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Effects of central administration of Cerebral dopamine neurotrophic factor (CDNF) on the behavior and serotonin system in the mouse brain

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Motivation and Aim: It is known that CDNF is able not only to protect the dopaminergic neurons of the brain, but also to participate in the control of various types of behavior. In turn, the serotonin (5-HT) system of the brain is involved in the regulation of many physiological processes and behavior and can potentially be under the influence of CDNF. Thus, the aim of this work was to study the effects of central administration of the recombinant CDNF protein on the behavior and of 5-HT in the mouse brain.
Methods and Algorithms: Male C56Bl6/J mice were injected with recombinant CDNF protein (3, 10, or 30 μg) or PBS into the left lateral ventricle of the brain. Movement activity, water and food intake, and sleep were recorded automatically in a home cage setting using the PhenoMaster for 3 days post-injection. Motor activity, anxious and exploratory behavior were measured in the open field test (OF) and elevated plus maze (EPM) Learning and memory were assessed using the Operant Wall module. 5-HT metabolism was assessed by HPLC in the midbrain raphe nuclei, frontal cortex, hypothalamus, thalamus, and hippocampus. The mRNA levels of *Htr1a*, *Htr2a*, *Htr7, Tph2, Maoa, Slc6a4, Creb1, Fos, Arc* and *Bdnf* were measured by real-time RT-PCR.
Results: It was found that the total distance traveled, as well as the distance and speed during the first 24 hours, were significantly increased in mice receiving 3 μg of CDNF. Also, this dose of CDNF significantly reduced the duration of sleep on the first day of testing. The total sleep time in the light phase of the day decreased in the mice of the 3 μg group. At the same time, the number of sleep episodes did not change in all experimental groups. Mice received CDNF demonstrated anti-anxiety behavior in the OF and EPM tests. CDNF at all doses significantly improved associative learning in mice compared to controls. CDNF caused significant changes in the mRNA level of *Htr1a*, *Htr2a*, *Htr7, Maoa, Creb1, Fos, Arc* genes in the different brain stractures. An increase in 5-HT catabolism was shown in all brain structures studied, except for the hypothalamus, in mice treated with CDNF at all dosages.
Conclusion: Thus, the anti-anxiety, antidepressant and procognitive effects of a single central injection of CDNF protein were demonstrated for the first time, which were accompanied by significant changes in 5-HT metabolism, as well as changes in the transcription of many genes importantly involved in the reception and degradation of 5-HT. It has been shown that central administration of CDNF at low doses can cause disturbances in the sleep/wake cycle.
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