

### Effect of Dietary Fatty Acids on Sleep and Stress Among Adults With Migraine: Secondary Analysis of a Randomized Controlled Trial

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**Objectives:** To determine whether dietary interventions that reduce headache also improve sleep and stress in adults with migraine.

**Methods:** We conducted a 16-week, three arm, parallel group, randomized, modified double blind, controlled trial in North Carolina. Participants were 182 adults (88% women, mean age 38y) with migraines on 5–20 days per month. The 3 diets were designed with EPA, DHA, and linoleic acid altered as controlled variables: H3 diet (n = 61)—increase EPA + DHA to 1.5 g/day and maintain linoleic acid at around 7% of energy; H3L6 diet (n = 61)—increase n-3 EPA + DHA to 1.5 g/day and decrease linoleic acid to  $\leq$  1.8% of energy; control diet (n = 60)—maintain EPA + DHA at <150 mg/day and linoleic acid at around 7% of energy. Sleep quality, stress rating, and the number of headache hours per day were pre-specified endpoints assessed daily with an electronic diary. Sleep quality was rated on a 1–4 scale, with

higher score indicating better quality. Stress was rated on a 0–10 scale, with higher score indicating more stress. Longitudinal mixed models were used to estimate between-group differences at end of study. Mediation analyses examining headache hours as a mediator (*paramed* command in Stata 17) controlled for baseline BMI, age, sex, headache hours, and baseline values of the respective outcome.

**Results:** At baseline, mean sleep quality was 2.5 (SD 0.5) and stress rating was 3.0 (SD 1.6). In intention-to-treat analyses, the H3L6 group significantly increased sleep quality and reduced stress level relative to the control group (difference 0.2, 95% confidence interval 0.05 to 0.3;  $-0.6$ ,  $-0.9$  to  $-0.3$ , respectively). There was a similar trend in the H3 vs. control group, although only statistically significant for increased sleep quality (0.1, 0.02 to 0.2) but not for reduced stress rating ( $-0.3$ ,  $-0.6$  to 0.02). In mediation analyses, the reduction in headache hours per day explained  $\sim$ 60% of the effect of the combined interventions on sleep quality (natural indirect effect = 0.09,  $p = 0.006$ ). For stress, the reduction in headache hours per day explained  $\sim$ 45% of the effect of the combined interventions (natural indirect effect =  $-0.14$ ,  $p = 0.078$ ).

**Conclusions:** The H3L6 intervention improved sleep quality and decreased stress. Findings suggest that these improvements occurred partially as a result of headache reduction.

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