

Phase-Amplitude Coupling of Theta and Gamma Rhythms During Rapid Eye Movement Sleep Predicts Verbal Memory in Alzheimer's Disease

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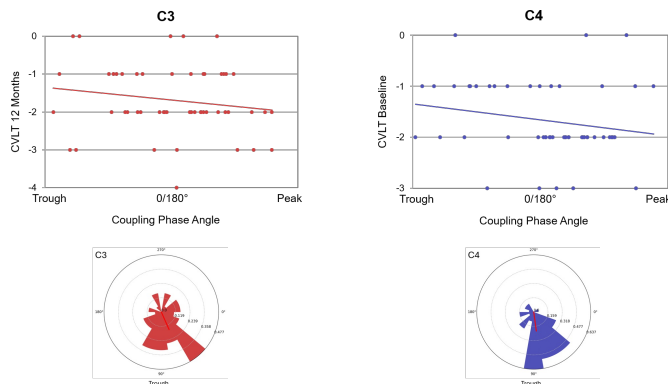
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INTRODUCTION

- Phase-amplitude coupling (PAC) supports memory consolidation and is disrupted in Alzheimer's disease (AD).
- Non-REM PAC and wake theta-gamma coupling decline with aging and AD.
- REM sleep theta-gamma coupling (REM-TGC) has not previously been investigated in humans.
- Elevated orexin-A in AD may disrupt REM sleep physiology.
- Whether REM-TGC relates to cognition and AD progression remains unknown.
- Aim: To determine whether REM-TGC is associated with cognitive performance in persons with mild-to-moderate AD and whether these relationships are influenced by orexin-A and neurodegeneration.**

RESULTS

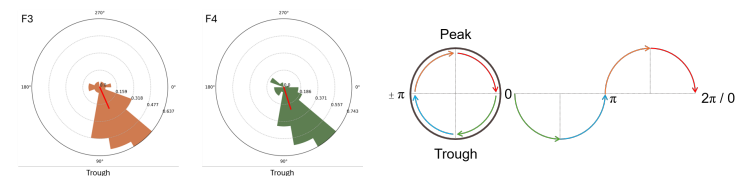
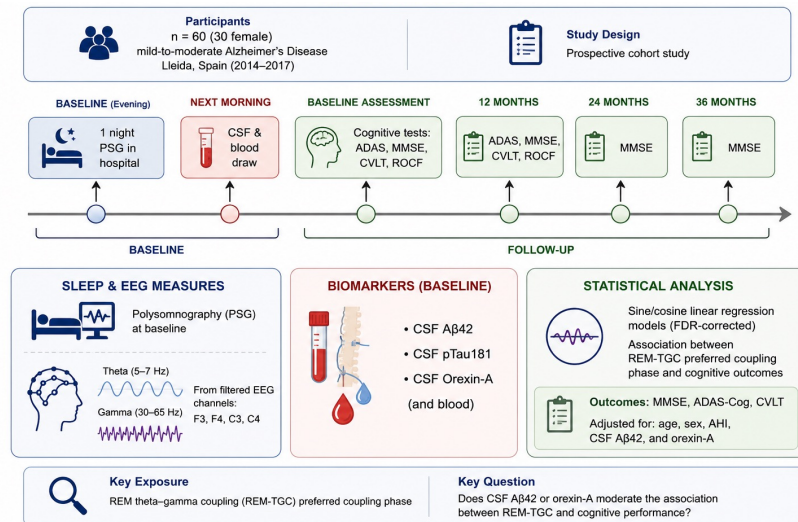
- REM-TGC at the theta trough predicts:**
 - CVLT at baseline (C4: $F(7, 32) = 9.439$, $\Delta R^2 = 0.291$, $p < 0.001$)
 - CVLT at 12 months (C3: $F(7, 32) = 5.625$, $\Delta R^2 = 0.155$, $p < 0.001$)
- Trend-level associations**
 - and MMSE at baseline (F4: $F(7, 32) = 2.950$, $\Delta R^2 = 0.138$, $p = 0.066$)
 - MMSE at 12 months (C3: $F(7, 32) = 4.128$, $\Delta R^2 = 0.444$, $p = 0.058$)



CONCLUSIONS

- REM theta-gamma coupling at the theta trough is associated with verbal memory in mild-to-moderate AD.
- This is the first study to characterize REM theta-gamma coupling in humans and in AD.
- Associations persisted after adjustment for CSF orexin-A and Aβ42
 - REM-TGC provides information beyond established AD biomarkers.
- REM-TGC may represent a novel electrophysiological biomarker of memory function in AD.
- Findings support further investigation of REM oscillatory coupling as a potential therapeutic target for memory preservation.

METHODS



Preferred coupling phase of REM theta-gamma coupling. Gamma amplitude was consistently coupled to the theta trough across frontal and central EEG channels.

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