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Depressant Effects of 2-PMPA through Reduction of p-CREB (Ser133) and mGluR5 Level in Prefrontal Cortex of C57BL/6 Mice

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Abstract : The N-acetylated-alpha-linked-acidic (NAAG) peptidase inhibitor 2-phosphonomethyl pentanedioic acid (2-PMPA) has demonstrated to be neuroprotective against glutamate-mediated neuron degeneration and neurological disorders such as ischemia. Several studies have demonstrated impaired psychiatric function by altered glutamate carboxypeptidase II expression, although 2-PMPA has not yet been studied. Thus, we investigated effect of 2-PMPA on depressive-like phenotype using C57BL/6 mice. Treatment of 2-PMPA (10 mg/kg for 6 days/daily, ip injection) on C57BL/6 naïve mice showed depressive-like symptoms such as decreased social preference, but did not affect the immobility measured by tail suspension test. Reduction of phosphorylated cAMP-responsive element binding (p-CREB) known as a representative marker of depressive-like behavior was observed in layer 1 and piriform cortex subregions of the prefrontal cortex of 2-PMPA-treated mice. The immunoreactivity of metabotropic glutamate receptors 5 (mGluR5) that mediate phosphorylation of CREB was also decreased in layer 1 and piriform cortex subregions of the prefrontal cortex of 2-PMPA injected mice. Thus, our results suggest that dysregulation of the GCPII or NAAG by 2-PMPA treatment is likely to be associated with pathogenesis of depression and further studies are needed to understand whether the reduced NAAG level or enhanced glutamate level in the brain is involved in this response.

Keywords : depression, GCPII, 2-PMPA, p-CREB, mGluR5
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