（様式4）(Form4)

学 位 論 文 の 内 容 の 要 旨

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A new type of simulated partial gravity apparatus for rats based on a pully-spring system.
（滑車システムを用いた新規なラット用部分重力装置）

The Earth’s unique gravitational environment and atmosphere protect humans from low gravity and various types of radiation. Nevertheless, since the first human mission into space and subsequent landing on the Moon, there has been a need to explore the effects of extraterrestrial environments on human health. This need for exploration has increased with the imminent return to the Moon and the potential for exploration of Mars. Current research findings indicate that nearly all systems in the human body will be adversely affected by the altered gravity in extraterrestrial environments; these adverse effects include bone injury, heart rate alterations, intracranial hypertension and visual impairment, and increased urinary stone risk. However, most research has focused on the musculoskeletal system because of its close relationship with gravity. In this study, we sought to devise a new type of simulated partial gravity apparatus (NA) for the hindlimbs of rats that could more efficiently and accurately simulate a partial gravity environment for rat hindlimbs, which will also reduce the impact of additional factors on the experiment results such as range of motion and number of weight measurements. We used the NA to simulate partial gravity, then assessed its reliability. Our new device may facilitate future utilization and refinement of partial gravity simulation devices.
An experiment was designed to verify the reliability and stability of the new apparatus. In this experiment, 25 seven-week-old male Wistar Hannover rats were randomly divided into five groups (n = 5 per group): hindlimb full weight-bearing control (1G), sham (1G), and the simulated gravity groups including Mars (3/8G), Moon (1/6G), and interplanetary space (microgravity: μG). The levels of partial gravity experienced by rat hindlimbs in the Mars and Moon groups were provided by a novel simulated partial gravity device. Changes in bone parameters [overall bone mineral density (BMD), trabecular BMD, cortical BMD, cortical bone thickness, minimum moment of area (MMA), and polar moment of area (PMA)] we evaluated using computed tomography in all rats at the proximal, middle, and distal regions of femur and tibia. Reduced gravity led to decreases in bone parameters in the simulated gravity groups, mainly in distal femur and proximal tibia. The proximal tibia, MMA, and PMA findings indicated greater weakness in the μG group than in the Mars group. The sham group design also excluded the decrease in lower limb bone parameters caused by the suspension attachment of the rat’s tail. The new simulated partial gravity apparatus can provide a continuous and stable level of partial gravity. These results suggest that the NA was able to provide a stable and accurate partial gravity level in rat hindlimbs; thus, the original design purpose of the NA was achieved.
Compared with previous devices, the new device has important advantages in terms of simulating partial gravity. First, the new device simulates partial gravity, which is determined by two factors: the DW of the rat and the weight of its balance container. The single daily assessment cuts down on the number of steps required for the experimenter and lessens the stress that too many measurements put on the rat. Second, The NA uses a flexible spring rope that allows the rat to have a range of motion within the cage similar to the control rats while ensuring that the hindlimbs are subjected to stable partial gravity. Using this spring rope in the NA reduces the risk of bone mass damage that a restricted range of motion may cause. Third, in this device, we did not use a suspension attachment to suspend the rat’s limbs, which It offers a reliable and valuable model for studying the effects of extraterrestrial gravity environments on humans.

Our NA experiment had some limitations. First, in the present study, we used tail suspension alone, rather than overall suspension. Tail suspension may gradually change the ratio of force on the four limbs of each rat; rats may begin to place more weight on their forelimbs, rather than their hindlimbs. In future long-term suspension experiments, we plan to refine the tail suspension, to overcome changes in force distribution in the forelimbs and hindlimbs. Second, this experiment analyzed the rat skeletal system without considering the muscular system; because muscles are sensitive to changes in gravity, the effects of the NA on muscle will be the mainly focus of future studies. Third, the micro-CT equipment we utilized was an early model, and the low scan resolution may be why we could not observe the decreased cortical bone thickness next to the knee joint. It also restricts our access to other bone parameters such as BV/TV, Tb. Th... We hope that new models of micro-CT devices will assist us in overcoming these objective issues in the future. Despite these limitations, we believe that the NA developed in this study offers a reliable simulator for studying the effects of changes in gravity on astronaut health during space missions; it may also be useful for studying the effects of gravity changes on the health of patients with various diseases who are bedridden and unable to support normal body weight. For researchers, the NA offers a promising new tool to study the alteration of gravity in space.