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## Combinatorial modulation of the spontaneous firings by glutamate receptors in dopamine neurons of the rat substantia nigra pars compacta

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Spontaneous firing rate and patterns of dopaminergic neurons in midbrain are key factors in determining the level of dopamine at target loci as well as in the mechanisms such as reward and motor coordination. Although glutamate, as a major afferent, is reported to enhance firing rate, the detailed actions of NMDA-, AMPA/kainate-, and metabotropic glutamate receptors (mGluR) on firing patterns are not clear. Thus we have investigated the role of glutamate receptors on the spontaneous firing activities using the network-free, acutely isolated dopamine neurons from substantia nigra pars compacta(SNc) of the 9-14 days rat. The isolated cells showed spontaneous regular firings of near 2.5 Hz, whose rate was enhanced by glutamate at submicromolar levels (0.3 □M) but abolished by high concentrations more than 10 □M. However, application of glutamate between 1~3 □M led to the initial disappearance and following big increase of the firing rates. When glutamate was removed, the enhanced firings were very slowly recovered after temporary disappearance of the firings. Agonist and antagonist experiments revealed that the initial disappearance of the firings was mediated by mGluR while the later disappearance on the washout period was related to NMDA- and AMPA-receptors. Although all the mGluR, AMPA/kainite, and NMDA receptors could raise firing rates, stimulation with AMPA showed a clear desensitization and stimulation of mGluR led to very late recovery after stopping stimulation. These data indicate that glutamate combinatorially modulates spontaneous firings by recruiting several glutamate receptors and the combinations may be one of mechanisms by which dopamine cells fire in various patterns *in vivo* in SNc.

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