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Cross-modal Sensory Integration: A New Strategy for SUD Treatment

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Background: Mediated by dopaminergic (DA) neurons in the reward pathway, zebrafish display robust conditioned place preference (CPP) to substances. The DA neurons receive input from GnRH-containing terminalis neurons (TNs) in the olfactory bulb. We have demonstrated that stimulation of the olfactory neurons activates TNs, which in turn, decrease dopamine content in the brain.

Hypothesis: Because the olfactory TNs synapse with brain DA neurons, it is conceivable that via cross-modal sensory integration, TN inputs (e.g., those triggered by odor stimuli through the olfactory system) lower dopamine content in the brain, and thereby reduce or prevent drug seeking behaviors.

Results: By recording the times that zebrafish required to pass through a water maze to enter a target area that contained caffeine, we evaluated the course of zebrafish CPP to substances with or without the activation of TN pathway. We found that when TNs were activated (e.g., in the presence of odorants, such as methionine), the animals' seeking behaviors for caffeine were reduced as compared to control animals. That is, the fish spent more time randomly swam around in the water maze, took longer times to arrive at the target area, or entered the target area by chance.

Future research: We intend to develop new strategies, via cross-modal sensory integration, for treatment of substance use disorders (SUDs). This may be achieved by applying certain chemical compounds, such as naturally occurred social-related odorants, sex hormones, or artificial scents, that effectively lower dopamine content in the brain, and thereby reduce or prevent drug seeking behaviors.