



## Elevated C-reactive protein and IL-6 signalling are not the only determinants of sleep quality and duration

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#### Letter to the Editor

We read with interest the article by Iakunchykova et al. on the association between chronic low-grade inflammation and usual sleep duration using genetically predicted levels of chronic inflammation represented by C-reactive protein (CRP), interleukin (IL)-6 signalling, and self-reported sleep duration (Iakunchykova et al., 2024). Elevated CRP levels <10 mg/L have been found to have a homeostatic effect, allowing sleep duration of 7–8 hours per day (Iakunchykova et al., 2024). Using polygenic score analysis, it was found that the homeostatic effect of CRP on sleep duration is primarily due to genetic variants within the *CRP* gene region (Iakunchykova et al., 2024). It was concluded that elevated CRP levels may causally facilitate the maintenance of optimal sleep duration (Iakunchykova et al., 2024). The study is impressive, but some points require further discussion.

The first point is that reducing sleep quality to a single inflammatory parameter represents a simplification of a complex, poorly understood phenomenon. Sleep duration and quality depend not only on an individual inflammatory response to acute stimuli (Iakunchykova et al., 2024), but also on several other exogenous and endogenous factors that influence sleep. These include neurological diseases (e.g. seizures, ischemic stroke, Parkinson disease, restless legs, neuropathic pain, headache), cardiac diseases (e.g. heart failure, arrhythmias), peripheral artery disease, lung diseases (e.g. chronic obstructive pulmonary disease, sleep apnea syndrome), urological diseases (e.g. pollakisuria, nocturia), orthopedic diseases (e.g. musculoskeletal pain), gastrointestinal diseases (e.g. nausea, gastritis, reflux), immunological disease (e.g. arthritis, colitis, Crohn's disease), or other concomitant diseases. The quality of sleep also depends heavily on lifestyle and exogenic factors such as eating habits, the timing of water and food intake, the use of illegal drugs, and the consumption of adrenergic stimulants such as nicotine, caffeine, cola, Red Bull, or alcohol (Antila et al., 2022). A noisy sleeping place, the noisy workplace, personality structure, the level of acute and chronic stress, and the pattern of social interactions can also influence sleep quality (Finsterer, 2024).

A second point is that CRP is a non-specific parameter, that can be elevated not only due to infectious diseases, but also due to immunological diseases, malignancies, obesity, lack of exercise, cigarette smoking, diabetes, or stress (Haldeman-et al.). We should know how these different causes could be ruled out as the cause of the CRP elevation.

The third point is that sleep quality was assessed using a questionnaire. The subjective assessment of sleep quality and duration has the disadvantage that it can differ greatly from the results of sleep laboratory and polysomnography (Benz et al., 2023). While polysomnography can determine good sleep quality, subjective assessment may confirm sleep quality as poor and duration as short. (Benz et al., 2023). Subjective and objective measurements can capture different aspects of sleep, even if they nominally consider the same value (sleep duration) (Benz et al., 2023). Subjective and objective measures of sleep duration do not agree in patients with insomnia disorder and those with good sleep, but in different directions (Benz et al., 2023).

In summary, the interesting study has limitations that put the results and their interpretation into perspective. Removing these limitations could strengthen the conclusions and support the study's message. Before good sleep quality is attributed to chronic mild inflammation, the various other influencing factors should be assessed and objective measures should be used to assess sleep duration.

#### Ethical approval

Not applicable.

#### Consent to participation

Not applicable.

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**Consent for publication**

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**Availability of data and material**

All data are available from the corresponding author.

**CRediT authorship contribution statement**

**Josef Finsterer:** Conceptualization, Data curation, Formal analysis, Writing – original draft.

**Declaration of competing interest**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Data availability**

No data was used for the research described in the article.

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