The fraction of activated N-methyl-D-aspartate receptors during synaptic transmission remains constant in the presence of the glutamate release inhibitor riluzole.

Abstract:
Excessive N-methyl-D-aspartate (NMDA) receptor activation is widely accepted to mediate calcium-dependent glutamate excitotoxicity. The uncompetitive, voltage-dependent NMDA receptor antagonist memantine has been successfully used clinically in the treatment of neurodegenerative dementia and is internationally registered for the treatment of moderate to severe Alzheimer's disease. Glutamate release inhibitors (GRIs) may also be promising for the therapy of some neurodegenerative diseases. During the clinical use of GRIs, it could be questioned whether there would still be a sufficient number of active NMDA receptors to allow any additional effects of memantine or similar NMDA receptor antagonists. To address this question, we determined the fraction of NMDA receptors contributing to postsynaptic events in the presence of therapeutically relevant concentrations of the GRI riluzole (1 microM) using an in vitro hippocampal slice preparation. We measured the charge transfer of pharmacologically isolated excitatory synaptic responses before and after the application of the selective, competitive NMDA receptor antagonist D-AP5 (100 microM). The fraction of activated NMDA receptors under control conditions did not differ from those in the presence of riluzole. It is therefore likely that NMDA receptor antagonists would be able to exert
additional therapeutic effects in combination therapy with GRIs.