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Nsomnia Sleep, USA

Arousal Threshold and Sleep Stability Endotypes Under Controlled GABAergic Modulation: A Prospective Cohort Study

Background

Arousal threshold is a key non-anatomical determinant of sleep stability in both obstructive sleep apnea (OSA) and insomnia-spectrum disorders, yet remains incompletely characterized outside of respiratory event-based frameworks. Low arousal threshold contributes to ventilatory instability and sleep fragmentation, while chronic hyperarousal states-common in trauma-exposed and autonomically dysregulated populations—may impair sleep continuity independent of overt respiratory events.

Polysomnography (PSG) effectively identifies respiratory and movement-related abnormalities but does not directly quantify intrinsic arousal stability or continuity resilience. We hypothesized that controlled GABAergic modulation under monitored anesthesia care (MAC) could serve as a translational physiologic model to probe arousal threshold behavior and characterize sleep stability endotypes independent of respiratory event burden.

Methods

In this prospective observational cohort, 50 ASA Physical Status I–II adults with chronic insomnia or non-restorative sleep despite normal or mild PSG findings underwent propofol-based MAC under standard ASA monitoring (ECG, noninvasive blood pressure, pulse oximetry, and capnography).

Propofol was titrated using processed EEG guidance (Patient State Index) to achieve controlled cortical inhibition. Continuous neurophysiologic data included Patient State Index (PSI), Spectral Edge Frequency (SEF95), Suppression Ratio (SR), artifact burden, and hemodynamic parameters.

A standardized modulation window (mean 30 minutes; mean dose 4 mg/kg) was maintained, followed by discontinuation and structured observation of post-modulation recovery dynamics.

Strict signal integrity criteria were applied, including exclusion of epochs with SR >2% and artifact-controlled spectral analysis. No claims of physiologic REM or NREM replication were made.

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Primary endpoints included feasibility, safety, and reproducible signal acquisition. Secondary analyses focused on identification of arousal-stability phenotypes based on recovery trajectories.

This approach utilizes controlled propofol-mediated GABAergic modulation under MAC to transiently reduce cortical arousal constraints and enable physiologic characterization of intrinsic stability patterns during recovery.

Results

All 50 patients completed the protocol. Target EEG ranges were achieved in 100% of cases.
No airway compromise requiring advanced intervention occurred. Transient hypotension occurred in <10% of patients and was managed per protocol. No sustained hypoxemia (<90%) beyond 30 seconds was observed. No unplanned admissions occurred.

Signal integrity gating successfully excluded suppression-contaminated epochs. Post-modulation recovery analysis demonstrated reproducible heterogeneity in stability dynamics, including:

- Rapid arousal re-emergence profiles consistent with low arousal threshold physiology
- Sustained spectral continuity profiles suggestive of higher stability resilience
- Fragmented recovery trajectories consistent with instability-dominant phenotypes

These patterns were observed despite normal or near-normal PSG findings.

Conclusions

Controlled propofol-mediated GABAergic modulation under MAC is feasible, safe, and reproducible as a translational model for probing arousal threshold behavior and intrinsic sleep stability dynamics.

These findings support the concept that arousal instability represents a measurable physiologic dimension independent of respiratory events and may define clinically relevant endotypes across insomnia and OSA spectra.

Transient modulation of cortical arousal pathways provides a novel physiologic window into sleep stability dynamics not captured by conventional PSG.

This framework has potential implications for refining phenotypic classification in sleep-disordered breathing, understanding non-anatomical contributors to ventilatory instability, and advancing precision approaches to perioperative sleep risk stratification.

Further investigation is warranted to correlate these phenotypes with arousal threshold metrics, ventilatory control parameters, and clinical outcomes.

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