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Salivary Stress Markers, Depression, Mood State and Back Pain in Healthy Men in Two Bed Rest Conditions: Validation of Two Models for Human Space Flight

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Abstract

The NASA promise to long-duration space flight includes astronauts who will be returning to the moon as well as those who will take part in human missions to Mars. Successful exploration will require a better understanding of the effects that extended missions pose for the behavioral health of astronauts, not just during flight but also pre and post-flight. The potential for psychiatric disorders developing in long-duration crews during or after missions requires that consideration be given to prevention and treatment .The objective of this study was to validate a ground-based models (Two bed rest conditions such as 6° head-down tilt (HDT) and bed rest position (HB) for microgravity and zero gravity and to study the effects of simulated condition on depression, mood state, back pain and biochemical stress markers. The aim of the present study was to determine the effects of 20-day HDT & HB on psychic stress, depression, mood-state, backache and headache in 10 healthy male volunteers. Psychological state was assessed by a stress test, mood state and cortisol was measured in saliva. During HDT and HB, all volunteers developed psychic stress, and the diurnal rhythm of cortisol secretion was significantly increased in simulated conditions. In addition, urine excretion of dopamine, epinephrine and norepinephrine were significantly increased. Thus 6° HDT & HB appears to be a valid model to induce psychic stress and neuroendocrine-related changes that could also be encountered by astronauts and marsonaunts during long-duration spaceflights.

Keywords: Head-down tilt; Bed rest position; Cortisol; Norepinephrine; Epinephrine

Introduction

Traditionally, the development of technology has taken the forefront in our efforts to sustain life underwater, in the air, in outer space, and in complex technological environments. The achievement of these technological and engineering feats provided an awareness of the physiological and biomedical stressors associated with operating in these environments. Myriad physiological conditions arising from spaceflight include Space Adaptation Sickness (SAS), bone demineralization, fluid shifts, and cardiovascular deconditioning [1]. Accordingly, the development of biomedical and physiological countermeasures was undertaken in an effort to begin overcoming these stressors. These countermeasures allow us to sustain human presence in flight for increasing periods as well as to participate in increasingly complex and lengthy missions [2]. Space flight, whether of long or short duration, occurs in an extreme environment that has unique stressors. Even with excellent selection methods, behavioral problems among space flight crews remain a threat to mission success. Assessment of factors that are related to behavioral health can help minimize the chances of distress and, thus, reduce the likelihood of behavioral conditions and psychiatric disorders arising within a crew. Correspondingly, countermeasures that spotlight on prevention and treatment can diminish the behavioral conditions and psychiatric disorders that, should they arise, would impact mission success.Russian experience in long duration spaceflight has revealed that among the most critical problems facing humans in long duration spaceflight, after the biomedical, are the psychological and psychosocial [3]. Physiological stressors inherent in the long-duration space environment pose the greatest challenge to human spaceflight [4]. The human body must physically adapt to the foreign microgravity environment and, in doing so, undergo cardiovascular, muscular, and skeletal deconditioning as well as changes in the immune and nervous systems, and radiation exposure [5,6]. Regarding the physical effects of adaptation to spaceflight, about 40-50% of flight crews during their first few days of microgravity experience a condition called Space Adaptation Sickness (SAS), which causes symptoms such as nausea, disorientation, headache, and a sea-sick or flu-like feeling. Some of the above named factors can be alleviated by exercise and pharmacological interventions, but others remain a significant obstacle in maintaining the health of astronauts during long duration missions [7]. Similarly, crews must undergo the stress associated with re-adapting to the 1-g environment on return journey to Earth. These physiological factors are a significant concern for a human mission to Mars. These and other adaptive physiological and physical processes represent change from a normal state of functioning for the astronauts and can thus contribute to increased psychological stress levels [8]. Many microgravity-induced responses in humans, including total body height increase and back pain, have been studied in simulation using 6 degrees of head-down tilt (HDT) [8-12]. Bed rest exposes humans to restricted mobility. It has been shown that HDT with balanced traction is a better method than horizontal bed rest (HBR) to induce back pain in healthy subjects [8]. There are very few studies on the correlation of Depression, Mood State, Back Pain and biochemical stress markers in simulating microgravity

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environments. Hence, this study was designed to examine depression, mood state, back pain and biochemical stress markers in normal healthy subject in two bed rest conditions (-6° head-down-tilt (HDT) bed rest and zero gravity of bed rest position (HB).

Materials and Methods

After sanction by the local ethics committee and acknowledgment of informed consent, ten healthy male volunteers (age 25.8, 7.5 (SE) yr, weight 64.2, 6.2 kg, height 167.7, 76.2 cm) were subjected to permanent bed rest for 20 days at 6° HDT and ten healthy male volunteers (age 26.5, 6.9 (SE) yr, weight 67.1, 5.6 kg, height 168.6, 7.8 cm) were subjected to permanent bed rest for 20 days at 6° H R. During the HDT period and HB, the subjects were not allowed to sit or to leave their bed; physical activities were limited to a very low state. The daily routine procedures were standardized and were kept constant during the entire study period. According to this study protocol, measurements were taken before the start of the HDT and HB period (Under normal conditions), at the first day and 20 days after the end of the bed rest (Post). The location of back pain and headache were measured using pain drawings [10], and intensity of pain was measured on a 10-cm visual analog scale between 2:00 and 3:00 PM daily and a set of analog scales was used to rate subjective feelings [10,12]. This set of scales consisted of 16 items grouped into three factors: alertness, contentedness, and calmness. Saliva was collected. Samples were frozen, and free-cortisol concentrations were quantified by a commercially available ELISA according to the instruction of the manufacturer (Orion Diagnostica, Espoo, Finland). Significant differences between mean values were tested with analyses of variance and paired *t* tests. The Wilcoxon signed-rank test was used for nonparametric tests.

Results

Back pain and headaches were significantly more intense during simulated microgravity and zero gravity as compared to after and before bed rest conditions (Table 1). Normal physiological variations in salivary cortisol secretion were higher in the morning followed by a decline down in the evening. Salivary cortisol concentration showed statistically significant increase during bed rest conditions as compared to normal condition and after (Table 2, P<0.001). Twenty-four-hour urine secretion of epinephrine, dopamine and nor epinephrine were significantly increased in both bed rest conditions. Beck Depression Inventory scores for all subjects were 0 before both bed rest conditions, while; during rest conditions scores were higher than subjects in normal condition ($p<.075$). All subjects had significantly higher scores on the activity scale of the Bond-Lader mood questionnaire (Bond and Lader, 1974) ($p< .068$) during both bed rest conditions.

Discussion

This study showed that subjects who had more back pain and headache were more depressed, and had lower activity scores on the mood state questionnaire during simulated conditions than before and after bed rest conditions. The pain intensity during simulated condition was similar to that reported by others in astronauts [9]. One possible explanation for the increased pain intensity during simulated condition could be significant increase and elongation of the spinal column, which could induce stretching of the lumbar nerve roots [8]. A headache was significantly more intense during both rest conditions as compared to after and normal condition, as observed in previous studies [7,13]. It could be due to increase in intracranial pressure. Intracranial pressure (ICP) increased by 2 mmHg immediately after the onset of HDT [8]. This increase in ICP is mainly due to the shift of CSF from the spine toward the head [13-16]. In this study, cortisol was determined in the saliva specimen for different reasons. Firstly, it represents a noninvasively method, secondly, determination of cortisol in saliva allows the detection of the protein-unbound free cortisol as well as unbound [17]. The free cortisol can reach target cells and their receptors [18] and hence reflects the biologically active cortisol that is responsible for the induction of physiological or pathophysiological effects. It has been reported that cortisol levels show a diurnal rhythm under physiological conditions [9]. In consequence, these finding may indicate that chronic stress which leads to alterations in the regulation of the hypothalamic-pituitary-adrenocortical axis, ending up in the suppression of its circadian regulation. Changes of the circadian rhythm of cortisol secretion during simulated microgravity and zero gravity due to excretion of catecholamines increased for dopamine and nor epinephrine and returned after simulated condition to lower concentrations, although amounts of catecholamines secreted and post were significantly elevated in part above pre values. Our study are alarming and have been included to emphasize the increased risk of behavioral health and psychiatric problems that is associated with extended stays in highly isolated, confined, and extreme environments;

Variables	HDT			HB		
	Pre- (before start of head-down tilt)condition (Mean(SD)	D20(last day of head-down tilt)Mean(SD)	Post Mean(SD	Pre- (before start of HB) condition (Mean(SD)	D20(last day of HB) Mean(SD)	Post Mean(SD)
Back pain	0	4.6 (3.4)	2.1 (1.6)	0	4.4 (3.2)	1.9 (1.1)
Headache	0	5.4 (2.6)	2.4 (1.3)	0	4.6 (1.2)	1.8 (1.2)

Table 1: Pain Intensities on a Visual Analog Scale (cm) before, during, and after HDT and HB.

Variables	HDT			HB		
	Pre- (before start of head-down tilt)condition (Mean(SD)	D20(last day of head-down tilt)Mean(SD)	Post Mean(SD	Pre- (before start of HB) condition (Mean(SD)	D20(last day of HB) Mean(SD)	Post Mean(SD)
Cortisol (morning 8 AM), nmol/l	13.63 (5.68)	24.65(6.89)	16.69(8.67)	13.25(5.64)	26.38(9.58)	12.68(6.87)
Cortisol (evening 8 PM), nmol/l	4.23(2.34)	12.69(5.21)	5.63(4.55)	3.99(1.21)	13.87(6.84)	4.68(2.35)
Epinephrine, mg/24 h	7.38(2.33)	16.65 (4.68)	6.02(3.05)	6.98(2.11)	14.63(4.56)	8.91(2.65)
Norepinephrine, mg/24 h	36.45(12.35)	71.12(21.68)	45.68(12.56)	35.66(11.56)	72.68(13.96)	46.96(22.68)
Dopamine, mg/24 h	214.25(44.56)	356.12(42.23)	201.34(45.68)	228.45(44.86)	328.12(45.67)	212.32(41.23)

Table 2: Saliva cortisol and urine catecholamine secretion parameter before, during and after HDT and HB.

such long durations are clearly at the outside boundary of our experience and evidence base. In view of long-duration flights on space stations or interplanetary mission such as Mars, there is a need for additional experiments by which the biological significance of spaceflight-induced changes of neuroendocrine system related in real microgravity such as in parabolic flight can be investigated further. In this respect, HDT and HB appear to be a helpful ground-based surrogate model.

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