

## 중력변화에 대한 전정반응

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## Vestibular Responses to Gravity Alterations

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Due to the adaptation to environments on Earth, various health-related issues are raised when exposed to different circumstances in space. Of environmental factors in space, gravity alteration has been considered as one of critical environmental changes. The primary inner organ to detect the gravity change is the vestibular system, especially otolith organs, and some limited researches have conducted to understand its mechanical and physiological properties. However, the related consequences were not consistent in despite of well description in systemic effects ranged from the peripheral vestibular system to the central nervous system. Here, we revisited the neuronal and behavioral effects of the gravity alteration on the relevant organs through this review. By representing previous studies for the gravity effects on the peripheral and central vestibular system, this review would provide the concrete understanding of the vestibular responses to the gravity alteration. Also, the physiological responses are expected to provide the useful resources to understand the systemic vestibular responses under the gravity alteration.

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## INTRODUCTION

Gravity is known as a critical factor to affect the function of cognition as well as behaviors [1-3]. The altered gravity was mainly detected in the peripheral vestibular system, especially otolith, and the corresponding neural information is sent to the central nervous system [4,5]. Initially, the changed gravity affects the membrane viscosity, which decreases or increases under hypo- or hypergravity, respectively [6]. The changes on the cell membrane modify the open state probability of ion channels,

influencing the resting potential which is closely related with the neuronal action potential threshold [6]. As shown in the serial reactions, all related processes are requisites for the homeostasis of body condition because all living creatures have adapted to the gravity on Earth. Therefore, the central vestibular system is the most relevant area for the readaptation by a gravity alteration, which is generally called as neural adaptation [7].

The gravity alteration initially affects the sensitivity of otolith afferents [8,9]. The relevant sensitivity was investigated by a

short-term model for the neuronal transmission. As known, the most critical factor to affect the neuronal activity is the open state probability of ion channels, and it directly induces the change in the conductance between two connected neurons. For instance, the microgravity (hypo-gravity) induces the decrease of the membrane conductance, and the consequence finally reduce the transmission of the related neural information [6]. The study using toadfish reported that microgravity increased the number of synaptic ribbons in the otolith hair cells, indicating the altered gravity induced the structural modification. Moreover, the type II hair cells and the afferent number of synaptic boutons of toadfishes were known to have a close relation with vestibular stimulation, implying the possibility in the structural rearrangement in the otolith relative to the macula [10]. Unlike accumulative physiological evidences, however, some studies failed to identify the structural alteration of otolith organs by the gravity. According to some previous studies, there were few experimental clues of the otoconial changes by the relatively long-term exposure to hypergravity induced by centrifugation [11,12]. For the concrete understanding of the vestibular responses to the gravity alteration, it is necessary to review the physiological responses to the gravity alteration at the cellular level. In this review, the revealed physiological responses to the hypo- and hypergravity would be revisited, providing the biological basis for the expected systemic and functional responses.

## NEURONAL RESPONSES TO GRAVITY ALTERATION: EXPERIMENTAL BASIS

Ion channel is the gate for the (de)polarization in a cell, and its function is generally expressed by the state probability [6]. Using *Escherichia coli*, the previous investigation demonstrated the relation between the gravity alteration and ion channels, showing the gravity dependence of the porin channel [13]. The mean open state probability was known to decrease dramatically under a microgravity while that under hypergravity increased. As there is no direct sensing structure in single neuron, the gravity-induced environmental change is certainly detected by the movement of the otolith hair cells. Thus, the structural changes of the otolithic organs affected the neuronal responses

and the membrane properties. Especially, the membrane viscosity shows a significant change under the gravity alteration, which indicates the change of fluidity in the membrane. This result was supported by the experiments using the human SH-SY5Y cells [14]. The resting potentials of the related neurons showed little difference as comparing before and after the exposure to the gravity alteration [15]. This result might be caused by the fast and reversible electrophysiological properties, which generally occurs within some milliseconds as exposed to the gravity alteration. Under the microgravity, the increase in the neuronal firing rate was reported [16]. However, this temporary effect might be ceased as considering the fast and reversible neuronal response to the gravity alteration. The fast reversibility of the neuronal activity, like the neuronal firing rate, can be the main reason for the failure to identify the neuronal responses to the gravity alteration.

On the other hand, the amplitude of the neuronal action potential directly shows the responding difference. Assessments of the amplitudes of H-reflexes and stretch reflexes identified the neural plasticity by the gravity alteration [17,18], and the experiment using a parabolic flight indicated the hypergravity induced the increase in the amplitude of neuronal spikes [19]. According to Watt [20], the weightless condition in the International Space Station (ISS) produced the decrease of H-reflexes, and the consequence was maintained until the human subjects came back to Earth. Therefore, these neuronal responses induced by the gravity alteration are the part of adaptation to the altered environment, and the corresponding effects last only until the alteration is retained.

## NEURONAL RESPONSES TO GRAVITY ALTERATION: MODELING BASIS

Considering the gravity in space, the microgravity is more desirable than the hypergravity, but the generation of microgravity on Earth is not applicable at this moment [21]. To overcome this obstacle, a model development can be another option. Especially, the constructed model provides some comparable outcomes to the experimental results, and it can show an insight which has been veiled. Also, the results are directly applicable to examine the expected behavioral consequences of the astro-

nauts, providing the biological changes at the molecular and cellular levels [6]. Furthermore, a model study can provide all different level of gravity including hypergravity.

In a model study, the microgravity affected the neuronal membrane as well as the ion channels. Under the condition, the fluidity increased by the decreased membrane viscosity, and it resulted in the decrease of the open state probability of ion channels. At the hypergravity, the results would be inversed. The resting potential is also affected by the gravity alteration. The polarized potential during the resting periods switched to depolarization under the microgravity and hyperpolarization under the hypergravity [6]. Even though the difference in the potentials was small (~several millivolts), this change made the neuron generate a following potential easily under microgravity. Thus, the gravity alteration affected the neuronal firing rates by modifying the threshold of its action potential. Due to the clear dependence on the neural communication, the velocity of the propagating action potential is also considered as a critical factor to show the conducting speed. By the reduced gravity, the latency was reported to increase, which implied the decreased velocity [6]. However, this modeling result was based on the activity in a single neuron, and there was a limit in the comparison with the results from previous experiments [6]. Nevertheless, the addressed effects were interpreted by the clear decrease in the velocity.

However, most results in the modeling study were limited as the gravity-induced effects in short-term and some scientific assumptions. Especially, the membrane viscosity and open state probability of ion channel covered some portions of the effects by the gravity alteration. One consistent outcome from previous modeling studies was that the open state probability of ion channels depended on the gravity alteration [13,22,23]. To overcome the current limitations of the interpretation, more comparative studies at the systemic level are also required as well as the expansion of physiological parameters for the cellular effects by the gravity alteration.

## BEHAVIORAL RESPONSES TO GRAVITY ALTERATION

Due to the gravity alteration sensed by the otolithic organs,

the neural information to the central nervous system should be undergone for neural adaptation, which modifies the systemic strategy for behavioral control [24]. Previous studies demonstrated the graviception initialized in the vestibular system, which is a neural process to recognize the gravity alteration [25,26]. In the behavioral responses to the gravity alteration, the most apparent function by the vestibular system is the body orientation to sustain the postural balance. Considering the behavioral strategy balancing between old and new tasks [27], the behavioral effects by the environmental changes would be undergone through a similar procedure by choosing one or the other. According to the study using the vestibular-gravitational signals in short-term, the subjects showed better performance in the routine and easy tasks by failing in accomplishing some newly provided tasks [28]. The results implied that the altered gravitational signals involved in reconstructing the conceptual preference for the balance between old and new tasks. Thus, the gravity alteration affected the performing capability for old and new tasks, and the subjects exposed to the gravity alteration tended to be in favor of the routine and familiar tasks.

The gravity alteration changes the motor responses as well as the cognitive change. Using the changed direction of gravity during a lean forward from upright standing, the body orientation was investigated [29]. As known, the body movement of leaning forward was constructed mainly by the vestibular information, and there was a clear relation between postural balance and movements. Thus, the balanced posture was a good example of the behavioral responses to the gravity alteration. The study presented the relation between the unbalanced gravitational torque and body balancing strategy by increasing the muscular responses in the ankle extensors. The contribution for this process was also evaluated using galvanic vestibular stimulation, and it supported that the electrical stimulation affected the body orientation even under a gravitational alteration.

## CONCLUSION

Current understandings on the gravity-induced physiological effects are limited. Based on the experimental and modeling studies under microgravity and hypergravity, the molecular and the cellular responses to the gravity alteration showed an

important role by the vestibular inner organs. The fast and reversible neuronal responses under the opposite conditions in gravity were useful to anticipate the effects by the gravity alteration. The changes in the neural responses induced the behavioral responses through the process of graviception, and the central vestibular system provided critical information for the neural adaptation. However, there are still some scientific assumptions to construct clear relation among the responses because of the lack of applicable gravity environment and responding parameters. Thus, the future researches should focus on the comparative studies between the experimental and the modeling researches at the systemic level by expanding the related parameters for the cellular effects by the gravity alteration.

중심 단어: 전정기관, 중력, 신경과학, 이석기관

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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