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Cerebral dopamine neurotrophic factor (CDNF) affects hippocampal neuroplasticity and fear memory in rats

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Cerebral dopamine neurotrophic factor (CDNF) is considered to be a protective factor for brain dopaminergic neurons. A little is known about the involvement of CDNF in the regulation of behavior aside from locomotor activity. There are some evidence indicating the role of CDNF in spatial memory, however, it is unknown whether CDNF is involved in the regulation of other forms of memory, e.g. fear memory. To address this question we used AAV-mediated gene delivery to induce CDNF overexpression in hippocampal neurons of adult Wistar rat males. We found that CDNF overexpression impaired conditioned response recall in fear conditioning paradigm by enhancement of the fear memory extinction. These alterations in fear memory were accompanied by elevated mRNA level of Creb implicated in Long-Term Potentiation formation. At the same time, CDNF overexpression lad to increase in mRNA levels of unfolded protein response markers Atf6, Perk and spliced Xbp1. In the rat primary hippocampal culture the CDNF overexpression stimulated the formation of burst activity and significantly increased not only the frequency of spikes, but also the number of spikes in a network burst. Also, it has been shown that CDNF increased not only the number of bonds per cell, but also the correlation of signals in neuronal culture. At the same time, both correlations between neighboring and distant cells were increased. The percentage of active cells in culture was increased by more than two times.

Thus, for the first time we have demonstrated that endogenously overexpressed CDNF can negatively regulate the fear memory formation that may be linked with the marked effects on hippocampal neuroplasticity produced by CDNF.

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