Abstract Preview - Step 3/4

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Theme: F Cognition and behaviour

Topic: F.2 Animal cognition and behaviour

Subtopic: F.2.h Learning and memory: pharmacology

Title: Simultaneous versus solitary pharmacological manipulation of NMDA- and AMPA -receptors: effects of new drugs on contextual learning and its extinction

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Text: Both the attenuation of the NMDA-receptor mediated transmission via low affinity blockade mechanism, and the stimulation of AMPA receptor-mediated signaling were shown to result in beneficial neurobiological effects, such as an enhancement of memory and neurogenesis. We aimed to compare the effects of acute pharmacological manipulations of these mechanisms, exerted simultaneously or solely in mice, on learning of two mouse tasks with distinct predominant dependency on either glutamate receptor subtype. In a step-down avoidance task, memantine, low affinity NMDA receptor blocker (5 mg/kg), but not ampakine QQX (5 mg/kg) increased memory scores. In contrast, extinction of contextual fear conditioning was significantly enhanced by the latter, but not by the first drug. Among four new isothiourea derivates used at the doses 0.5-1 mg/kg, one compound that showed a maximal potency with respect to both glutamatergic mechanisms, as well as dimebon (1 mg/kg), had the most prominent memory enhancing effects. Thus, simultaneous low affinity blocade of the NMDA receptor and stimulation of AMPA-mediated transmission can result in eminent pro-cognitive activities. These data point to the importance of multi-target drug mechanism in the regulation of cognitive functions and suggest its potential for clinical implications.

Author Keywords: Alzheimer´s disease, AMPA-receptors, Dimebon, fear conditioning, hippocampus, memory extinction, mouse, NMDA receptor

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