Effect of the protonophore carbonyl cyanide-p-trifluoromethoxyphenyl-hydrazon on the glutamate release from rat brain nerve terminals under altered gravity conditions.

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L-glutamate acts within the mammalian central nervous system as the predominant excitatory neurotransmitter and as a potent neurotoxin. The balance between these physiological and pathological actions of glutamate is thought to be kept in check by the rapid removal of the neurotransmitter from the synaptic cleft. The majority of uptake is mediated by the high-affinity, Na^+-dependent glutamate transporters. Depolarization leads to stimulation of glutamate efflux mediated by reversal of the high-affinity glutamate transporters. The effects of the protonophore carbonyl cyanide-p-trifluoromethoxyphenyl-hydrazon (FCCP) on the glutamate release from isolated nerve terminals (rat brain synaptosomes) were investigated in control and after centrifuge-induced hypergravity (rats were rotated in a long-arm centrifuge at ten-G during one-hour period). The treatment of synaptosomes with 1 μM FCCP during 11 min resulted in the increase in L-[^{14}C]glutamate release by 23.0$\pm$2.3 % of total accumulated synaptosomal label in control animals and 24.0$\pm$2.3 % animals, subjected to hypergravity. FCCP evoked release of L-[^{14}C]glutamate from synaptosomes was not altered in animals exposed to hypergravity as compared to control. Glutamate transport is of electrogenic nature and thus depends on the membrane potential. The high-KCl stimulated L-[^{14}C]glutamate release in Ca^{2+}-free media occurred due to reversal of the glutamate transporters. Carrier –mediated release of L-[^{14}C]glutamate (6 min) slightly increased as a result of hypergravity loading (7.7$\pm$2.8 % and 11.0$\pm$2.0 % of total accumulated label in control and animals, subjected to hypergravity, respectively). In contrast, high-KCl stimulated L-[^{14}C]glutamate release from synaptosomes preliminary treated with 1 μM FCCP considerably increased from 27.0$\pm$2.2 % to 35.0$\pm$2.3 % of total accumulated synaptosomal label after centrifuge-induced hypergravity as compared to control animals (Ð$\leq$0.05). We found the competitive nontransportable glutamate transporter inhibitor DL-threo-β-benzyloxyaspartate to inhibit FCCP-high KCL-stimulated release of L-[^{14}C]glutamate. The release would be expected to occur via high-affinity plasma membrane glutamate transporters. Changes observed may be connected with augmentation of cytosolic pool of neurotransmitter.