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# Investigating Sleep Fragmentation in Murine Models of Nf1

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# Investigating Sleep Fragmentation in Murine Models of *Nf1*

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Neurofibromatosis type 1 (NF1) is a common monogenic disorder caused by a single germline mutation in the *NF1* gene, affecting 1 in 3,000 people worldwide. Children with Neurofibromatosis type 1 are at increased risk for sleep issues which negatively affect their quality of life, cognitive function, and behavior. Past cross-sectional studies have demonstrated that children with NF1 were more likely to have more sleep disturbances while initiating and maintaining sleep, arousal, and sleep-wake transition. Preliminary studies using genetically engineered mouse (GEM) models of NF1 have shown that female *Nf1*+/+ (wild-type) mice spend less time in non-REM sleep than male *Nf1*+/+ mice, and their male and female *Nf1* mutant counterparts Leveraging new electroencephalogram (EEG) technologies in collaboration with Dr. Wong's laboratory, the sleep difference between wild-type and their respective mutants was seen, indicating that NF1 plays a major role in sleep fragmentation. The loss of a major sleep pathway regulator, orexin, has been shown to induce sleep fragmentation in mice. Based on these observations, NF1 would be negatively affecting levels of orexin because of the sleep fragmentation that was seen in the mutant mice. To determine if NF1 affected transcription or translation of orexin in the murine brain, hypothalamic orexin expression in wild-type and *Nf1*-mutant mice was assessed by quantitative RT-PCR and Western blotting. Female *Nf1*-mutant mice had much lower levels of hypothalamic orexin compared to *Nf1*+/+ females, while orexin expression did not differ between male Nf1-mutant and wild-type mice, indicating that orexin was not causing the sleep fragmentation found in both male and female Nf1-mutant mice. Therefore, this study narrowed down potential candidates that could be causing this sleep fragmentation in NF1 mutant mice, which is one-step closer in elucidating the obscure molecular pathway of NF1 and sleep.