ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

Published by JK Welfare & Pharmascope Foundation   Journal Home Page: www.ijrps.com

Effect of vestibular stimulation on cold water stress-induced neurological changes in Wistar rats

Rama Kranthi T[1], Archana R[*2], Senthilkumar Sivanesan[3]

[1]Department of Physiology, Prathima Institute of Medical Sciences, Nagunur, Karimnagar, Telangana -505529, India
[2]Department of Physiology, Saveetha Medical College, Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai - 602105, Tamilnadu, India
[3]Department of Research and Development, Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai - 602105, Tamilnadu, India

Article History:

Received on: 10 Nov 2019
Revised on: 11 Dec 2019
Accepted on: 18 Dec 2019

Keywords:

Caloric vestibular stimulation,
Coldwater swimming stress,
Corticosterone,
Histopathological changes,
Stress

ABSTRACT

The current study was undertaken to see the effects of cold-water stress on the brain and to evaluate the beneficial effect of vestibular stimulation on stress-induced brain changes. Healthy, male, Wistar rats, weighing 180 to 250 gm with 3-6 months of age, were used for the study. Stress was induced by making the animals swim in cold water maintained at 10^0C for 30 min a day, for 14 days. Following cold water swimming stress, bilateral hot water caloric vestibular stimulation was given to the animals using 41^0C temperature water for 15 days. Rats were sacrificed and histopathological brain changes were studied by Hematoxylin & Eosin staining. Serum corticosterone level has increased significantly after cold water swimming stress ($p<0.01$). Corticosterone was less in animals that received caloric vestibular stimulation in comparison with the animals which did not receive caloric vestibular stimulation ($p<0.05$). Coldwater swimming stress had induced focal neuronal atrophy, nuclear pyknosis with congested blood vessels and infiltration of mononuclear inflammatory cells in the hippocampus and hypothalamus. Stressed animals that received caloric vestibular stimulation recovered well and showed the cerebral cortex with the normal neuroglial arrangement. Hypothalamus showed normal morphology and the hippocampus showed a pyramidal layer with a normal thickness in comparison to the animals which did not receive caloric vestibular stimulation. We conclude Caloric vestibular stimulation was effective in reversing the cold-water stress-induced serum corticosterone and histopathological changes in the brain.

*Corresponding Author

Name: Archana R
Phone: +91-9840608149
Email: dr.rarchana@gmail.com

ISSN: 0975-7538

DOI: https://doi.org/10.26452/ijrps.v13i2.88

Production and Hosted by

IJRPS | www.ijrps.com

INTRODUCTION

The name "stress" was first used by Hans Selye, founder of the stress theory. Any alteration in the physiological balance is stress. The reaction to stressor varies largely between individuals and the stress cycle is comprised of four phases: the resting ground phase, the tension phase, the response phase and the relief phase [1] . One of the important systems responding to stress is the activation of the hypothalamic-pituitary-adrenal (HPA) axis to ensure an appropriate response to the stressor.

Chronic stress, which is associated with changes in the hippocampus, may be associated with the onset of psychotic disorders [2]. Vestibular apparatus is the sense organ for equilibrium and becomes functional from the 5^{th} month of gestation. Traditionally controlled vestibular stimulation was used for neurological diagnosis, but it could be used to investigate and treat other clinical conditions [3]. Controlled vestibular stimulation has proven to be helpful in dementia [4], modulation of brain aging neurotransmitters [5] and in the improvement of depression and anxiety. But very little is known about the effects of vestibular stimulation on stress-induced changes in the brain. The present study is taken up to evaluate the effect of cold water stress on changes in the brain of Wistar rats and to evaluate the effect of caloric vestibular stimulation on stress-induced changes in the brain of Wistar rats.

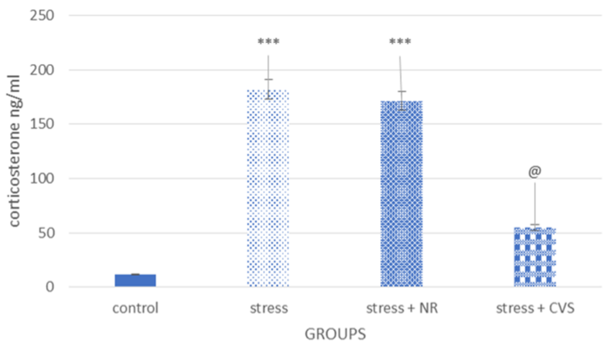

Figure 1: Serum corticosterone levels in control, stress, stressfollowed by natural recovery and stress followed by caloric vestibularstimulation-induced Wistar rats

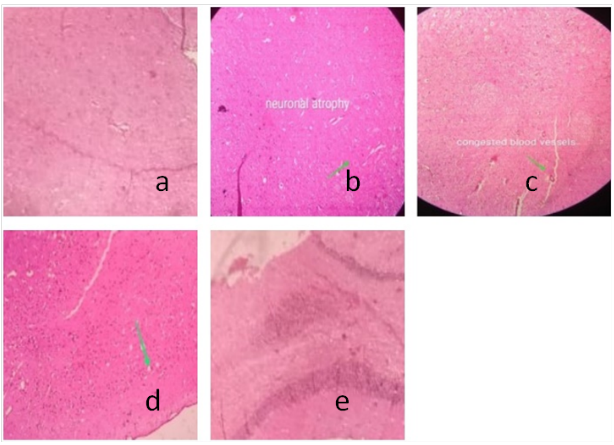

Figure 2: Histopathology hippocampus a. control b. neuronal atrophy c. Congestedblood vessels d. nuclear pyknosise. following controlled vestibular stimulation

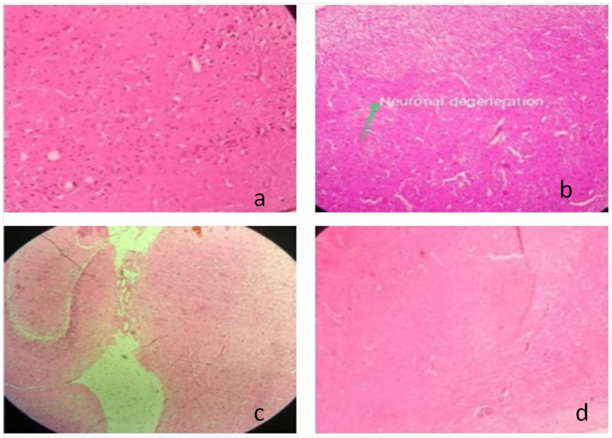

Figure 3: Histopathology of Hypothalamus a. control b. nuclear degenerations. Mononuclearcell inflammatory infiltrated. following controlled vestibular stimulation

MATERIALS AND METHODS

Animals

Male, Wistar rats of 3 -6 months of ageweighing180 to 350 gm were included in the study. Animals were maintained as per the guidelines of the Committee for Control and Supervision of Experiments on Animals. Pellet diet was provided with water *ad libitum*. Four animals were housed in a polypropylene cage. The present study was carried out after obtaining Institutional animal ethical committee clearance (1/PIMS/2017 Dated 24/08/2017).

Experimental design

The animals were randomly selected and grouped as follows,

Group I (n=6) – Control (neither stress nor caloric Vestibular stimulation)

Group II (n= 6) –stress for 14 days (cold water swimming stress for 14 days)

Group III (n= 6) – stress for 14 days + natural recovery(NR) for 15 days

Group IV (n= 6) – stress for 14 days + caloric vestibular stimulation (CVS) for 15 days

Coldwater swimming stress

Rats were made to swim in cold water maintained at ten ^{0}C for 30 min a day between 9.00 AM to 12.00 PM. Plastic containers of 60 cm height, 40 cm diameter were used and the water level was maintained at 30 cm [6].

Caloric vestibular stimulation

Caloric vestibular stimulation was given by irrigating external auditory meatus with 2ml of water

Table 1: Bodyweight in control, stress, stress followed by natural recovery and stress, followed by vestibular stimulation groups in Wistar rats.

Parameter	Control	Stress	Stress followed by natural recovery	Stress followed by caloric vestibular stimulation
Body-weight(grams)	287.75 ±14.32	279 ± 23.84	318.75 ± 28.17	303.33 ± 14.13

Results are expressed as mean ±SEM (n=6).<p-0.05 considered to be significant

maintained at 41^{0}C using a polyethylene tube bilaterally for 15 days [7].

At the end of the experiment, the blood sample was obtained by retro-orbital puncture and animals were sacrificed by decapitation. Blood was allowed to clot and serum was obtained after centrifugation for 20 min at a speed of 3000 rpm. Serum corticosterone was analyzed using a solid-phase enzyme-linked immunosorbent assay (ELISA) method. For analysis of histopathological changes brain was placed in 10% neutral buffered formaldehyde. After proper fixation, sections of 3-5 mm were prepared and submitted to dehydration, clearing impregnation and embedding. Sections were made by microtome and stained by Hematoxylin and Eosin (H&E).

Statistical analysis

Data was analyzed using SPSS 20. One-way analysis of variance followed by Tukey's post hoc test was used for multiple comparisons and expressed as mean ±S.E.M. p-value < 0.05 was considered to be statistically significant.

RESULTS AND DISCUSSION

Table 1 explains the changes in body weight in control, stress, stress followed by natural recovery and stress, followed by caloric vestibular stimulation groups. Results are expressed as mean ±SEM (n=6). Statistical analysis showed no significant changes between the groups.

As given in Figure 1 shows that, Results are expressed as mean ±SEM (n=6). ***p<0.001as compared to the control group. @ p<0.05as compared to the stress group, followed by the NR group; corticosterone has increased significantly in the stress group (181.88±36.32) when compared to the control group (11.74 ± 0.52). Animals that received caloric vestibular stimulation showed lower levels of corticosterone(54.77±9.54) in comparison to animals which were left for natural recovery (171.46 ±35.78) after 14 days of stress.

Coldwater swimming stress-induced neuronal atrophy, nuclear pyknosis with congested blood vessels in Hippocampus (Figure 2).

Nuclear degeneration, mononuclear cell inflammatory infiltrate was observed in Hypothalamus (Figure 3). Stressed animals that received caloric vestibular stimulation recovered well and showed the cerebral cortex with the normal neuroglial arrangement. Hypothalamus showed normal morphology and the hippocampus showed a pyramidal layer with a normal thickness in comparison to the animals which did not receive caloric vestibular stimulation. When Stress is applied for a long duration, it causes hyperactivation of the hypothalamic-pituitary-adrenal (HPA) axis [8], which is mediated by the hippocampus [9]. The prolonged exposure of the hippocampus to the glucocorticoids disturbs the metabolism of the neurons by inhibiting glucose uptake and makes them more sensitive to metabolic inputs [10]. Stress inhibits the inhibitory input to the hypothalamic-pituitary-adrenal (HPA) axis [11], resulting in overactivation of the HPA axis, which increases corticosterone. Brain areas which are targeted by the stress are hippocampus, amygdala and prefrontal cortex [12]. Stress is known to cause morphological rearrangement [13], dendritic atrophy in hippocampal pyramidal neurons especially in the CA3, CA4 region and an impairment of neurogenesis in the dentate gyrus [14–16], and causes thinning of motor cortex [17]. Our current study also proves stress induces pathological and morphological changes in the hippocampus and hypothalamus. The vestibular system has extensive connections with various structures of the brain, which include the hippocampus, amygdala, thalamus, prefrontal cortex [18]. Our previous studies have shown the effectiveness of vestibular stimulation in improving auditory and visual reaction time in stress [19]. Caloric vestibular stimulation can inhibit Hypothalamo Pituitary Adrenal (HPA) axis and Sympatho Adrenal Medullary axis by direct pathway and also by increasing the release of GABA and activating hippocampal formation [20] and decreases corticosterone levels.

CONCLUSIONS

Caloric vestibular stimulation is effective in reversing the cold water stress-induced corticosterone levels and changes in the brain. The decrease in corticosterone might be the reason for changes in the brain following caloric vestibular stimulation.

Funding Support

The authors declare that they have no funding support for this study.

Conflict of Interest

The authors declare that they have no conflict of interest.

REFERENCES

[1] O Rom and A Z Reznick. The Stress Reaction: A Historical Perspective. 905:1–4, 2016. Advances in experimental medicine and biology.

[2] L J Phillips, P D Mcgorry, B Garner, K N Thompson, C Pantelis, S J Wood, and G Berger. Stress, the hippocampus and the hypothalamic-pituitary-adrenal axis: implications for the development of psychotic disorders. *Australian and New Zealand Journal of Psychiatry*, 40(9):725–741, 2006.

[3] S M Miller and T T Ngo. Studies of caloric vestibular stimulation: implications for the cognitive neurosciences, the clinical neurosciences and neurophilosophy. *Acta Neuropsychiatrica*, 19(3):183–203, 2007.

[4] K V Jinu, J K Mukkadan, and R Archana. Effect of bilateral and unilateral caloric vestibular stimulation in scopolamine-induced dementia in Wistar albino rats. *Biomedical Research*, (15):29–29, 2018.

[5] K Sai Sailesh, R Usha, P Padmanabha, J Abraham, and J K Mukkadan. Can Controlled Vestibular Stimulation Delay Brain Aging? *Asian Journal of Health Sciences*, 2(1), 2014.

[6] H S Nagaraja and P S Jeganathan. Forced swimming stress-induced changes in the physiological and biochemical parameters in albino rats. *Indian Journal of Physiology and Pharmacology*, 43(1):53–59, 1999.

[7] V P Varghese, S S Kumar, R Archana, and J K Mukkadan. Vestibular modulation of thyroid function in forced cold water swimming stress-induced Wistar albino rats. *International Journal of Research in Ayurveda and Pharmacy*, 6(4):513–515, 2015.

[8] K Alkadhi. Brain Physiology and Pathophysiology in Mental Stress. ISRN Physiology. pages 1–23, 2013.

[9] L. J Zhu, M. Y Liu, H Li, X Liu, C Chen, Z Han, and Q. G Zhou. The Different Roles of Glucocorticoids in the Hippocampus and Hypothalamus in Chronic Stress-Induced HPA Axis Hyperactivity. *PLoS ONE*, 9(5), 2014.

[10] R M Sapolsky, D R Packan, and W W Vale. Glucocorticoid toxicity in the hippocampus: in vitro demonstration. *Brain Research*, 453(1-2):90180–90181, 1988.

[11] M Joëls, H Karst, D Alfarez, V M Heine, Y Qin, E Riel, Van, and H J Krugers. Effects of Chronic Stress on Structure and Cell Function in Rat Hippocampus and Hypothalamus. *Stress*, 7(4):221–231, 2004.

[12] J D Bremner. Traumatic stress: effects on the brain. *Dialogues in Clinical Neuroscience*, 8(4):445–461, 2006.

[13] B S Mcewen. Plasticity of the Hippocampus: Adaptation to Chronic Stress and Allostatic Load. *Annals of the New York Academy of Sciences*, 933(1):265–277, 2006.

[14] E Fuchs, G Flügge, F Ohl, P Lucassen, G K Vollmann-Honsdorf, and T Michaelis. Psychosocial stress, glucocorticoids, and structural alterations in the tree shrew hippocampus. *Physiology & Behavior*, 73(3):285–291, 2001.

[15] B S Mcewen. Stress and hippocampal plasticity. *Annual Review of Neuroscience*, 22(1):105–122, 1999.

[16] K M Gill and A A Grace. Differential effects of acute and repeated stress on the hippocampus and amygdala inputs to the nucleus accumbens shell. *International Journal of Neuropsychopharmacology*, 16(9):2013–2025, 2013.

[17] A R Khan, C D Kroenke, O Wiborg, A Chuhutin, J R Nyengaard, B Hansen, and S N Jespersen. Differential microstructural alterations in rat cerebral cortex in a model of chronic mild stress depression. *PLOS ONE*, 13(2), 2018.

[18] C Gurvich, J J Maller, B Lithgow, S Haghgooie, and J Kulkarni. Vestibular insights into cognition and psychiatry. *Brain Research*, 1537:244–259, 2013.

[19] A Rajagopalan, S Kumar, and J Mukkadan. Effect of vestibular stimulation on auditory and visual reaction time in relation to stress. *Journal of Advanced Pharmaceutical Technology & Research*, 8(1):34–38, 2017.

[20] Kumar, sai sailesh, and Mukkadan. Can controlled vestibular stimulation reduce stress. *Health Sciences*, 2(3):JS001, 2013.

