

# Chronic inflammation and subsequent depressive symptoms: The mediating role of sleep

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## Background

Chronic inflammation has been associated with the onset of depression, but the mechanisms underlying this relationship remain elusive. This study examined whether sleep explained the association between elevated levels of inflammatory markers and subsequent depressive symptoms in an English nationally representative sample.

## Methods

The sample consisted of 2,953 men and women (aged 50+) recruited from the English Longitudinal Study of Ageing (ELSA) an ongoing, open, representative prospective cohort study. Four waves of data between 2008/09 (wave 4) and 2016/17 (wave 8) were analysed. Serum levels of inflammatory markers (CRP, fibrinogen) and covariates (age, sex, education, wealth, body mass index, smoking, cholesterol, triglyceride) were measured at wave 4 (considered here as the baseline). Self-reported sleep disturbance (versus no sleep disturbance) was examined via three items of the Jenkins Sleep Problems Scale (difficulty falling asleep, trouble remaining asleep and morning tiredness) at a four-year follow-up (wave 6, 2012/13). Depressive symptoms were assessed at baseline and six years later (wave 7, 2014/15) using the 8-item version of the Centre for Epidemiological Studies Depression Scale (CES-D) (excl. item on sleep). Binary mediation analysis was used to investigate whether sleep mediated the relationship between systemic inflammation and depressive symptoms, adjusting for the full set of covariates.

## Results

High baseline levels of CRP were significantly associated with greater odds of subsequent depressive symptoms, independent of age, sex and baseline depressive symptoms (Odds Ratio (OR)=1.32 (95% Confidence Intervals (CI)) 1.02-1.70). Further adjustment for socio-economic variables (education, wealth status) attenuated this relationship to non-significance (OR=1.17 (95% CI) 0.90-1.53). High CRP levels at baseline were significantly related to higher odds of reporting sleep disturbance at wave 6 (OR: 1.44; (95% CI) 1.14-1.82). Sleep disturbance was associated with greater odds of subsequent depressive symptoms (OR: 2.69 (95% CI) 2.03-3.57). Mediation analyses revealed that sleep problems mediated the relationship between high CRP and depressive symptoms, explaining a total of 65.61% of this association.

## Conclusions:

In this nationally representative sample, we found that sleep disturbance is a partial mediator of the relationship between high CRP and subsequent depressive symptoms. Interventions targeting sleep disturbance may be effective in ameliorating inflammation-associated depressive symptoms.

Keywords: Keywords: depressive symptoms, chronic inflammation, mediation analysis, sleep

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