

SCAN ME



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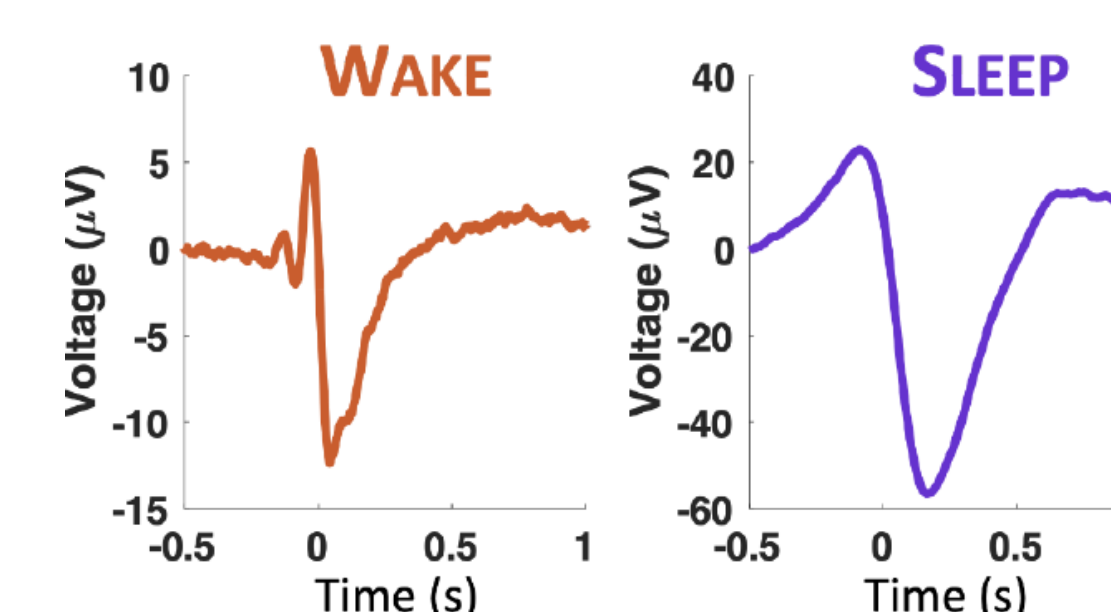
Resting-state EEG wake slow waves predict cognition and two-year amyloid conversion in preclinical Alzheimer's disease

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INTRODUCTION

An increasing body of evidence has underscored the critical role of **sleep slow waves** in facilitating the clearance of brain waste, affecting the accumulation of Alzheimer's disease (AD) brain lesions. Recent studies have identified **sleep-like slow waves in wake EEG** of young adults, often interpreted as intrusions of **local sleep during wakefulness**. The occurrence of these **wake slow waves (wake SW)** is known to increase during sleep deprivation, and can predict behavioral errors across various tasks.



Wake and sleep slow waves.
(Andrillon et al., 2021)

AIMS

- 1 Do wake SW cross-sectionally relate to **cognition**?
- 2 Can wake SW **predict the transition to amyloid positivity (A+)** in the next years?

MATERIAL & METHODS



INSIGHT-preAD cohort

n = 274 (63% of women)

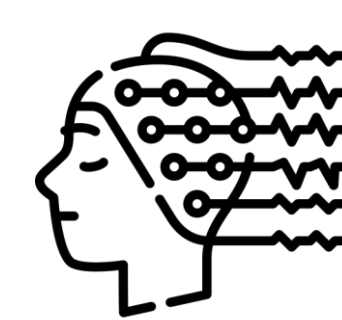
Age: 70-85 y.o

Subjective Cognitive Decline (SCD):

- with memory complaints
- without objective memory deficits

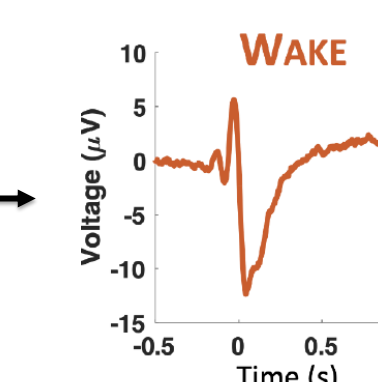


TEP ¹⁸F-florbetapir (baseline + 2 years later) → **Amyloid status** (A+ or A-)



Resting-state EEG

2 min eyes closed + 2 min eyes open
256 channels



wake SW (> 5µV) in delta (1-4 Hz) and theta (4-7 Hz) bands
→ Extraction of their density (nb/min) and amplitude (µV)



Neuropsychological tests

→ **Composite scores**: memory, attention, executive functions

Aim 1: Relationships between wake SW metrics and cognition

1) Linear regression model on each EEG channel:

$EEG \sim 1 + age + sex + educational\ level + memory\ composite\ score + attention\ composite\ score + executive\ functions\ composite\ score$

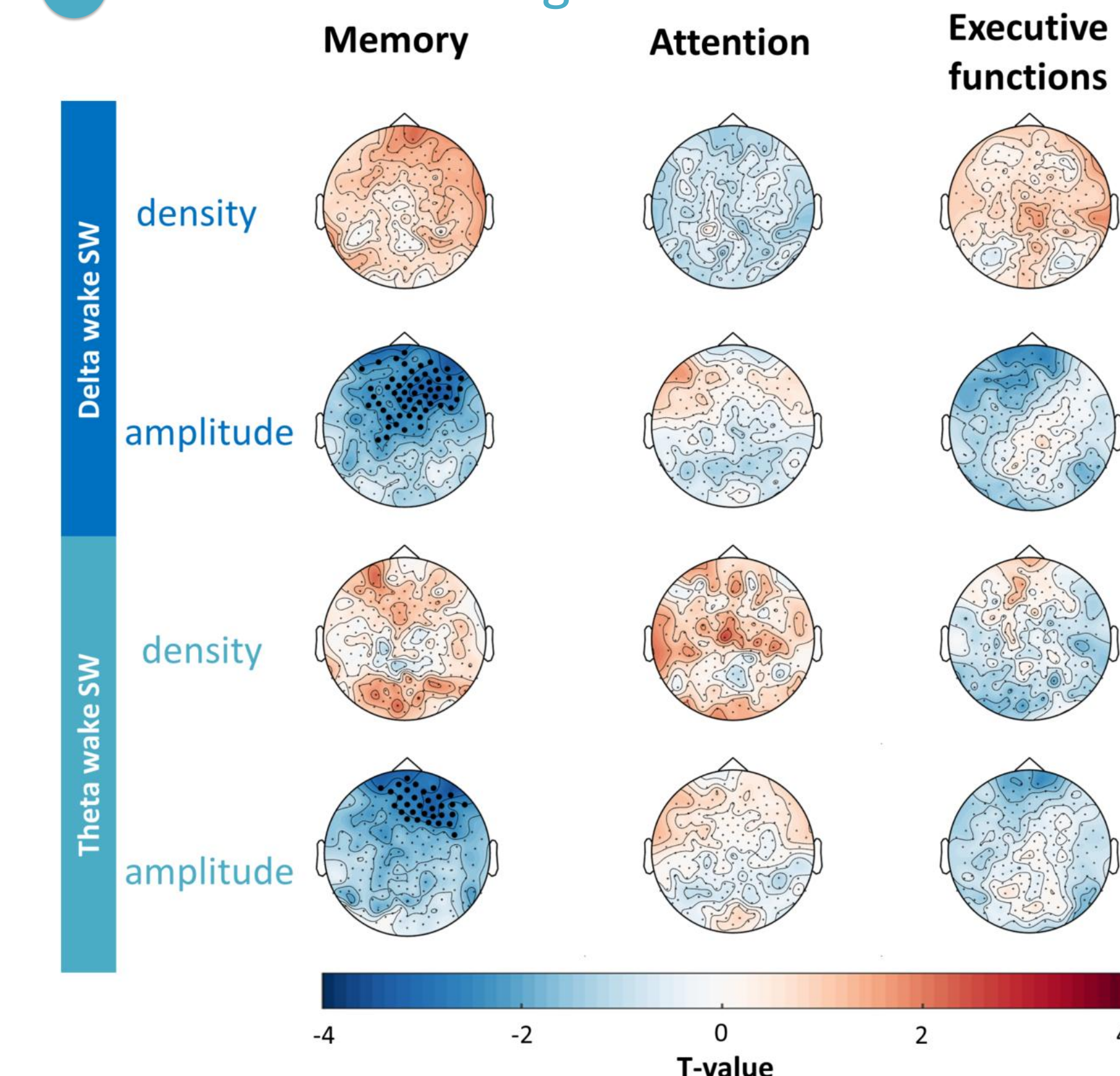
2) Cluster based permutation correction (1000 permutations)

Aim 2: Prediction of converters (A- → A+) based on averaged wake SW metrics at baseline with repeated 5-fold cross-validation (x100) procedure

- Split data into training (80%) and test (20%) data
- Logistic regression wake SW metric ~ converters (on training dataset)
- Determine Youden index to differentiate optimal threshold differentiating converters to individuals remaining A-
- Classify individuals of the test dataset with this optimized threshold

RESULTS

1 Wake SW and cognition



Statistical maps of the associations wake SW ~ cognition.
• = significant clusters of electrodes

2 Prediction of A+ converters with wake SW

Convertors (n=16)

A- stable individuals (n=157)

	Sensitivity (TP rate)	Specificity (TN rate)	Balanced accuracy
Delta wake SW amplitude	0.61 [0.50-0.65]	0.81 [0.81-0.82]	0.71 [0.66-0.73]
Theta wake SW amplitude	0.62 [0.53-0.65]	0.85 [0.85-0.85]	0.73 [0.69-0.75]
Baseline ¹⁸ F-florbetapir PET SUVr	0.92 [0.80-0.95]	0.69 [0.69-0.70]	0.81 [0.75-0.82]

Prediction of individuals who will convert from A- to A+ during the 2-year follow-up period.

Mean values and 95% confidence intervals (in brackets) are reported. Abbreviations: TN (True Negative), TP (True Positive).

CONCLUSION

1 Higher wake SW amplitude at rest was correlated with poorer memory performance. Previous literature showed that wake SW during behavioral tasks can predict errors and slowed cognitive processing at the trial level (Andrillon et al. 2021; Sheybani et al., 2023) likely due to the neuronal silencing associated with wake SW. Our results show that **resting-state wake SW can also provide information about cognition.**

2 Both delta and theta wake SW amplitude yielded good performance for predicting which individuals will convert to A+ in the next 2 years.

→ Wake SW may serve as an early EEG biomarker of AD pathology and help identifying A- individuals at risk of transitioning to amyloid positivity (A+), even before the onset of objective cognitive decline (see other results in our paper).