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## Background

- ALS: characterized by upper and lower motor neuron degeneration and **extra-motor network disruption**
- Auditory oddball task during EEG**
  - Sensory and involuntary attention switching networks
  - Analysis of ERP (**mismatch negativity**) detects malfunction in cognitive cortical activity in ALS[1] BUT: non-phase locked oscillatory activity not considered
  - Intertrial variance (ITV) – Measures non-phase locked oscillations** – previously uncharacterised, may provide measures of ALS-related dysfunction

## Results: Control ERSP

- Standard and deviant tones induce **alpha band non-phase locked ERS (Fig 3A)**, distinct from ERPs (fig 3B)

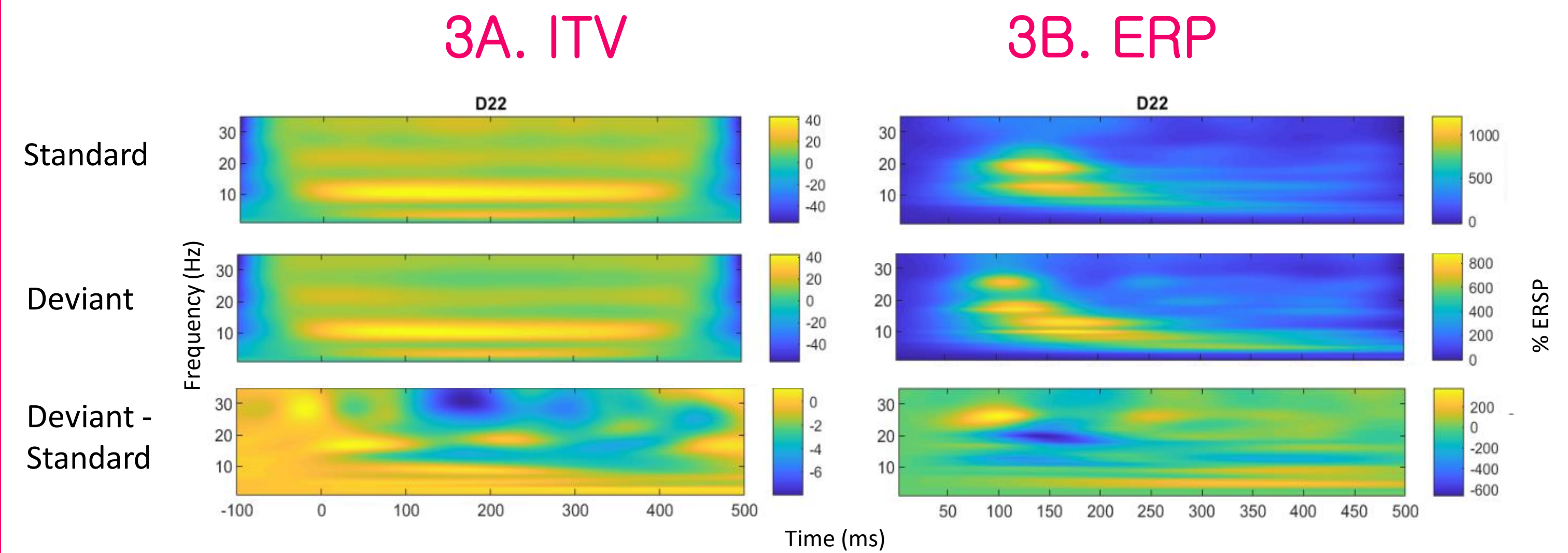


Fig 3. Non-phase locked (A) and phase-locked (B) oscillation ERSPs in response to standard and deviant tones, as well as the difference between deviant and standard. The color bar on the left represents the percentage of perturbation, where yellow = ERS, blue = ERD.

**Aims – Characterise non-phase locked oscillations during auditory oddball task and determine if they are abnormal in ALS**

## Results: Differences in people with ALS

### ALS vs. controls:

- Greater alpha-beta ERS during deviant tones over left temporal lobe (Fig. 4)**

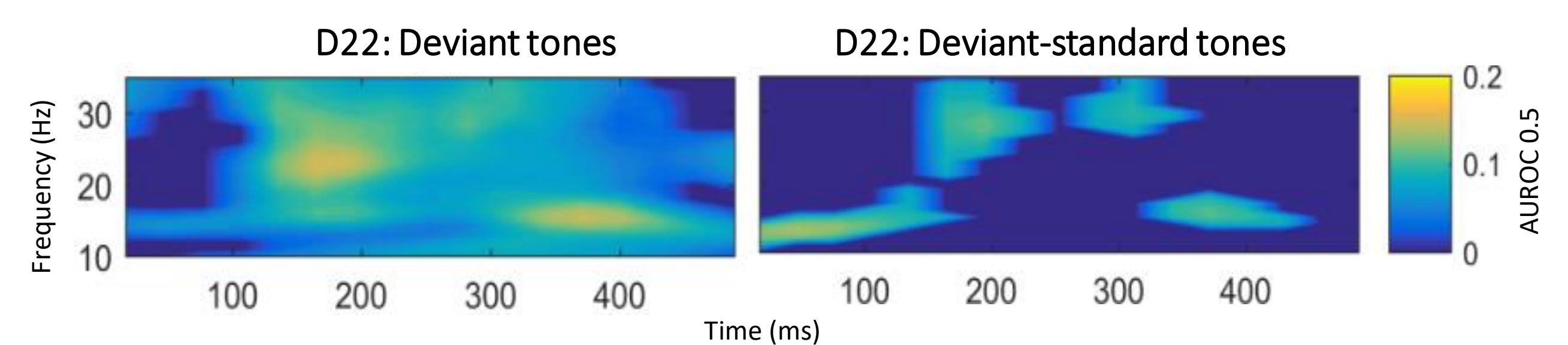


Fig 4. Significant differences (5% FDR) in non-phase locked ERSPs in ALS compared to controls.

## Methods

- 123 people with ALS (32f, median age 61.5)
  - ALS subgroups: 11 C9orf72+, 27 bulbar onset, 73 deceased
- 115 age-matched controls (75f, median age 59)

### Clinical data:

- Beaumont Behavioral Inventory (BBI)
- Edinburgh Cognitive and Behavioral ALS Screen (ECAS)
- Revised ALS Functional Disability Rating (ALSFRRS-R)

### Auditory Pitch Oddball Paradigm:

- Silent black-and-white movie
- Regular standard tones: 720Hz
- Rare (~10%) deviant tones: 800Hz
- Interstimulus interval: 833ms
- 3\*8min sessions
- Participants told to ignore tones

### EEG data:

- 128 electrodes, 512 Hz
- 5 electrodes selected (fig 2)
- Trial epoch: -100ms to +500ms



Fig. 1. EEG setup.\*

### Data analysis:

- Edge padding
- Complex Morlet wavelet transform (CMWT):**
  - Separately for standard, deviant
  - Alpha and beta band frequencies
- Phase-locked oscillations**
  - Average across trials before CMWT
  - =ERP in time-frequency domain
- Non-phase locked oscillations (ITV)**
  - Subtract average signal before CMWT
  - Average across epochs after
- ERSP = % change in oscillations vs. baseline**
  - Event related desynchronisation (ERD) – ↓ from baseline
  - Event related synchronisation (ERS) – ↑ from baseline

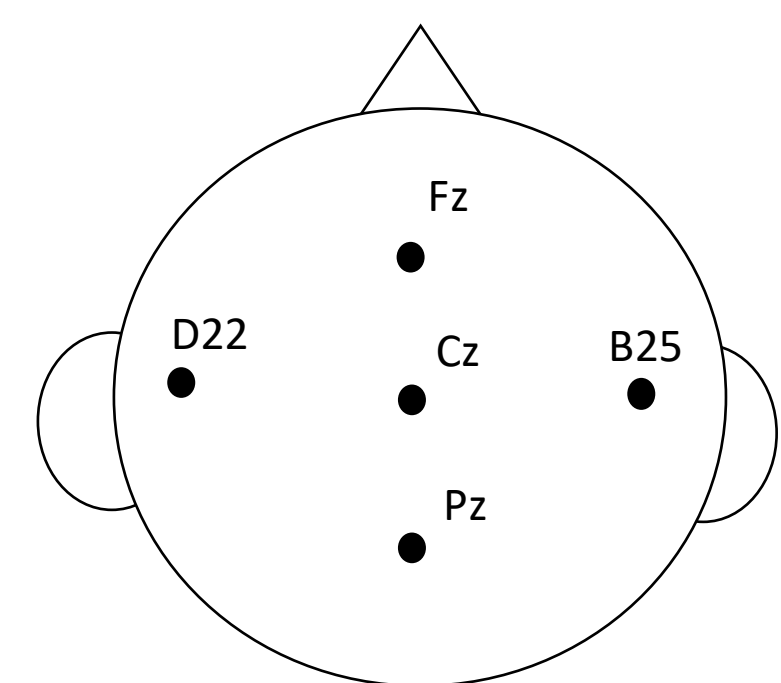


Fig. 2. Location of selected electrodes.

### Subgroup differences:

- Greater alpha-beta ERS during deviant tones in ALS with bulbar vs spinal onset (Fig. 5)**

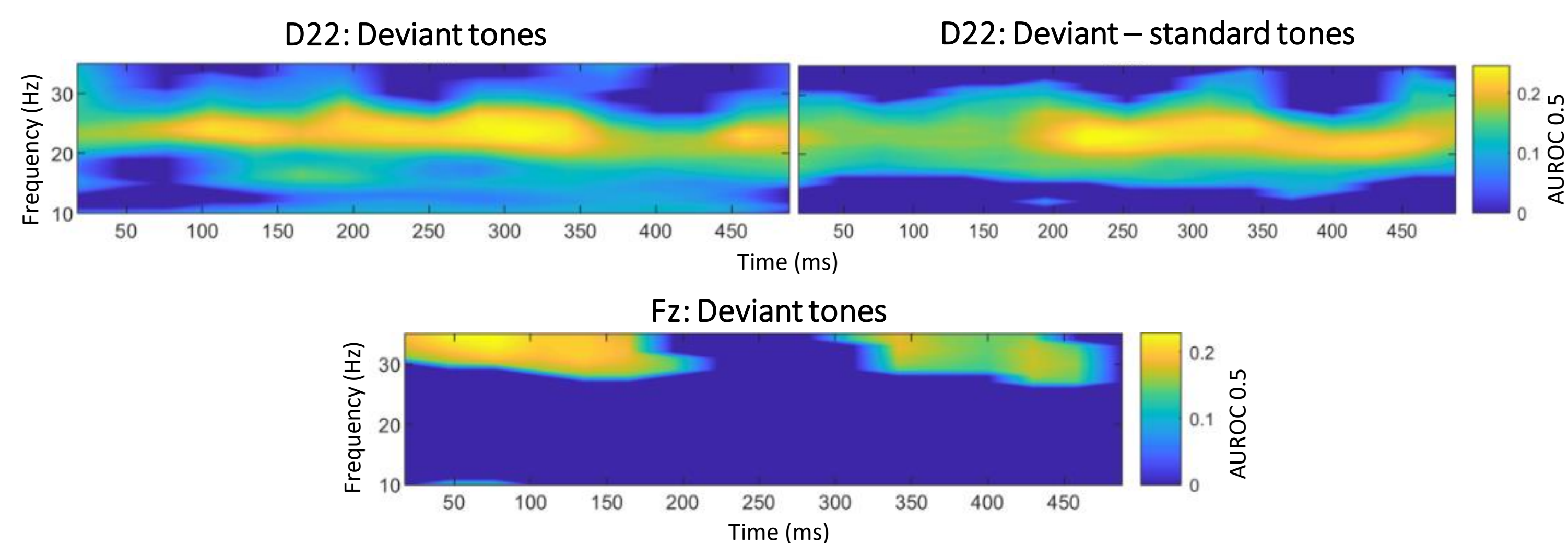


Fig 5. Significant differences (5% FDR) in non-phase locked ERSPs in left temporal and prefrontal lobe for bulbar- vs. spinal-onset ALS.

- Significant gender effect:** Less non-phase locked alpha ERS over prefrontal lobe in females than males
- No significant differences for phase-locked oscillations

### Correlations:

- Negative correlations:**
  - Disease duration and alpha band in deviant tones over the D22 channel ( $\rho = -0.39$ ,  $p < 0.001$ )
  - Disease duration and alpha band in deviant-standard tones over the Pz channel ( $\rho = -0.30$ ,  $p < 0.001$ )

## Limitations

- Low number of C9orf72- ALS – Underpowered subgroup analysis
- Gender effect – To be accounted for in future analyses

## Discussion/Conclusion

- Auditory oddball paradigm elicits non-phase locked alpha and beta temporal ERS, distinct from ERPs
- Non-phase locked ERSP changes in ALS, no difference in phase-locked
- Non-phase locked oscillatory activity useful for characterising ALS