

## Optogenetic recording and manipulation of median raphe serotonin neurons in reward-related behavior.

Hiroyuki Kawai, Yuma Nagai, Masashi Koda, Kazuki Nagayasu, Hisashi Shirakawa, Shuji Kaneko

*Dept. Mol. Pharmacol., Grad. Sch. Pharmaceut. Sci., Kyoto Univ.*

Reward processing is an essential function for survival of individuals. Impairment in reward processing induces an objectively incorrect judgment about the value of reward, leading to drug addiction or anhedonia. Increasing evidences implicate that serotonergic neurons as well as dopaminergic neurons play a critical role in the reward processing. Median raphe nucleus (MRN), containing lots of serotonergic neurons, is suggested to be involved in this process. However, it is not fully understood whether MRN serotonergic neurons respond to reward and how they regulate reward-related behavior, partly because of the difficulty of specific recording and manipulation of MRN serotonergic neurons. Here, we determined whether and how MRN serotonergic neurons control reward system and reward-related behavior by optogenetic recording and manipulation. Fluorescent calcium indicator, GCaMP6s, was expressed in MRN serotonergic neurons, by serotonergic neuron specific viral vectors. Then we measured the fluorescence in the MRN before and after sucrose licking by using fiber photometry. We found that the fluorescence started to decrease just after sucrose licking, indicating that reward inhibits MRN serotonergic neurons. Moreover, optogenetic inactivation of MRN serotonergic neurons increased the number of nose-poke and spent time in the chamber associated with stimulation in self-stimulation paradigm and conditioned place preference paradigm, respectively. Our results suggest the MRN serotonergic neurons play a key role in the reward processing.