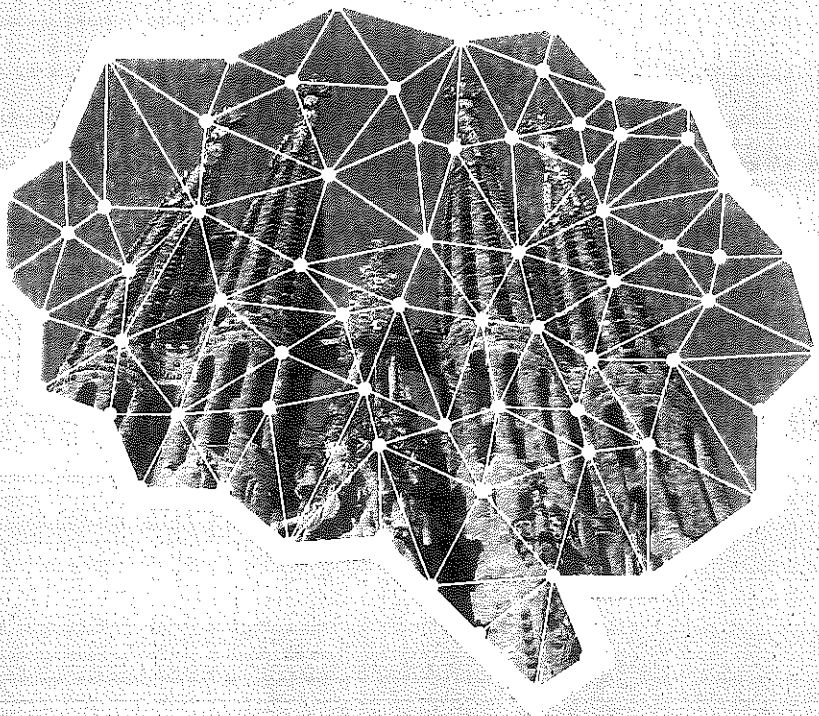

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Effects of adipokinetic hormone/red pigment-concentrating hormone family of peptides on MK-801 induced schizophrenia models in rats

O. Mutlu [1], T. Páleníček [2], N. Pinterová [3], K. Šíchová [3], J. Horáček [2], K. Holubová [4], C. Höschl [2], A. Stuchlík [4], F. Erden [1], K. Valeš [4]

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The adipokinetic and red pigment-concentrating hormone (AKH/RPCH) family of peptides controls fat, carbohydrate and protein metabolism in insects. It is suggested that adipokinetic hormone (AKH) may contribute to neuronal function in the human central nervous system. In our previous study [1], we showed that AKH possesses antidepressant, anxiolytic, and analgesic effects, causes hyperlocomotion and exerts neuroprotective effects and increased brain neurotropic factors in mice. Because AKH was effective in depression and anxiety by affecting the central nervous system, it might also be important to study whether AKH has an antipsychotic effect profile in the model of schizophrenia in animals. The aim of this study is to investigate the effects of Anax imperator AKH (Ani-AKH), Libellula auripennis AKH (Lia-AKH) and Phormia-Terra hypertrehalosemic hormone (Pht-HrTH) on MK-801-induced memory deterioration in the active allothetic place avoidance test (AAPA) and MK-801-induced sensorimotor gating deficit in the prepulse inhibition test (PPI). In the AAPA task, Long Evans rats were treated with Ani-AKH (2 mg/kg), Lia-AKH (2 mg/kg), Pht-HrTH (2 mg/kg), MK-801 (0.15 mg/kg) and the combination of MK-801 with the hormones sub-chronically. In the prepulse inhibition test, Wistar-albino rats were treated with Ani-AKH (1 mg/kg), Lia-AKH (1 mg/kg), Pht-HrTH (1 mg/kg), MK-801 (0.1 mg/kg) or the combination of MK-801 with hormones acutely before the test. Successful performance of the active allothetic place avoidance task, in which the rat has to differentiate between relevant and irrelevant stimuli, depends on the mode of information processing disturbed in schizophrenic patients. PPI is a neurological phenomenon in which a weaker prestimulus (prepulse) inhibits the reaction of an

organism to a subsequent strong startling stimulus (pulse). Many studies have shown that PPI is disturbed in many diseases and disorders, especially in schizophrenia. MK-801 disturbs PPI and can be used as a pharmacological model of schizophrenia and psychosis . The results of the AAPA and PPI tests were evaluated by one-way ANOVA followed by Tukey's post hoc test when significant differences were detected. In the AAPA test, MK-801 significantly increased locomotion and this effect was partially reversed by Ani-AKH 2 and Lia-AKH 2 mg/kg while Pht-HrTH 2 mg/kg showed no reversing effect. In the AAPA test, MK-801 treatment significantly increased the number of entries and the number of shocks while Ani-AKH 2 mg/kg, Lia-AKH 2 and Pht-HrTH 2 mg/kg significantly reversed these effects. In the AAPA test, MK-801 treatment significantly decreased the maximum time of avoidance while Ani-AKH 2, Lia-AKH 2 and Pht-HrTH 2 mg/kg significantly reversed the MK-801-induced decrease in the maximum time of avoidance. Lia-AKH (1 mg/kg) significantly potentiated the MK-801-induced PPI disruption, while Ani-AKH (1 mg/kg) partially potentiated the impairment caused by MK-801, and Pht-HrTH did not modify the effect of MK-801. In conclusion, AKH/RPCH family peptides may demonstrate improved effects on cognitive dysfunction in MK-801-induced cognition deficit, while Lia-AKH and Ani-AKH likely increase MK-801-induced sensorimotor gating deficits in the PPI test, while Pht-HrTH had no effect.

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