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IBRO WORKSHOP

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ABSTRACT DETAILS

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BEHAVIORAL EFFECT OF GABA RELEASE FROM FOREBRAIN CHOLINERGIC NEURONS

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Márton I. Mayer¹, Virág T. Takács¹, Katalin E. Sós¹, Zsuzsanna Bardóczy¹, Hunor Sebők¹, Katalin Sviatkó¹, Balázs Hangya¹, Manó Aliczki², Éva Mikics², Tamás F. Freund¹, Gábor Nyiri¹

¹ Department of Cellular and Network Neurobiology, Institute of Experimental Medicine, Budapest, 2Department of Behavioural Neurobiology, Institute of Experimental Medicine, Budapest

The basal forebrain cholinergic system comprises several nuclei that provide innervation to cortical areas. It contributes to arousal, attention and memory, including fear and extinction learning, and it is implicated in anxiety and post-traumatic stress disorder. We have recently shown that cholinergic terminals synaptically release not only acetylcholine, but GABA as well, the release of which can be modulated independently. Although previous studies demonstrated that the alteration of GABAergic cotransmission is possible and has functional consequences in other non-cholinergic brain regions, the role of GABA release from forebrain cholinergic cells is unknown. We created a conditional knockout mouse strain (ChAT-vGAT-cKO) to decrease GABA release from cholinergic neurons. Our preliminary behavioral tests showed that these mice had increased hippocampal theta activity during sleep and performed significantly better in a cognitive task, likely due to a relatively more efficient cholinergic effect. However, ChAT-vGAT-cKO mice showed significant deficits in fear extinction learning after cued fear conditioning. These results may provide a formerly unrecognized mechanism for certain pathological conditions.

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