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# **Before Attributing Sleep Deprivation in ALS to Depression or Muscle Weakness,** All Other Factors Influencing Sleep Quality Must Be Excluded

### Josef Finstere

MD, PhD Neurology Dpt., Neurology & Neurophysiology Center, Vienna, Austria, Orcid: 0000-0003-2839-7305

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## LETTER TO THE EDITOR

We were interested to read the article by Diaz-Abad et al. on a cross-sectional study of sleep quality in 43 patients with newly diagnosed amyotrophic lateral sclerosis (ALS) assessed using the Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale (ESS), the Beck Depression Inventory-Revised (BDI-II) and the ALS Functional Rating Scale (ALSFRS) [Diaz-Abad, M. et al., 2018]. Only patients with definite or probable ALS according to the El Escorial criteria were included [Diaz-Abad, M. et al., 2018]. Twenty-eight patients had limb-onset alS and 15 patients had bulbar-onset alS [Diaz-Abad, M. et al., 2018]. The mean PSQI was higher in ALS than in control subjects, and poor sleep quality (PSQI >5) was found in 63% of ALS patients [Diaz-Abad, M. et al., 2018]. The PSQI correlated positively with the BDI-II and the inability to turn in bed [Diaz-Abad, M. et al., 2018]. The study is appealing, but some points should be discussed.

First, sleep quality in ALS depends not only on the ability to turn over in bed and mood, but also on many other extrinsic and intrinsic factors that determine sleep quality. Intrinsic determinants of sleep quality include personality type, coping strategies for managing stress, levels of acute and chronic stress, balance between sympathetic and parasympathetic tone, hormonal balance, level of social interactions, strategies for processing daytime experiences, level of physical activity, genetic background and comorbidities.

Comorbidities that can disrupt sleep include diseases of the central nervous system (CNS) (e.g. epilepsy, headaches, pituitary dysfunction, Parkinson's disease, restless legs syndrome, sleep apnoea syndrome, sweating), lung diseases (e.g. asthma, infections, chronic bronchitis, COPD), cardiovascular diseases (e.g. heart failure, malignant ventricular arrhythmias, hypertension) lung diseases (e.g. asthma, infections, chronic bronchitis, COPD), gastrointestinal diseases (e.g. nausea, gastritis, reflux, diarrhea, constipation, flatulence, bloating), chronic or acute infectious diseases (e.g. dental foci, cystitis, urethritis), urological diseases (e.g. pollakisuria, nocturia), metabolic diseases (e.g. hypoglycemia), immunological diseases (e.g. arthritis, colitis, Crohn's disease), orthopaedic diseases (e.g. musculoskeletal pain), occult malignant diseases and a number of non-specific abnormalities such as pain, fever, acidosis/alkalosis or autonomic disorders.

External factors that affect sleep quality include noises inside (e.g., partner's snoring, pets, air conditioning, refrigerator, telephone, computer) or outside the bedroom (e.g. animals, bells, cars, garbage collection, neighbors, airplanes), brightness, temperature, humidity, electrosmog, air quality, vibrations, presence/absence of insects or other animals in the bedroom, relationship with neighbors in the adjacent apartment, eating habits (e.g. quantity, timing and quality of food and liquids) and current medication (e.g. ASM, hypnotics, sedatives, neuroleptics, antidepressants, illegal drugs, alcohol, coffee, cola, black tea or Red Bull). These factors must be included in the analysis before final conclusions can be drawn. In particular, comorbidities and concomitant medications must be specified.

The second point relates to the criteria according to which ALS was diagnosed [Diaz-Abad, M. *et al.*, 2018]. The diagnosis of ALS according to the El Escorial criteria is rather old-fashioned. Currently, the most commonly used diagnostic criteria are the revised Gold Coast criteria [Ferullo, L. *et al.*, 2024]. Did all included patients also fulfill these new criteria? How many of the patients with definite or probable ALS according to the El Escorial criteria did not have ALS according to the revised Gold Coast criteria?

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Third, pulmonary function was not included in the analysis. Since ALS patients with bulbar involvement and those with respiratory muscle involvement may suffer from ventilatory dysfunction leading to hypoxygenation [Sales de Campos, P. *et al.*, 2023], it would have been crucial to assess the impact of respiratory parameters on sleep quality. Was sleep quality worse in bulbar ALS than in ALS with limb involvement?

The fourth point is that no longitudinal data was collected. To assess whether the sleep disturbance is progressive and also correlates with the ALSFRS in more advanced stages of ALS, it would have been interesting to see data from a repeated examination a few months after the first study.

To summarize, this interesting study has limitations that put the results and their interpretation into perspective. Removing these limitations could strengthen the conclusions and reinforce the message of the study. All outstanding questions need to be addressed before readers can uncritically accept the study's conclusions. Before sleep deprivation in ALS can be attributed to depression or muscle weakness, all other factors affecting sleep quality must be ruled out.

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