

Sleep abnormalities and the involvement of neuroinflammation in Prader-Willi Syndrome

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Objective: In Prader-Willi Syndrome patients, sleep abnormalities are often present as one of important symptoms, which also affects the cognitive functions. In this study, we aimed to investigate the underlining links between neuroinflammation and sleep disruption in the PWS mouse model. We explored the effects of anti-inflammation drugs on this sleep disruption.

Methods: *Snord116* is a gene that had been indicated to manifestation of several important symptoms of PWS. We used paternal *Snord116del* mice as our model. We compared the sleep pattern alterations with the wild type litter mate using EEG recording. Different neuroinflammation biomarkers were used to visualize the change between groups. Finally, we used interleukin-1 receptor antagonist (IL1ra) as pharmacological interference to provide the direct evidence of the involvement of neuroinflammation.

Results: *Snord116del* mice showed increases in REM sleep, but not altered in NREM sleep. It also didn't show significant change in circadian rhythm. The episodes and duration of REM both increased in *Snord116del* mice. We also observed the REM intrusion in waking period, which aligns with the narcolepsy-like symptom recorded in human PWS patients. In brain slices with immunofluorescence staining and protein expression from the Western blot, we also observed increasing amount of neuroinflammation biomarkers in the hippocampus and suprachiasmatic nucleus (SCN). These brain regions play an important role in cognitive function and sleep regulation.

Conclusion: In summary, our results suggest the potential contribution of inflammatory cytokine IL-1 β on the sleep disruption of PWS mice. Following this finding, we used IL1ra to block the IL-1 β signaling. These results indicate that targeting neuroinflammation might be beneficial in controlling the symptom of sleep abnormalities in PWS.

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