# Intranasal CRISPR psychotropic reduces anxiety-related behavior in mice

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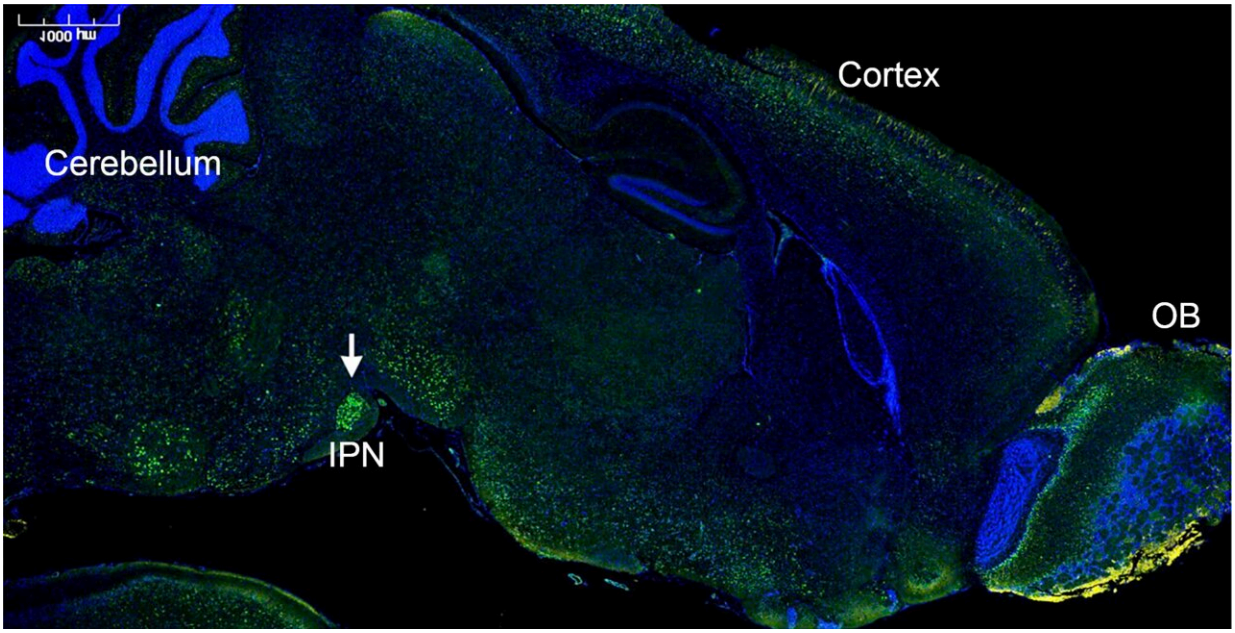


Representative, low-field immunofluorescence sagittal image following treatment, fixation in formalin, and immunolabeling using a specific antibody against green-fluorescence protein (GFP). GFP-positive neurons positively transfected with guide RNA were identified in most brain regions including the olfactory bulb (OB), cortex, cerebellum, and numerous sub-cortical areas including the interpeduncular nucleus (IPN), a major connectome for stress-mediated pathways. Credit: Rohn et al.

A study in mice reports a CRISPR/Cas9 gene-editing delivery system, capable of bypassing the blood-brain-barrier and modulating neuronal

receptor pathways, to treat chronic anxiety.

Troy Rohn and colleagues targeted 5HT-2A, a serotonin receptor known to play a role in anxiety and depression. The authors used a vector based on an inactivated adeno-associated virus to deliver the vector through the nose. The vector delivers a guide RNA to neurons. The guide RNA binds to the target receptor gene, HTR2A, which is then cut at a specific location by the enzyme Cas9. The work is published in the journal *PNAS Nexus*.

Five weeks after intranasal delivery of the vector and package, 75 mice were tested with standard behavioral assays measuring mouse anxiety. For example, anxious mice will choose to spend more time in dark areas and tend to bury unfamiliar objects such as marbles in sawdust rather than letting them be.

Treated mice spent 35.7% more time in light areas than controls and showed a 14.8% decrease in the number of marbles buried compared with controls. Mice treated with the CRISPR package showed an 8.47-fold decrease in HTR2A expression in their brains, compared with control mice. According to the authors, noninvasive, intranasal delivery of CRISPR/Cas9 therapeutics may help patients who exhibit treatment-resistant anxiety.

**More information:** Troy T. Rohn, Genetic modulation of the HTR2A gene reduces anxiety-related behavior in mice, *PNAS Nexus* (2023). DOI: 10.1093/pnasnexus/pgad170

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