Acute and sustained excitotoxicity differentially influence riluzole’s neuroprotective effect
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Introductions

Excitotoxicity is initially defined as an acute insult to neurons that leads to their death by excessive activation of glutamate receptors. Acute and massive glutamate release is thought to occur and play a role in various severe insults including cerebral ischemia, traumatic brain injury, hypoglycemia, and epilepsy. Amyotrophic lateral sclerosis (ALS) is a chronic neurodegenerative disease where implication of excitotoxicity has been reported. In contrast to the acute excitotoxicity, more chronic and sustained exposure to milder elevations of glutamate is believed to mediate excitotoxicity in neurodegenerative disease such as ALS.

Objective

The present study is to investigate the impact of acute (10 - 60 min) and sustained (24 h) exposure to low (10 μM) and high (75 μM) concentration of glutamate on the injury and viability of primary neuronal cultures. The neuroprotective effect of riluzole (the unique FDA-approved ALS drug) is comparatively assessed under the two glutamate exposure conditions.

Material and Methods

The extent of injury is measured by the amount of lactate dehydrogenase (LDH) released in the cell culture supernatants and cell viability is measured by the ATP consumption by the cell cultures.

The mechanism of neuronal damage induced by acute exposure to glutamate is largely insensitive to riluzole.

In contrast, the neuronal damage induced by sustained exposure to low concentration of glutamate is largely riluzole-sensitive mechanism. This observation is in accordance with the argument in favor of the chronic slow excitotoxicity hypothesis in ALS.

Neuronal damage induced by exposure to high concentration of glutamate is mediated by mechanisms sensitive and insensitive to riluzole treatment.