Modulating beta oscillations using neurofeedback training in PD

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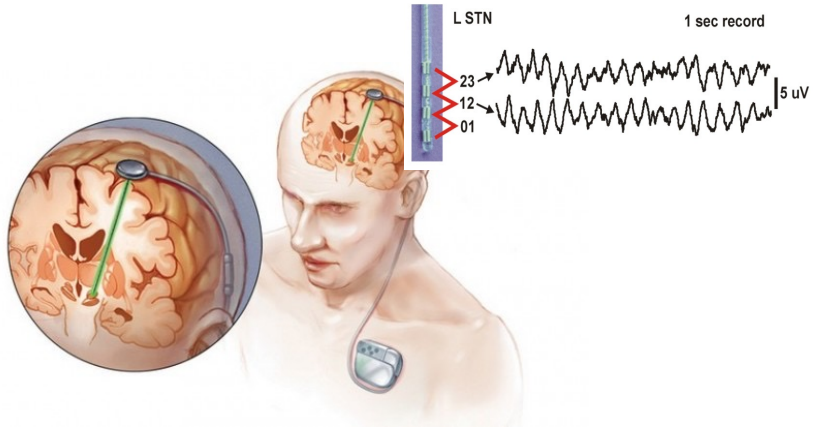
Provide understanding, methodology and treatments that can be applied to the motor and cognitive dysfunction

Clinical Translation

Improving DBS, new protocols for aDBS



Foundational Neuroscience

Underlying circuit pathophysiology, the consequences of neural oscillations in the motor and cognitive functions

Biomedical Engineering

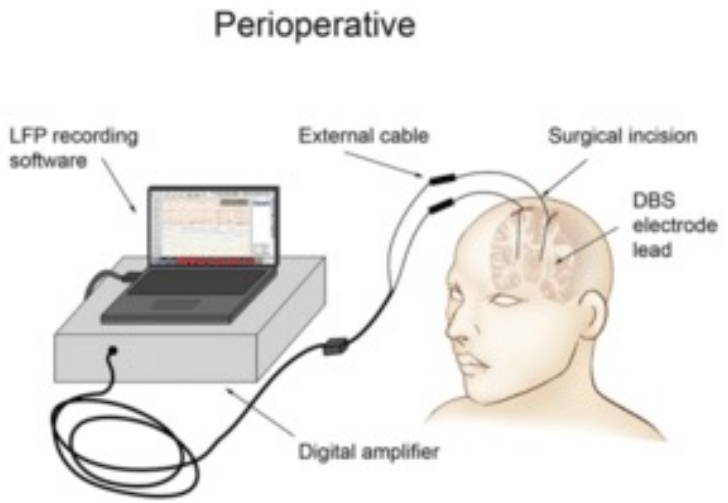
Developing and testing new hardware and algorithms

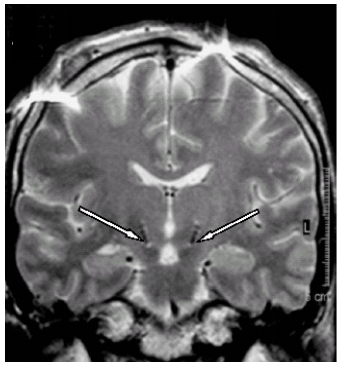
NFB training targeting beta oscillations in PD

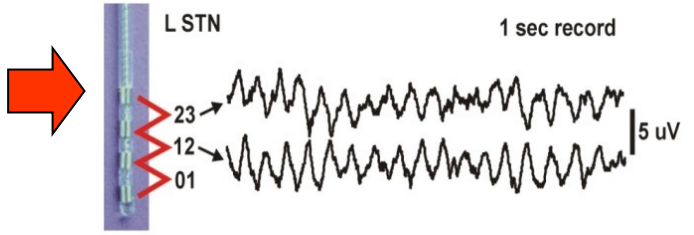
- Background/Rationale and research questions
- Methods and experimental design
- Neurofeedback training (NBT) targeting beta oscillation in the sensorimotor network
  - With cortical EEG in healthy participants
  - With STN LFPs in PD patients after DBS
- Discussion: some lessons learnt

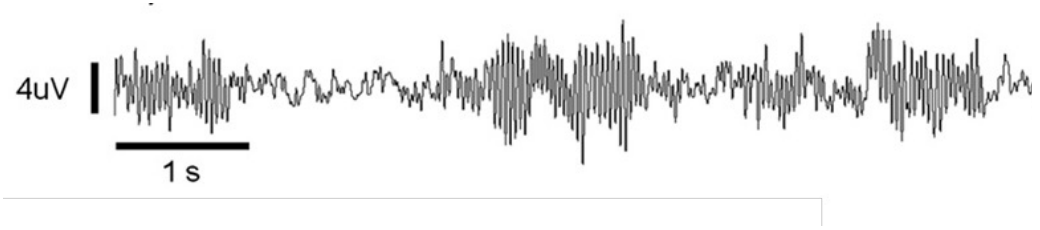
1. Background and Research Questions

Neural Biomarkers of bradykinesia and rigidity in PD







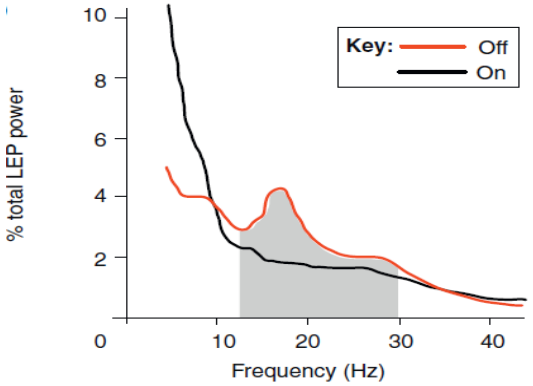


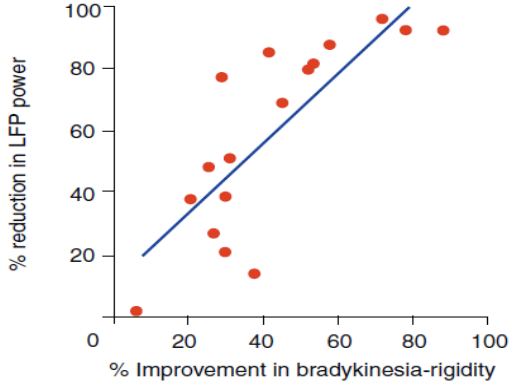
Prof. Peter Brown

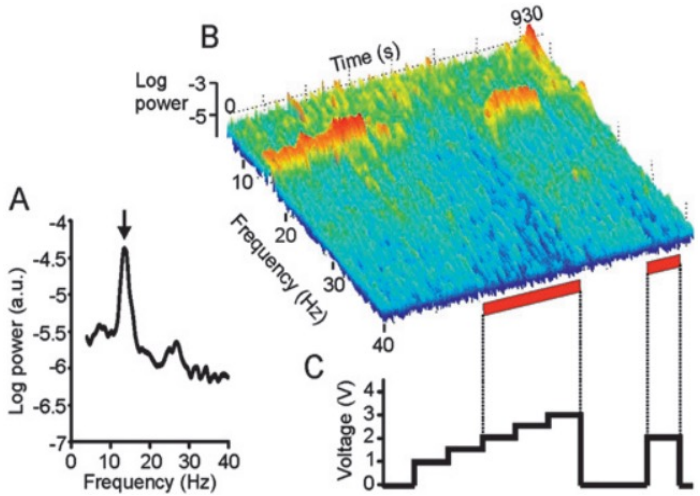
- Beta oscillations (13-30 Hz) is enhanced in PD (Brown et al. 2001; 2006;)
- Correlated with the bradykinesia and rigidity

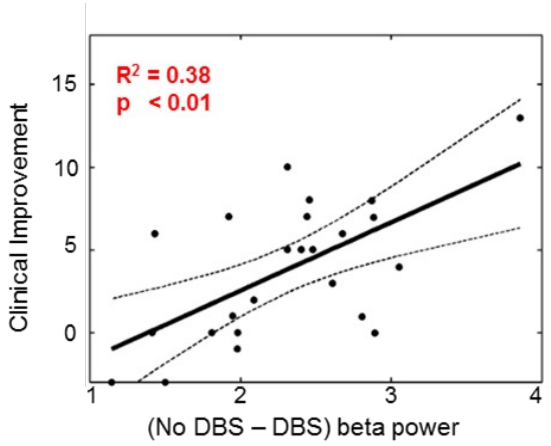
Beta oscillations a biomarker

- Successful treatment of ‘rigidity and bradykinesia’ is associated with the suppression of beta oscillations in the basal ganglia





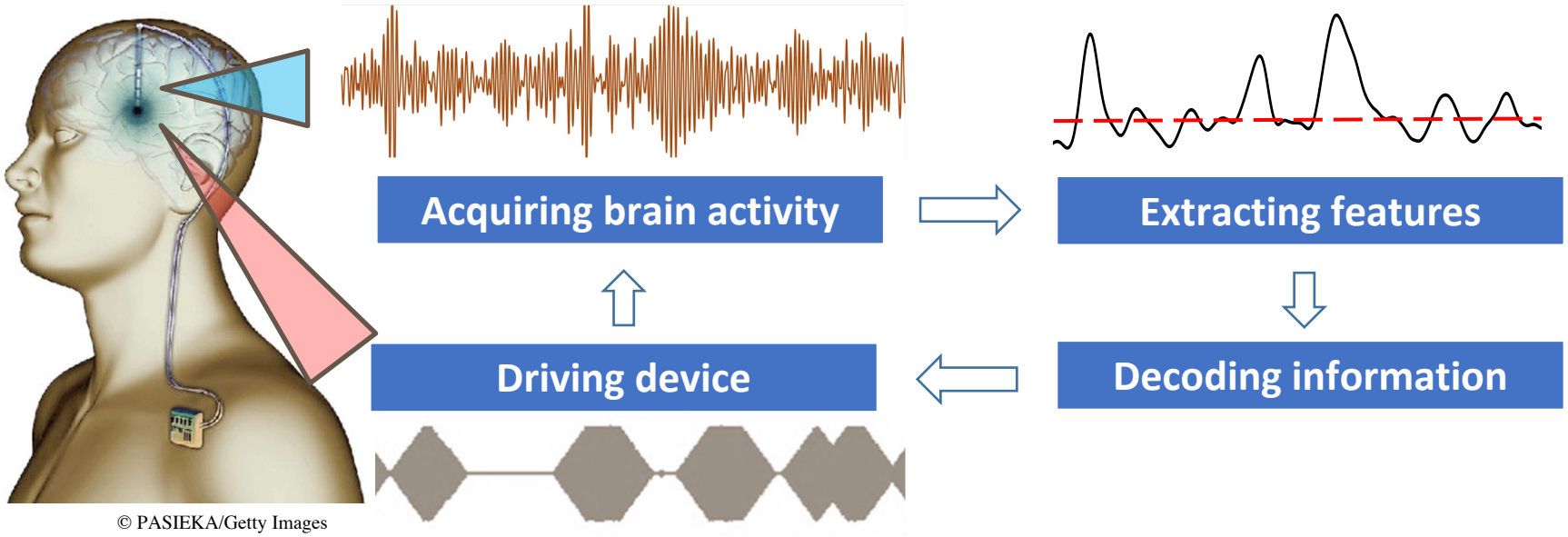




Kühn et al, 2005;
Weinberger et al, 2006;
Eusebio et al,2011

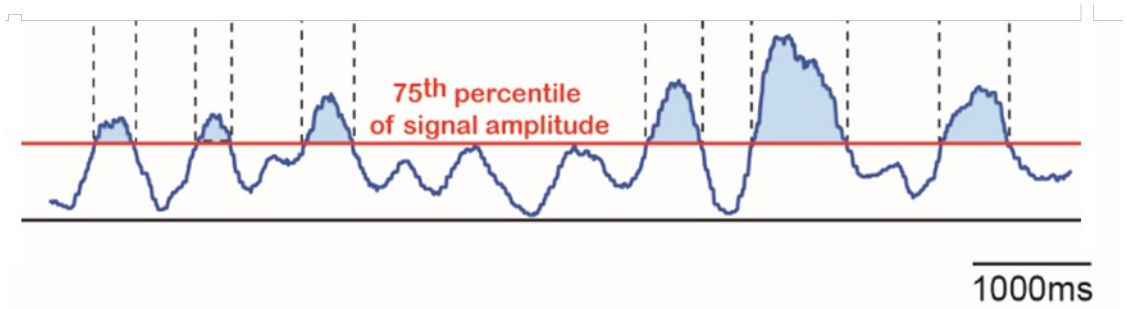
Beta Triggered Closed-loop DBS

- Adaptive DBS of STN using beta oscillation in LFP as biomarker (Little et al. 2013 Ann Neurol.): substantial improvements in UPDRS motor scores and may be superior to conventional continuous DBS in PD

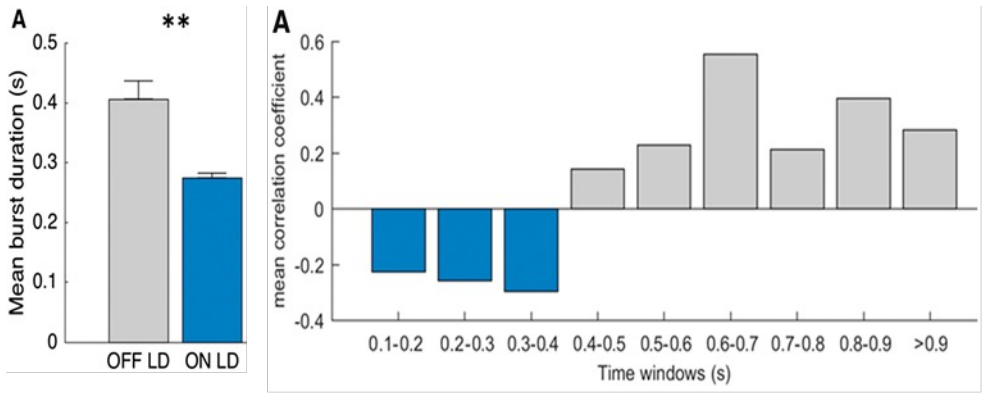


Dynamics and of the beta oscillations are important

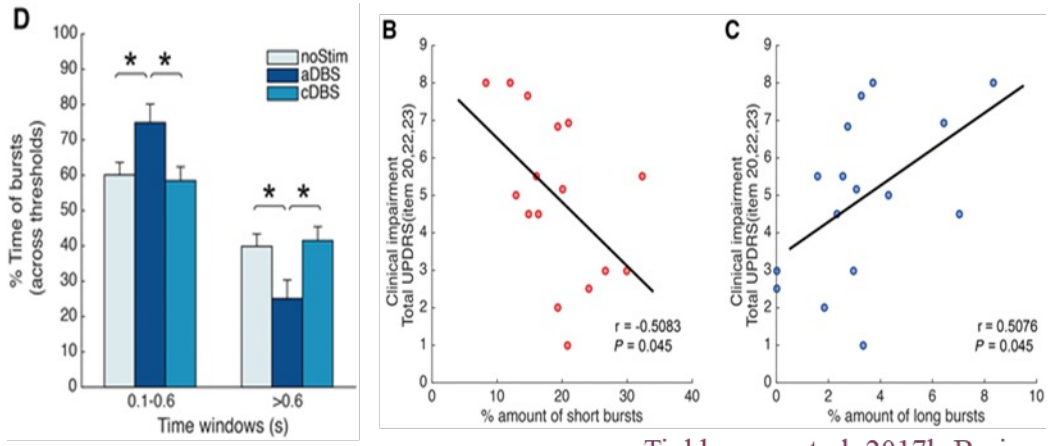
- Temporal dynamics of beta oscillations



- Longer bursts in the STN are more likely to be pathological (Tinkhauser et al, 2017a&b)



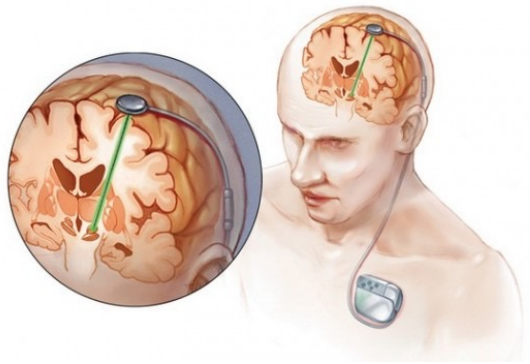
Tinkhauser et al, 2017a Brain

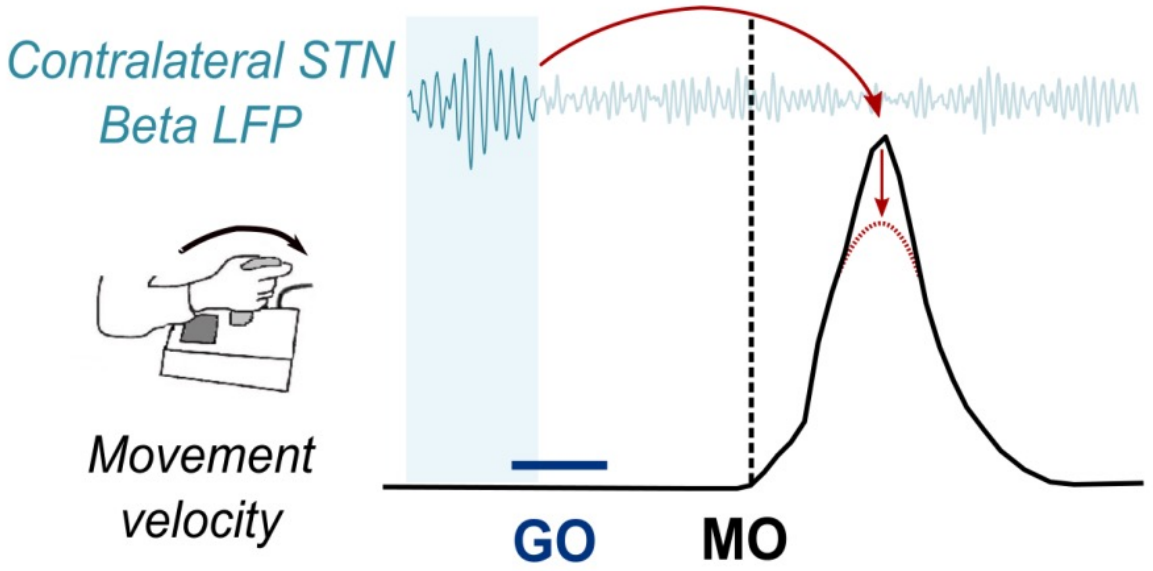


Tinkhauser et al, 2017b Brain

Timing of the beta bursts are important

- Beta bursts occurred before the go cue slowed down movements and facilitate movement cancellation (Torrecillos et al., 2018 J Neurosci; Little et al., 2019 PloS Biol ; Wessel, 2020 J Neurosci)





Research questions

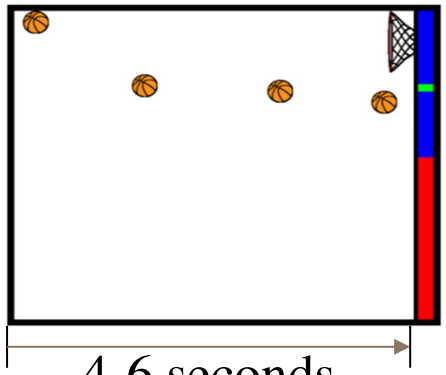
- Whether the participants can learn to suppress beta bursts through neurofeedback training?

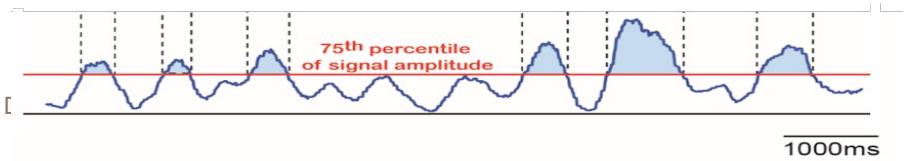
- Whether the training improves motor performance?

2. Methods and Experimental Design

Neurofeedback of the beta bursts

- Duration of the NFB training:
  - Short training sessions across multiple days
  - Short trials with breaks between within a session
- How to present the feedback?
  - Quick fluctuations in the feedback signal can lead to confusion and loss of motivation
  - Long smoothing can lead to long delay in responses
  - A trade-off between responsiveness and not too much flickering

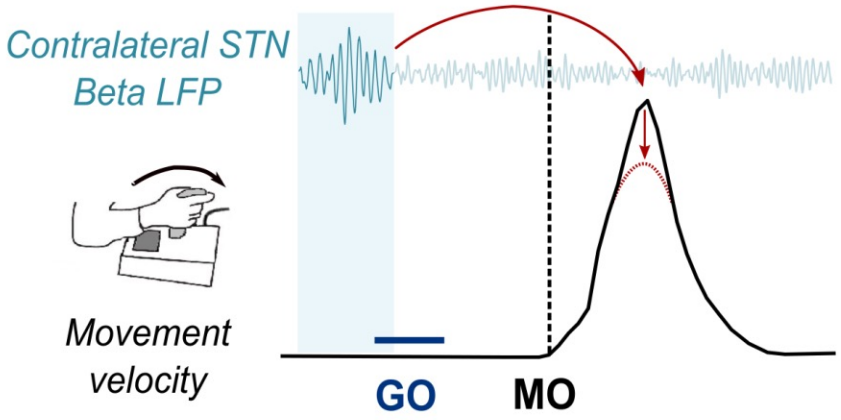


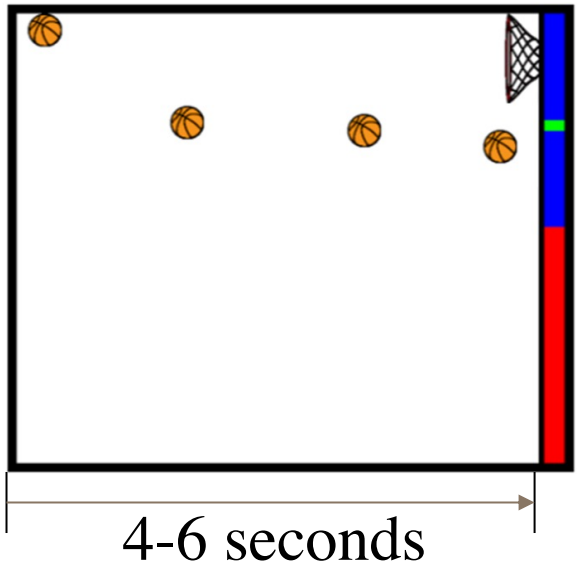


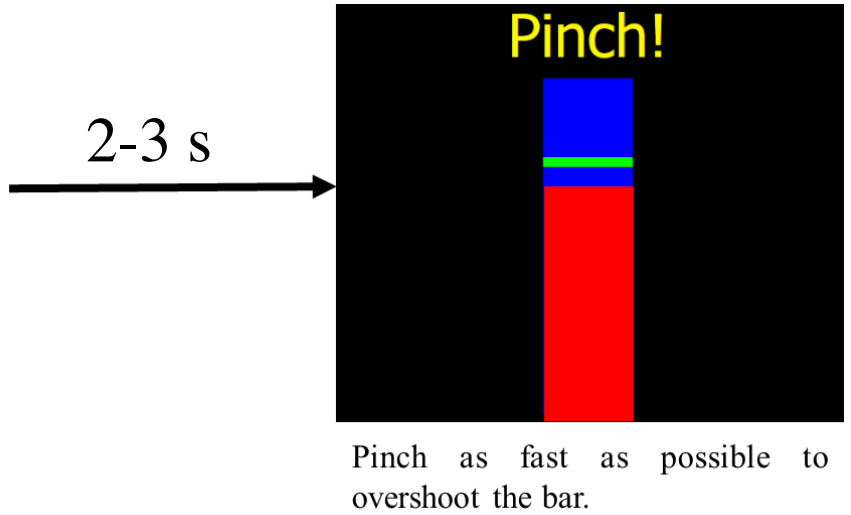
- Position of the basket ball was updated every 250 ms;
- Constant displacement with each update on horizontal axis
- Displacement on the vertical axis was related to beta burst: movement one level downwards when beta amplitude was over a predefined threshold

Motor task to evaluate the effect of the NFB

- Cued pinching task to measure the short-term, immediate effects of the NFB

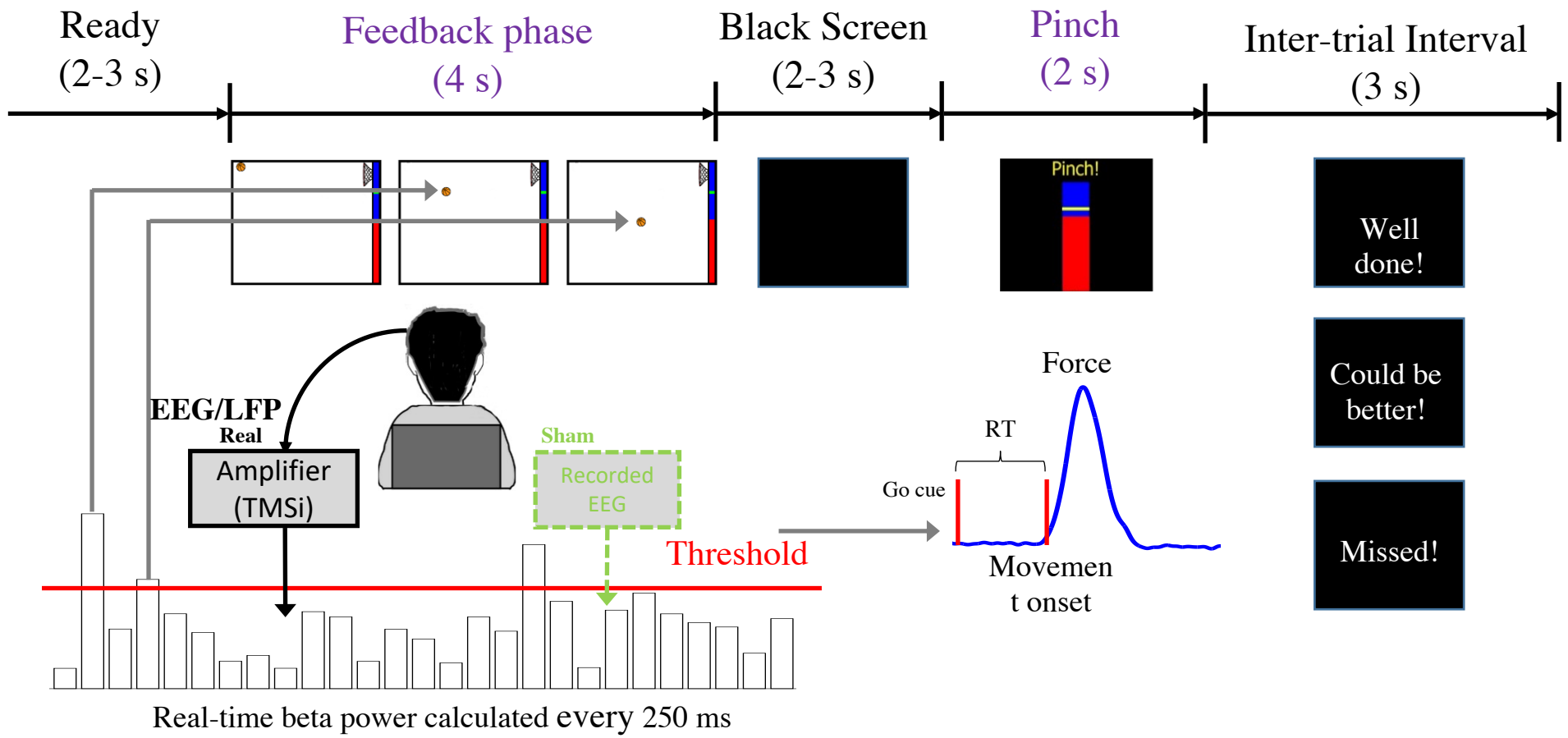






Pinch as fast as possible to overshoot the bar.

Experimental design



- Randomised 'NFB' trials and 'control' trials within one session for each participant.
- Explicitly instructions/suggestions: imaging movements

Sham Control

- Important since motor imagery reduces beta
- Some strategies for sham:
  - No feedback (not suitable here because visual attention to moving objects might induce a reduction in beta band activities);
  - Replay (not possible/easy for double blinded design)
  - Random feedback
  - Double blinded
- Only in healthy participants

Participants

- 20 healthy participants: (He et al. 2020 in J Neurosci)
  - Targeting beta measured from the motor cortex using EEG
  - One real NFB group and one sham group
  - Each participants were recorded for three times over three different days within one week
  - Two hemispheres were tested separately

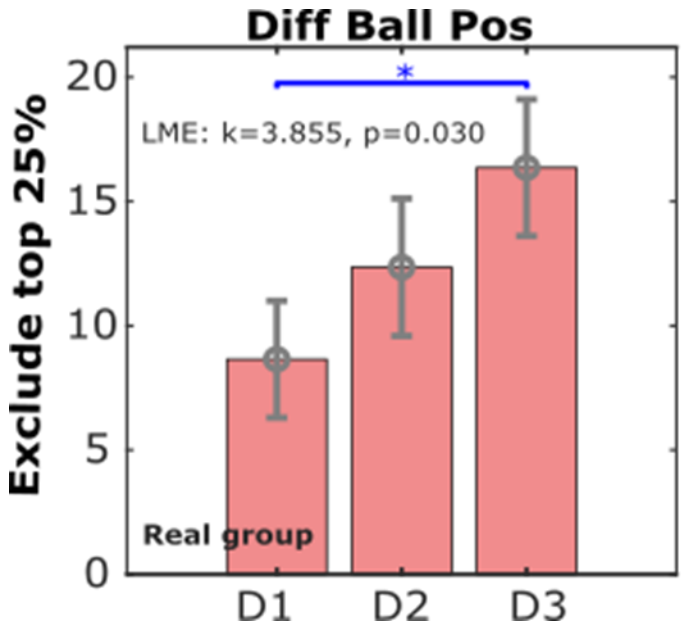
- 12 PwPD undergoing DBS targeting beta in the STN LFPs:

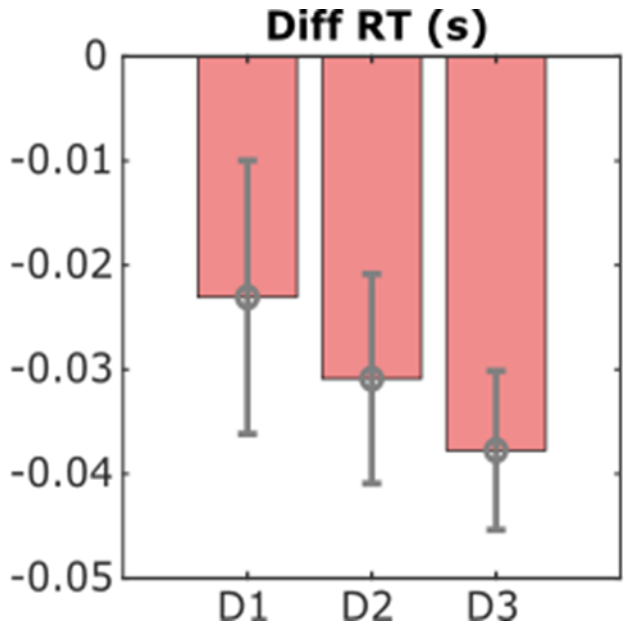
  (He et al. 2020 in eLife)
  - Two sessions over two consecutive days when OFF medication

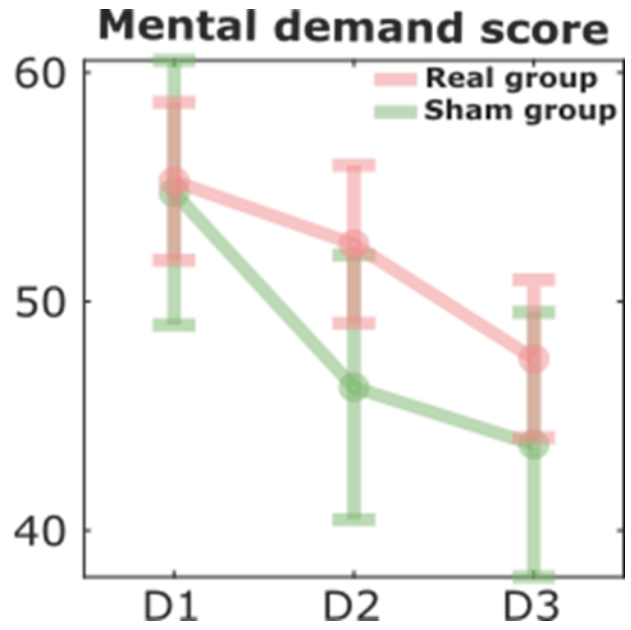
3. Effect of NFB targeting cortical beta in young healthy

Participants can modulate beta with NFB training

- Performance of Neurofeedback control of beta was getting better across days



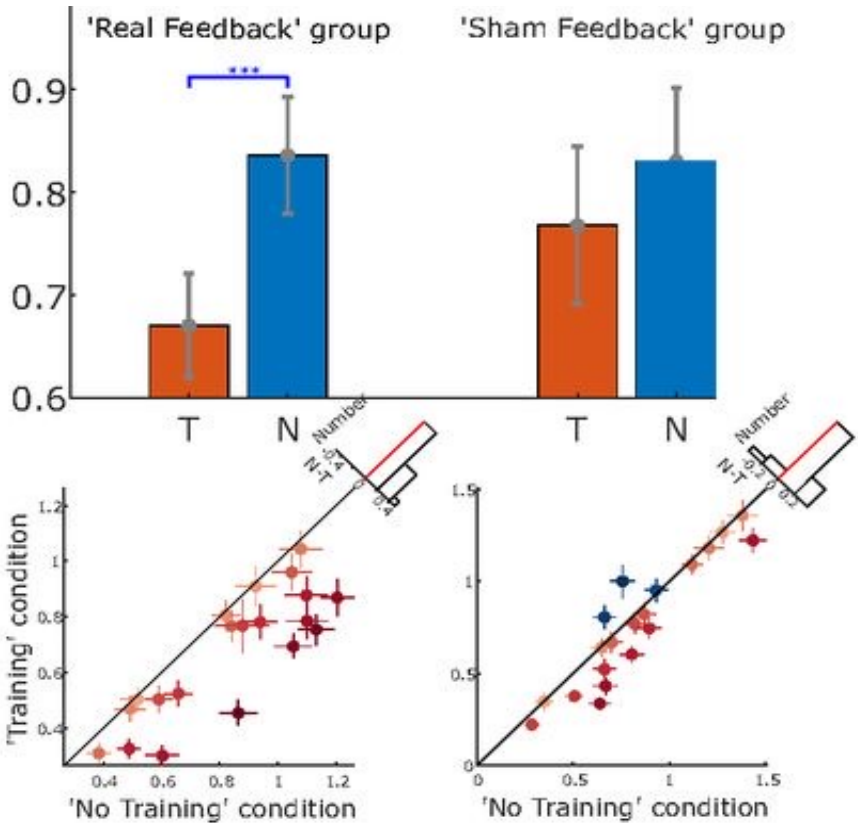




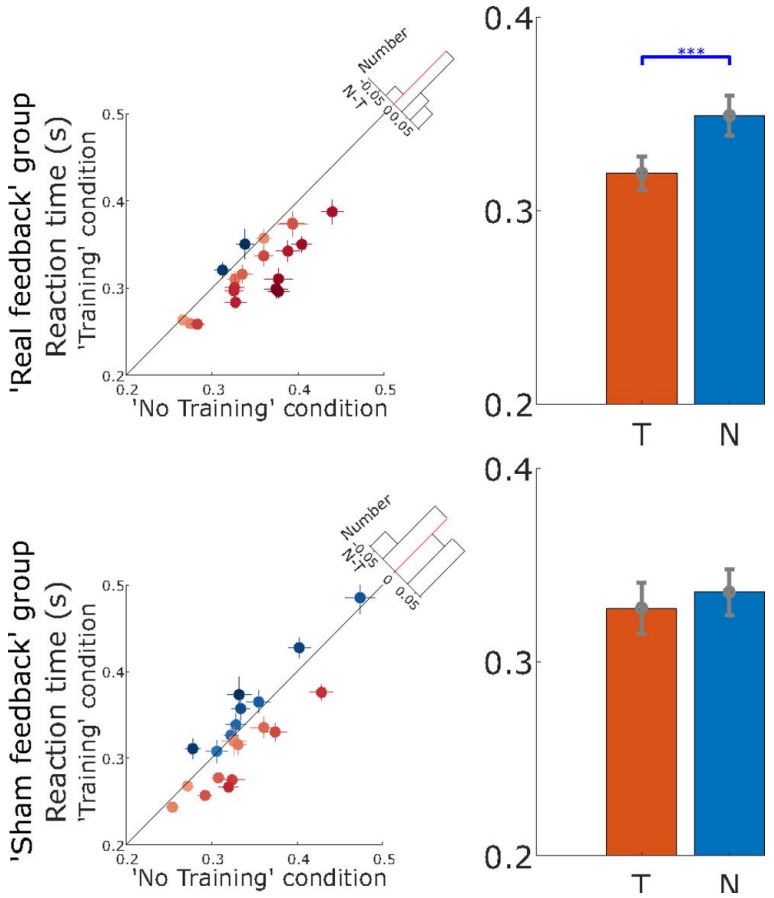
He et al, 2020 J Neurosci

Participants can modulate beta with NFB training

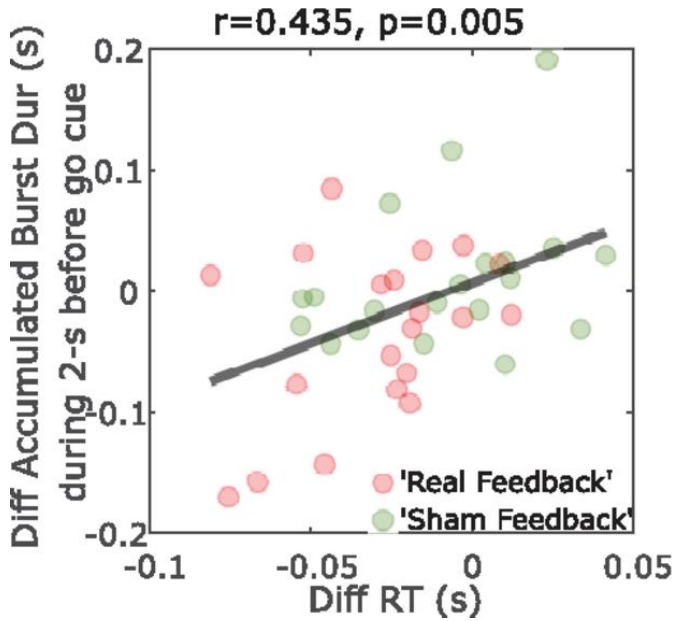
Bursting activities were reduced by NFB training



Reaction time was shorter after NFB training



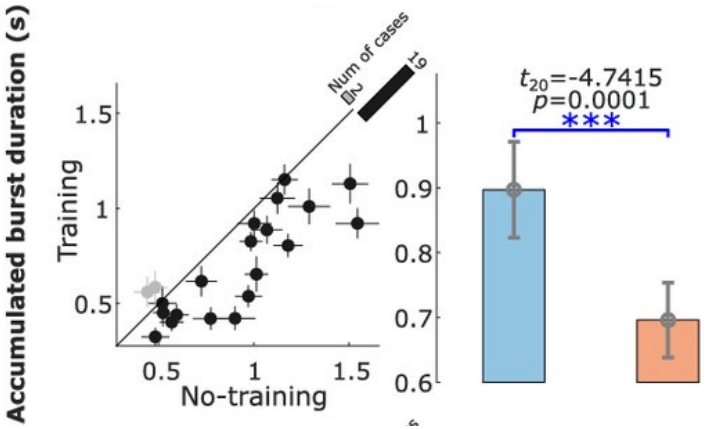
Reduced bursting activity correlated with reduced RT



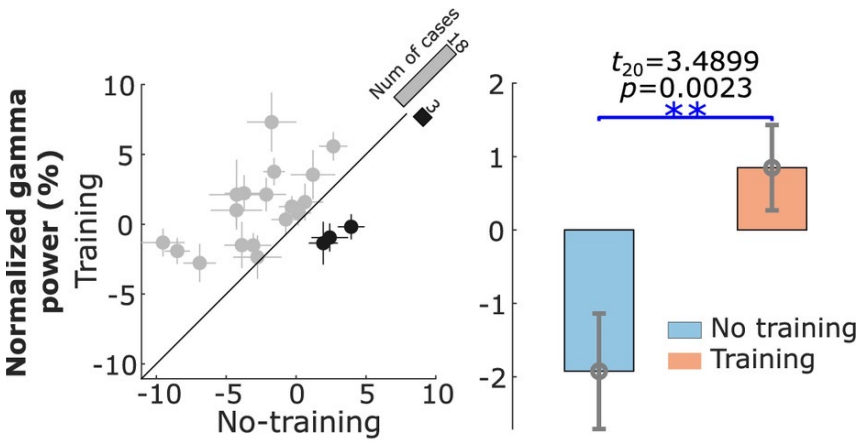
He et al, 2020 J Neurosci

3. Effect of NFB targeting beta in STN LFPs in PD

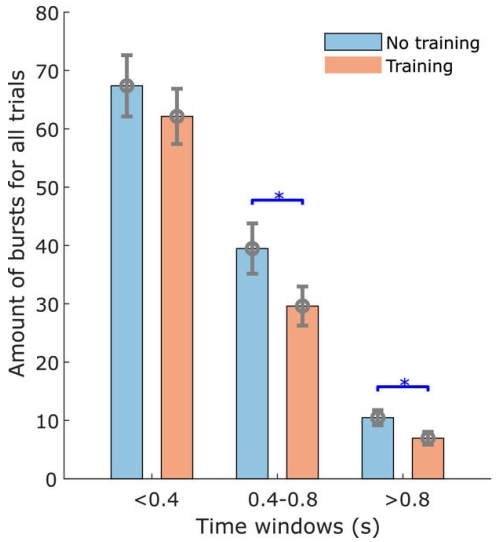
NFB training targeting STN beta bursts for patients with PD



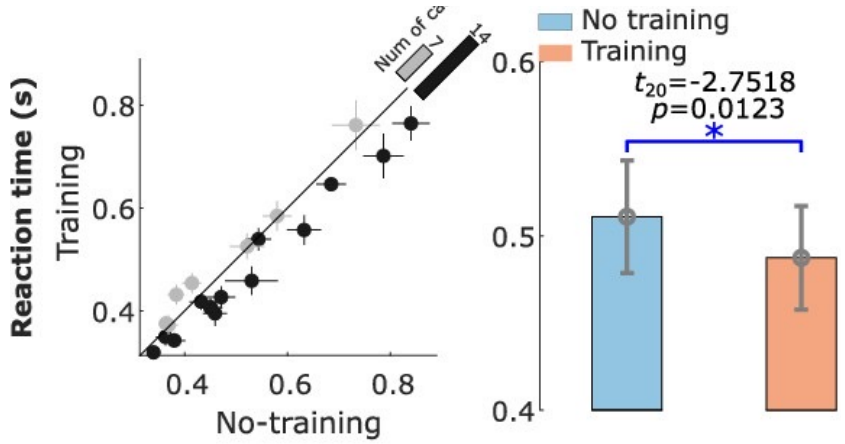
Beta reduced during NFB



Gamma increased during NFB



Longer bursts reduced more than shorter bursts



Reaction time was shorter after NFB

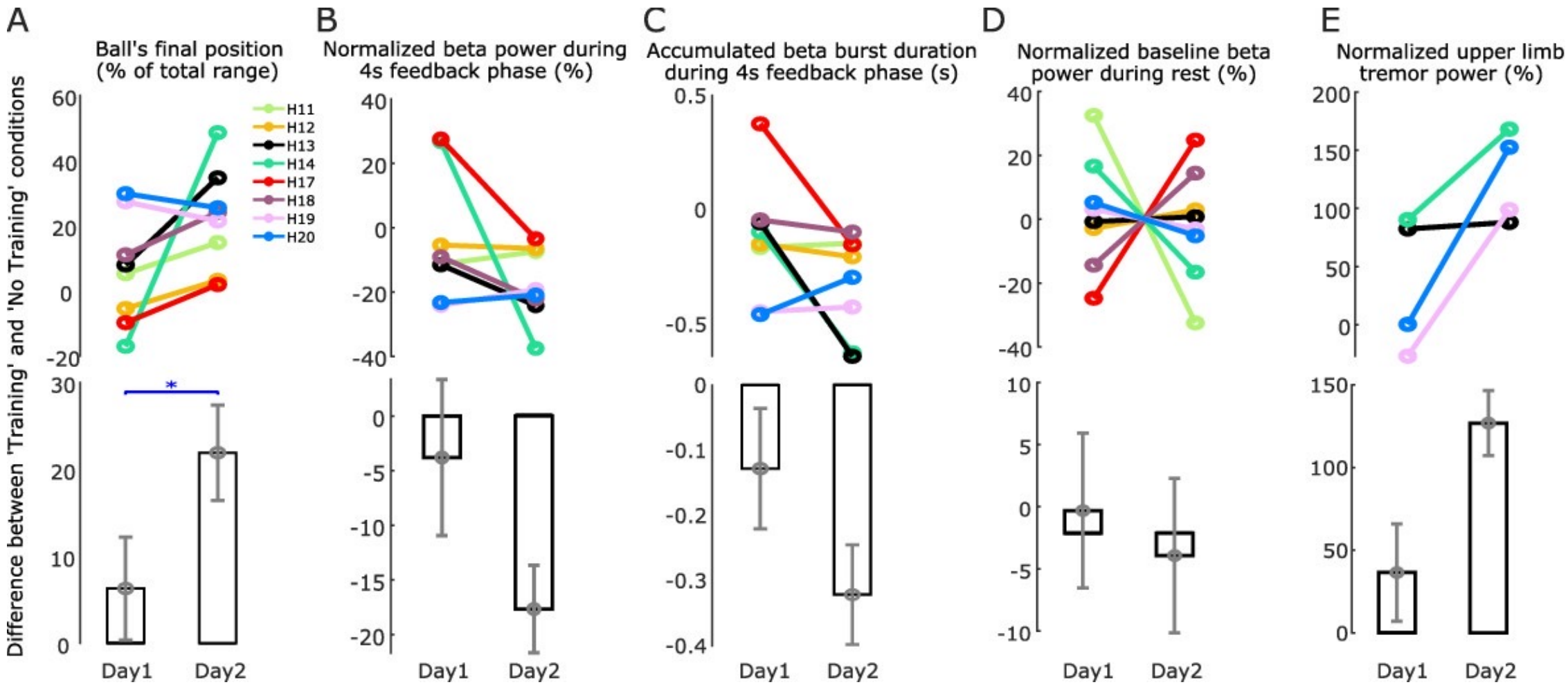
$$\mathrm{RT} = k_1 TorN + k_2\beta + k_3\gamma + k_4\alpha + 1|\mathrm{Sub}$$

$k_1 = -0.0154 \pm 0.0071$, p = **0.0297**
$k_2 = 0.0061 \pm 0.0020$, p = **0.0017**
$k_3 = -0.0085 \pm 0.0026$, p = **0.0014**
$k_4 = 0.0029 \pm 0.0022$, p = 0.1948

He et al, 2020 eLife

NFB training targeting STN beta bursts for patients with PD

Neurofeedback training effect was stronger on Day2 compared with Day1



He et al, 2020 eLife

Interim Summary

- PwPD can learn to suppress beta bursts with NFB
- Beta targeted-neurofeedback training could potentially be used to facilitate movement initiation.
- Effect of NFG on non-targeted neural signals
  - +: increased gamma which invigorate movements
  - -: increased tremor in some patients which is not due to cognitive load
- Long-term effects of NFB remain to be tested

Discussion: some lessons learnt on NBF targeting beta

- Presentation mode: need to be creative to keep participants engaged and motivated
- Dynamics of the target signal => refreshment rate of the feedback
- Sham control: important tease out the effect of NFB compared to practicing a mental strategy
- Behavioural measurements as the effect of the NBF
- Impact of the NFT in other activists：gamma and tremor band activities in PD

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All the participants!

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