

Role of glutamate release from melanin-concentrating hormone neurons in REM sleep regulation

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Neurons containing melanin-concentrating hormone (MCH) localized in the posterior lateral hypothalamus and have a crucial role in rapid eye movement sleep (REMs) regulation. As MCH neurons also contain a variety of other neurotransmitters such as glutamate. However, the specific neurotransmitter responsible for REMs regulation is not known. We hypothesized that glutamate, the primary fast-acting neurotransmitter in MCH neurons, is necessary for REMs regulation. To test this hypothesis, we generated mice deleted vesicular glutamate transporter (Vglut2; necessary for synaptic release of glutamate) specifically from MCH neurons by crossing MCH-Cre mice (expressing Cre recombinase only in MCH neurons) with Vglut2^{fllox/fllox} mice (expressing LoxP-modified alleles in Vglut2). We then studied the amounts, architecture and diurnal variation of sleep-wake states in baseline conditions. Next, we activated the MCH neurons lacking glutamate release using chemogenetic methods and tested whether these MCH neurons still promoted REMs. Our results indicate that glutamate in MCH neurons contributes to normal diurnal variability of REMs by regulating the levels of REMs during the dark period, but MCH neurons can promote REMs even in the absence of glutamate.