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A new model of depressive-like behavior in rats and mice for preclinical drug discovery

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Emotional stress is primarily triggered by the cognitive processing of negative input; it is regarded as a serious pathogenetic factor of depression that is challenging to model in animals. While available stress paradigms achieve considerable face and construct validity in modeling depressive disorders, broader use of naturalistic stressors instead of the more prevalent models with artificial challenges inducing physical discomfort or pain may substantially contribute to the development of novel antidepressants. Here, we investigated whether a three-week exposure of Wistar rats and BALB/c mice to unpredictably alternating frequencies of ultrasound between the ranges of 20–25 and 25–45 kHz, which are known to correspond with an emotionally negative and with a neutral emotional state respectively, for small rodents in nature can induce behavioral and molecular depressive like changes. Both rats and mice displayed decreased sucrose preference, elevated despair behavior in a swim test, reduced locomotion and social exploration. Rats showed an increased expression of SERT and 5-HT2A receptor, a decreased expression of 5-HT1A receptor in the prefrontal cortex and hippocampus, diminished BDNF on gene and protein levels in the hippocampus. Fluoxetine, administered to rats at the dose of 10 mg/kg, largely precluded behavioral depressive-like changes. Thus, the applied paradigm of emotional stress is generating an experimental depressive state in rodents, which is not related to any physical stressors or pain. In essence, this ultrasound stress model, besides enhancing animal welfare, is likely to provide improved validity in the modeling of clinical depression and may help advance translational research and drug discovery for this disorder.

Biography

Anna Morozova is working on her PhD project in the Department of Basic and Applied Neurobiology, V P Serbsky Federal Medical Research Center for Psychiatry and Narcology. She is also a Medical Doctor (Psychiatrist) in a mental hospital named Gilyarovskiy. She has published more than 10 papers. The last paper deals with a new approach in modeling of depressive-like behavior in rats and mice. She also studied the Ultrasound of alternating frequencies cause variable emotional impact which evokes depressive syndrome in mice and rats.

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