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2. Title
   Roles of Orexin Neurons and Nicotinic Acetylcholine Receptors in Reward-based Cognitive Behavior

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4. Summary
   Orexin neurons in the hypothalamus regulate physiological functions, including energy homeostasis and wakefulness. Moreover, orexin receptors are also involved in nicotine reward and addiction. However, it remains unknown how orexin neurons are related to reward motivation and reward-based cognitive behavior secondary to nicotine addiction. In this study, we investigated role of orexin neurons in reward-based cognitive behaviors. We used orexin-Cre and DRD2-Cre rats. We used progressive ratio test using touch screen operant machine to examine reward motivation. Rats were subjected to touch responding for food pellets under a progressive ratio schedule. When orexin neurons were activated by DREADD system, breaking point was increased in progressive ratio test. When orexin neurons were dysregulated by diphtheria toxin, breaking point was reduced in the test. Under FR5 or FR20 conditions, the activity in orexin neurons was increased after the fifth or 20th screen touch. The increase in FR20 was higher than fifth screen touch. Taken together, cell-specific excitatory manipulation of orexin neurons resulted in high motivation to reward in orexin-Cre rats. Moreover, the orexin neuron activities changed in motivative behaviors, and were depended on degree of effort to obtain a reward. Further research will be required to develop AAV knock-out system.