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# Optimizing Sleep Architecture and Its Effects on Cognition in New-Onset Temporal Lobe Epilepsy

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## Introduction

- Temporal lobe epilepsy (TLE) is characterized by altered neural network activity.
- Beyond seizures, individuals with TLE experience cognitive<sup>1</sup> and sleep problems, contributing to poor school performance, underemployment and lower socioeconomic status.
- Sleep fragmentation in TLE disrupts memory consolidation and sustained attention, both of which are impaired in this disorder.
- These comorbidities often appear before the first recognized seizure and can worsen even with successful seizure treatment, suggesting an early network abnormality that affects seizures, sleep and cognition together.
- Few studies have addressed the mechanisms underlying sleep and cognitive problems in TLE.

## Hypothesis & Aims

- Central hypothesis:** disordered networks in new-onset TLE alter sleep architecture, disrupting memory consolidation and attention.
- In healthy sleep, NREM slow oscillations are phase-locked with sleep spindles (SW-SSO coupling), which supports memory consolidation. In TLE, interictal discharges and seizures may disrupt this coupling.
- Acoustic stimulation (AS) enhances slow-wave activity and memory in healthy adults but has not been studied in TLE.
- Aim 1:** characterize sleep architecture in TLE and link it to cognition.
- Aim 2:** determine whether AS enhances slow-wave sleep, memory and attention in TLE.

## Approach

**Participants:** 78 young adults enrolled (40 healthy controls, 38 with TLE); 53 completed both nights.

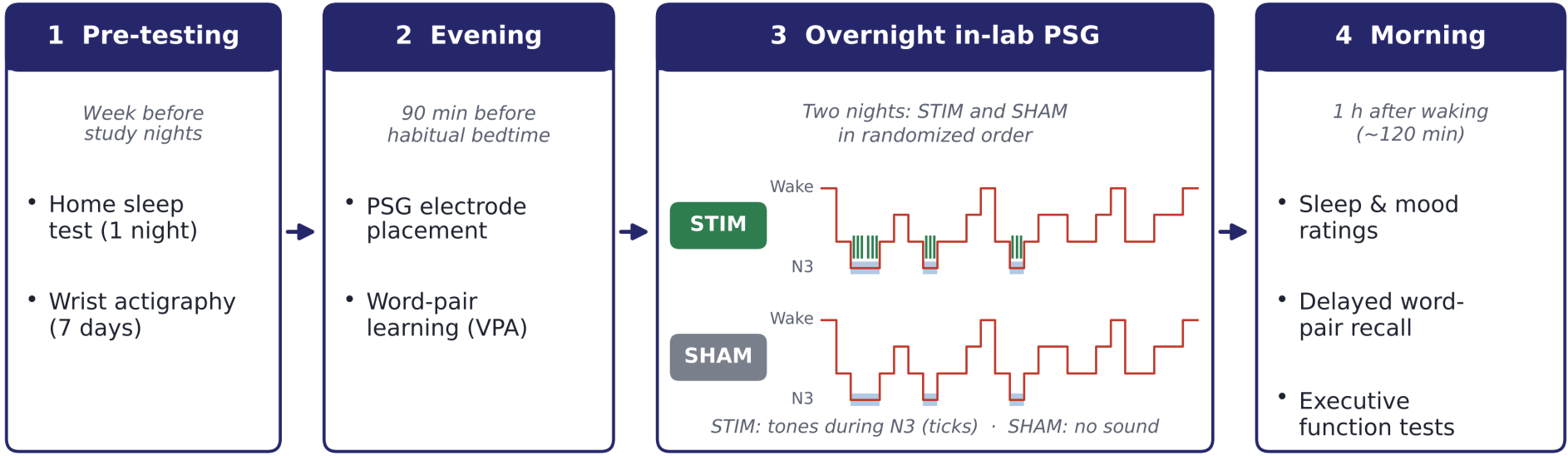
**Design:** randomized, sham-controlled, two-night crossover. Each participant had one night of acoustic stimulation (STIM) and one sham night (SHAM) in randomized order, using the Philips SmartSleep Deep Sleep Headband, which delivers phase-locked tones during slow-wave sleep and records stimulation dose ("deep-sleep boost" minutes).

**Sleep:** in-lab polysomnography (PSG) on both nights.

**Cognition & mood:** word-pair learning (CANTAB Verbal Paired Associates, VPA) ~90 min before bedtime; starting 1 h after waking: VPA delayed recall, NIH Toolbox DCCS, Flanker and Picture Sequence Memory, and sleepiness/mood scales (Epworth, Karolinska, Global Vigor and Affect).

**Analysis:** linear mixed-effects models (random intercept per participant) adjusted for night and group; stimulation dose analyzed as a continuous variable (0 on sham night). Exploratory;  $p < .05$ .

### Study design



## Participants

Table 1. Participant demographics

| Characteristic                      | Overall (n = 78) | Healthy controls (n = 40) | Epilepsy (TLE) (n = 38) | p      |
|-------------------------------------|------------------|---------------------------|-------------------------|--------|
| Age, years, mean (SD)               | 26.4 (6.4)       | 23.9 (5.1)                | 30.0 (6.3)              | < .001 |
| Education, years, mean (SD)         | 14.5 (1.6)       | 14.8 (1.2)                | 14.0 (1.8)              | .07    |
| Sex assigned at birth, n (%)        |                  |                           |                         | .16    |
| Female                              | 40 (69.0)        | 26 (76.5)                 | 14 (58.3)               |        |
| Male                                | 18 (31.0)        | 8 (23.5)                  | 10 (41.7)               |        |
| Handedness, n (%)                   |                  |                           |                         | 1.00   |
| Right                               | 53 (93.0)        | 31 (93.9)                 | 22 (91.7)               |        |
| Left                                | 4 (7.0)          | 2 (6.1)                   | 2 (8.3)                 |        |
| Race, n (%)                         |                  |                           |                         | .35    |
| White                               | 28 (47.5)        | 16 (47.1)                 | 12 (48.0)               |        |
| Asian                               | 13 (22.0)        | 10 (29.4)                 | 3 (12.0)                |        |
| Black or African American           | 2 (3.4)          | 0 (0.0)                   | 2 (8.0)                 |        |
| Native Hawaiian or Pacific Islander | 1 (1.7)          | 0 (0.0)                   | 1 (4.0)                 |        |
| More than one race                  | 3 (5.1)          | 2 (5.9)                   | 1 (4.0)                 |        |
| Other                               | 5 (8.5)          | 3 (8.8)                   | 2 (8.0)                 |        |
| Not provided                        | 7 (11.9)         | 3 (8.8)                   | 4 (16.0)                |        |

Age and education: Welch t-tests. Sex and handedness: Fisher exact tests. Race: permutation chi-square test (20,000 permutations). Race was a select-all item; participants choosing two or more categories are counted once under "More than one race."

## Results

### 1. Stimulation increased deep sleep

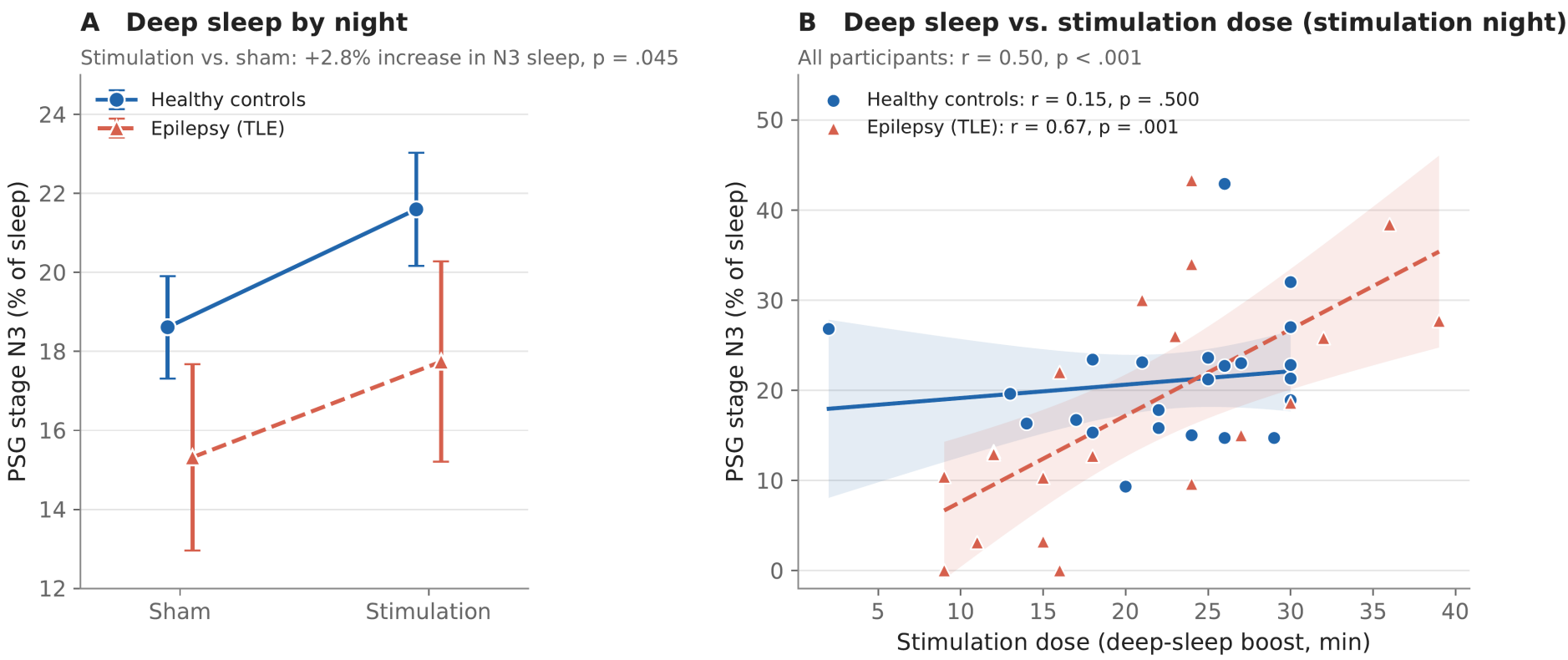


**Figure 1.** Deep sleep (stage N3) with acoustic stimulation. (A) In-lab PSG N3 percentage on sham and stimulation nights (mean  $\pm$  SEM). N3 was 2.8 percentage points higher on stimulation nights (linear mixed model adjusted for night and group,  $p = .045$ ). (B) N3 percentage on the stimulation night vs. stimulation dose, with linear fits  $\pm$  95% CI. Higher stimulation dose was associated with more N3 overall ( $r = .50$ ,  $p < .001$ ), driven by the epilepsy group primarily.

### 2. Stimulation reduced next-morning tension

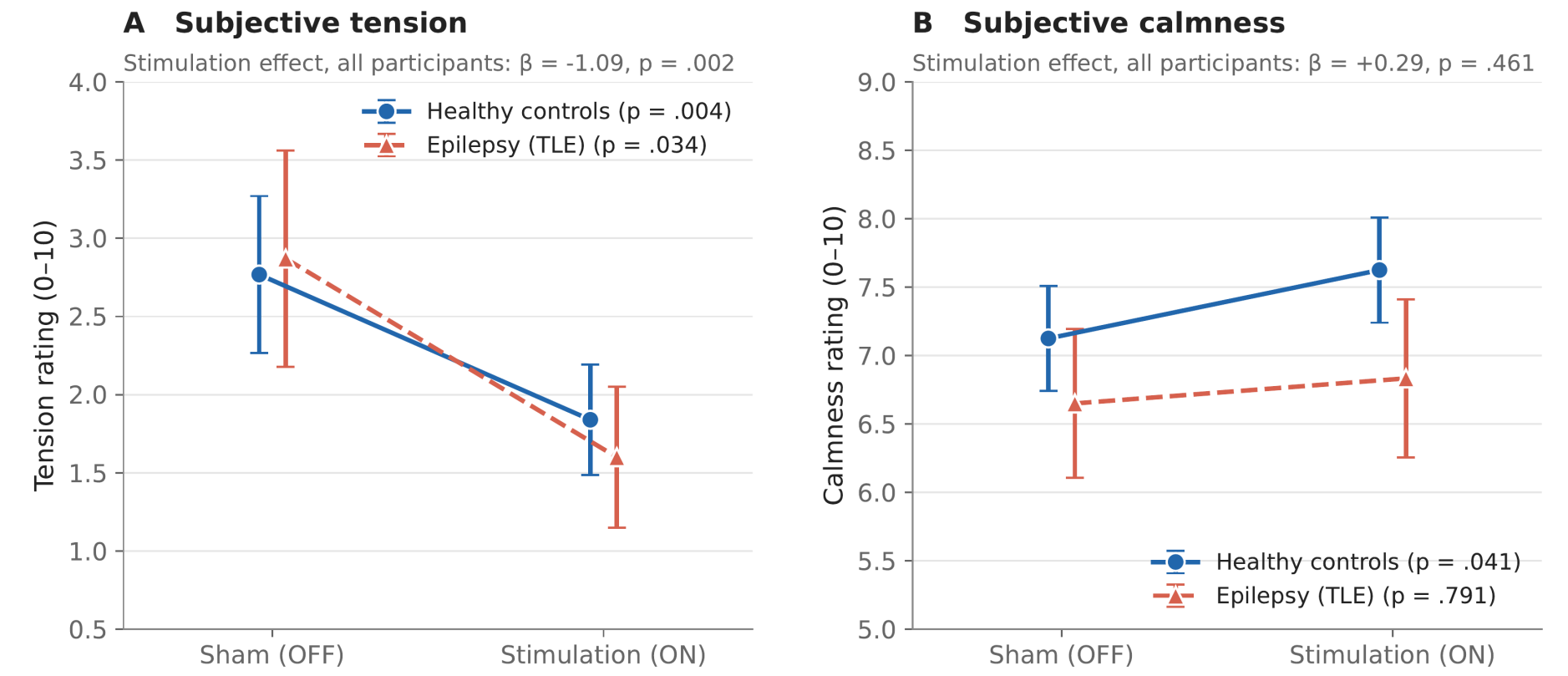


**Figure 2.** Subjective tension and calmness after sham and stimulation nights. Visual analogue scale ratings (0–10; mean  $\pm$  SEM) of (A) tension and (B) calmness the morning after each night. Stimulation reduced tension across participants ( $p = .002$ ), in both healthy controls ( $p = .004$ ) and epilepsy participants ( $p = .034$ ). Calmness increased modestly in healthy controls ( $7.12 \rightarrow 7.62$ ,  $p = .041$ ).

### 3. Stimulation dose tracked next-morning cognition

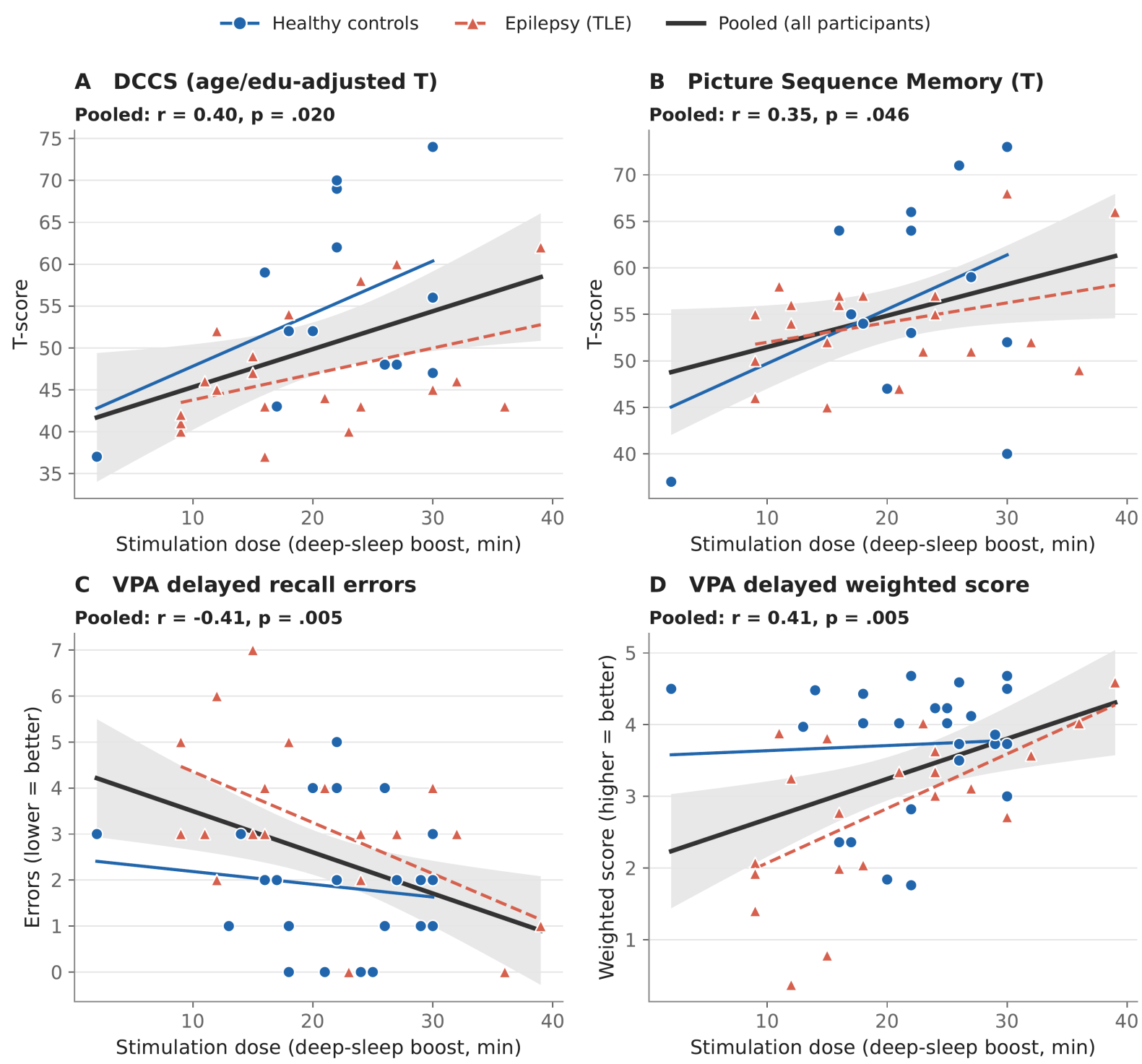


**Figure 3.** Next-morning cognition vs. stimulation dose on the stimulation night. (A) DCCS age/education-adjusted T-score, (B) Picture Sequence Memory age/education-adjusted T-score, (C) VPA delayed recall errors, and (D) VPA delayed weighted score, each plotted against stimulation dose. Black line and gray band: pooled linear fit  $\pm$  95% CI (all participants); colored lines: fits within each group. Higher stimulation dose was associated with better performance on all four measures (pooled  $r = .35$ –.41,  $p \leq .046$ ). For delayed verbal memory (C, D), the association was driven primarily by the epilepsy group.

Dose effects held after adjusting for age, sex, race and education.

## Conclusions

- Acoustic stimulation modestly increased slow-wave sleep and reduced next-morning tension in both TLE and healthy controls.
- Higher stimulation dose was associated with better next-morning memory, particularly in epilepsy.
- These preliminary results support acoustic stimulation as a feasible, non-invasive approach to enhance sleep-dependent memory in TLE, warranting larger multi-night trials.
- Future work will examine SW-SSO coupling and its relationship to cognition and seizures in TLE.

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