

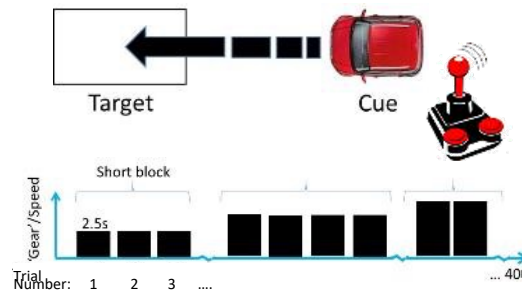
## Introduction

Patients with frontotemporal lobar degeneration (FTLD) are typically impulsive and disinhibited, with an impaired ability to adapt and update behaviours in response to a changing environment<sup>1,3</sup>. We use Magnetoencephalography with a novel visuo-motor learning task (CAR Task) to understand these abnormal behaviours in the context of impaired GABAergic neurotransmission, and potential restoration by GABA-reuptake inhibition using Tiagabine (TGB, GAT1 transporter inhibitor).

## Methods

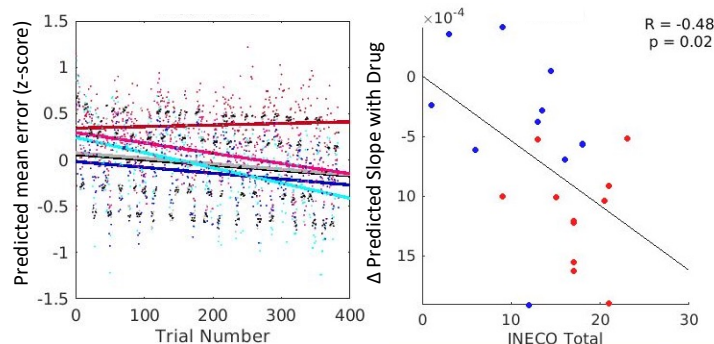
- Design:** Double blind placebo controlled cross over design. 10mg Tiagabine / placebo
- Participants:** 11 bvFTD, 11 PSP, 18 healthy controls (mean age 66, SD 7.5)
- MEG Sensor:** Individual linear models of trial covariates. ANOVA of group and drug effects.
- MEG Source of Beta:** LCMV Beamformer & connectivity (amplitude envelope correlations) using Desikan-Killiany Atlas (5000 permutations,  $p < 0.05$  corr)

## Controlled Action Response (CAR) Task



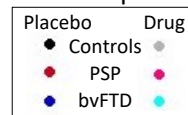
## Behaviour: Linear Mixed Model

$$\text{MeanError} \sim 1 + \text{TrialNumber} * \text{DrugSession} + (1 + \text{Gear} | \text{Subject})', \text{FitMethod}', \text{'REML'}$$

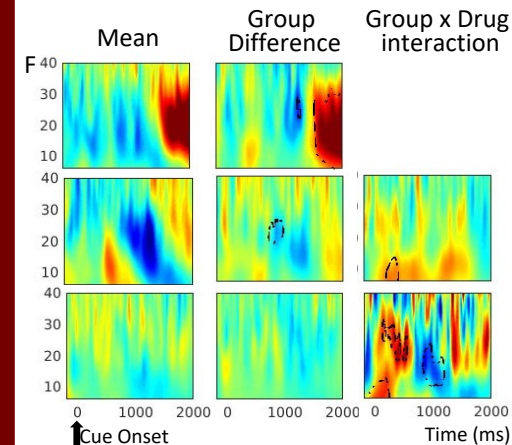


Performance over trials was improved on drug for patients.

Improvement on drug correlated with INECO – patients with better cognitive performance showed more improvement on drug.



## MEG Power spectra of behavioural covariates



**Movement time** related spectra.

ERD/ERS is diminished in patients vs controls

**Mean Error:** Better accuracy associated with greater ERD, reduced in patients. TGB increases alpha power in bvFTD but decreases it in PSP, with greater accuracy.

**Trial No.** TGB enhances ERD in PSP, but elevates Beta power in bvFTD as trials progressed.

-----  $p < 0.001$  FWE cluster corrected

## LCMV Beamformer & Amplitude Envelope Correlation of beta



**Group Mean:** Task related beta modulation vs baseline, and mean network connectivity

**Group x Drug Interaction:** TGB enhances ERD in right IFG, and enhanced frontal connectivity in patients.

## Discussion

GABA modulation improved motor learning in bvFTD and PSP patients, by differential enhancement of Beta power, within a primary source of right prefrontal cortex. This is a key region in a frontal network for behavioural control and inhibition, and a region known for loss of GABA neurotransmission in FTLD<sup>2,3</sup>.

## References

- Hughes et al., (2018) Brain, 2. Murley et al., (2018) Brain 3. Murley et al., (2020) Brain