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A novel paradigm in ground-based space simulated modelling developed to study presynaptic event conundrum in brain intensified inhibitory and attenuated excitatory processes in nerve terminals.

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Terrestrial organisms are well adapted to the gravity they are constantly being subjected to. The exposure to altered gravity conditions leads to the changes in a wide variety of neuronal systems. The physiological changes seen in humans, vertebrate and simple organisms in spaceflight may originate from dysfunction of basic biological mechanisms caused by microgravity. The adaptation to weightlessness and hypergravity and the later re-adaptation are complex processes involving different brain areas and nervous pathways. For space research it is of high importance to understand the influence of gravity on the properties of the central nervous system. Until now it is not much know about how neuronal tissue can sense gravity. The biochemical basis underlying the effects of altered gravity on the process of nervous signal transmission is essentially unknown.

The effects of simulated hypergravity on the presynaptic events have been investigated in order to provide further insight into regulation of glutamate and gamma-aminobutyric (GABA) neurotransmission and correlation between excitatory and inhibitory responses under altered gravity conditions. Exposure of animals to hypergravity (centrifugation of rats at 10G for 1 hour) has been found to cause changes in the synaptic processes of brain, in particular neurotransmitter release and uptake in rat brain synaptosomes. Hypergravity loading resulted in more than two-fold enhancement of [^{3}H]GABA transporter activity (Vmax increased from 1.4 ± 0.3 nmol/min/mg of protein in the control group to 3.3 ± 0.59 nmol/min/mg of protein for the animals

exposed to hypergravity ($p \leq 0.05$)). The maximal velocity of L-[^{14}C]glutamate uptake decreased from 12.5$\pm$ 3.2 to 5.6 $\pm$ 0.9 nmol/min/mg of protein under artificial gravity conditions. To clarify these kinetic changes of the glutamate uptake the study assessed the competitive transporter inhibitors DL-threo-beta-benzyloxyaspartate and L-threo-beta-hydroxyaspartate for the abilities to affect the glutamatergic transmission. We found that inhibitors became more potent under hypergravity.

Depolarization-evoked exocytotic release of the neurotransmitters has also changed in response to simulated hypergravity. It increased for GABA (7.2 $\pm$ 0.54 % and 11.74 $\pm$1.2 % of total accumulated label for control and hypergravity, respectively ($p \leq 0.05$)), but reduced for glutamate (14.4 $\pm$ 0.7 % and 6.2 $\pm$ 1.9 %, for control and hypergravity, respectively). Thus, comparative analysis of the neurotransmitter uptake and release has demonstrated that short-term centrifuge-induced 10G hypergravity loading intensified inhibitory and attenuated excitatory processes in nerve terminals. The activation or reduction of neurotransmitter uptake appeared to be coupled with similarly directed alterations of the neurotransmitter release.

The findings would be expected to provide valuable experience for the use of artificial gravity during long-term or planetary exploration mission, for example during next steps of space exploration: human missions to moon, Mars and to worlds beyond with the goal of living and working there for increasingly extended periods of time.