cross-cultural adaptation into Arabic of the shortened Revised Child Anxiety and Depression Scale (RCADS-25). *Confl Health*. 2021 Jul 1;15(1):51. doi: 10.1186/s13031-021-00386-1. PMID: 34210326; PMCID: PMC8247224.
13. Gormez V, Kılınçaslan A, Cahid Orengul A, Ebesutani C, Kaya I, Ceri V, et al. Psychometric properties of the Turkish version of the Revised Child Anxiety and Depression Scale Child Version in a clinical sample. *Child Psychiatry Hum Dev*. 2017;48(6):922-33.
14. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Circulation*. 1996;93(5):1043-65.
15. Chalmers JA, Quintana DS, Abbott MJA, Kemp AH. Anxiety disorders are associated with reduced heart rate variability: A meta-analysis. *Front Psychiatry* [Internet]. 2014 [cited 2023 Sep 08];5:80 [about 11 p.]. Available from: https://www.frontiersin.org/journals/psychiatry/articles/10.3389/fpsyt.2014.00080/full.
16. Koch C, Wilhelm M, Salzmann S, Rief W, Euteneuer F. A meta-Analysis of heart rate variability in major depression. *Psychol Med.* 2019;49(12):1948-57.
17. van der Kooy KG, van Hout HPJ, van Marwijk HWJ, de Haan M, Stehouwer CDA, Beekman ATF. Differences in heart rate variability between depressed and non-depressed elderly. *Int J Geriatr Psychiatry.* 2006;21(2):147-50.
18. Vloet TD, Jans T, Frey A, Häußler M, Vloet A, Geissler J, et al. Mean Heart Rate and Parameters of Heart Rate Variability in Depressive Children and the Effects of Antidepressant Medication. *Z Kinder Jugendpsychiatr Psychother*. 2019 May;47(3):253-260. doi: 10.1024/1422-4917/a000672. Epub 2019 Apr 11. PMID: 30971175.
19. Blood JD, Wu J, Chaplin TM, Hommer R, Vazquez L, Rutherford HJV, et al. The variable heart: High frequency and very low frequency correlates of depressive symptoms in children and adolescents. *J Affect Disord*. 2015;186:119-26.
20. Yeragani VK, Pohl R, Balon R, Ramesh C, Glitz D, Jung I, et al. Heart rate variability in patients with major depression. *Psychiatry Res*. 1991;37(1):35-46.
21. Lyonfields JD, Borkovec TD, Thayer JF. Vagal tone in generalized anxiety disorder and the effects of aversive imagery and worrisome thinking. *Behav Ther.* 1995;26(3):457-66.
22. Cheng YC, Su MI, Liu CW, Huang YC, Huang WL. Heart rate variability in patients with anxiety disorders: A systematic review and meta-analysis. *Psychiatry Clin Neurosci*. 2022;76(7):292–302.
23. Thayer JF, Friedman BH, Borkovec TD. Autonomic characteristics of generalized anxiety disorder and worry. *Biol Psychiatry*. 1996;39(4):255-66.
24. Cohen H, Benjamin J, Geva AB, Matar MA, Kaplan Z, Kotler M. Autonomic dysregulation in panic disorder and in post-traumatic stress disorder: application of power spectrum analysis of heart rate variability at rest and in response to recollection of trauma or panic attacks. *Psychiatry Res.* 2000;96(1):1-13.
25. Hauschildt M, Peters MJV, Moritz S, Jelinek L. Heart rate variability in response to affective scenes in posttraumatic stress disorder. *Biol Psychol*. 2011;88(2–3):215-22.
26. Pittig A, Arch JJ, Lam CWR, Craske MG. Heart rate and heart rate variability in panic, social anxiety, obsessive-compulsive, and generalized anxiety disorders at baseline and in response to relaxation and hyperventilation. *Int J Psychophysiol.* 2013;87(1):19-27.
27. Alvares GA, Quintana DS, Kemp AH, Van Zwieten A, Balleine BW, Hickie IB, et al. Reduced heart rate variability in social anxiety disorder: associations with gender and symptom severity. *PLoS One* [Internet]. 2013 Jul 30 [cited 2024 Feb 20];8(7). Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0070468.
28. Blase K, Vermetten E, Lehrer P, Gevirtz R. Neurophysiological approach by self-control of your stress-related autonomic nervous system with depression, stress and anxiety patients. *Int J Environ Res Public Health*. 2021;18(7):3329.
29. Hammel JC, Smitherman TA, McGlynn FD, Mulfinger AM, Lazarte AA, Gothard KD. Vagal influence during worry and cognitive challenge. *Anxiety Stress Coping.* 2011 Mar;24(2):121-36. doi: 10.1080/10615806.2010.490912. PMID: 20544417.
30. Henje Blom E, Olsson EM, Serlachius E, Ericson M, Ingvar M. Heart rate variability (HRV) in adolescent females with anxiety disorders and major depressive disorder. *Acta Paediatr.* 2010;99(4):604-11.