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# Stress, Fever and Sixth Sense: A Review of the Links.

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## ABSTRACT

Stress induced hyperthermia" is a regulated change in temperature (a true fever). Psychological stress has been shown to cause a rapid rise in the body temperature of rats rabbits and humans. The present review suggests that vestibular stimulation: A sixth sense, can influence stress induced hyperthermia. Further work is necessary to examine the role of vestibular stimulation in stress induced hyperthermia. **Keywords:** Fever, Stress, Vestibular stimulation



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#### INTRODUCTION

"Stress induced hyperthermia" is a regulated change in temperature (a true fever). Psychological stress has been shown to cause a rapid rise in the body temperature of rats rabbits and humans.[1] The existence of emotional hyperthermia in humans was established.[2] Clinical studies have implicated adolescence as an important and vulnerable period during which traumatic experiences can predispose individuals to anxiety and mood disorders. Juvenile stress can induce long-term alterations in body temperature regulation and heighten the increase in temperature associated with anticipation of social defeat. [3] The degree of body temperature is an important indication of health as well as illness and often constitutes the basis for deciding whether or not to initiate treatment. [4] When mammals, including man, are confronted with a stressful event, their core body temperature rises, stress-induced hyperthermia. Body temperature recording is recommended to include as a physiological readout parameter of stress. [5, 6]

Stimulating vestibular system: A sixth sense, [7] by controlling direction, duration, frequency and intensity is called controlled vestibular stimulation. There exists abundant physiological evidence a unique linkage between the neuro-vestibular system and the regulation of homeostasis, circadian rhythms, and body composition. [8] The hypothalamus ensures normal (e.g., feeding, thermoregulation, cardiovascular, fluid balance) and adaptive (e.g., stress, exercise) homeostasis by altering a variety of neural and endocrine effector mechanisms, including the balance among sympathetic and parasympathetic outflow. [9]Abundant anatomical evidence that the vestibular nuclei project directly to hypothalamus and to numerous brainstem autonomic nuclei that, in turn, project to the hypothalamus.

Moreover, a number of these nuclei have been shown to influence homeostatic and circadian function. Such nuclei include the parabrachial, caudal raphe nuclei, solitary nucleus, and the locus coeruleus. [10-14] Vestibular stimulation, depending on side of stimulation, has a modulating effect on mood and affective control. [15]

The purpose of this article is to review research reports related to vestibular stimulation and its effect on stress induced hyperthermia and to establish a hypothesis and to suggest translational research in this area.

### MATERIALS AND METHODS

Articles were selected from searches at google.com, pubmed.com, British medical journal.com, Medline, ERIC, frontiersin.org, hindawi.com, scopus.com and other online standardized journals.

### Vestibular stimulation effects stress induced hyperthermia through hypothalamus

The fundamental autonomic stress response to psychological stress is hyperthermia. Stress induces hyperthermia through hypothalamic medullary monosynaptic stress pathway which stimulates sympathetic neurons and induces thermogenesis in brown adipose tissue. It was observed that rostral medullary raphe region (rMR) and dorsomedial hypothalamus (DMH) mediate a psychosocial stress-induced thermogenesis. DMH stimulates paraventricular hypothalamic nucleus and cause release of stress hormones. [16] Glucocorticoids may have a role in stress-induced fever. [17] The main characteristic of the stress response is activation of the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic adrenomedullary (SA) system. [18] Chemical thermogenesis is mediated by epinephrine. [19] Raise in the body temperature during emotional excitement may be due to unconscious tensing of muscles. [20]

Single, paired, and rhythmic stimulation of the vestibular nerve and lateral vestibular nucleus of Deiters produces three types of response from hypothalamic neurons, with short, long, and intermediate latent periods. [21] PVN neurons receive vestibular afferents bilaterally according to the intensity of vestibular stimulation, with the information received probably integrated in the hypothalamus to participate in vestibulo-autonomic reflexes. [22] Neurons of the PVN showed different patterns of response with various combinations of inhibition and excitation sequences following caloric vestibular stimulation. [23] Vestibular stimulation inhibits both HPA axis and decreases cortisol level and heart rate and blood pressure within normal limits and brings to stress- less condition. [24] Caloric stimulation (CS) of the vestibular apparatus inhibited noradrenergic neuronal activity in the locus coeruleus (LC). [25]

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#### Vestibular stimulation effects stress induced hyperthermia through food intake

Eating has been theorized as a coping strategy for stressful situations. [26] Stress was correlated with being overweight in children. [27] Consumption of carbohydrate may relieve depressive moods and this has been considered as part of the causal link for developing obesity. Increased consumption of carbohydrate dense foods such as sweets, cookies, snacks, and fast food was associated with higher perceived stress in females. [28] Stress can cause a rapid increase in energy expenditure. Stress hormones circulate the blood and communicate to cells to break down energy stores ready to provide a greater supply of energy. [29] Food intake was increased overall during the 6 days of repeated stress and body temperature was increased during stress and during recovery from stress during 6 days of repeated stress. [30] The process of heating the body through dietary sources is known as thermogenesis, or diet-induced thermogenesis. [31]

Sympathetic discharge and adrenaline cause an immediate increase in the rate of metabolism due to due to uncoupling of oxidative phosphorylation that is oxidation of food stuffs is associated with release of heat rather than generation of ATP. Heat produced in this way is called chemical thermogenesis. [20] Vestibular system is having extensive interactions with hypothalamus, dorsal raphe nucleus, nucleus tractus solitarius, locus coeruleus, hippocampal formation and regulates food intake. [32]

### Vestibular stimulation effects stress induced hyperthermia through cutaneous circulation

Psychological stress causes activation of 5-HT2A receptors in neural pathways that control thermogenesis in the brown adipose tissue and facilitate cutaneous vasoconstriction. [33] The central hypothalamic-pituitary-adrenal (HPA) axis is activated following stress signals such as 5-hydroxytryptamine, acetylcholine, and inflammatory cytokines. Stress signals also activate the locus coeruleus (LC) of the brain stem eliciting a sympathetic nervous system response. Human skin expresses CRH as well as CRH receptors (CRH-R). The CRH-R1 $\alpha$ isoform is the predominant CRH receptor in skin and is expressed in all major cell populations of epidermis, dermis, and subcutis. By contrast, CRH-R2 is expressed predominately in hair follicles, sebaceous and eccrine glands, muscle and blood vessels. [34] Vestibular inputs can entrain the firing of cutaneous sympathetic neurones and increase their normally weak pulse-related rhythmicity. [35] Bilateral sinusoidal galvanic vestibular stimulation (sGVS), evokes a potent entrainment of sympathetic outflow to muscle and skin. Very low frequencies of sGVS modulate skin sympathetic nerve activity (SSNA). [36]

### CONCLUSION

Collectively, the present review suggests that between vestibular stimulation can influence stress induced hyperthermia. Further work is necessary to examine the role of vestibular stimulation in stress induced hyperthermia.

### REFERENCES

- [1] LONG, N. C., A. J. VANDER AND M. J. KLUGER. Stress-induced rise of body temperature in rats is the same in warm and cool environments. PHYSIOL BEHAV. 47(4) 773-775, 1990.
- [2] Briese E. Emotional hyper thermia and performance in humans. Physiol Behav. 1995 Sep; 58(3): 615-8.
- [3] Yee N, Plassmann K, Fuchs E. Juvenile stress impairs body temperature regulation and augments anticipatory stress-induced hyperthermia responses in rats. Physiol Behav. 2011 Sep 1;104(3):408-16.
- [4] Ma<sup>•</sup> rtha Sund-Levander, Christina Forsberg and Lis Karin Wahren. Normal oral, rectal, tympanic and axillary body temperature in adult men and women: a systematic literature review. Scand J Caring Sci; 2002; 16; 122–128.
- [5] Vinkers CH, Penning R, Hellhammer J, Verster JC, Klaessens JH, Olivier B, Kalkman CJ. The effect of stress on core and peripheral body temperature in humans Stress. 2013 Sep;16(5):520-30.
- [6] Olivier B, Zethof T, Pattij T, van Boogaert M, van Oorschot R, Leahy C, Oosting R, Bouwknecht A, Veening J, van der Gugten J, Groenink L. Stress induced hyperthermia and anxiety: Pharmacological validation. Eur J Pharmacol. 2003 Feb 28;463(1-3):117-32.
- [7] Kumar Sai Sailesh, Archana R, Mukkadan J K. Thinking with your sixth sense. RJPBCS. 2014; 5(4): 481-485.



- [8] Patrick M. Fuller, Timothy A. Jones, Sherri M. Jones, and Charles A. Fuller. Neurovestibular modulation of circadian and homeostatic regulation: Vestibulohypothalamic connection? PNA. November 26, 2002; 99(24):15723–15728.
- [9] Paxinos, G. The Rat Nervous System (Academic, New York), 1995; 2nd Ed.
- [10] Saper, C. B. & Loewy, A. D. Brain Res. 1980; 197, 291–317.
- [11] Herbert, H., Moga, M. M. & Saper, C. B. J. Comp. Neurol.1990; 93, 540–580.
- [12] Balaban, C. D. & Porter, J. D. (1998) J. Vestib. Res.1998; 8, 7–16.
- [13] Kumar Sai Sailesh, J.K.Mukkadan Can Controlled Vestibular Stimulation reduce stress A Review." Health sciences. 2013; 2(3):js001.
- [14] Kumar Sai Sailesh, George Jissa, Mukkadan J.K. Cancer pain relief by vestibular stimulation A hypothesis. . Health sciences. 2013; 4(2): jS004D.
- [15] Nora Preuss, Gregor Hasler, Fred W. Mast. Caloric vestibular stimulation modulates affective control and mood. Brain stimulation. 2014; 7: 133-140.
- [16] Naoya Kataoka, Hiroyuki Hioki, Takeshi Kaneko, Kazuhiro Nakamura. Medullary raphe circuit driving brown adipose tissue thermogenesis and hyperthermia. Cell metabolism. 2014;20(2): 346-358.
- [17] Soszyński D. Stressful increase in body temperature-hyperthermia or fever. Postepy Hig Med Dosw. 1999; 53(6):855-70.
- [18] Navarro-Oliveira CM, Vassilieff VS, Cordellini S. The sympathetic adrenomedullary system, but not the hypothalamic-pituitary-adrenal axis, participates in aorta adaptive response to stress: nitric oxide involvement. Auton Neurosci. 2000 Oct 2; 83(3):140-7.
- [19] Lauralle Sherwood. Essentials of Physiology.Delhi. cengage Learning India Private Limited. 2012; 4<sup>th</sup> edition: P 519.
- [20] Sabyasachi Sircar. Principles of Medical Physiology. New York. Thieme Stuttgart. 2008;PP 697-699.
- [21] S. S. Grigoryan, O. G. Baklavadzhyan, S. M. Minasyan, Ts. I. Adamyan, É. S. Gevorkyan, S. G. Sarkisyan. Responses of hypothalamic neurons to stimulation of vestibular nerve and lateral vestibular nucleus in the rabbit. Neuroscience and Behavioral Physiology. 1999, Volume 29, Issue 1, pp 61-66.
- [22] Liu F, Inokuchi A, Komiyama S. Neuronal responses to vestibular stimulation in the guinea pig hypothalamic paraventricular nucleus. Eur Arch Otorhinolaryngol. 1997; 254(2):95-100.
- [23] G. B. Azzena, F. Melis, M. A. Caria, G. P. Teatini, G. Bozzo. Vestibular projections to hypothalamic supraoptic and paraventricular nuclei. Archives Italiennes de Biologie. 1993; 131(2-3).
- [24] Sailesh KS, Mukkadan JK. Psychoneuroimmuno modulation by controlled vestibular stimulation. J Clin Exp Res. 2013; 1(3): 68-70.
- [25] Nishiike S, Takeda N, Uno A, Kubo T, Yamatodani A, Nakamura S. Cholinergic influence on vestibular stimulation-induced locus coeruleus inhibition in rats. Acta Otolaryngol. 2000 Mar;120 (3):404-9.
- [26] Jenkins S, Horner SD: Barriers that influence eating behaviors in adolescents.J Pediatr Nurs. 2005, 20:258-267.
- [27] Koch FS, Sepa A, Ludvigsson J: Psychological stress and obesity. J Pediatr. 2008, 153:839-844
- [28] Rafael T Mikolajczyk, Walid El Ansari and Annette E Maxwell. Food consumption frequency and perceived stress and depressive symptoms among students in three European countries. Nutrition Journal 2009, 8:31.
- [29] <u>http://www.emedexpert.com/tips/metabolism-tips.shtml</u>
- [30] Bhatnagar S, Vining C, Iyer V, Kinni V. Changes in hypothalamic-pituitary-adrenal function, body temperature, body weight and food intake with repeated social stress exposure in rats. J Neuroendocrinol. 2006 Jan;18(1):13-24.
- [31] http://www.livestrong.com/article/483701-foods-to-increase-body-temperature/
- [32] Kumar Sai Sailesh. Vestibular Balance of Food intake. Int J Pharm Bio Sci 2014 July; 5(3): (B) 1069 1073.
- [33] Ootsuka Y, Blessing WW, Nalivaiko E. Selective blockade of 5-HT2A receptors attenuates the increased temperature response in brown adipose tissue to restraint stress in rats. Stress. 2008 Mar;11(2):125-33.
- [34] Jessica M. F. Hall, desAnges Cruser, Alan Podawiltz, Diana I. Mummert, Harlan Jones, and Mark E. Mummert, "Psychological Stress and the Cutaneous Immune Response: Roles of the HPA Axis and the Sympathetic Nervous System in Atopic Dermatitis and Psoriasis," Dermatology Research and Practice, vol. 2012, Article ID 403908, 11 pages, 2012.



- [35] James C, Stathis A, Macefield VG. Vestibular and pulse-related modulation of skin sympathetic nerve activity during sinusoidal galvanic vestibular stimulation in human subjects. Exp Brain Res. 2010 Apr;202(2):291-8.
- [36] Hammam E, Dawood T, Macefield VG. Low-frequency galvanic vestibular stimulation evokes two peaks of modulation in skin sympathetic nerve activity. Exp Brain Res. 2012 Jun;219(4):441-6.