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RESEARCH ARTICLE

Modulation of immune responses in stress by vestibular stimulation

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ABSTRACT

Background: We hypothesized that stress induced suppression of immunity may be prevented by vestibular stimulation by inhibiting the stress axes. **Aims and Objectives:** The present study was undertaken to assess effectiveness of vestibular stimulation in the modulation of immune responses in stress. **Materials and Methods:** A total of 240 healthy college students were randomly divided into four groups control male and female group and vestibular male and female groups with 60 participants in each group. Vestibular stimulation was administered by making the participants to swing on a swing in back to front direction, according to their comfort. After recording base line values, vestibular stimulation was administered to the intervention groups, and post-intervention values were collected during regular classes and during pre-examination period. Blood cell count was performed using Sysmex Machine (Model Sysmex XP 100) (an automatic multi parameter blood cell counter) manufactured by Sysmex India Pvt. Ltd. **Results:** Vestibular stimulation limited stress induced changes in total leukocyte count, neutrophil, lymphocyte, monocyte, eosinophil, and absolute eosinophil count, counts in both male and female intervention groups. Stress induced decrease was prevented in female intervention group. **Conclusion:** Our study provides further evidence for beneficial effects of vestibular stimulation in limiting stress induced changes in immune responses.

KEY WORDS: Vestibular Stimulation; Immunity; Stress; White Blood Cells; College Students

INTRODUCTION

The term "immunity" refers to the resistance exhibited by the host toward injury caused by microorganisms and their products. In addition to its generalized innate immunity, the resistance that an individual acquires during life is known as acquired immunity.[1] Origination of human immune system is in the bone marrow where they mature, migrate and circulate in the body tissues and blood stream. The innate immune system components include granulocytes or polymorph nuclear leukocytes, the group to which neutrophils, eosinophils and basophils, macrophages/ monocytes, and natural killer cells (NK cells). Acquired immunity components include B lymphocytes, a major defense against infections and T lymphocytes responsible to proliferation of antigen.[2]

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Stress is defined as a way in which environmental demands on strain on individual's adaptive capacity, resulting in both psychological demands as well as biological changes that could place at risk for illness.[3] It affects different functions of the human body such as body metabolism, digestion, appetite, sleep, sexuality, and fertility.[4] Acute and chronic psychological stress harms immune system. It was reported

that cellular and humoral immunity is suppressed by chronic stress whereas acute stress suppresses cellular immunity.[5,6]

Studies show that lymphocytosis, mobilization of specific lymphocyte subtypes includes cytotoxic cells such as NK cells and CD8T cells, increased NK cell cytotoxicity, increased salivary and serum immunoglobulin A secretion rate, stimulation of aspects of the complement system, enhanced vaccination response, and faster wound healing, immune cell subtypes such as T regulatory cells, memory T cells, and immune cells specific to certain pathogens, such as cytomegalovirus, are sensitive to acute psychological stress.[7]

The vestibular stimulation is the sensory apparatus of the inner ear that helps the body maintain its postural equilibrium. It influences our activities of daily life. Vestibular system is connected with hippocampus, raphe nucleus, locus coeruleus, thalamus, amygdala, insular cortex, anterior cingulated cortex, prefrontal cortex, cerebellum, occipital cortex, putamen, parietal lobe and other areas of brain[8] and plays a major role in relieving stress, cancer pain, promotes sleep, improves immunity, improves cognition, and also treats endocrine disorders.[9-11] The present study was undertaken to assess effectiveness of vestibular stimulation in the modulation of immune responses in stress and hypothesized that stress induced suppression of immunity may be prevented by vestibular stimulation by inhibiting the stress axes.

MATERIALS AND METHODS

Study Design

This was a longitudinal follow-up study in which, participants were assessed 3 times. Baseline values were recorded during regular classes (with no examination in preceding 2 weeks and coming 2 weeks). After recording base line values, vestibular stimulation was administered to the intervention groups, and post-intervention values were collected after 8 months (during regular classes) (146 ± 5.6 days in males and 147 ± 6 days in females) and after 16 months (during pre-examination period) (268 ± 5 days in males and 268 ± 6 days in females) followed by vestibular stimulation. Vestibular stimulation was not administered to the control group. However, values were recorded at the corresponding points in time.

Setting

The present study was conducted at Little Flower Medical Research Centre, Kerala, and Little Flower Institute of Medical Sciences and Research, Kerala, India.

Study Population

A total of 240 healthy young adults of the age group of 18-24 of either sex were a part of this research after obtaining written consent from them. Participants involved in drug/alcohol abuse, and those taking any kind of medication or suffering from any somatic or mental disorders, participants with a history of use of corticosteroids in the past year, with a history of antidepressant medication, on hormone supplements including oral contraceptives, those with ear infections or any vestibular disturbances, cardiorespiratory disorders those already following stress management methods and were excluded. Selected participants were randomly assigned to four groups:

Group MC (n = 60): Control male group (no vestibular stimulation was administered).
Group FC (n = 60): Control female group (no vestibular stimulation was administered).
Group MV (n = 60): Intervention male group (vestibular stimulation was administered).
Group FV (n = 60): Intervention female group (vestibular stimulation was administered).

Vestibular Stimulation

Vestibular stimulation was administered by making the participants swing on a swing, according to their comfort (back to front direction) once in a day, for 5 days in a week at their leisure time (8:30-9:30 am, 11:00-12:00 am, 1:00-2:00 pm, and 4:00-5:00 pm in four groups) as described earlier.[12]

Assessment of Immunity

Blood cell count was performed using Sysmex Machine (Model Sysmex XP 100) (an automatic multi parameter blood cell counter) manufactured by Sysmex India Pvt. Ltd.

Ethical Consideration

The study was approved by Institutional Ethics Committee. The study was performed in accordance with the "Ethical Guidelines for Biomedical Research on Human Participants, 2006" by the Indian Council of Medical Research and the Declaration of Helsinki, 2008.

Data Analysis

Statistical analysis was performed using SPSS 20.0 version. Mean and standard deviations of all the observations were calculated. Comparison between the groups was performed by two-way ANOVA and *post hoc* by Bonferroni posttest. Significance was accepted at $P < 0.05$.

RESULTS

Total leukocyte count decreased significantly and remained in normal limits, followed by vestibular stimulation in intervention females ($P < 0.05$) when compared with control group females. Stress induced increase in total leukocyte count was limited in both male and female intervention groups (Tables 1 and 2).

Neutrophil count decreased significantly and remained in normal limits, followed by vestibular stimulation in intervention males ($P < 0.01$) when compared with control group males. Stress induced increase was prevented in both male and female intervention groups (Tables 1 and 2).

Lymphocyte count increased significantly and remained in normal limits, followed by vestibular stimulation in intervention males ($P < 0.001$) when compared with control group males. Stress induced decrease was prevented in both male and female intervention groups (Tables 1 and 2).

Eosinophil count and absolute eosinophil count was not significantly changed followed by vestibular stimulation in both male and female intervention groups. However, the stress induced decrease was prevented in both male and female intervention groups (Tables 1 and 2).

Monocyte count significantly decreased and remained in normal limits, in both male and female intervention groups ($P < 0.001$) when compared with corresponding control groups. Stress induced increase was prevented in both male and female intervention groups (Tables 1 and 2).

Basophil count significantly decreased and remained in normal limits, in intervention group females when compared with control group females ($P < 0.05$). Stress induced decrease was prevented in female intervention group (Tables 1 and 2).

DISCUSSION

We have observed an alteration in the blood cell parameters followed by vestibular stimulation indicating a positive impact on immunity. Earlier studies reported that examination stress increases neutrophils, and platelets, and decreases eosinophil's, monocytes basophils, and lymphocytes.[13] In contrast, increase in the absolute number of leukocytes, lymphocytes, $CD8^+$ cells, and $CD16^+$ cells observed during mental stress.[14] Interestingly, it was reported that effect

Table 1: TLC and differential leukocyte count of the male participants before and after vestibular stimulation

Parameters	MV			MC		
	D0	D1	D2	D0	D1	D2
TLC	8700.00±1680.87	8343.33±1039.77	8473.33±948.48***	8646.67±1372.04	8740.00±1317.22	9766.67±1486.57
Neutrophils	63.10±9.02	58.58±7.86**	59.68±6.47***	63.07±6.17	62.88±6.75	73.53±8.07
Lymphocyte	28.05±9.31	35.47±8.58***	34.03±7.01***	28.68±6.36	28.50±6.79	17.55±7.02
Eosinophil	4.38±2.66	3.75±2.49	3.73±2.62***	4.03±2.22	4.13±2.52	1.07±1.01
Monocyte	4.05±2.19	1.92±1.89***	2.22±2.15***	3.88±3.27	4.18±3.45	7.72±4.63
Basophil	0.27±0.44	0.25±0.43	0.30±0.46	0.33±0.47	0.30±0.45	0.13±0.34
Absolute eosinophil count	233.92±114.33	233.35±72.91	234.10±74.93***	265.35±164.39	267.28±156.83	142.75±101.46

Data were presented as mean±SD. TLC: Total leukocyte count, MV: Vestibular males, MC: Control males, D0: Pre-intervention score (during regular classes), D1: Post-intervention score (during regular classes), D2: Post-intervention scores (during pre-examination period), *P<0.05, **P<0.01, ***P<0.001

Table 2: TLC and differential leukocyte count of the female participants before and after vestibular stimulation

Parameters	FV			FC		
	D0	D1	D2	D0	D1	D2
TLC	8498.33±1602.45	7951.67±1076.18*	8015.00±1061.26***	8534.98±1055.29	8638.33±1089.20	9740.00±1261.11
Neutrophils	63.67±7.99	62.08±8.39	62.98±6.44***	62.78±8.77	62.65±6.90	75.47±7.01
Lymphocyte	29.78±9.29	33.38±7.23	32.43±6.02***	30.22±7.75	30.75±6.32	18.20±6.27
Eosinophil	2.73±2.27	2.63±1.67	2.78±1.88***	3.12±2.32	2.77±2.43	1.13±1.16
Monocyte	3.22±2.46	1.38±1.33***	1.43±1.21***	3.20±2.59	3.18±2.73	5.03±2.44
Basophil	0.62±0.63	0.40±0.49*	0.45±0.53**	0.68±0.50	0.65±0.54	0.17±0.37
Absolute eosinophil count	266.58±136.77	270.42±111.47	268.83±133.08***	264.53±138.96	261.33±115.74	155.60±72.05

Data were presented as mean±SD. FV: Vestibular females, FC: Control females, D0: Pre-intervention score (during regular classes), D1: Post-intervention score (during regular classes), D2: Post-intervention scores (during pre-examination period), *P<0.05, **P<0.01, ***P<0.001

of stress on immunity varies based on the type of stress, as acute stress increases in natural immunity and decrease in specific immunity and exam stress mainly suppresses cellular immunity and chronic stress suppress both cellular and humoral immunity.[5] Stress influence immunity through sympathetic fibers which descends from brain to primary and secondary lymphoid tissues.[15] These fibers releases variety of substances which binds to receptors on white blood cells.[16] Stress also influence immunity through hypothalamic-pituitary-adrenal axis, the sympathetic-adrenal-medullary axis, and the hypothalamic-pituitary-ovarian axis.[17] Stress also influence immunity through behavioral changes.[18,19] It was reported that normal functioning of hippocampus is essential for normal humoral immunity and ventral hippocampal formation was reported to modulate specific immunity.[20,21] Interestingly, normal vestibular functioning is essential for normal functioning of hippocampus.[22,23] Hence, we hypothesized that vestibular stimulation may modulate immune functions through hippocampus.[6] Vestibular stimulation may limit stress induced changes in immunity by inhibiting both the stress axes, as both animal and human studies reported decrease in cortisol and blood pressure followed by vestibular stimulation.[24-26] Interestingly, vestibular lesions cause increase in cortisol levels.[27] Animal and human case studies reported that vestibular stimulation has limited stress induced changes in hematological parameters.[28,10] Our results support earlier studies as we have observed that vestibular stimulation effectively limited stress induced changes in immune responses. Strength of the study was the participants who are allied health sciences, who frequently exposed to heavy examination stress. Limitation of the present study includes, the subjects represented in this study were only students of Kerala. Thus, the results cannot be generalized to other levels of education, cities, cultures, and other universities.

CONCLUSION

Our study thus proves the beneficial effects of vestibular stimulation in balancing stress induced changes in immune responses. We recommend further detailed studies including more parameters to gain the explorative knowledge regarding the positive effects vestibular stimulation.

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