

# Sleep Quality in Neuromyelitis Optica Spectrum Disorder: A Systematic Review and Meta-Analysis

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## Objective

Neuromyelitis optica spectrum disorder (NMOSD) is a severe autoimmune demyelinating disease of the central nervous system. Recent literature highlights sleep disturbance as a common complaint of patients with NMOSD, with significant implications for quality of life and symptom management. In this review, we summarize the literature on sleep quality in NMOSD and discuss these findings in the context of current knowledge on sleep physiology.

## Methods

Literature search was performed using Ovid MEDLINE, EMBASE and Scopus from inception to September 2020. All included studies reported at least one measure of sleep quality in patients diagnosed with NMOSD. Pittsburgh Sleep Quality Index scores of 183 patients from four studies were compared with those from a dataset of 4864 healthy female controls.

## Results

Thirteen studies describing 1041 NMOSD patients, of whom 82.2% were female, were included in the review after screening 625 records. Disturbed sleep was demonstrated across subjective metrics based on patient surveys and objective metrics, such as polysomnography. An estimated 70% of NMOSD patients can be classified as poor sleepers. Standardized mean difference between Pittsburgh Sleep Quality Index scores of 183 NMOSD patients and those of 4864 female controls was 0.53 (95% CI 0.38-0.67,  $P < 0.001$ ). Decreased sleep quality was significantly associated with decreased quality of life and increases in anxiety, depression, and disability status. Sleep disturbances in NMOSD were similar in severity to those in MS.

## Conclusion

- Sleep disturbances are a major contributor to NMOSD disease burden and may arise from the disruption of sleep circuitry, in addition to physical and psychological complications.
- Multiple processes involved in sleep regulation may be affected, such as but not limited to neural circadian circuit disruption, direct effects of inflammation, aminergic projecting system abnormalities, glymphatic system impairment, development of sleep disorders such as restless legs syndrome/sleep apnea and medication side effects. Ultimately, while there are many theorized causes of poor sleep in NMOSD, the most likely explanation involves a combination of many of these factors.
- In order to address sleep-related complaints, clinicians managing NMOSD should closely investigate all of these factors as they present uniquely in each patient.
- Finally, a better understanding of these mechanisms is necessary for developing effective therapies for NMOSD-associated sleep disturbances.