Abstract

Background: PCP/NMDA hypothesis of schizophrenia was supported by several lines of studies, but few studies have tested whether known electrophysiological abnormalities of schizophrenic patients such as P300 and mismatch negativity (MMN) could be elicited by NMDA receptor antagonism.

Methods: We have administered sub-anesthetic dose of ketamine (0.65mg/kg) to healthy volunteers to explore the role of NMDA receptor on P300 and MMN. Fourteen healthy volunteers underwent placebo-controlled ketamine infusion. Brief Psychiatric Rating Scale (BPRS) was administered.

Electrophysiological change was evaluated with P300 in Sternberg paradigm and MMN.

Results: BPRS score was significantly increased by ketamine infusion ($t = -7.83$, df = 13, $p = 0.000003$). Dysfunction in recognition memory task ($t = 2.436$, df = 13, $p = 0.03$) and P300 amplitudes (Pz, $t = 3.059$, df = 10, $p = 0.012$) were observed during...
ketamine administration. Ketamine had no effect on MMN.

Conclusions: Observed abnormalities in psychopathology, recognition memory, and P300 supported PCP/NMDA hypothesis of schizophrenia. MMN abnormalities in schizophrenia could not be explained by PCP/NMDA hypothesis. Different pathological mechanism might be involved in impaired MMN generation.

Keywords: schizophrenia, PCP/NMDA hypothesis, ketamine, mismatch negativity (MMN), recognition memory, P300

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