

Altered sleep architecture, rapid eye movement sleep, and neural oscillation in a mouse model of human chromosome 16p11.2 microdeletion

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Sleep, Volume 42, Issue 3, March 2019, zsy253, <https://doi.org/10.1093/sleep/zsy253>

Published: 12 December 2018 **Article history** ▼

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Abstract

Sleep abnormalities are common among children with neurodevelopmental disorders. The human chr16p11.2 microdeletion is associated with a range of neurological and neurobehavioral abnormalities. Previous studies of a mouse model of human chr16p11.2 microdeletion (chr16p11.2df/+) have demonstrated pathophysiological changes at the synapses in the hippocampus and striatum; however, the impact of this genetic abnormality on system level brain functions, such as sleep and neural oscillation, has not been adequately investigated. Here, we show that chr16p11.2df/+ mice have altered sleep architecture, with increased wake time and reduced time in rapid eye movement (REM) and non-REM (NREM) sleep. Importantly, several measurements of REM sleep are significantly changed in deletion mice. The REM bout number and the bout number ratio of REM to NREM are decreased in mutant mice, suggesting a deficit in REM-NREM transition. The average REM bout duration is shorter in mutant mice, indicating a defect in REM maintenance. In addition, whole-cell patch clamp recording of the ventrolateral periaqueductal gray (vlPAG)-projecting gamma-aminobutyric acid (GABA)ergic neurons in the lateral paragigantocellular nucleus of ventral medulla of mutant mice reveal that these neurons, which are important for NREM-REM transition and REM maintenance, have hyperpolarized resting membrane potential and increased membrane resistance. These changes in intrinsic membrane properties suggest that these projection-specific neurons of mutant mice are less excitable, and thereby may play a role in deficient NREM-REM transition and REM maintenance. Furthermore, mutant mice exhibit changes in neural oscillation involving multiple frequency classes in several vigilance states. The most significant alterations occur in the theta frequency during wake and REM sleep.

[chr16p11.2 microdeletion](#), [REM sleep](#), [neural oscillation](#), [theta rhythm](#), [vlPAG](#), [LPGi](#), [GABAergic neurons](#)

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Online ISSN 1550-9109

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