

Predictive encoding of deviant tone sequences in the human prefrontal cortex

Olgerta Asko^{1*}, Vegard A. Volehaugen¹, Sabine L. Leske¹, Ingrid Funderud^{2,3}, Anaïs Llorens^{4,5,6}, Jugoslav Ivanovic⁷, Torstein R. Meling⁸, Pål Gunnar Larsson⁷, Robert T. Knight⁴, Tor Endestad^{1,2}, Anne-Kristin Solbakk^{1,2,7}, Alejandro O. Blenkmann¹

1. RITMO, Univ. of Oslo, Norway; 2. Helgeland Hospital, Mosjøen, Norway; 3. Regional Department of Eating Disorders, Univ. Hosp., Oslo, Norway; 4. Helen Wills Neuroscience Inst, UC Berkeley, USA; 5. Université de Franche-Comté, Besançon, France; 6. Université Paris Cité, Paris, France; 7. Univ. Hosp., Rikshospitalet, Oslo, Norway; 8. Nat. Hosp., Rigshospitalet, Denmark;

* olgerta.asko@psykologi.uio.no

Abstract

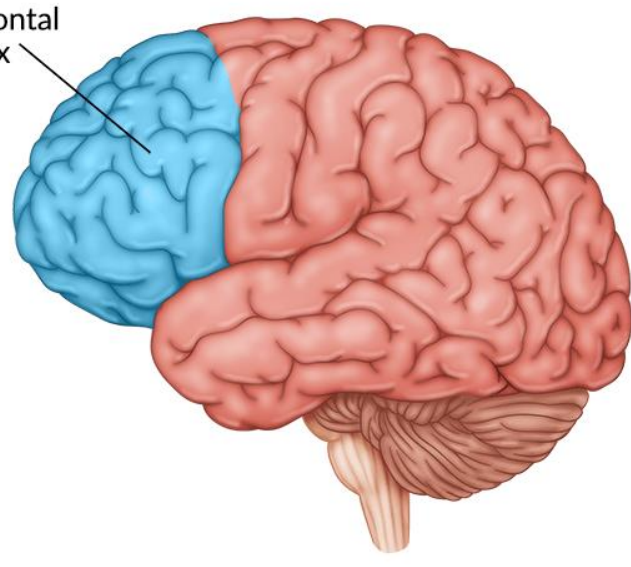
Background: The **prefrontal cortex (PFC)** plays a key role in using predictive information to guide perception and action, yet the specific roles of its subregions in predictive processes remains unclear. Recent perspectives propose that the **orbitofrontal cortex (OFC)** generates predictions about perceptual events and actions, while the **lateral prefrontal cortex (LPFC)** supports prospective functions related to predictive processes.

We recently showed that **OFC lesions** affect the detection of **auditory prediction violations** at two levels of rule abstraction, with altered MMN and P3a responses, suggesting the OFC's role in generating prediction error signals related to **top-down expectation** (Asko et al., 2024). Here, we present new findings on the involvement of **PFC subregions** in **anticipation** of violations informed by predictive information.

Methods: Using an **auditory local-global deviance detection task**, we recorded EEG in healthy control participants (n=15), patients with focal lesions to the OFC (n=12) and LPFC (n=10) and SEEG from the same areas in epileptic patients (n=7). 22 healthy participants performed a modified version of the experiment (without EEG), detecting deviant sequences with a button press.

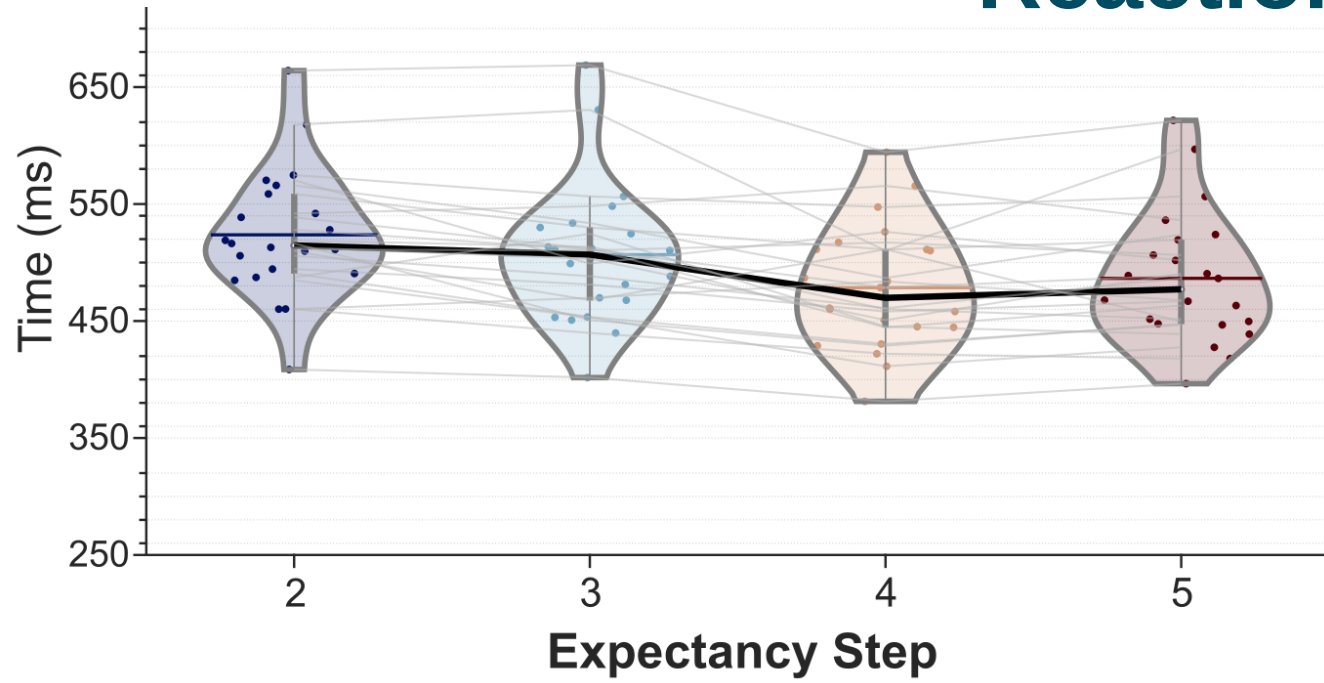
Results: Healthy adults showed modulations of the **Contingent Negative Variation (CNV)** with **higher expectancy** of deviant sequences leading to a higher CNV drift rate. Intracranial recordings revealed similar **expectancy modulation** of the **high-frequency broadband activity (HFBA)** in OFC and LPFC electrodes, with **earlier** activity modulation for OFC. Patients with OFC lesions lacked CNV-sensitivity to the predictive context, while patients with LPFC lesions showed moderate sensitivity. Behaviorally, **expectancy enhanced** deviance detection **speed**.

Conclusion: Electrophysiological and causal evidence is provided for the distinct roles of two PFC areas in using predictive information to prepare action.



Results

Reaction time task



Expectancy increases the detection speed of deviant sequences (n=22)

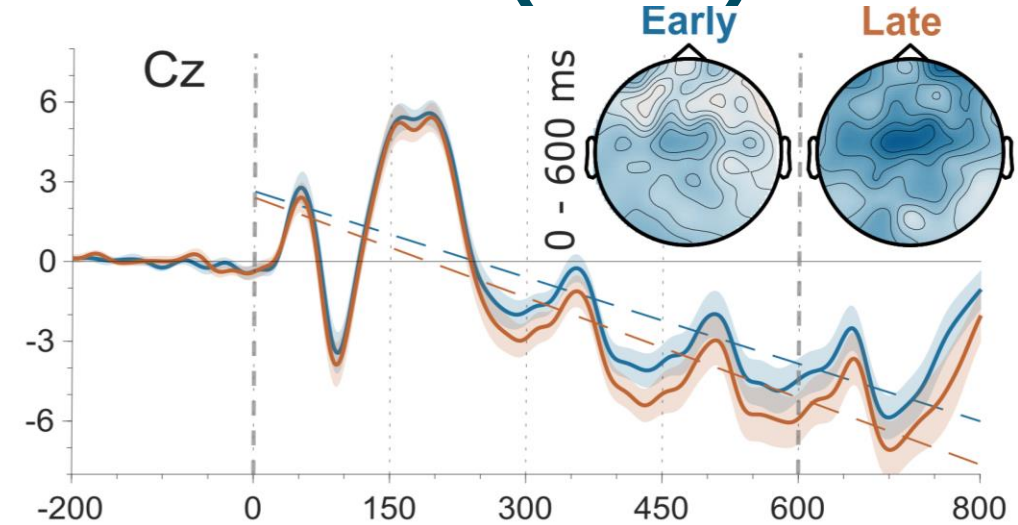
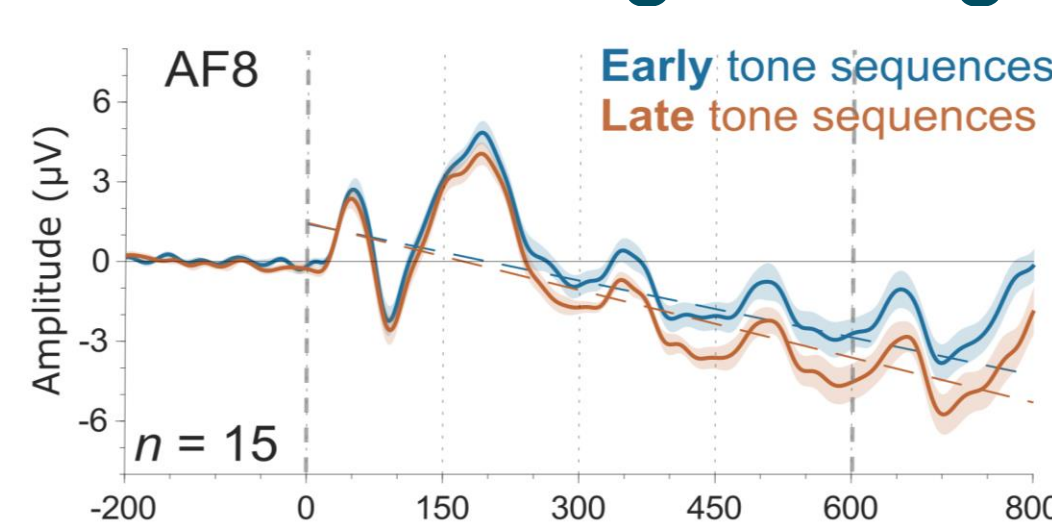
Linear mixed-effects model
 $RT \sim 1 + Expectancy Step + (1|Participant)$
 $\beta = -0.013, p < 0.001$

Scalp EEG

Contingent Negative Variation (CNV)

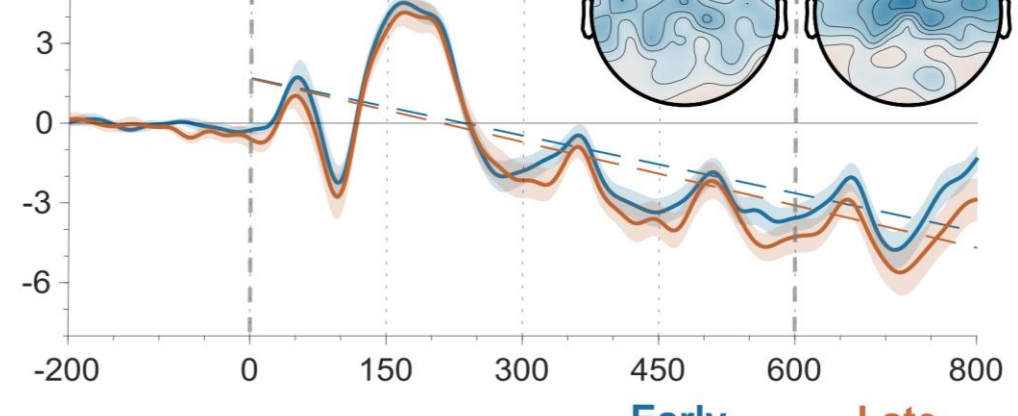
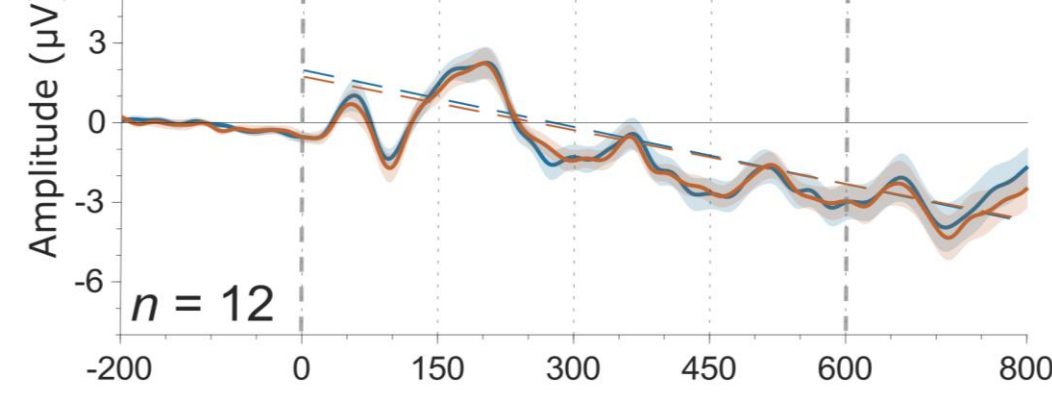
CNV in healthy controls

Significant effect of **expectancy step** in a group of 48 fronto-central channels



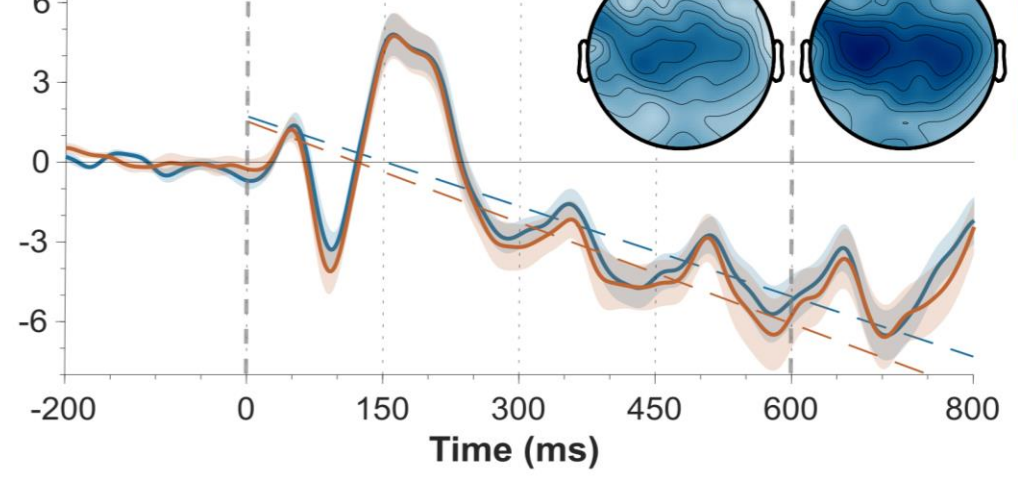
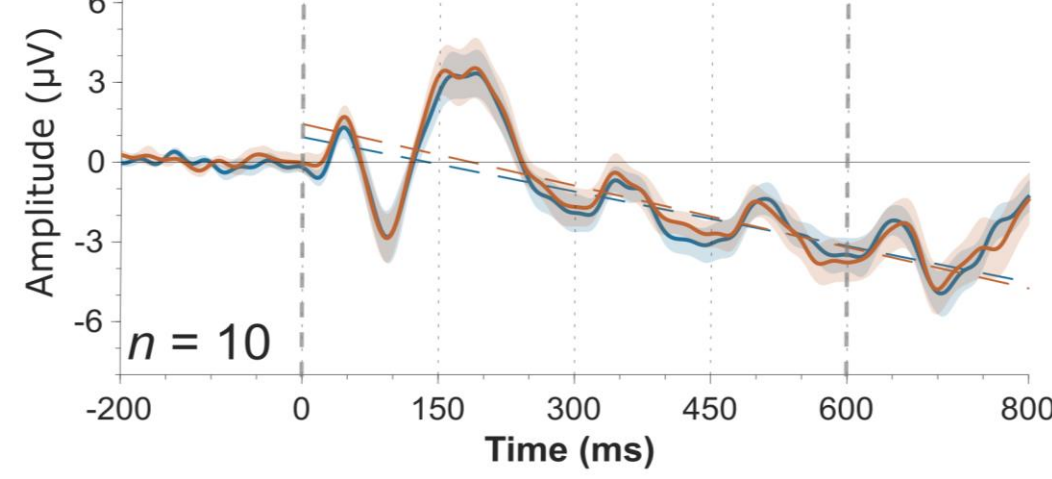
OFC lesion group

No significant effect of **expectancy step**



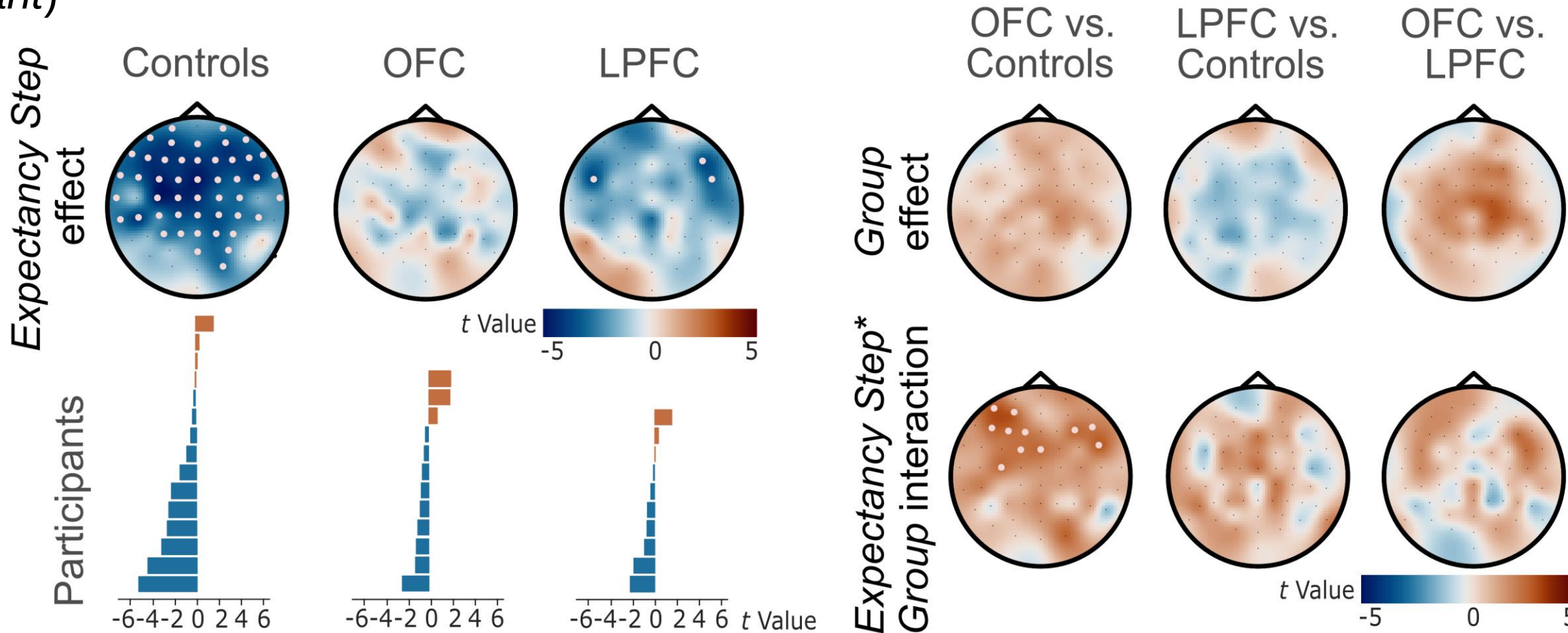
LPFC lesion group

Significant effect of **expectancy step** in three channels



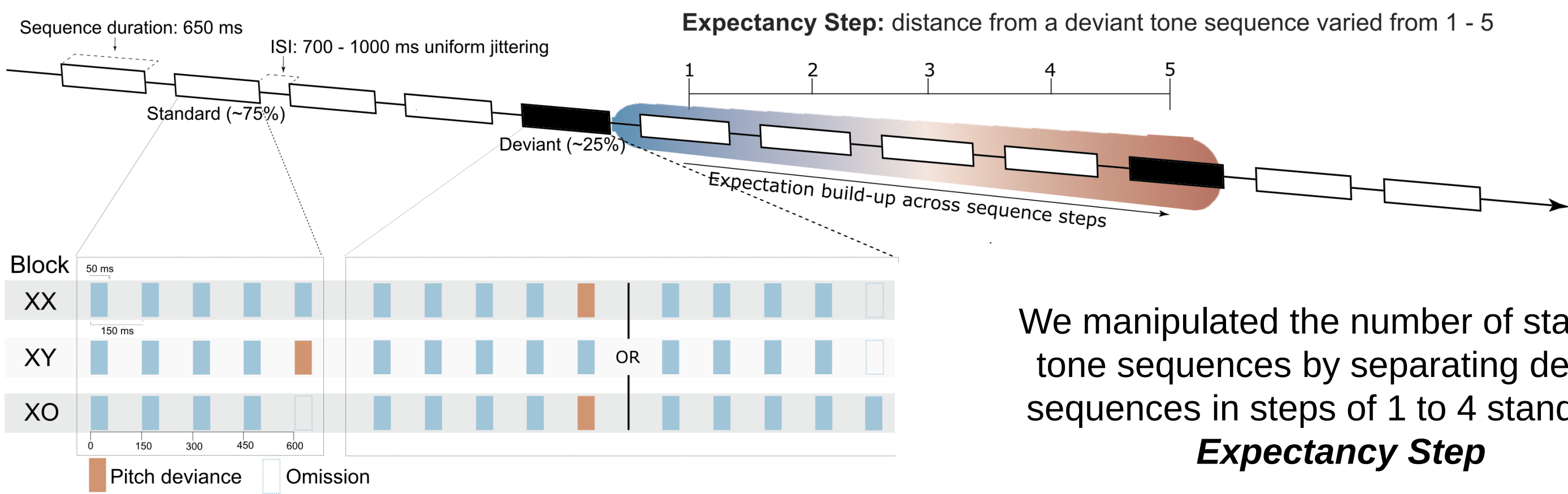
Linear mixed-effects model

Effect of **Expectancy step** per group: $Slope \sim 1 + Expectancy Step + (1|Participant)$
Effect of **group** and **interaction**: $Slope \sim 1 + Expectancy Step + Group + Expectancy Step * Group + (1|Participant)$



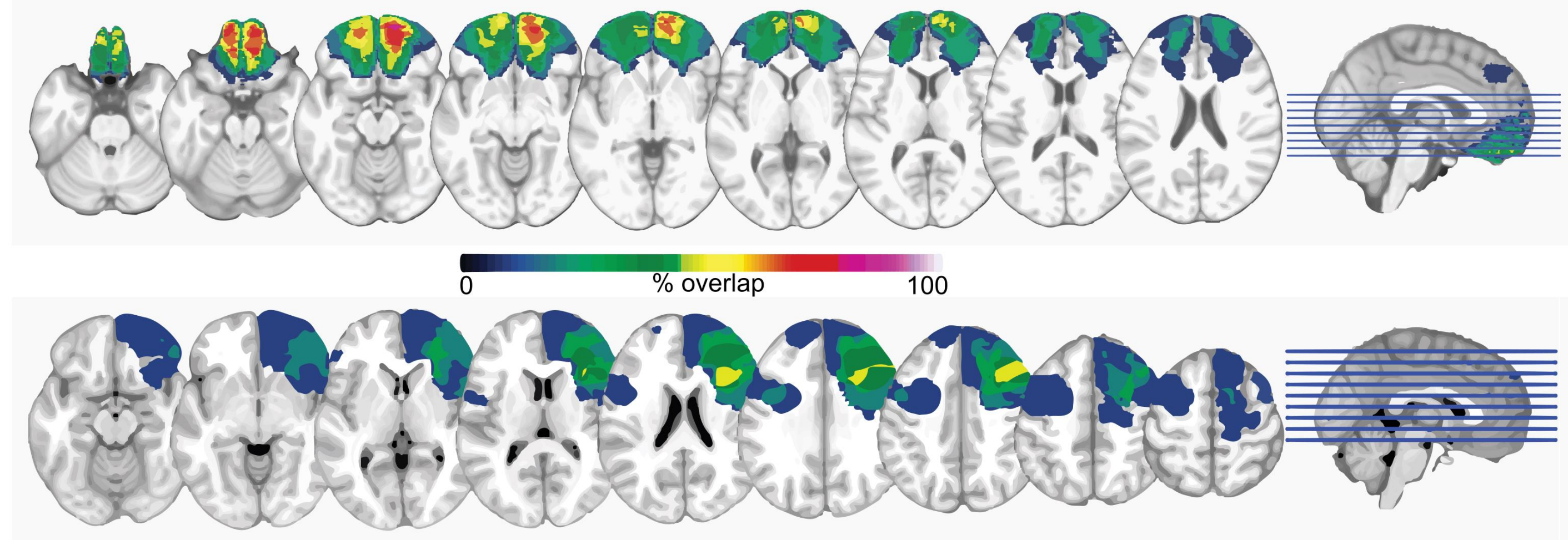
Methods

The auditory local-global deviance detection task

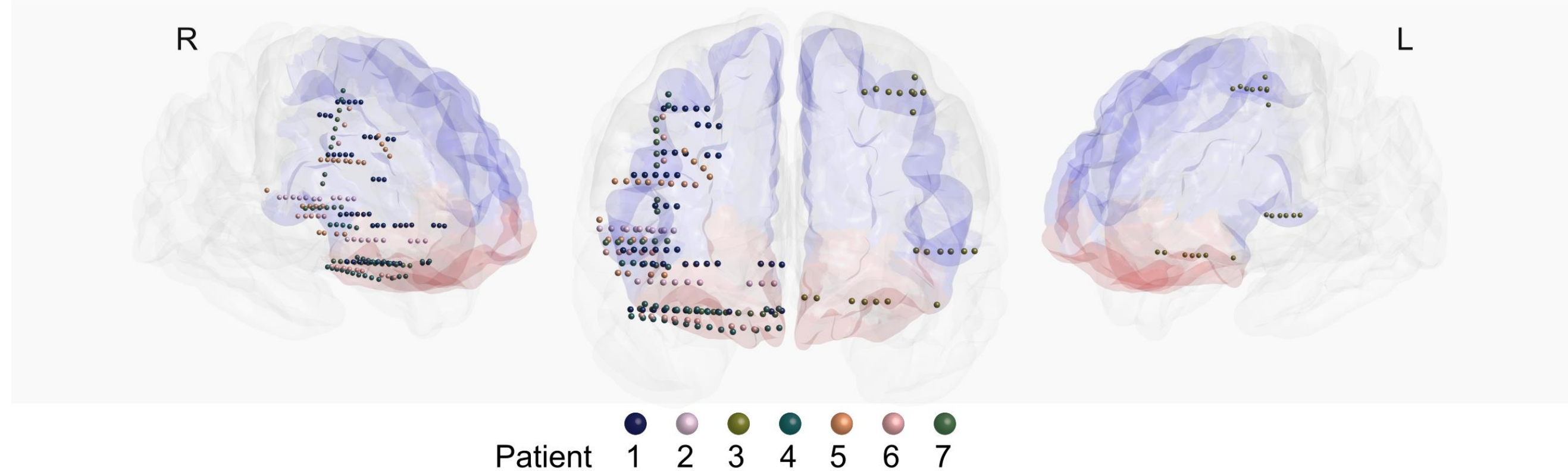


We manipulated the number of standard tone sequences by separating deviant sequences in steps of 1 to 4 standards: **Expectancy Step**

OFC and LPFC Lesion Reconstruction



Intracerebral depth electrodes in patients with epilepsy



EEG

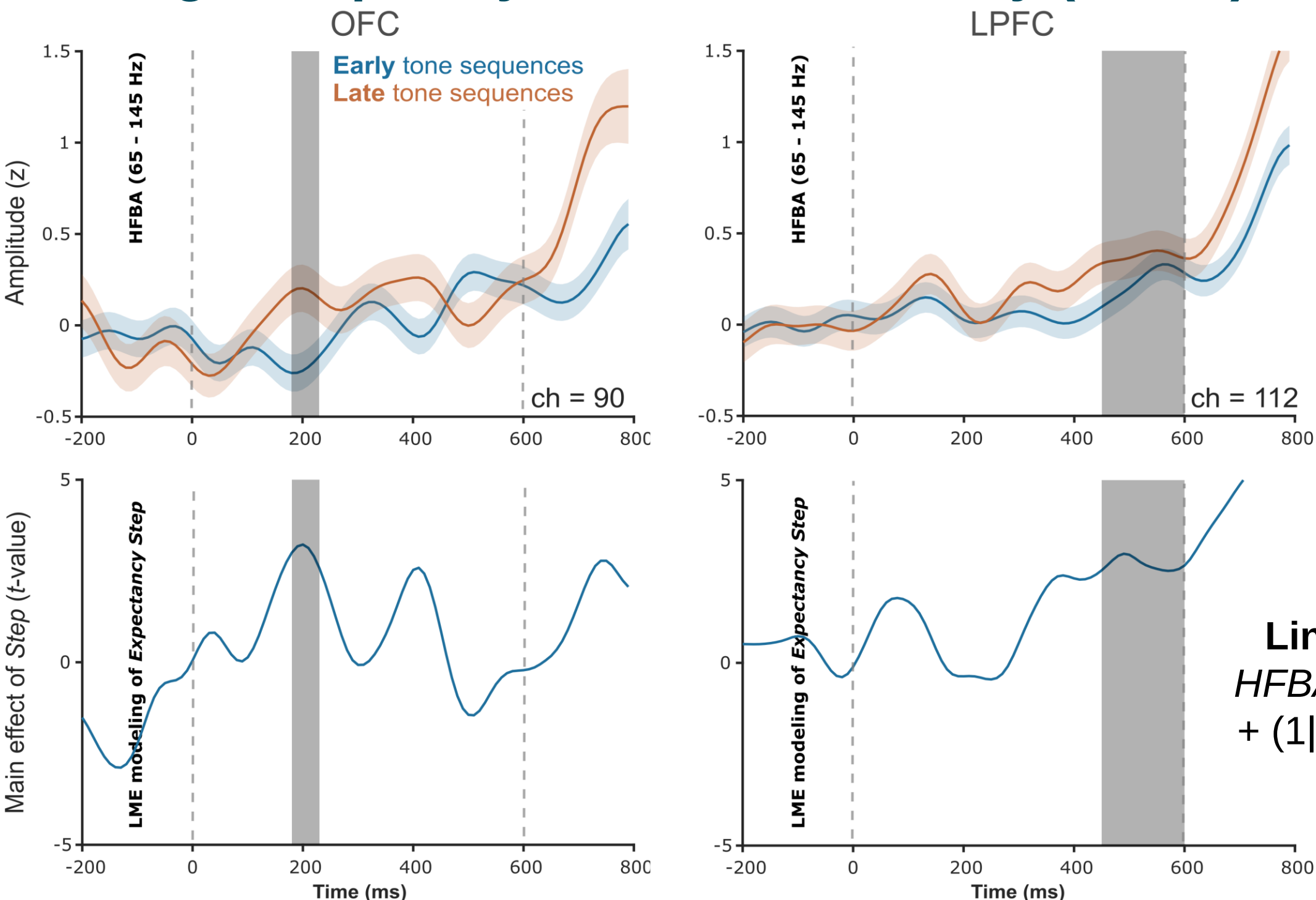
Biosemi ActiveTwo System (64-channel); Sampling rate: 1024 Hz

SEEG

8-18 contacts/arrays; 3.5 mm inter-electrode distance; ATLAS (Neuralynx, USA; n = 4) or Brain Quick (Micromed, Italy; n = 3) system; Sampling rate: 16 000 or 2048 Hz, respectively

*Fieldtrip toolboxes and costume made scripts in MATLAB were used.

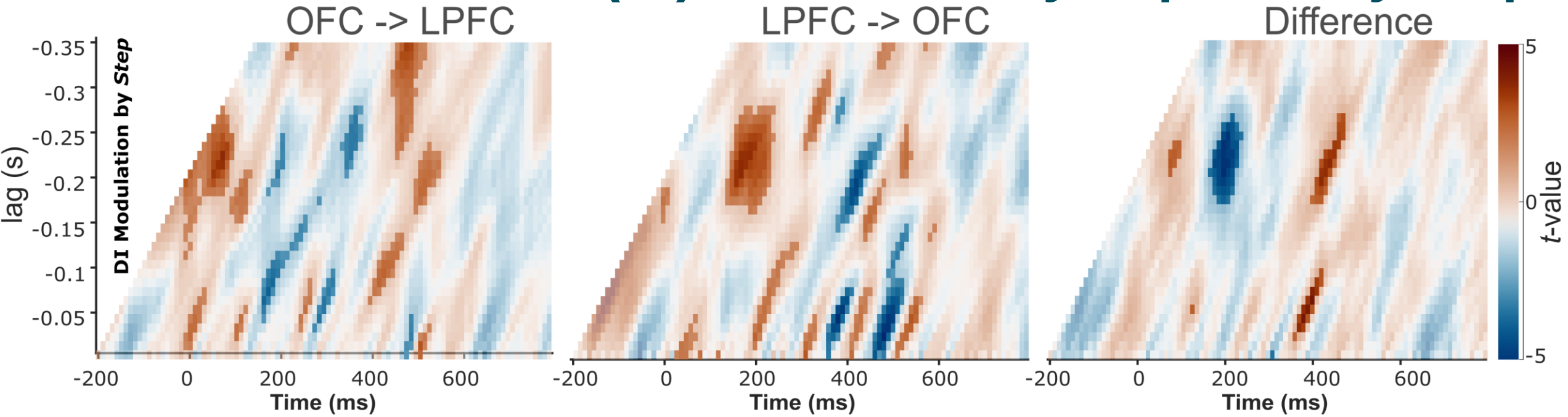
High-frequency broadband activity (HFBA)



Intracerebral HFBA (65 to 145 Hz) encodes **expectancy** of global deviants in distinct time-windows for OFC (180-230 ms, $p < 0.05$) and LPFC (450-600 ms, $p < 0.05$)

Linear mixed-effects model
 $HFBA_{\mu}(t) \sim 1 + Expectancy Step + (1|Participant) + (1|Participant: Channel)$

Directed Information (DI) modulated by Expectancy Step



DI quantifies directional connectivity, how well past activity of a "sender signal" (e.g., HFBA from OFC) predicts future activity of a "receiver signal" (e.g., HFBA from LPFC). Opaque colored areas: time windows and lags where **DI modulation** by **expectancy step** was significant ($p < 0.05$)

References

Asko, O., Blenkmann, A. O., Leske, S. L., Foldal, M. D., Llorens, A., Funderud, I., Meling, T., Knight, R. T., Endestad, T., & Solbakk, A.-K. (2024). Altered hierarchical auditory predictive processing after lesions to the orbitofrontal cortex. *Elife*, 13, e86386.



Conclusions

The **PFC** plays a key role in **anticipating auditory deviances** using **top-down predictive information**. Specifically, **OFC lesions** reduced sensitivity to predictive context, weakening CNV modulation by expectancy, with **LPFC lesions** only moderately affected CNV sensitivity to expectancy. **Intracranial** recordings showed early activity modulation in the OFC, followed by the LPFC, both tracking deviant sequence expectancy. **OFC likely provides predictive context** to LPFC, which adjusts sensory processing to anticipate deviances.

