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Effect of listening music (Rabindra Sangeet) on autonomic dysfunction in patients with generalized anxiety disorder: A power spectral analysis of heart rate variability

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Abstract

Background: Power spectral analysis of heart rate variability (HRV) is a complex method for assessing cardiac autonomic nerve function (CANF) in generalized anxiety disorder (GAD) patients which is a common mental disorder in the world. Recently, music therapy is used as an adjunct to pharmacotherapy in clinical psychiatry for GAD. **Objective:** To observe the effect of music therapy on CANF by power spectral analysis of HRV in GAD patients was designed. **Methods:** This prospective non randomized intervention study was done in 2019 on 60 newly diagnosed GAD patients aged 20- 40 years, both male and female. Among them 30 patients were under music therapy with listening of Raga Bhairabi based Rabindra sangeet for 3 months and 30 patients were without music therapy for three months. Age, sex and BMI matched healthy control were also enrolled. HRV of all GAD patients and control were recorded at baseline and after three months of follow up. HRV were recorded by Power Lab 8/35. For statistical analysis Bonferroni's Post Hoc test and paired sample't' test were done. **Results:** Total power, LF power, HF power, LF n.u, HF n.u and LF/HF and were significantly lower in all GAD patients compared to healthy control at baseline. After 3 months of music therapy, significant increment of Total power, HF power, HF n.u and significant decrement of LF n.u and LF/HF occurred whereas no change of these except HF n.u were noted in patients without music after

3 months. Moreover, after three months of music therapy, Total power, HF n.u, and LF/HF were almost same to control. **Conclusion:** So this study concluded that music therapy (Rabindra sangeet) improved autonomic dysfunction in GAD patients and can be used as an adjunct to pharmacotherapy in clinical psychiatry for good cardiac health in GAD patients.

Keywords: Music, TP, HF power, LF power, HF n.u, LF n.u, LF/HF, GAD

Introduction

Generalized anxiety disorder (GAD) is a highly disabling mental health condition affecting 9% people of all ages across the world.[1.] In Bangladesh, 6 million people suffering from GAD has been reported[2].It can negatively impact a patient's quality of life and disrupt important daily activities[3-6].It is manifested by chronic and severe uncontrolled anxiety associated with restlessness, lack of concentration, irritability, muscle tension, easily fatigued and sleep disturbance more than 6 months[7]. High prevalence of anxiety and stress in modern lifestyle have adverse effect on autonomic functions even in healthy subjects[1]. Autonomic nervous system(ANS) tends to preserves homeostasis by adjusting the regulation of various organ and system which was disturbed due to stressful situations. Association of autonomic symptoms in GAD patients demonstrated the autonomic dysfunction in this group of patients which is manifested by sympathetic hyperactivity and parasympathetic hypoactivity[3-5]. Previous studies found that GAD is associated with autonomic dysfunction which predict higher risk of increasing cardiovascular morbidity[3,5-7].

Heart Rate Variability (HRV) is a popular tool for quantitative, non invasive assessment of individual component of autonomic activity. It represents the variation of consecutive RR interval as well as instantaneous heart rate which can measure the output from central autonomic modulation. Power spectral analysis of Frequency domain measures of HRV focus distribution of ECG signal into specific frequency bands and reflects the power of heart rate fluctuation at different frequency ranges. This difference in power of the signal at different frequency ranges can differentiate the sympathetic and parasympathetic tonic discharge at rest attributed to the heart rate fluctuation. Therefore, power spectral analysis represents more precise assessment of cardiac autonomic activity [8-10]. Among the spectral measures of HRV total power indicate variability of autonomic discharge whereas High frequency (HF) component is a specific index of cardiac parasympathetic activity. Interpretation of Low frequency (LF) component is controversial because some considered it as marker of sympathetic modulation and by others it reflects the interaction between sympathetic and parasympathetic activity. LF/HF ratio is considered an important marker of sympathovagal balance[10].

In recent days various relaxation technique including meditation, breathing exercise, yoga, biofeedback mechanism are popularly advocate to elevate anxiety and stress. A randomized control trial in stress induced subjects demonstrated reduction of sympathetic and elevation of parasympathetic symptoms after listening to music.[11] Recent evidence on benefit

of music therapy has been the basis of its use in various clinical conditions[12]. Music have therapeutic effect in preoperative and postoperativepatients, cancer, autism, metabolic syndrome, schizophrenia, major depressive disorder.[13-17] But little is known about the effect of vocal therapy by listeing Rabindra sangeet on autonomic dysfunction in GAD. Music has a beneficial role when combined with standard care. In clinical settings, GAD is usually treated by medication together with psychiatric counseling. A RCT demonstrated the value of music therapy to reduce anxiety level in GAD.[12] But the potential of vocal music therapy for improvement of autonomic dysfunction in GAD has not been largely explored. Therefore this study has been designed to investigate the effect of vocal music therapy in the form of raga based Rabindra sangeet on autonomic function by analyzing frequency domain measures of HRV in GAD patients.

Methods

Study design, setting

This prospective interventional study was carried out from March 2019 - February 2020 at the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka. The protocol of this study was approved by the Institutional Review Board of BSMMU.

Participants

This study was conducted on newly diagnosed GAD patients, aged 20-40 years of both genders who were recruited from the outpatient Department of Psychiatry of BSMMU diagnosed by the psychiatrist according to DSM-V criteria. All patients were equally divided according to intervention with music therapy into 30 patients who received music therapy (Raga Bhairavi based Rabindra Sangeet) in addition to medication prescribed by psychiatrists and 30 patients under same medication but without music therapy.

For comparison 30 apparently healthy subjects with similar age range and gender were taken as controls that also were assessed by GAD-7 criteria before enrollment. Controls were hospital staffs and attendant of the patients at BSMMU.

Sampling

Total 60 GAD patients were enrolled by purposive sampling technique from Outpatient Department of Psychiatry. All patients were studied at baseline before music therapy and follow-up. 30 patients were given music therapy for 3 months and 30 patients were without music therapy. All patients were under similar medication and under psychiatric counseling. Data were collected after 3 months in both groups of GAD patients. Control subjects were not under music therapy and data were collected from them at baseline and 3 months of follow-up.

Exclusion criteria

The GAD patients with previous history or currently suffering from- cardiovascular disorders, respiratory disorders, renal insufficiency, liver disease, arthritis, neurological disorders, thyroid disorders, other psychiatric disorders, malignancy, pregnancy and also the patients under medications for cardiac disease or respiratory disease or for other reasons which might interfere with autonomic nervous system balance or serum mineral status, current smokers were excluded from this study.

Intervention

To provide music therapy10 preselected low frequency Raga Bhairavi based Rabindra Sangeet (Tagor's song) sung by both male and female vocalists were uploaded in patients' mobile phone. The songs were selected according to the choice of the patient. To determine the choice some specific songs of some specific singer was made to listen by the patient. The songs were selected which the patients feel

comfortable. Then he/she was advised to listen to the songs with the help of earphone in a comfortable position every day at evening or any preferable time for half an hour for three consecutive months. Patients were monitored by communicating through telephone 2/3 times per week To ensure the compliance of the intervention the attendant were also enquired about the daily listening practice of the patient.

Data collection procedure

After explaining about the aim and purpose of the study, informed written consent was taken from each subject. Before recording HRV, patients were advised to follow some special preparation. After enrollment the subjects were advised to follow some instruction in the previous night of HRV test day. They were advised to finish their meal by 9:00 pm and to have a sound sleep to remain free from any type of stress and without sedative on the test day. They were requested to take light breakfast without tea and coffee and to attend the autonomic nerve function test laboratory in the Department of Physiology, BSMMU between 8:00 am to 10:00 am on the test day. All patients' data were recorded during same time period. A thorough physical examinations including pulse, BP, height, weight were measured and BMI was calculated. The subject was advised to take rest for 15-20 minutes in a controlled laboratory environment with 25^{o}c temperature and dim light. During this rest period he was not allowed to talk, eat or drink, to perform physical or mental activity, even sleep. ECG was recorded on lead II for 5 minutes by a data acquisition device Power Lab 8/35 (An AD instrument, Australia). ECG data was analyzed by Lab chart software which gives auto generated sheet of HRV data value and statistics. Patient was advised to come with a mobile phone capable of playing mp3 music. Then preselected Raga Bhairavi based Rabindra Sangeet (Tegor's song) was uploaded in his/her mobile. Then with the help of earphone he/she was advised to listen to the songs in a comfortable position every day evening or any preferable time for half an hour for three consecutive months. Patient was advised to come for follow up assessment after 3 months in the same department. HRV data of control subjects were also recorded in similar manner.

Statistical analysis:

Data were expressed as Mean ± SD. Data analysis was done using SPSS version 22. Statistical analysis was done by One-way ANOVA followed by Bonferroni's Post Hoc test to compare data among the groups and between the groups and Paired sample "t" test was used to compare the data between paired groups. p value of ≤ 0.05 was considered as statistically significant.

Results

In this study, age, BMI of all groups were almost similar and number of male and female were also similar among the groups (Table I). At baseline pulse and blood pressure was significantly higher and frequency domain measures were significantly lower except LF n.u, LF/HF in GAD patients compared to control. Moreover all these parameters were significantly not different in two groups of GAD patients (Table II).In addition, pulse rate, SBP ,DBP,LF n.u, LF/HF were significantly reduced but TP, HF power, HF n.u significantly increased in GAD patients whereas after three months follow up, GAD patients without music therapy did not show significant changes in these parameters when compared to their baseline values(Table III).On further analysis post intervention values of SBP, TP, HF power, HF n.u significantly increased whereas LF Power, LF n.u, LF/HF and pulse showed significant lower in music group compared to their non music group. Furthermore, SBP, TP, HF n.u and LF/HF in GAD patients listening music reached close to control value. Though LF power, HP Power, LF n.u were still away from the control group after 3 month (Table IV).

Table I: Age, BMI of different groups (N=84)

Parameters	music GAD(n=28)	Non Music GAD (n=26)	Control (n=30)
Age(years)ME±SD	29.79 ± 5.78	31.69±6.66	31.1±3.69
BMI(kg/m2)ME±SD	22.86±1.52	21.87±1.96	22.07±2.12
Male no (%)	14(50%)	12(46.15%)	15(50%)
Female no (%)	14(50%)	14(53.85%)	15(50%)

Statistical analysis were done by One-way ANOVA (among groups) followed by Bonferroni's Post Hoc test (between groups);BMI= Body Mass Index; N= Total number of subjects; n=number of subjects in each group.

Table II: Baseline values of Frequency domain measures and pulse rate, SBP and DBP) in different groups (N=84)

Parameters	Music GAD (n=28)	Non music GAD (n=26)	Control (n=30)
TP **(ms²)**	1108.7±379.68••• (654.45-2234)	919.25±399.14••• (479.2-1796)	1567.8±570.75 (678-2543)
LF power **(ms²)**	295.53±179.98•• (132.40-767.0)	293.1±129.87•• (111.10-612.90)	467.09±276.40 (158.80-991.00)
HF power **(ms²)**	342.92±144.27••• (143-693)	252.92±134.31••• (116.6-695.7)	623.08±169.74 (336.1-890.1)
LF norm **(n.u.)**	64.26±8.58••• (50.23-78.41)	66.23±13.94••• (38.37-95.70)	39.46±9.28 (21.34-61.39)
HF norm **(n.u.)**	33.71±8.93••• (13.76-48.74)	34.13±11.91••• (10.09-59.71)	59.12±9.31 (34.23-76.73)
LF/HF ratio	2.08±0.74••• (1.06-3.65)	2.26±1.08••• (0.64-4.68)	0.71±0.29 (0.28-1.65)
Pulse (beats/min)	87.11±10.51••• (61-110)	87.23±13.94••• (69-125)	73.87± 5.6 (60-90)
SBP(mm of Hg)	126.79±5.13••• (110-135)	122.69±7.10••• (110-130)	110.83±8.10 (100-130)
DBP(mm of Hg)	84.11±5.78••• (70-90)	83.58±4.12••• (75-90)	72.00±5.96 (60-85)

Data were expressed as Mean ± SD. Values in parentheses indicate ranges. Statistical analysis were done by One-way ANOVA (among groups) followed by Bonferroni's Post Hoc test (between groups); SBP=Systolic Blood Pressure; DBP=Diastolic Blood Pressure; TP- Total power; LF power- Low frequency power; HF power- High frequency power; LF norm- Low frequencypower in normalized unit; HF norm- High frequency power in normalized unit; LH/HF ratio- Low frequency power/High frequency ratio. N=number of subjects; n=number of subjects in each group. •••=Control baseline vs. music GAD baselinevs. non music GAD baseline.

Table III : Pre and post intervention/follow up values of nonlinear measures and pulse rate, systolic blood pressure (SBP) and diastolic blood pressure (DBP) in different groups of GAD (N=84)

Parameters	Music GAD (n=28)		Non music GAD (n=26)	
	Pre	Post	Pre	Post
TP	1108.7±379.68	1418.6±455.98***	919.25±399.14	989.34±376.74
(ms^2)	(654.45-2234)	(674.1-2347)	(479.2-1796)	(546.30-1908)
LF power	295.53±179.98	246.26±98.73	293.1±129.87	273.79±154.37
(ms^2)	(132.40-767.0)	(120.56-489.00)	(111.10-612.90)	(117.00-728.1)
HF power	342.92±144.27	502.68±194.55***	252.92±134.31	281.36±148.49
(ms^2)	(143-693)	(156.00-790.00)	(116.6-695.7)	(103.5-750.0)
LF norm	64.26±8.58	46.35±13.30***	66.23±13.94	62.62±9.85
(n.u)	(50.23-78.41)	(22.53-74.55)	(38.37-95.70)	(38.49-80.97)
HF norm	33.71±8.93	55.91±11.10***	34.13±11.91	44.29±10.55***
(n.u)	(13.76-48.74)	(25.80-76.46)	(10.09-59.71)	(24.82-70.87)
LF/HF	2.08±0.74	1.03±0.61***	2.26±1.08	1.99±0.99
Ratio	(1.06-3.65)	(0.29-2.89)	(0.64-4.68)	(0.37-3.72)
Pulse rate	87.11±10.51	79.36±9.63**	87.23±13.94	85.19±10.93
(beats/min)	(61-110)	(56-100)	(61-110)	(66-125)
SBP(mm of Hg)	126.79±5.13	114.46±7.11***	122.69±7.10	119.81±6.24
	(110-135)	(100-125)	(110-130)	(110-130)
DBP(mm of Hg)	84.11±5.78	79.82±5.18**	83.58±4.12	83.35 ±3.77
	(70-90)	(70-85)	(75-90)	(75-92)

Data were expressed as Mean ± SD. Statistical analysis was done by Paired sample t-test; SBP= Systolic Blood pressure; DBP= Diastolic Blood Pressure; TP- Total power; LF power- Low frequency power; HF power- High frequency power; LF norm- Low frequencypower in normalized unit; HF norm- High frequency power in normalized unit; LH/HF ratio- Low frequency power/High frequency ratio; N= Total number of subjects; n=number of subjects in each group. * P<0.05 **p<0.01 *** P<0.001.*= baseline GAD vs. post music GAD

Table IV : Post intervention/follow up values of Frequency domain measures and pulse rate , systolic blood pressure (SBP) and diastolic blood pressure (DBP) in different groups of GAD (N=84)

Parameters	Music GAD (n=28)	Non music GAD (n=26)	Control (n=30)
TP(ms^2)	1418.6±455.98$^{\$\$}$	989.34±376.74	1607.8±473.54
	(674.1-2347)	(546.30-1908)	(941.7-2548)
LF power(ms^2)	246.26±98.73$^{¥¥¥}$	273.79±154.37	447.78±279.99
	(120.56-489.00)	(117.00-728.1)	(161.20-980.00)
HF power(ms^2)	502.68±194.55$^{\$\$\$¥}$	281.36±148.49	635.36±169.82
	(156.00-790.00)	(103.5-750.0)	(341.7-907.00)

Table IV : (Contd.)

Parameters	Music GAD (n=28)	Non music GAD (n=26)	Control (n=30)
LF (n.u.)	46.35±13.30$^{\$\$\$¥¥}$ (22.53-74.55)	62.62±9.85 (38.49-80.97)	37.05±10.08 (18.21-56.44)
HF (n.u.)	55.91±11.10$^{\$\$\$}$ (25.80-76.46)	44.49±10.55 (24.82-70.87)	61.41±9.79 (41.39-77.79)
LF/HF ratio	1.03±0.61$^{\$\$\$}$ (0.29-2.89)	1.99±0.99 (0.37-3.72)	0.65±0.28 (0.24-1.36)
Pulse rate(beats/min)	79.36±9.63$^{¥}$ (56-100)	114.46±7.11 (100-125)	79.82±5.18 (70-85)
SBP(mm of Hg)	85.19±10.10 (66-125)	119.81±6.24 (110-130)	83.35 ±3.77 (75-92)
DBP(mm of Hg	72.53±7.48$^{¥¥¥}$ (62-90)	112.67±6.79 (100-125)	73.00±5.66 (60-85)

Data were expressed as Mean ± SD. Statistical analysis was done by One-way ANOVA (among groups) followed by Bonferroni's Post Hoc test (between groups); SBP= Systolic Blood pressure; DBP= Diastolic Blood Pressure; TP- Total power; LF power- Low frequency power; HF power- High frequency power LF norm- Low frequencypower in normalized unit; HF norm- High frequency power in normalized unit; LH/HF ratio- Low frequency power/High frequency ratio; N=Total number of subjects; n=number of subjects in each group. $^{\$}$= post music GAD vs. post non music GAD; $^{¥=}$ post music GAD vs. control follow up. $^{\$=}$P<0.05, $^{\$\$}$ = ≤ 0.01, $^{\$\$\$}$ =≤0.001. $^{¥=}$P≤0.05, $^{¥¥}$ = ≤ 0.01, $^{¥¥¥}$ =≤ 0.001,

Discussion

In this study analysis of values of frequency domain measures demonstrated the quantity both sympathetic and parasympathetic tonic discharge at rest as well as state of autonomic balance during the data recording period [10]. In GAD at baseline higher resting pulse rate, SBP, DBP,LF n.u and LF/HF as well as lower TP, HF power, HF n.u compared to control suggest that all drug naive GAD patients had cardiac autonomic dysfunction with increased sympathetic activity and poor parasympathetic tonic activity [6,18-24]. These results agree to previous studies on GAD with hypertension and CVD risk [5,6,21].

Recently impact of music therapy on autonomic dysfunction has been investigated on major depressive disorder patients and found a good impact on ANS[17].

In the current study improvement of autonomic balance by increased parasympathetic and decreased sympathetic tone after 3 months of listening vocal Bhairav rag based rabindra sangeet was evident on current series of GAD patients with impaired autonomic function. Here HF,HF nu ,TP significantly increase and LF, LFnu and LF/HF significantly decrease after music therapy in GAD. In addition no significant change were observed in non music GAD patients who were not given music therapy.This good impact of music was further supported by the unchanged impaired autonomic status in GAD patients over 3 months who were not under music therapy. It

was also noted that both sympathetic and parasympathetic tone were significantly improved compare to non music GAD patients after 3 months of therapy.

After listening Rag based song for three months the significant decrement of pulse rate, SBP and DBP in patients from their baseline suggest improvement of cardiac autonomic regulation which agreed to the result of others [11,14,17,25] .

Improvement of autonomic balance in GAD patients after music therapybrought significant increment in Total power, HF power, HF n.u. and significant decrement in LF n.u. and LF/HF ratio after 3 months of musical intervention agrees to others studies on patients with other diseases [11,25-29]. Moreover, SBP in music group of patient were close to healthy subjects which in turn strongly support the good effect of music on autonomic dysregulation in GAD.

The outcome of these findings suggests improvement of impaired autonomic balance as well as improvement of sympathetic and parasympathetic dysfunction resulted from music therapy in GAD.

Lack of significant change in non music group after 3 months of follow-up demonstrated negligible effect of medication on autonomic dysfunction in GAD.

Moreover, significant difference in autonomic data in music group patients compared to non music group of patients at the end of 3 months of study further emphasizes the good impact of this type of music therapy over medication on the improvement of autonomic function in GAD.

Though little is known about the scientific mechanism of autonomic regulation improvement in GAD patients but it was suggested that music can directly entrain the cardiovascular rhythm which is obviously due to synchronization of higher centers of autonomic control induced by music therapy which may be applicable in these cases [30.] Furthermore, it has been suggested that relaxation response on hypothalamic and limbic system induced by soothing music may reduce neuroendocrine activity and stress response by enhancing parasympathetic activity and decreasing sympathetic activity [31]. This fact may explain the enhance parasympathetic activity and reduced sympathetic activity in GAD patients from the relaxation effect of Rag based Rabindara sangeet used in this current series of GAD patient

Conclusion

From the results of the present study,it can be finally concluded that music therapy (rabindra songeet) is an effective measure to improve autonomic dysfunction in GAD and it can be successfully used as an adjunct to medication and thereby protect the patients with generalized anxiety disorder from cardiovascular risk.

Ethical clearance

The protocol of this study was approved for ethical aspects by Intuitional Review Board of BSMMU, Dhaka, Bangladesh.

Conflict of interest

The authors declare no conflict of interest.

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