Objectives:
Orthostatic intolerance is one of the physical impairments that occur after space flight. Although several candidate mechanisms have been proposed, the physiological mechanism underlying this condition remains unclear. Recently, we have demonstrated that the vestibular system has a significant role in controlling arterial pressure (AP) during gravitational stress (vestibulo-cardiovascular reflex). The vestibular system is known to be highly plastic; i.e., the sensitivity of the vestibular system is altered if subjects are maintained in a different gravitational environment. Thus, it is possible that microgravity induces a plastic alteration in the vestibulo-cardiovascular reflex that may result in inadequate adjustment of the AP upon postural change (changes in direction of gravity). To examine this hypothesis a series of experiments are conducted both conscious rats and human subjects.

- Whether gravitational alteration induced plasticity of the vestibulo-cardiovascular reflex in conscious rats?
- To examine the role of the vestibular system for controlling AP in animals, the AP responses to gravitational changes have been compared between intact and vestibular lesioned (VL) animals. However, in human studies such invasive and irreversible methods like VL could not be used. Accordingly, an alternative method for acutely interrupting the vestibular-mediated AP response to gravitational change is required. Whether a continuous application of galvanic vestibular stimulation (GVS) might obscure the gravity-based input to the vestibular organs and/or might reset the vestibulo-cardiovascular system, and then reduces the vestibular-mediated AP response to gravitational change?
- Using GVS, the role of the vestibular system in AP control during 60° head-up tilt (HUT) was examined young healthy subjects.
- The role of the vestibular system in AP control during HUT was examined elderly subjects.

Summary of Results:
- Rats were maintained in a 3-G or a normal 1-G environment for 2 weeks, and the AP responses to free drop-induced microgravity were determined. In 1-G rats, the microgravity increased the AP by 37 ± 3 mmHg; this pressor response was significantly attenuated by VL (24 ± 3 mmHg) or body stabilization (29 ± 2 mmHg). Thus, the microgravity-induced pressor response was mediated by both the vestibular and nonvestibular systems; the input of the latter system was blocked by body stabilization. In the 3-G rats, the pressor responses were significantly suppressed compared to those in the corresponding 1-G rats; i.e., the AP increased by 24 ± 2 mmHg in freely moving 3-G
rats, by 10 ± 4 mmHg in 3-G rats with VL, and by 13 ± 4 mmHg in stabilized 3-G rats. Furthermore, there was no difference between the 1-G and 3-G rats in terms of the pressor response induced by stressors such as a loud noise or an air jet. These results indicate that pre-exposure to 3-G for 2 weeks induces plasticity in both the vestibular- and nonvestibular-mediated AP responses to microgravity.

- GVS itself induced pressor response in an intensity dependent manner. This pressor response was completely abolished by vestibular lesion, suggesting that the GVS-induced response was mediated by vestibular system. The pressor response to microgravity (35 ± 3 mmHg) was significantly reduced by simultaneously applied GVS (19 ± 1 mmHg) and pressor response to 3 G load was also significantly reduced by GVS. However, GVS had no effect on air jet-induced pressor response. The effects of GVS on pressor response to gravitational change were qualitatively and quantitatively similar to that caused by the VL. These results indicate that GVS reduced vestibular-mediated pressor response to gravitational change, but has no effect on the nonvestibular-mediated pressor response. Thus, GVS might be employed for the acute interruption of AP response to gravitational change.

- AP did not change during posture transition from supine to HUT if GVS was not applied. However, on application of GVS during HUT, AP immediately and significantly decreased by 17 ± 2 mmHg. Without posture transition, lower body negative pressure (LBNP) induced the same degree of footward fluid shift as HUT, as assessed from the right calf circumference; AP was observed to decrease significantly regardless of GVS. This decrease in AP during LBNP testing was similar to that under HUT with GVS. Thus, GVS modifies the AP response during HUT but not during LBNP: LBNP elicits only a footward fluid shift, while HUT elicits footward fluid shift and alterations in the vestibular input. Hence, GVS can be used for investigating the vestibulo-cardiovascular responses in humans and clarifying whether the vestibular system plays an important role in AP and PR control during posture transition.

- Contrary to the young healthy subjects, the AP response in elderly subjects (70-80 yo) was not altered by GVS application. At the 15 s after the HUT, the AP decreased by 19 ± 5 mmHg without GVS and by 22 ± 4 mmHg with GVS. These results indicate that the role of vestibular system in controlling AP upon postural change in elderly subjects is minimal, and thus if vestibulo-cardiovascular reflex was blocked by GVS, the AP response to HUT was not affected. In elderly subjects, daily input to the vestibular system might be reduced, this might induce a plastic alteration of the vestibulo-cardiovascular reflex, and then the intolerance of orthostasis might occur.

9. Publication List

10. URL
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