

EEG measures of arousal and capacity for consciousness in Alzheimer's Disease

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Introduction

Consciousness is relevant in dementia, as unlike discrete states such as general anaesthetic and light sleep one cannot intuit consciousness from observation alone, especially in more severe cases (1, 2).

- Observations of patients with dementia seem to show reduced awareness and arousal, however clinically there is significant variability and fluctuation (2).
- Data exists comparing patients with mild cognitive impairment in AD to patients without AD, typically showing an increase in slow-speed brainwaves, similar to that seen in sleep-like states (3).
- EEG markers of wakefulness (the Alpha Theta ratio) and complexity (e.g. Lempel Ziv Complexity) provide surrogate measures of aspects of consciousness (4, 5).
- Changes in brain network properties and types of interactions have also been observed in people with undergoing a general anaesthetic (6).
- There is little to no evidence on the changes observed in these markers of consciousness in more advanced and severe dementia highlighting a key area of research.

Methods

This research used 47 participants which were categorised into 3 groups: Control (no-AD), Mild AD and Severe AD based on their Global Dementia Rating (GDR). The patients were sitting, mostly still throughout the recording and EEG recordings were all over a minute-long.

- **Preprocessing** When EEG data is recorded, it is filled with noise from the surroundings. Preprocessing attempts to remove this. This was done in Python (7).
- **Alpha Theta Ratio** The most basic measure of wakefulness is the proportion of slow waves to faster waves. Theta waves represent slow lower frequency oscillations and these predominate in sleep, whereas higher frequencies typically predominate in wakeful consciousness (8, 9).
- **Signal Entropy (e.g. Lempel Ziv Complexity)** This is a measure of temporal signal complexity. “Capacity for consciousness” has often been described as having more complex EEG activity. This has been found to be reduced in mild cognitive impairment patients (10).
- **Connectivity and Network Analysis** The brain forms connections between different regions (11). All these individual connections can be put together to create a larger network or graph (11). Changes in the layout and type of connection formed in these graphs has been shown to change in suppressive anaesthesia with loss of consciousness (8, 9, 12). As part of our research we used multiple methods of estimating connectivity to isolate different types of interactions between brain regions.
- **Statistical Analysis** This was carried out using R (13).

Results

- There was a statistically significant decrease in Alpha Theta ratio when comparing Control and Mild groups and Control and Severe groups ($p < 0.0001$ and $p = 0.0002$ respectively) as determined by linear mixed effects, however no difference between Mild and Severe groups ($p = 0.5411$). See Figure 1.
- Lempel Ziv Complexity (LZC) also demonstrated statistically significant reduction from Control to Mild and Control to Severe groups ($p < 0.0001$ and $p = 0.0004$ respectively) while failing to discriminate between Mild and Severe groups ($p = 0.9678$). See Figure 1.
- Network analysis showed statistically significant changes in “Small World” network properties and the amount of connectivity. However the exact direction of these changes varied depending on the method used to calculate connectivity between regions.

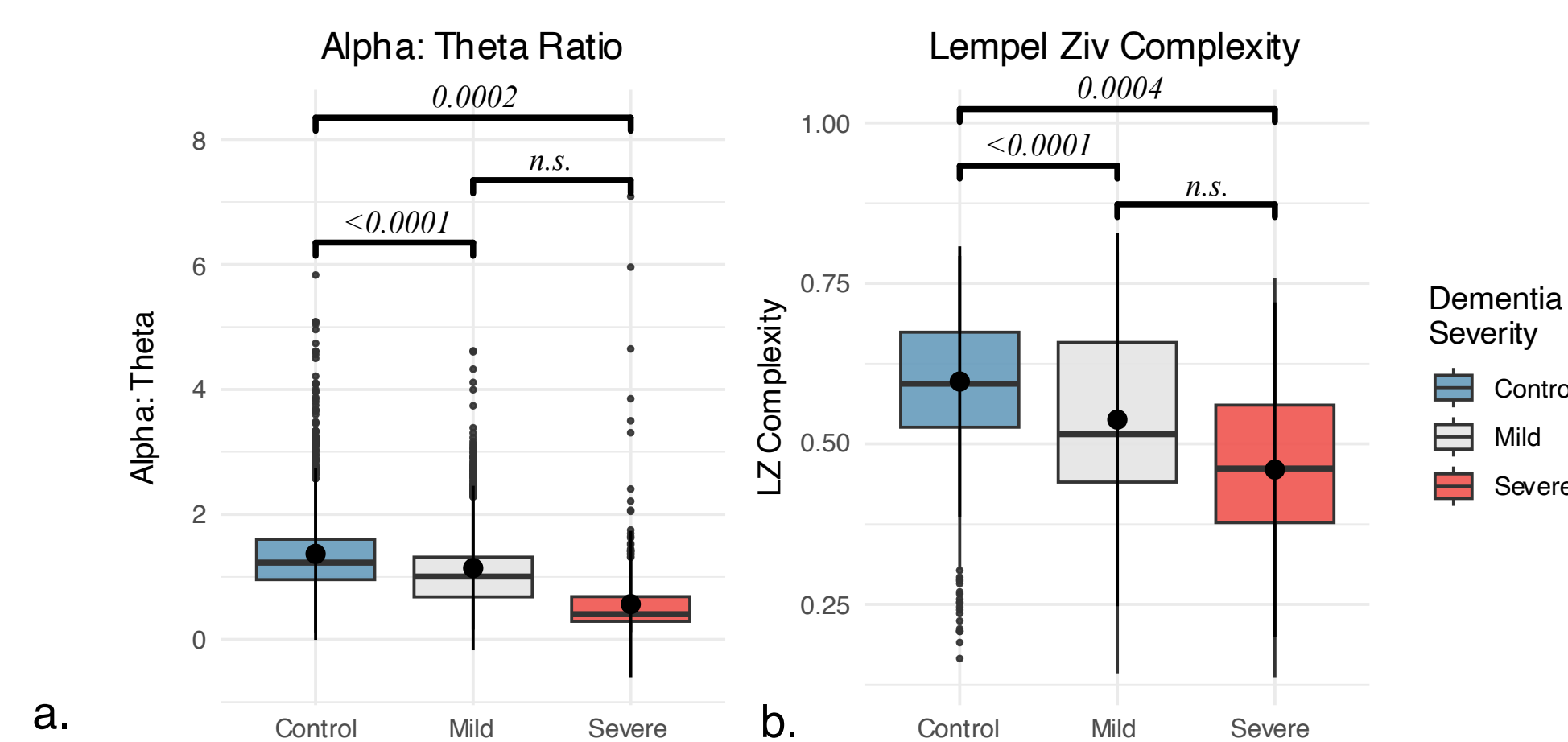


Figure 1: a. box plot of Alpha:Theta Ratio showing a statistically significant reduction between Control and Mild, however no difference between Mild and Severe. b. Box plot of Lempel Ziv showing the changes as seen in Alpha:Theta Ratio.

Visual Summary of Findings

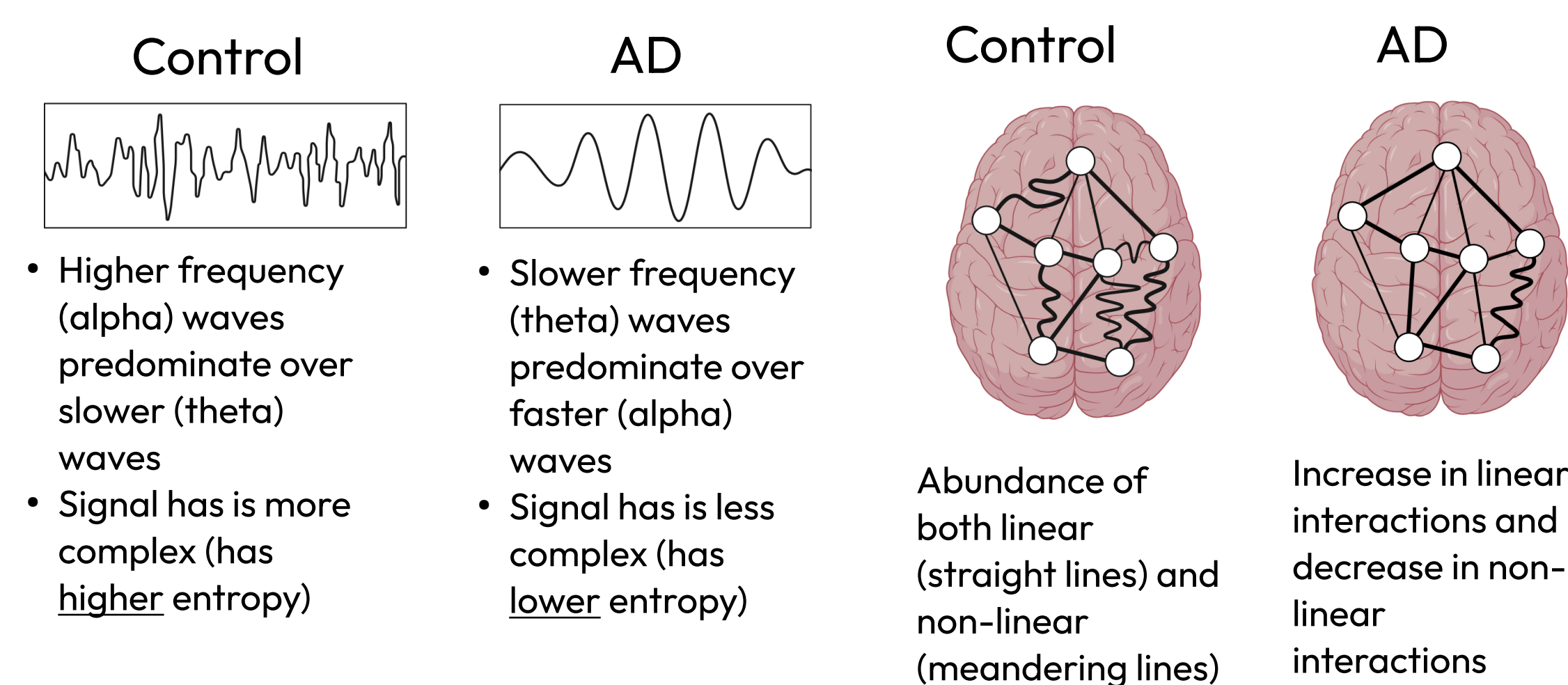


Figure 2: Summary of Findings. Created in *BioRender.com*

Discussion and Conclusion

Results showing a shift toward less complex and slower wave dominant state as AD severity increases agrees with existing literature on mild cognitive impairments and shows this state persists in severe dementia.

- These measures are often said to describe an individual's “Capacity for Consciousness”, suggesting that as dementia advances, patients' ability to experience the range of conscious phenomena had by those without dementia decreases.
- Both LZC and Alpha Theta ratios correlate highly with levels of wakefulness, and the results seen herein describe a conscious experience similar to that seen in the induction of general anaesthesia, just at a much slower rate. This suggests that AD may be a disorder of consciousness.
- Gross network changes observed in this group whilst statistically significant, somewhat contradict one another depending on the method used. This can be accounted for when considering that measures used such as imaginary coherence (imCOH) measure almost entirely simple (linear) region to region interactions whilst measures such as wSMI measure mostly complex (non-linear) interactions (9).
- When considered together this data suggests a transition from more complex non-linear region to region connectivity to more simple connectivity: a phenomenon seen also seen in following the induction of anaesthesia (8, 14).
- Whilst this data suggests that people with severe AD may have reduced consciousness, considering that they often remain mobile, and may be responsive or restless (2), further research is needed into the variability and fluctuation of consciousness in severe AD, and also the reliability of these EEG measures to describe the conscious state seen in dementia

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Any Questions?

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