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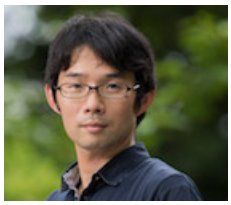
Identification of neurons regulating REM sleep and insights to the mechanisms of REM sleep behavior disorder



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Abstract

Over the night, our sleep cycles between two distinct states, rapid eye movement (REM) sleep and non-REM sleep. Abnormal balance of the two sleep states is a common and early symptom in various neurological disorders, suggesting that each sleep state plays crucial roles. Little is known, however, about the individual roles and neural substrates of these two states. These states are identified only in some vertebrate animals species and thus might be involved in higher order brain functions. We applied mouse genetics to functionally dissect neurons in the brainstem and identify neurons involved in regulating REM sleep and non-REM sleep. With this approach, we previously identified glutamatergic and GABAergic neurons in the pontine tegmental area that negatively regulate REM sleep (*). Recently, we further searched for molecular markers in this brain area that allow precise manipulation of neuronal subgroups. In one group of neurons, genetic inhibition led to a drastic decrease in REM sleep, suggesting that these neurons play an essential role in generating REM sleep. Moreover, the mice frequently exhibited aggressive movements during REM sleep, resembling REM sleep behavior disorder (RBD). RBD is a sleep disorder in which patients act out of their dreams and exhibit violent behavior during REM sleep. We expect that these neurons are a key to understanding the neural circuitry of REM/non-REM sleep and that our genetic mouse model provides important implications about the neural mechanisms of RBD. *Hayashi et al., Science 350, 957-961, 2015.