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RESEARCH ARTICLE

Gender-based comparison of salivary stress marker among healthy individuals after intervention with three melodic scales of Indian music – Exploration with a pretest-posttest design

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ABSTRACT

Background: Music is used as entertainment, but it has potential health benefits. Evidence regarding Indian music in controlling stress is meager. Hindustani music (a type of Indian music) has its system of musical scales (ragas). **Aims and Objectives:** The objective was to evaluate change in stress using salivary alpha-amylase (sAA) after passive listening to Hindustani ragas and its variation with gender. **Materials and Methods:** Healthy individuals were randomly divided into three groups that received music intervention (ahir bhairav, kaunsi kanada, and bhimpalas ragas/scales). Stress was assessed with salivary alpha-amylase including pre, during, post-intervention (each for 10 min) among both the genders were compared. SPSS 20.0 was used to analyze the data. **Results:** All three ragas reduced sAA level (not significant). However, a significant difference in sAA level during and post music ($P = 0.016$) was observed. **Conclusions:** Passive listening to any of the three Indian scales reduced stress, like the western melodic scales. Music medicine (passive listening to music) thus has therapeutic implications as an alternative therapy for stressed/anxious individuals in medical disorders. Gender-specific effects with each melodic scale were noted.

KEY WORDS: Music; Stress; Salivary Alpha-Amylase

INTRODUCTION

Music is an esthetic stimulus that evokes a subjective experience in every individual involved in it, be it in production of new music or a simple exercise such as listening to music. Seven different functions of music are put forth such as memory recall, entertainment, diversion, social bondage, regulation of self and emotions, and self-reflection.[1] However, little did we know that artistic practice of music has potential health benefits. Music can reduce perioperative and operative anxiety, reduce blood pressure (BP), respiratory rate, and heart rate during endoscopy,[2] colonoscopy,[3] cardiac catheterization,[4] and cardiac patients.[5] Music therapy is also used in pain clinics, intensive care units, perioperative set ups, coronary care, oncology, positron emission tomography scanning waiting rooms, and pediatric units.[6,7]

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Recent studies emphasize the effect of different types of music in promoting relaxation and reducing stress levels.[8-11] Meditative classical music lowers the neurohumoral markers of stress.[12,13] Dementia patients and caregivers had reduced stress when music was given at home.[14] Stress can be

measured using different questionnaires or assessment of biomarkers of stress. Classically biomarkers that change with the level of stress are serum cortisol, catecholamines, amylase, and plasma interleukins. One of the non-invasive ways of measuring stress is detection of stress markers in the saliva. Saliva biomarkers are equally sensitive as blood biomarkers.[15,16] Salivary alpha-amylase (sAA) is one of the major enzymes that are released on sympathetic stimulation.[17]

Hindustani and Carnatic music are the two broad branches of Indian music with its respective system of melodic scales (ragas). "Raga" (musical/melodic scale) is a set of tones presented in a specific order to generate a tune/melody and is said to have the "effect of coloring the hearts of men.[18]" Each raga can evoke a rasa/emotion. For example, raga "Kapi" causes a cool, soothing, and deep mood, and raga neelambari evokes sleep.[19,20] Gandharva veda, a part of sama veda, and the manuscript, "Raga chikistsa" (Available at Saraswati Mahal Library in Tanjore), have mentioned various ragas to have health benefits and cure various ailments.[21] To name a few, raga malkauns for hypotension and raga behag for insomniacs.[22]

Umpteen literatures exist on the health benefits of Mozart music and other genres of music. Despite the presence of a lot of folklore on Indian music, medical science has barely explored the benefits of Indian music. Change in stress with music has been evaluated in a few studies.[23,24] Exploration of the effect of Indian music on stress is limited. Gender-based differential response to stress has been documented.[25,26] To the best of our knowledge, it remains unknown if music intervention to reduce stress also varies with gender.

As part of a larger project, the present study objective was to evaluate the effect of three chosen Hindustani ragas (melodic scales) – Ahir bhairav, kaunsi kanada, and bhimpalas, on stress using the level of salivary stress markers. The manuscript is part of a larger project (RAGA-1 study on clinicalTrials.gov - NCT02691585). The primary outcome measure was to evaluate the change in salivary alpha-amylase levels with 10 min of Indian music intervention. The secondary outcome measure was to assess if stress response varies with gender and to explore the gender-specific effect of a specific melodic scale on levels of stress biomarker.

MATERIALS AND METHODS

Ethical Approval

The study protocol was approved by the institutional ethical and scientific committee (Submission reference: MSRMC/EC/2016; dated: 11/02/2016 ; MSRMC/EC/2017; dated: 25/07/2017). The study period was from 2016 to 2019 (October 2016 – first recruitment and December 2019 – last recruitment). Research was conducted in accordance with the Declaration of Helsinki, apart from registration through online questionnaire, where an informal consent, to answer the online questionnaire and further participation, was taken by the participants. A written, informed consent to volunteer for the study was taken from all participants.

Study Design

A randomized intervention uncontrolled trial (pre-test post-test triple-blinded design) was conducted. Sample size was calculated to be 105 that was randomly divided into three intervention groups (n = 35 subjects in each group), each receiving one of the three randomly chosen ragas (Group A – raga A [ahir bhairav], Group B – raga B [kaunsi kanada], and Group C – raga C [bhimpalas]). The ragas were coded as A, B, and C by one of the subjects (who were not involved in the project). Subjects had to listen to music with a relaxed mind, with their eyes closed, for 10–12 min duration.

Basis for Sample Size

In a previous study, it was found that the change in anxiety scores from before to after the procedure was 33.3 (23.3–41.7) and 30 (20–40), respectively (median [interquartile range]). This study had an effect size of 0.2. In the present study, sample size calculated to be 104, considering power of 80%, effect size of 0.276, and an alpha error of 5%.[27]

Subjects – Recruitment

Subjects were recruited from Ramaiah Group of Institutions with different education backgrounds, undergraduate and postgraduate level. Subjects were invited to participate in the study through online and notice board advertisements. Anyone who is healthy aged 18–30 years of either gender was asked to volunteer. Online Google Forms questionnaire was sent to those who responded to the call. About 150 subjects volunteered to participate and 122 of them completed the questionnaire. Exclusion criteria were subjects with medical disorder including psychiatric disorder, pregnancy, body mass index (BMI) >30 kg/m^2, hearing issues, and anyone consuming drugs that can affect the BP or autonomic status of the individual. All subjects BP were measured, and only non-hypertensive and non-tachycardis were included.

Baseline Demographic Data Recording

An online pre-designed, pre-tested questionnaire contained details of sociodemographics, education background, smoking and alcohol history, present or past self-history, and family history of non-communicable diseases. Subjects' preference to music, genre, duration of listening to music, and previous experience/training with music (instrumental or vocal) were also included. After subjects filled the online form, they were invited for further data collection in the laboratory. Among the 122 subjects who answered the online questionnaire, 12

subjects were excluded based on their own data in the form. A total of 110 subjects reported to the laboratory. They were explained the study protocol, and cooperation expected from them and their rights to withdraw their participation. During general health check-up, BMI was calculated and BP in sitting position was measured twice after 5 min rest (sphygmomanometer) in between. Only normotensives were included and thus three subjects were further excluded.

Randomization

Simple randomization technique was implemented to randomize recruited subjects (n = 107) into three groups. The random numbers were generated through Microsoft Excel (3 sets of 35 each) and the generated numbers were kept in a sealed, opaque envelope. This envelope was opened and subjects were assigned to each of the three groups randomly (Groups A, B, and C) by the research assistant.

Baseline (Pre) and Post-Intervention Readings

Participants were instructed to take light breakfast, and abstain from tea, coffee about 2 h before the recording. They were asked to avoid exhaustive exercise, alcohol intake, and smoking for the past 24 h. Recordings were carried out between 09:00 and 10.00 am in an isolated noise-free (and disturbance-free) laboratory at a stable temperature of 20–22°C. Subjects were asked to rinse the mouth with fresh water (for saliva collection) and then to lie supine and relax (10 min before the tests), with their eyes closed. Salivary oral swab was given, to be kept sublingually, for collection of saliva. The first 10 min of baseline collection of saliva commenced (pre-intervention). At the end of 10 min, the inserted saliva swab was removed with the sterile steel blunt forceps and the swab inserted into the pre-labeled Salivette. At end of 10 min, a fresh saliva swab was placed in the mouth without disturbing the subject much, other than "open your mouth and bite out the swab, keeping your eyes closed" instruction. Music intervention with respective raga as per the random group allocated was then administered. At the end of 10 min of music, saliva swab was removed and one more fresh swab was inserted into the mouth for another 10 min. At the end of 10 min (post-intervention), the subject was asked to open the mouth and the last saliva swab was taken out. The subjects were then relieved. The saliva samples were centrifuged for 15 min at 3000 rpm and supernatant saliva was stored at –80°C, until further analysis. Analysis of sAA levels (enzyme-linked immunosorbent assay) at 3 time points – pre, during, and post music was done.

Salivary Amylase

Saliva for baseline stress markers (sAA) was collected as per protocol given. Subjects were asked to rinse their mouth before lying in supine position. Saliva was collected using the SalivaBio Oral Swab (Salimetrics, State College, PA). This synthetic swab enables better volume collection, subject comfort, and compliance and is validated for the analysis of salivary markers. The reagents were stored at 2–8°C. On the day of assay, saliva samples were thawed and then vortexed and centrifuged for 15 min at 1500 g. In a 96-well microtiter plate, the enzymatic action read of α-amylase on chromogenic substrate, 2-chloro-p-nitrophenol linked with maltotriose, and yielded 2-chloro-p-nitrophenol, which was then spectrophotometrically measured at 405 nm (salimetrics.com). The rise in absorbance at 405 nm is directly proportional to the amount of sAA activity. Range of sAA as per protocol sheet was 3.1–423.1 units/mL. The intraassay precision or coefficient of variation (%) was 2.5–7.2% and interassay precision was 3.6–5.8%.

Music Intervention

As per gandharva veda and raga chikitsa literature, ragas that can normalize tension and BP are ahir bhairav, bhupali, puriya, bhimpalas, hindol, kaunsi kanada, and todi.[21,28] Of these ahir bhairav, kaunsi kanada and bhimpalas were used for the present study. The subjects were made to listen to the music through headphones,[29] connected at uniform volume (50%) through a laptop. Based on the group, the subject is allotted to a particular musical clip played for 10 min duration. The musical clip had instrumental (Bansuri) music playing alaap portion in the respective scale/raga recorded by an eminent flautist. Subjects had to passively listen to this with eyes closed and their minds relaxed. Ahir bhairav (ahiri or abhiri), an ancient raga, the raga A of this study. Arohana (ascent): S r G M P D n S and avarohana (descent): S n D P M G r S. S, G, M, P, D. All notes in this scale are shuddha (natural) except r and n which are komal (flat). Ahir bhairav is typical uttarang raga, played in the first prahar of the morning (06:00–09:00 am). Chakravakam scale of Carnatic music resembles ahir bhairav.[30] The ascent sounds pensive, while descent and the second half is filled with positivity, hope, and feeling of unconditional love.[31] Raga kaunsi kanada is malkauns scale during ascent and Darbari scale during descent. The notes of arohana are S g M d n S and avarohana are S n d P M g R S. Best time for this scale is between 12:00 and 03:00 am (3rd prahar of the night). Kaunsi kanada is an exceptionally sophisticated scale of Hindustani music that can color our minds.[32] Kaunsi kanada was the raga B in this study. Bhimpalas is a soft scale that evokes feelings of love and yearning. It is a "late-afternoon" raga. In South Indian classical music, the counterpart of this scale is raga "Abheri.[33]" The notes of this scale are arohaṇa: S G M P N S. Avarohaṇa: S N D P M G R S (chathusruthi rishabh, sadharana gandhar, suddha madhyam, chathusruthi dhaivath, and kaisiki nishadha). Bhimpalas was the raga C in this study.

Statistical Analysis

Data were analyzed using SPSS software version 20.0 (SPSS Inc., Chicago). The continuous variables were analyzed using descriptive statistics (mean and SD). The qualitative/

categorical variables were presented as frequency and percentage. The Kolmogorov–Smirnov test was used to check for normalcy of the data. At baseline, the difference in proportion of categorical variables was tested using Chi-square test and one-way ANOVA was used for continuous variables. The independent t-test was used to analyze the differences between the groups. Multivariate forward logistic regression analysis was implemented to study the effect of confounders (namely, age, gender, smoking, alcoholism, involvement in mind-body relaxation technique, physical activity, and music training). $P \leq 0.05$ was considered statistically significant.

RESULTS

Online questionnaire was completed by 122 subjects, 110 subjects reported to the laboratory, of which data of 107 subjects were found to be satisfying both inclusion and exclusion criteria and thus used for final analysis [Figure 1]. The three groups were comparable based on sociodemographic data. Age group of 19–21 years was predominant in all the groups, maximal in Group B (74.3%) [Table 1]. About 16 each in Group B and C and 13 in Group A were trained in music (more trained in Indian music). With respect to musical training, the groups were comparable. Most preferred type of genre among the subjects was Hindi movie songs. When asked to name a few ragas that the subjects were familiar with, only about 17 individuals of the whole group could name the ragas such as anandabhairavi, bhairav, bhageshri, hamsanandi, hamsadhwani, kalyani, and saveri.

There was no significant difference in the sAA levels, based on between-group and gender-wise comparisons. Based on pairwise time-based comparison, mean differences in sAA – pre and during music intervention ($P = 0.458$) and pre and post music intervention ($P = 0.192$) – were not significant. There was a significant difference in the saliva values between during and post music ($P = 0.016$). However, note that in all three groups, sAA level tended to reduce with music and then slowly increased back toward normal after music was stopped, though statistically not significant [Table 2 and Figure 2]. Subjects who were given music intervention salivary amylase levels reduced maximally with raga B intervention (mean difference between before and during music was 8.32 U/mL), though this was statistically not significant. Nevertheless, based on gender-wise comparison, it was observed that males showed a specific rise in salivary amylase level with music (+11.75 U/mL) and after music intervention with raga ahir bhairav, while females exhibited a rise in amylase levels with raga C, bhimpalas (+8.94 U/mL) during music that reduced toward baseline after music was stopped, these changes were, however, statistically not significant. However, on multivariate analysis after adjusting for the effect of various covariates, namely, age, gender, smoking, alcoholism, involvement in mind-body relaxation technique, physical activity, and music training, it was found that salivary markers were not affected by the above-mentioned covariates.

DISCUSSION

In this study, we have attempted to study Indian classical music in the form of three Hindustani ragas/scales, and their effect on stress using stress marker [sAA], on normal healthy individuals and the variation based on gender. In the current study, sAA levels reduced in all three groups, sAA level tended to reduce with music and then slowly rose back toward normal after music was stopped, though statistically not significant. Among the three interventions, raga kaunsi kanada reduced salivary alpha-amylase maximally during music intervention though it was insignificant statistically. Gender-based comparison of mean differences in salivary amylase before and during music showed males had an increase in salivary amylase level with raga ahir bhairav, while females exhibited

Table 1: Sociodemographic characteristics and music questionnaire data of subjects in the intervention groups – Group A (Raga A), Group B (Raga B), and Group C (Raga C)

Variables	Group	A *n*=36 (%)	B *n*=35 (%)	C *n*=36 (%)	*P*
Age (years) Mean±SD		21±2.85	20.34±2.1	20.14±2.2	0.339
Gender	Female	19 (32.8)	17 (29.3)	22 (37.9)	0.557
	Male	17 (34.7)	18 (36.7)	14 (28.6)	
Type of diet	Non-veg	24 (34.3)	24 (34.3)	22 (31.4)	0.79
	Veg	12 (32.4)	11 (29.7)	14 (37.8)	
Mean BMI (kg/m^2) Mean±SD		23.71±4.8	23.82±4.3	23.5±4.7	0.956
Training in music	No	23 (37.1)	19 (30.6)	20 (32.3)	0.79
	Yes	13 (28.9)	16 (35.6)	16 (35.6)	
Genre of music	Indian	23 (37.1)	19 (30.7)	20 (32.3)	0.474
	Western	10 (25.6)	15 (38.5)	14 (35.9)	
	Unanswered	3 (50)	1 (16.7)	2 (33.3)	

n is the number of subjects in each group. All the values of the two groups are in absolute values and in parenthesis are in percentages. $P < 0.05$ is considered significant. *P* calculated using Chi-square test/Fisher's exact test. Mean age comparison was done using ANOVA. BMI: Body mass index, SD: Standard deviation

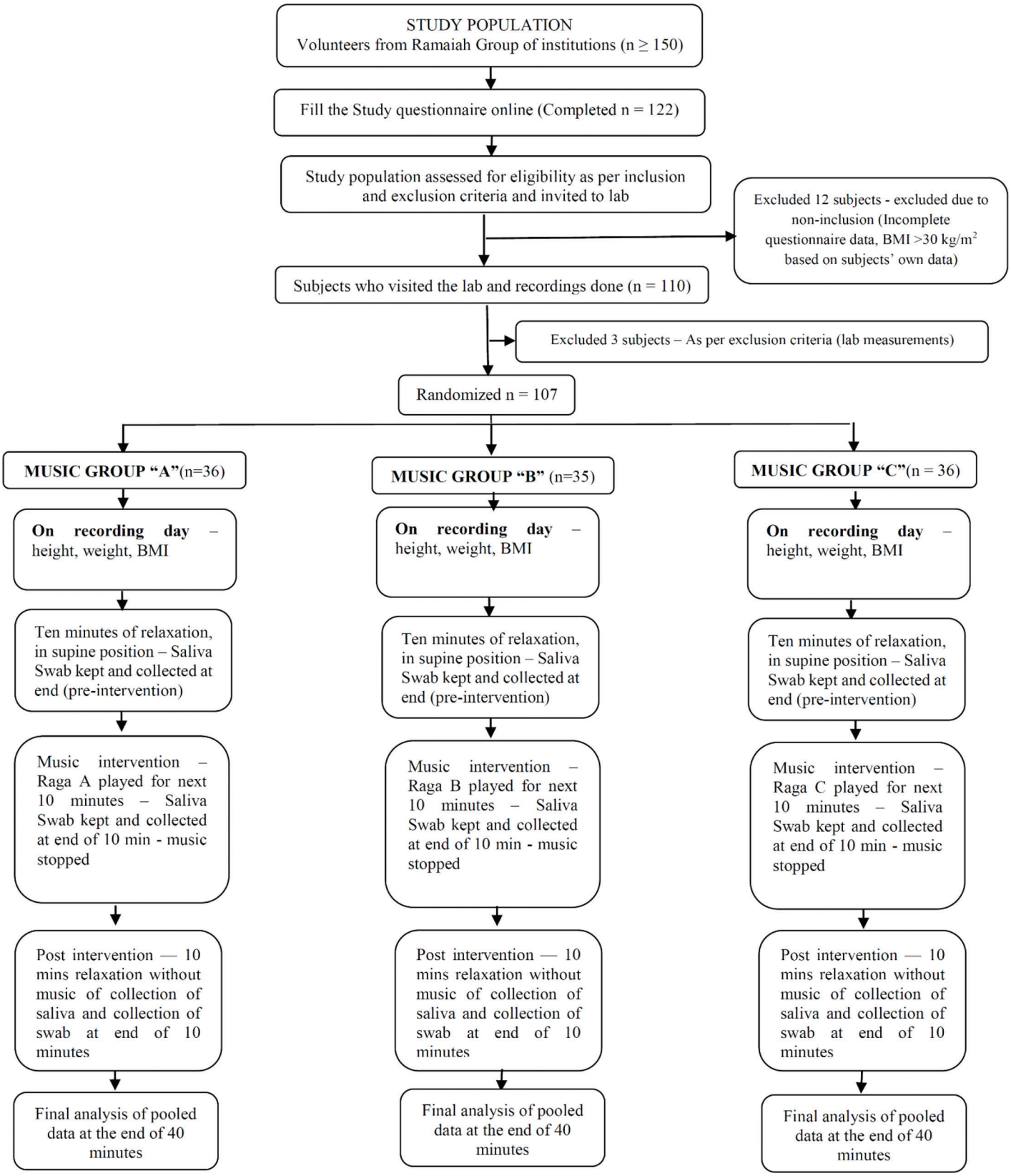

Figure 1: Consort diagram of participant recruitment, distribution, and follow-up

a rise in amylase levels with raga bhimpalas; these changes were, however, statistically not significant.

Music research has studied stress response using both serum and salivary cortisol and amylase. Stress markers vary with gender. In one study, listening to music reduced serum cortisol in women, but increased alpha-amylase among men. Couples who shared musical preferences it was observed that men had lower cortisol levels when women listened to their preferred music. Both genders had higher sAA levels

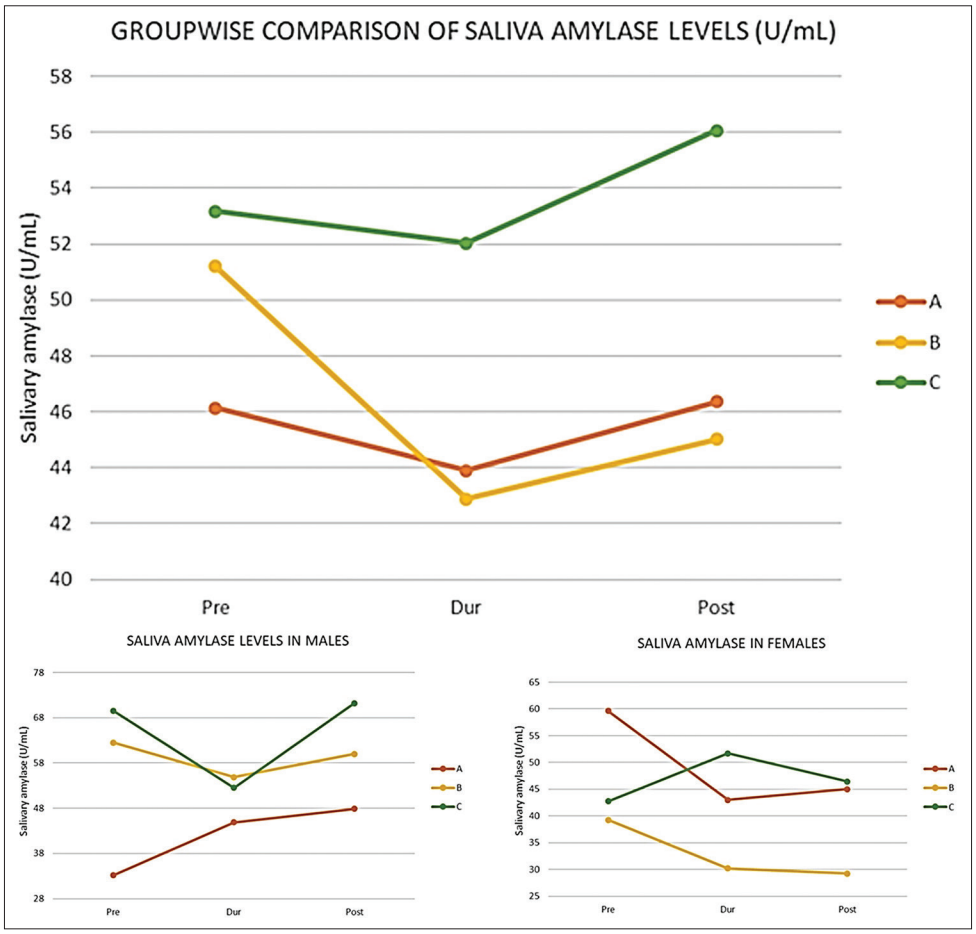

Figure 2: Salivary amylase level in different groups

Table 2: Comparison of saliva between the intervention groups (pre, dur, and post music intervention) (***n***=107)

Group	Mean			*P*
	Pre	Dur	Post	
Group A				
A (*n*=36)	46.13±16.3	43.89±52.4	46.37±49.2	0.979
Male (*n*=17)	33.15±29.2	44.9±54.6	47.9±51.5	0.731
Female (*n*=19)	59.64±84.8	43±51.8	45±48.5	0.854
Group B				
B (*n*=35)	51.20±40	42.88±35.9	45.01±42.3	0.379
Male (*n*=18)	62.5±43.9	54.83±36.2	60±51	0.546
Female (*n*=17)	39.24±32.5	30.23±32.1	29.25±23.1	0.685
Group C				
C (*n*=36)	53.18±58.4	52.03±57.4	56.07±68.1	0.892
Male (*n*=18)	69.56±85.4	52.55±76.3	71.22±97.6	0.75
Female (*n*=17)	42.76±29.6	51.7±43.3	46.42±39.7	1.0

n is the number of subjects in each group. All the values are in mean and standard deviation (SD) – univariate ANOVA. $P<0.05$ was considered significant – Levene's test of equality. **P* calculated using RM-ANOVA

when their partner listened to their respective preferred music.[34] Serum cortisol levels decreased maximally in groups that listened to Mozart/Strauss music with drop in men being higher than women.[35] Music listening was effective in reducing subjective stress levels along with lower cortisol concentrations. Alpha-amylase increased with energizing music and decreased with relaxing music.[8] Among healthy students, impact of 6 weeks of background music during preclinical laboratory on stress and anxiety showed that there was a positive relationship between attraction to music and its role as a device in reducing stress.[36] Music also reduced anxiety and depression of college students.[37] Music reduced perceived stress levels and increased the coping abilities.[38,39] Reduction in anxiety has been the most consistent finding found in research works with patients[40-42] and laboratory-based investigations[40,41,43] after listening to music. Music significantly decreased baseline sAA levels in autism and intellectual disability patients.[44] Among healthy females, passive listening to music significantly reduced the cortisol levels.[24] Tibetan music usage reduced sAA levels during pre-surgery waiting time.[45] With music performance, sAA levels increased 1 min before the performance and remained at that level until after the performance, before dropping to lower than baseline levels. In contrast, salivary cortisol levels peaked at 15 min after the performance. This study showed that sAA is an important biomarker to understand performance-related stress.[46]

Not many Indian studies are documented. We recorded a significant reduction in state and trait anxiety (using STAI) score among pre-hypertensives and hypertensives after listening to raga bhimpalas for minimum 15 min a day, for at least 5 days/week, for 3 months duration.[47] Patients who heard classical Indian instrumental music had reduced psychological distress during a gastroscopic examination.[48] Stress as evaluated using galvanic skin response decreased on listening to religious songs (hymns).[49] Perceived stress reduced among medical students after listening to light instrumental music.[50] It may thus be observed that across studies, predominantly stress reduced after listening to music, as measured by salivary stress markers as shown in the current study.

The strength of the study is that three Indian ragas have been systematically and scientifically studied, among normal healthy individuals, and compared based on gender, with a randomized pretest-posttest design, for the 1st time. Subjects of homogenous age groups were compared. Stress was measured using a validated biomarker. Music had only melody (alaap) against a drone instrument, without any percussion instruments or lyrical component, as they can produce different effects on physiological parameters. The study did have a few limitations such as: As this study was first of its kind, a control group though included, only baseline assessments were taken, thus making statistical comparison difficult. Having a control group with 30 min of relaxation without any musical stimulus, would have been a better design to draw clear conclusions. Music choice was not given to the subjects. Literature review shows that self-chosen music has better pain suppression effect.[51-55] However, a number of other research works show that experimenter chosen music is also good.[56] while few others reported that choice did not matter.[57] All subjects were considered clinically normal, but laboratory measurements were not conducted to confirm the same. Salivary cortisol, that indicates a different axis of stress mechanism, was not measured. Note that the ragas used in the current study are from different thaats (Hindustani music scale system). Therefore, future studies should look into an effect by a particular raga, based on its individual notes, sequence of notes, and the thaat it arises from.

CONCLUSIONS

Indian music intervention reduced stress and salivary stress markers. In that raga, kaunsi kanada seemed to have the best effect on subjective stress while both raga ahir bhairav and bhimpalas reduced salivary alpha-amylase levels. Gender-specific effects of each melodic scale used were further noted.

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