
2. Research Term: FY2000~2002

3. Research Fields: Space Medicine

4. Research Categories: Phase I (A) Research and ISAS Grant for Basic Study Oriented to Utilization of Space Station

5. Research Theme:
   - Role of gravity in the neuromuscular development: study using rats
   - Responses of neuromuscular system in human and rats to exposure to microgravity
   - Exercise-induced muscle damage, recovery, and regeneration after hypokinesia/hypodynamia in rat

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8. Summary of Research
   The mechanism responsible for the plasticity of neuromuscular system is still unclear. Thus, this study was performed to investigate the role of gravitational loading on the development of neuromuscular system. It is essential to develop the suitable prescription for improvement of normal growth and/or recovery of functional capacities of neuromuscular system, which was inhibited or damaged by chronic space flight, bedrest, diseases, or accident. The major purposes of the study were to investigate 1) effects of hindlimb suspension or loading at 2-g during the first 3-month of life on the development of neuromuscular system in rats, 2) effects of exposure to actual microgravity (µ-g) on neuromuscular activities in human and rats, and 3) effects of reloading after 16 days of unloading on the characteristics of rat soleus muscle.

   The growth of ankle plantar-flexor soleus was inhibited by hindlimb suspension of new-born rats. Although the growth-related increases of muscle fiber number and longitudinal growth were not affected, the increase of fiber cross-sectional area, fiber-type transformation toward slow-twitch type, and the change of fiber innervation from multiple to single were inhibited by suspension. These phenomena were associated with lowered levels of myonuclear number, DNA content within a nucleus, and/or satellite cell number. However, the effects of suspension on the growth of other plantar-flexors, gastrocnemius and plantaris (fast twitch muscle), were minor, even their growth was inhibited in some degree. The growth of dorsi-flexors, extensor digitorum longus and tibialis anterior (TA, fast twitch muscle), was not influenced by suspension at all. It was suggested that the growth-associated shift of muscle fiber type in soleus is not programmed genetically but is closely related to the tonic activity of the muscle itself. The significant effect of afferent input, which is directly influenced by muscle activity, on the differentiation of fiber type was also suggested. Analyses of gene and protein expression in soleus and spinal cord (L5 segmental level) have been also performed.

   The electromyogram (EMG) activity of soleus recorded on the floor was increased when the gravity level was increased during the ascending phase of parabolic flight and was decreased during the exposure to µ-g. Similar response was noted in a plantar-flexor lateral gastrocnemius. The EMG activities of TA, and neck (rhomboideus capitis) and back muscles (internal oblique) were even increased during the µ-g period. The EMG of TA may be increased, because TA is passively stretched due to the plantar-flexion of ankle joints. Co-contraction of ankle dorsi- and plantar-flexors was also observed. The level of afferent neurogram was inhibited, as well as soleus EMG, during the exposure to µ-g. This phenomenon may be related to the plantar-flexion-related passive
shortening of muscle. Tension development (in situ) of soleus muscle, length of single muscle fibers and sarcomere, and sarcomere number were also analyzed before and after 2 weeks of hindlimb suspension in order to study the mechanism responsible for the responses of soleus EMG and afferent input to gravitational loading. Hindlimb-suspension-related plantar-flexion of ankle joints resulted in shortened sarcomere length and decreased tension development. However, muscle fiber length and sarcomere number per fiber decreased after 2 weeks of hindlimb suspension and the mean sarcomere length at a given ankle joint angle increased. These data indicated that reorganization of sarcomere and muscle fibers was induced during 2 weeks of hindlimb suspension. Thus, tension development was increased, even when the ankle joint was plantar-flexed. It was suggested that the soleus EMG and afferent neurogram are closely related to the fiber and sarcomere length and tension development.

The EMG activities of lateral gastrocnemius, back, and neck muscles in human during standing position increased at 1.5- and 2-g and decreased during µ-g. The EMG of TA was not influenced by the gravity levels. Although the latency of the appearance of M and H wave was constant throughout the parabolic flight, the magnitude of H-wave was increased during the exposure to µ-g. However, Hoffman-reflex was not influenced by the hypergravity, which was created before and after the µ-g period. These phenomena were not directly related to the fluid shift within the body.

We have a plan to perform an experiment to investigate the effect of exposure to actual µ-g environment during the early postnatal period on the development of neuromuscular system in rats using the international space station. The current study was performed as one of the pilot study. As the results, some valuable suggestions, which may be helpful for the future experiment in space, were obtained. The successful recording of neuromuscular activities using telemetry system during the parabolic flight in the current study suggested that this method could be utilized in the space environment with chronic µ-g.

9. Publication List

10. URL
Home page address: http://www.hss.osaka-u.ac.jp/kenkyu/shintai_bunka/index.html