

BEHAVIOR

**Role of serotonin in mother-child bond**

Liu, Y. et al. *Neuron* (2023) <https://doi.org/10.1016/j.neuron.2023.02.010>

Most mammals' first social relationship is with their mother. This early mother-child bond is critical for survival and might influence other behaviors later in life, including adult social behavior. A new study in *Neuron* reveals the critical role of serotonin in maternal affiliation by infants.

More than 10 years ago, while studying sexual preference in mice, Liu et al. noticed that the loss of the neurotransmitter serotonin (5-hydroxytryptamine; 5-HT) through knockout of tryptophan hydroxylase 2 (*Tph2*) – a gene encoding an enzyme required for synthesizing 5-HT in the brain – induced defective behavior in mouse pups. In their new work, the researchers generated mutations for *Tph2* in rodents and non-human primates, and analyzed the behavior in *Tph2*<sup>-/-</sup> infants through a series of behavioral assays.

Their findings show that after separation from mothers, *Tph2*<sup>-/-</sup> mouse pups

produced less ultrasonic vocalizations (USVs) – a signal to attract maternal caring – than *Tph2*<sup>+/+</sup> and *Tph2*<sup>+/-</sup> pups. When presented with bedding from their mothers vs. bedding from other dams or vs. clean bedding, both *Tph2*<sup>+/+</sup> and *Tph2*<sup>+/-</sup> mouse pups spent more time on maternal bedding, whereas *Tph2*<sup>-/-</sup> mouse pups showed no preference. Similarly, during separation from their mothers, *Tph2*<sup>-/-</sup> rat pups produced less USVs than *Tph2*<sup>+/+</sup> rats, and showed no preference in the bedding preference assays. Analysis of videos of daily behaviors of monkey infants and their mothers in their home cage revealed that *Tph2*<sup>-/-</sup> infants interacted less with their mother than *Tph2*<sup>+/+</sup> infants, indicating reduced affiliation. Altogether, these results demonstrate a conserved role for 5-HT in maternal-infant bonding, from mice to monkeys. “This is the first report of a

molecule shown to play a behavioral role conserved from mice, rats to monkeys by genetic targeting,” write the investigators in their report, adding that their work should stimulate further research on the role of 5-HT in human infants.

By combining, genetics, pharmacology, optical imaging, immunocytochemistry, and chemogenetics, Liu et al. also showed that oxytocinergic neurons in the paraventricular nucleus, responsible for producing oxytocin, act downstream of serotonergic neurons in the raphe nucleus to regulate maternal affiliation in pup mouse, thereby demonstrating the role of the serotonin-oxytocin relationship in the regulation of this early social behavior.

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