

Altered hierarchical predictive processing after lesions to the orbitofrontal cortex

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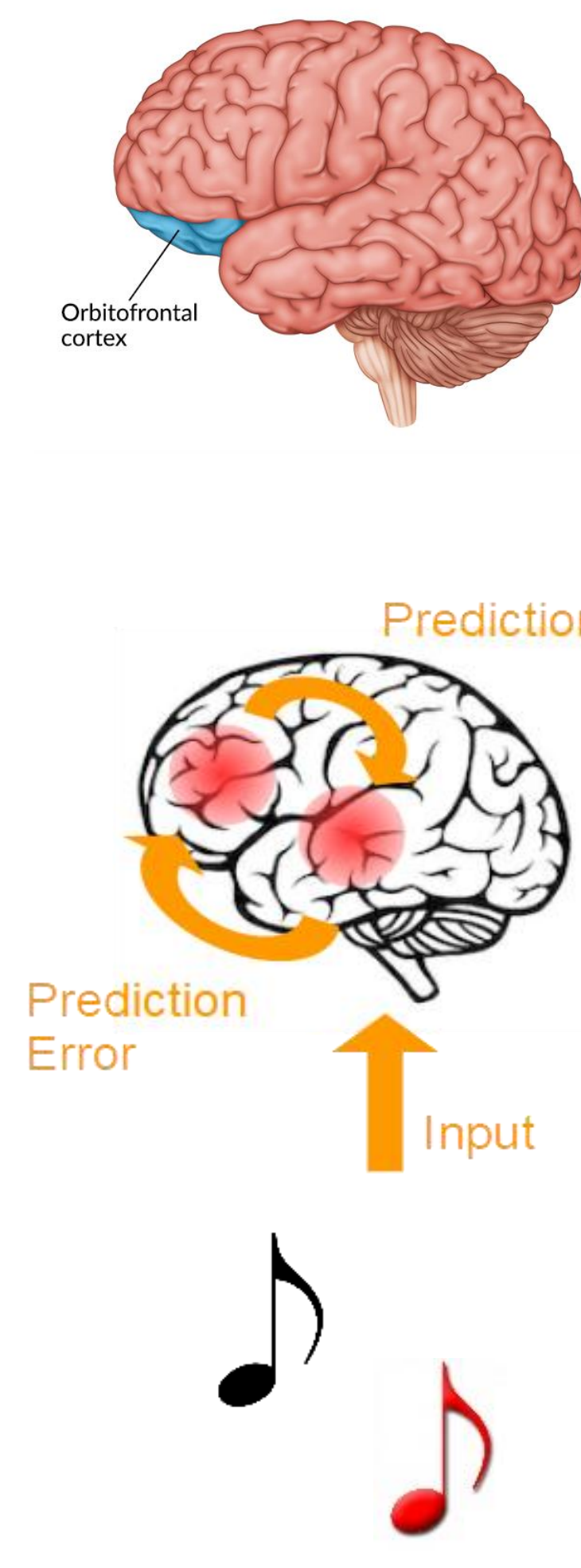
1. Abstract

Background: Recent perspectives about the functional role of the **orbitofrontal cortex (OFC)** propose that OFC generates *predictions* about perceptual events, actions, and their outcomes, possibly via a “cognitive map” that contains representations of all relevant sensory, temporal, and contextual features needed to predict the environment.

Methods: We tested the causal involvement of the OFC in detecting violations of prediction at different levels of abstraction (i.e., hierarchical predictive processing) by studying the **event-related potentials (ERPs)** of patients with focal OFC lesions (**n = 12**) and healthy controls (**n = 14**) while detecting deviant tones in an auditory **local-global task**.

Results: Deviant tones at the “local” level produced an **early mismatch negativity (MMN)** followed by a frontally distributed P3a component, which might reflect a prediction error (PE) process at lower hierarchical areas. Deviant tones unpredicted by the global rule (i.e., “local+global” level deviants) produced a **long-lasting MMN**, followed by a P3a/P3b complex, indicating the contribution of higher-order predictions and their violations. However, standard tones unpredicted by the global rule (i.e., “global” level deviants) elicited only a posterior P3b. In OFC patients, ERPs elicited by the predicted standard tones were unaffected compared to controls. However, patients showed an **reduced MMN to “local” violation** and **reduced and later in latency MMN** and P3a to “local+global” violation, while the P3b was unaffected.

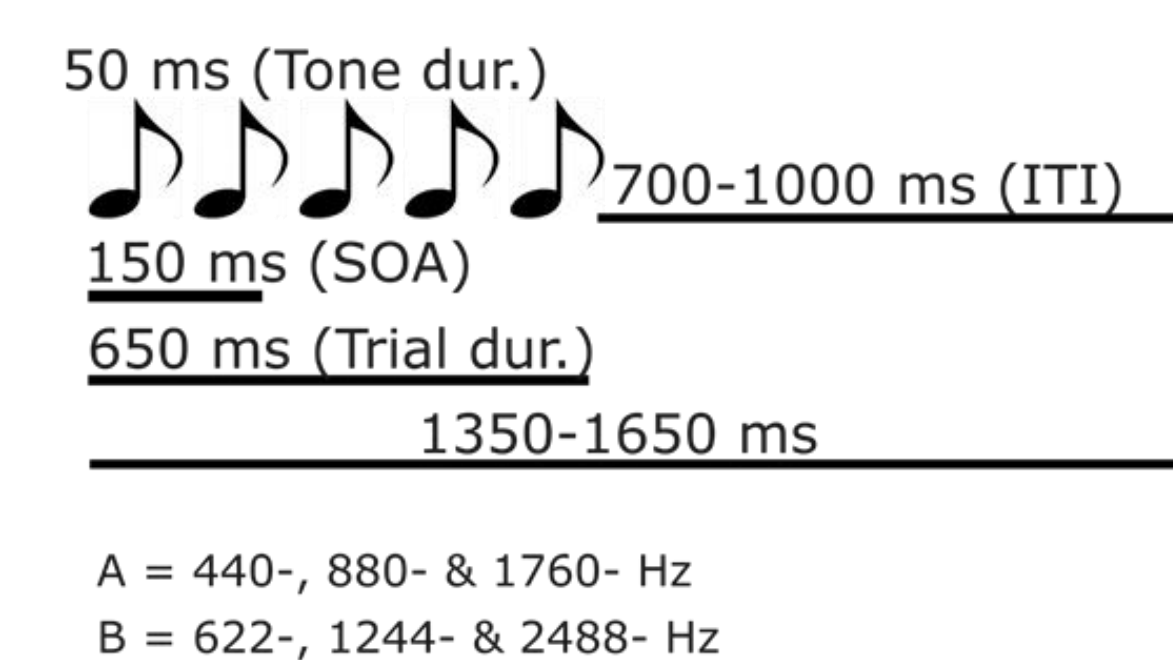
Conclusion: The OFC plays a role in predictive processing of auditory deviance at different hierarchical levels.



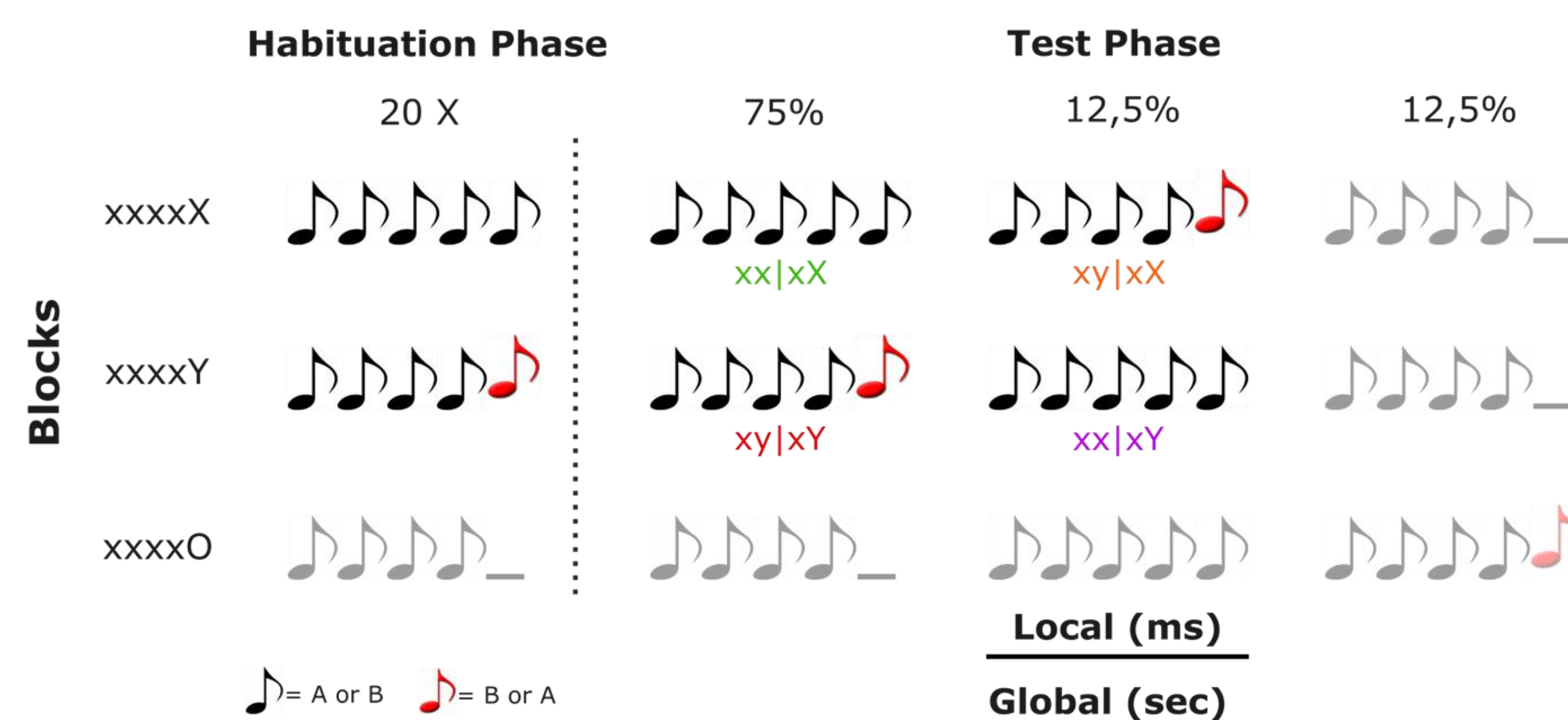
2. Methods

Task Design

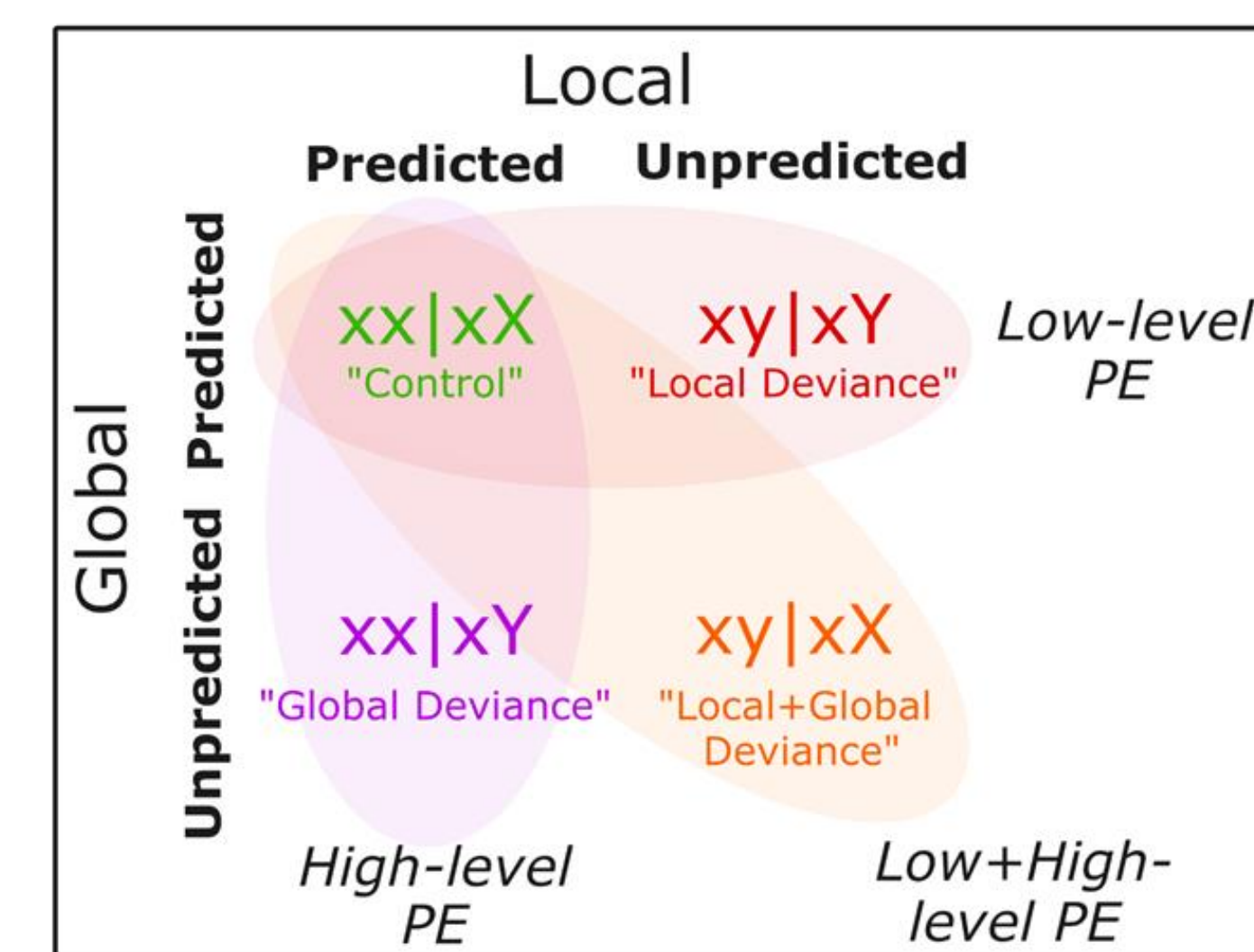
A Trial design



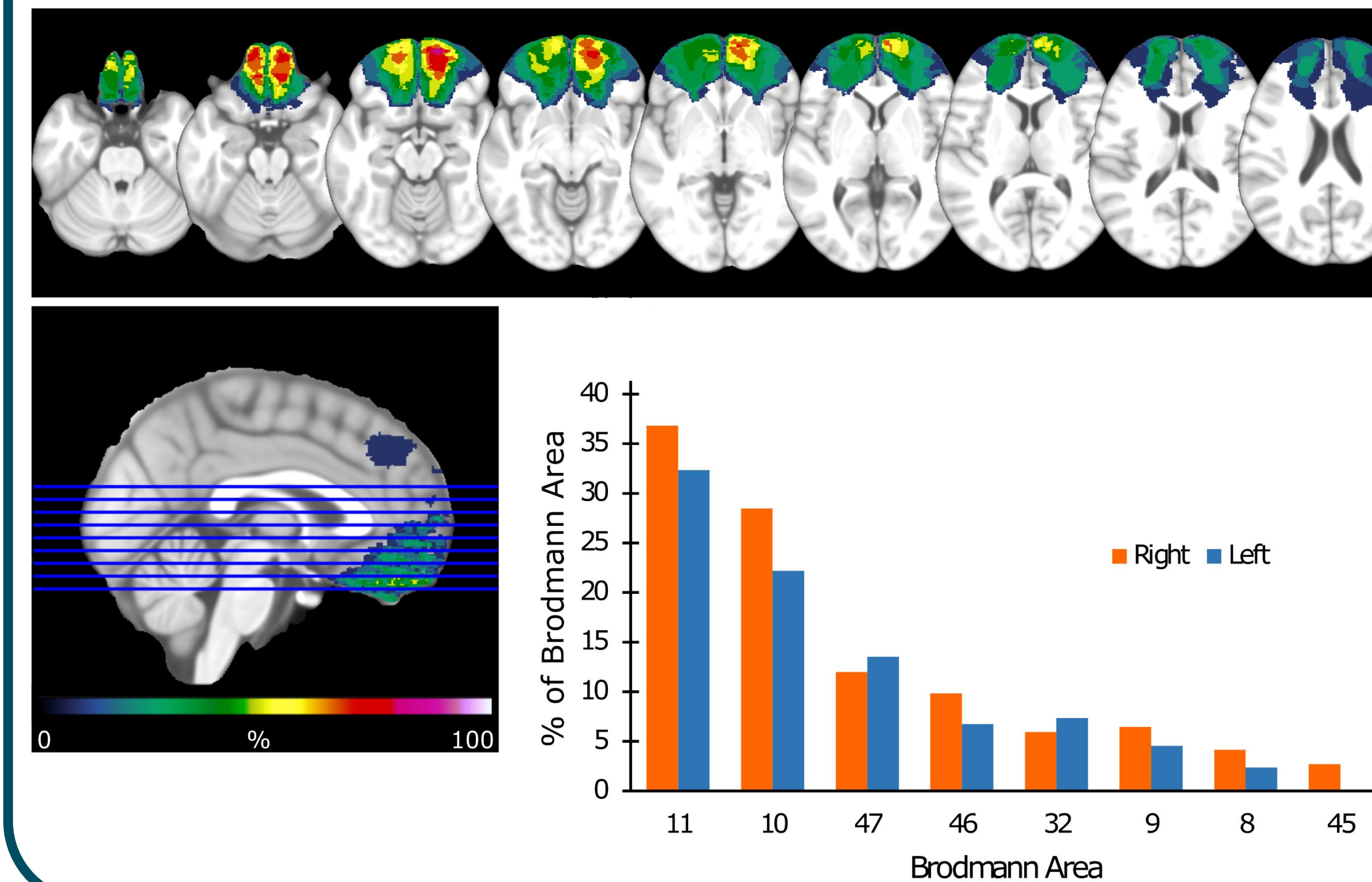
B Block design



C Condition Contrasts



OFC damage reconstruction



Participants

OFC Patients (n=12)

F/M: 8/4
Age: 47.9 yrs
Edu.: 15 yrs
IQ: 112.2
Lesion Etiology:
Olfactory Meningioma (9)
Traumatic Brain Injury (2)
Low Grade Glioma (1)

Healthy Controls (n=14)

F/M: 8/6
Age: 47.6 yrs
Edu.: 16.1 yrs
IQ: 115.4

EEG

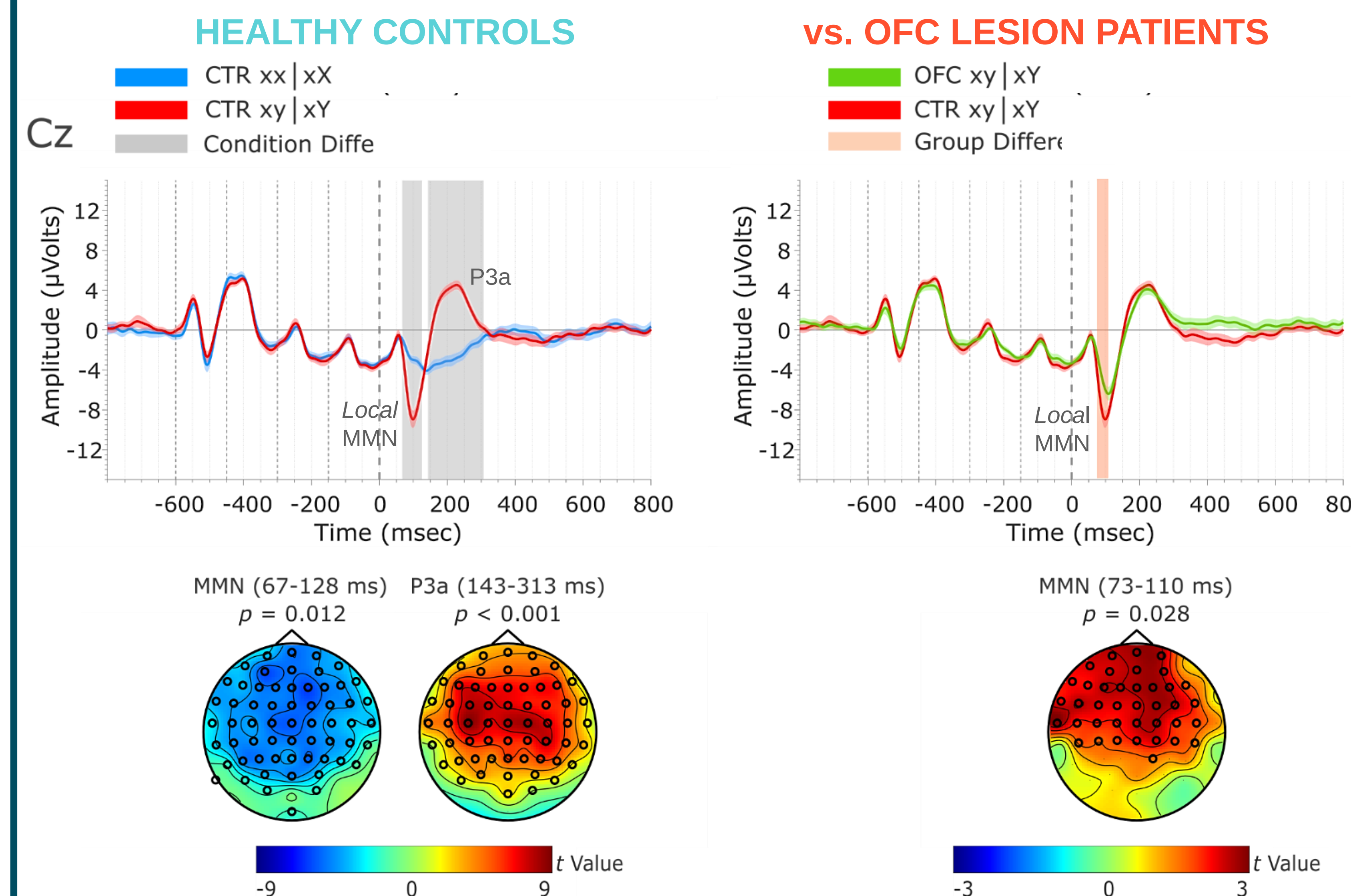
Acquisition: Biosemi ActiveTwo System (64-channel); Sampling rate: 1024 Hz;

Preprocessing: Referencing: earlobes; Filtering: high-pass, infinite impulse-response (IIR) zero-phase Butterworth filter (order: 3), half-amplitude cutoff at 0.01 Hz; Data cleaning: Visual inspection for noisy channels & segments, ICA eye movements, spherical spline channel interpolation; Epochs: -1800 to 2400ms from tones onset.

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

3. Results

Local Deviance: low-level prediction error (PE)

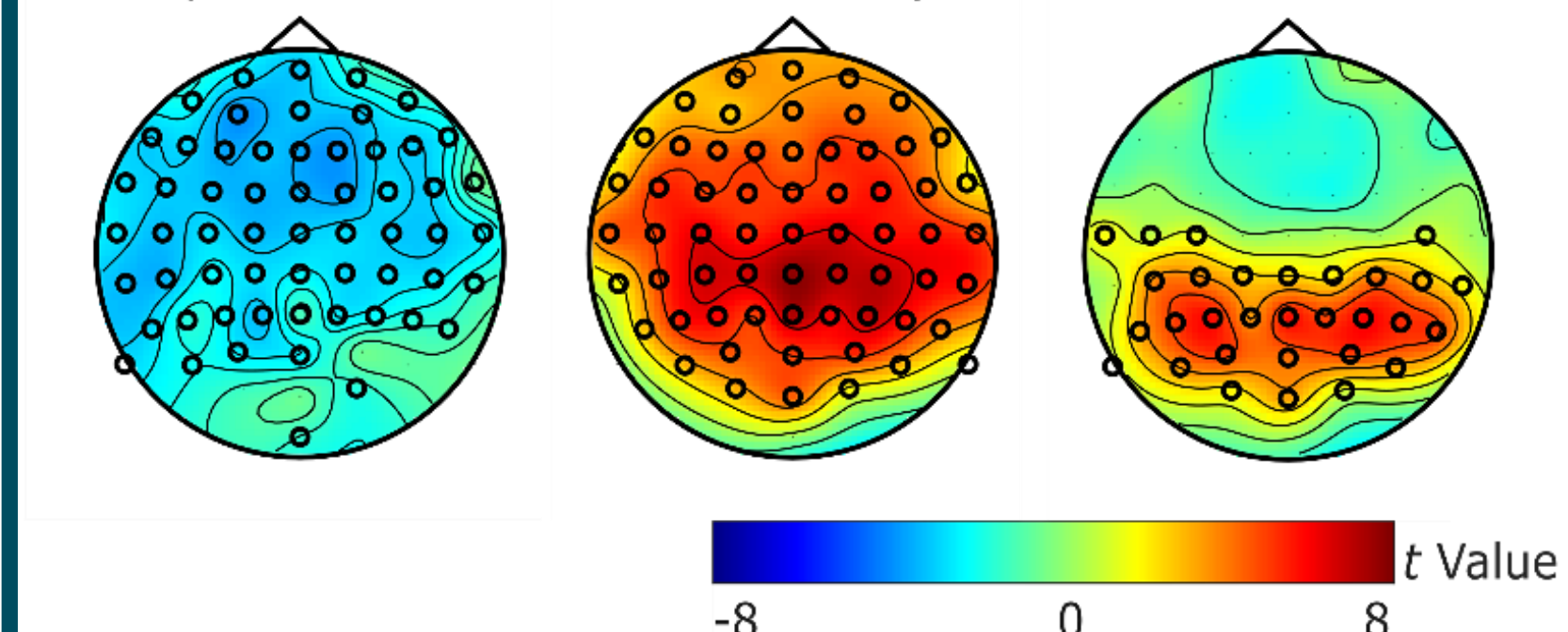
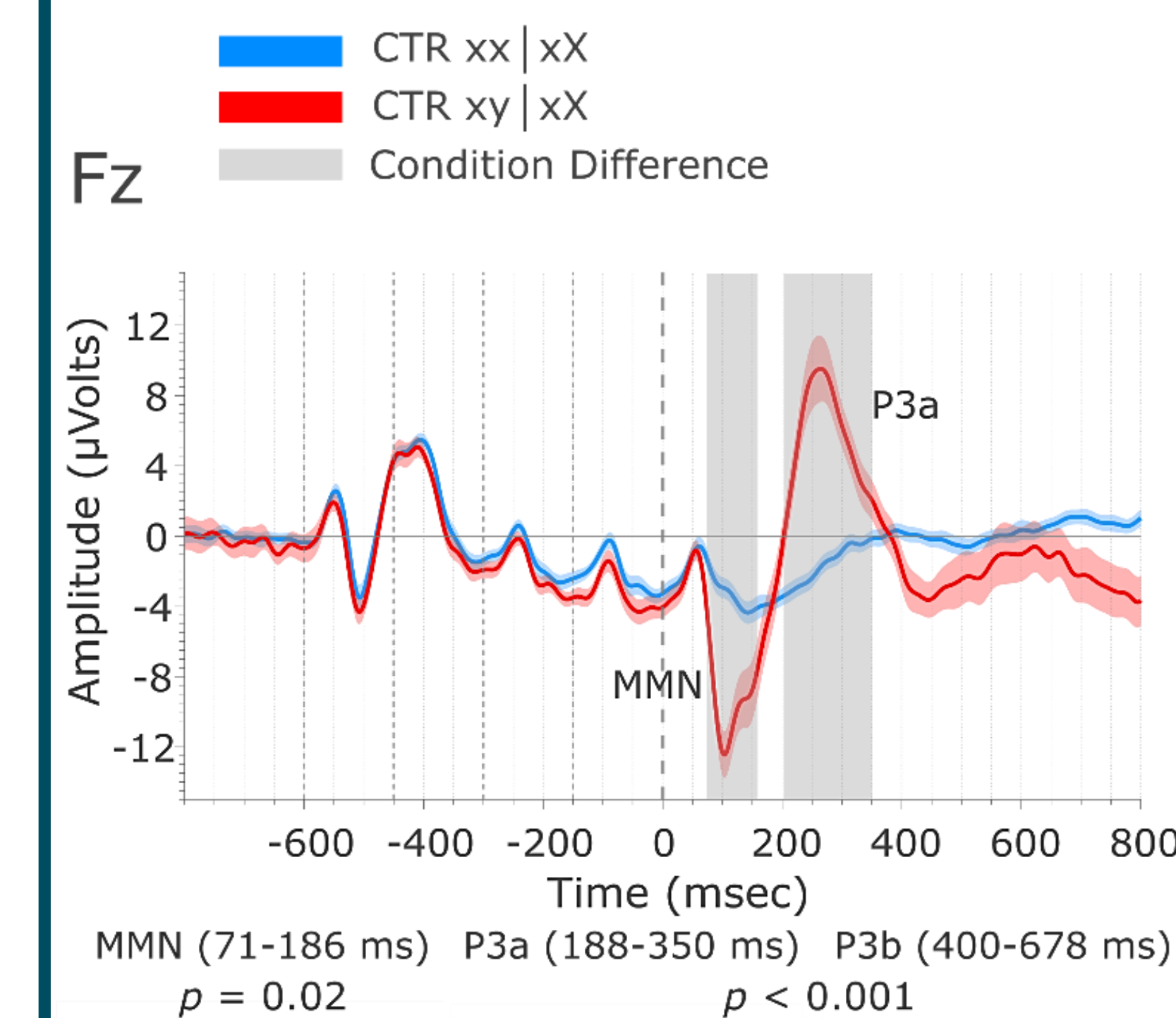


Cluster-based permutation t-test (CBPT):
Healthy controls: early MMN (67-128 ms; neg. cluster: $p = .012$) followed by a P3a (143-313 ms; pos. cluster: $p < .001$).

Independent-samples CBPT t-test:
reduced MMN for **OFC patients** ($p = .028$). No significant difference for the P3a.

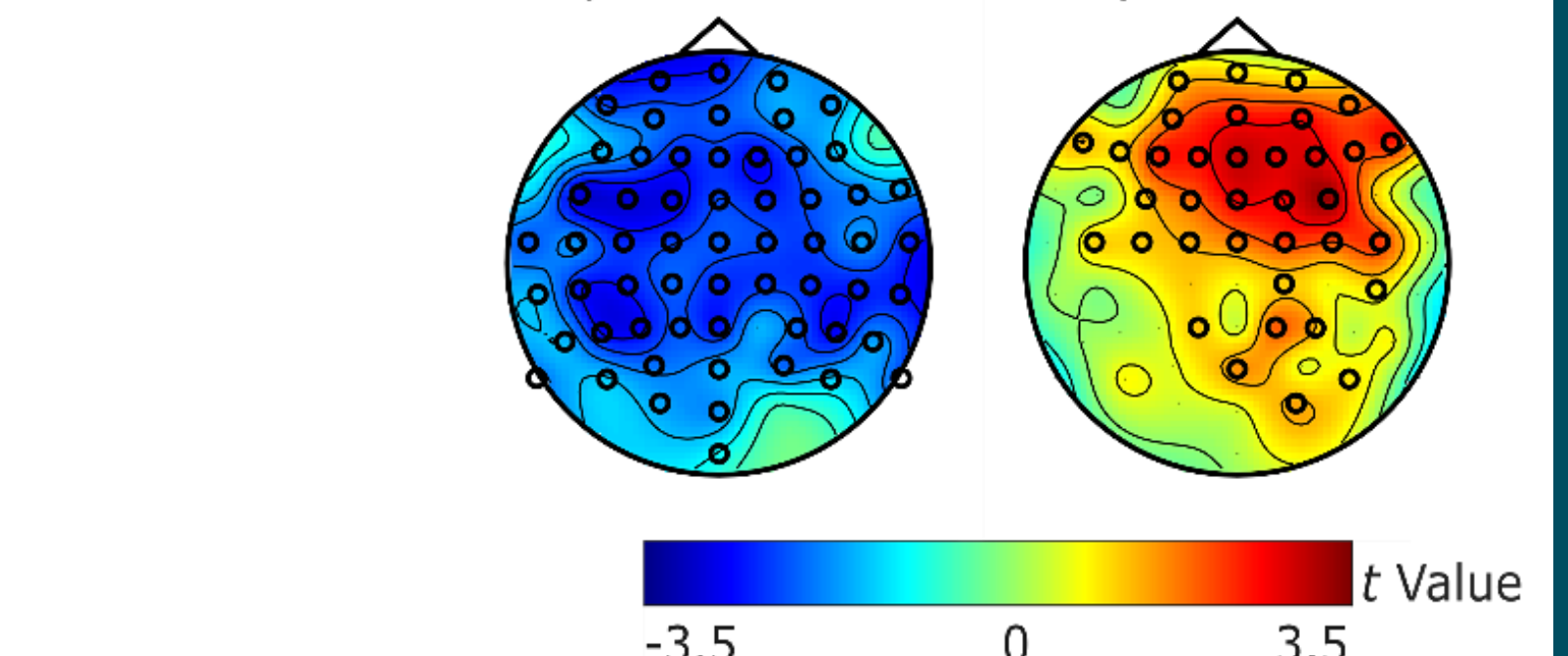
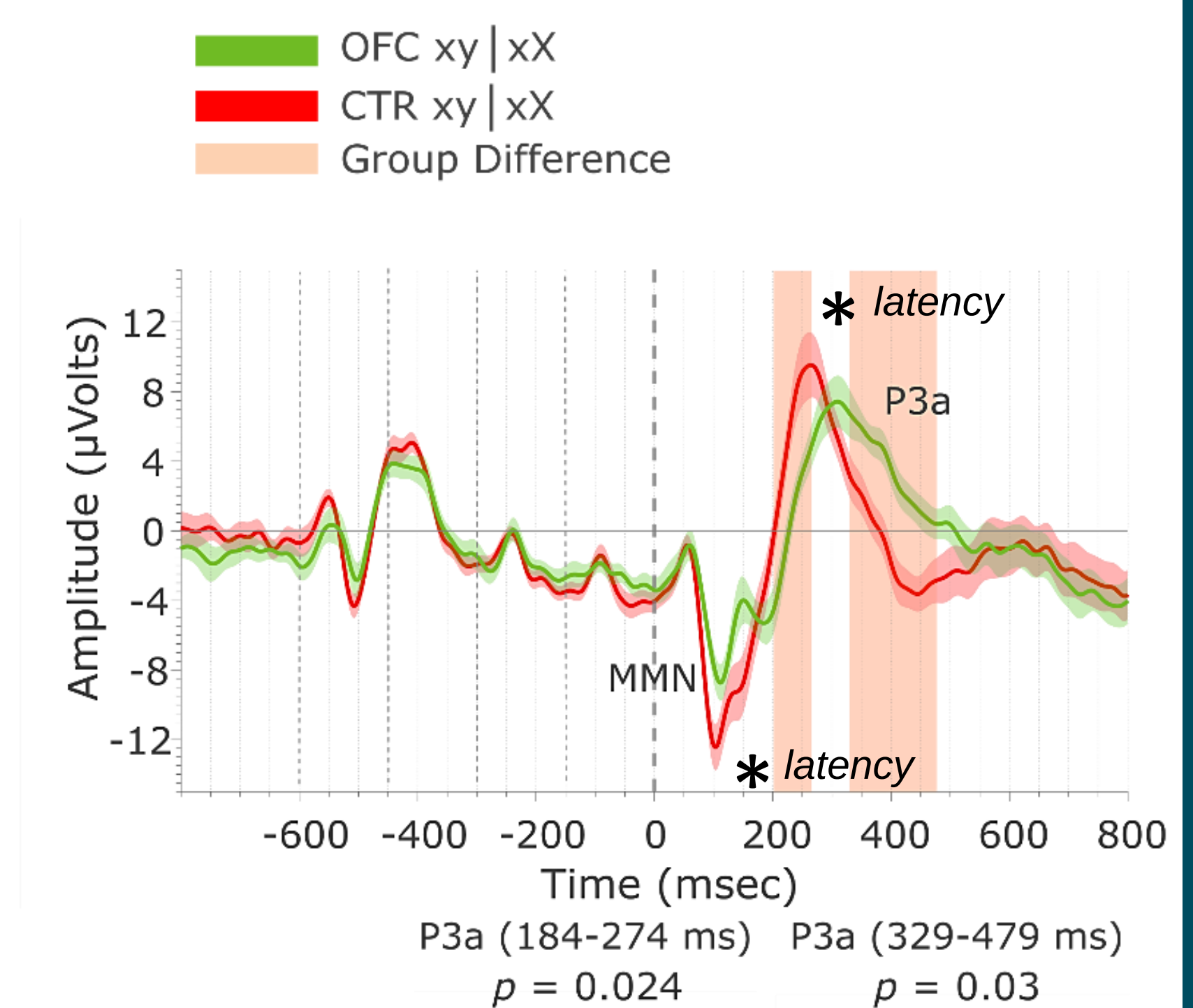
Local + Global Deviance: low + high-level prediction (PE) error

HEALTHY CONTROLS



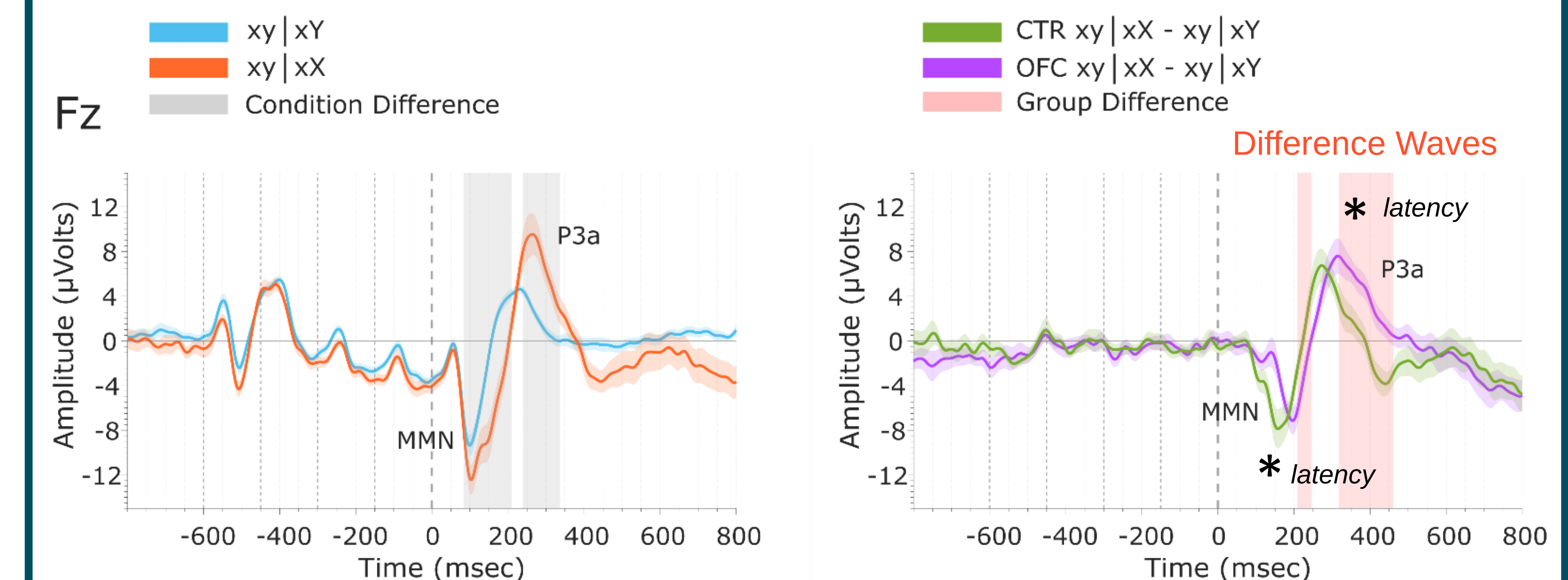
Healthy controls: (biphasic) **long-lasting MMN** with an anterior distribution (71-186 ms; neg. cluster: $p = .02$) followed by a **P3a/P3b complex** (188-678 ms; pos. cluster: $p < .001$).

vs. OFC LESION PATIENTS



OFC patients: **reduced MMN** and **P3a** (neg. cluster, $p = .024$ at 184-274 ms; pos. cluster, $p = .03$ at 329-479 ms). ≈ 25 ms later latency for the MMN; ≈ 50 ms for the P3a

Local vs. Local + Global Deviance: interaction



Condition differences at the time-window of **MMN** ($p = .018$; 85-210 ms) and **P3a** ($p < .01$; 221-684 ms).

Group differences at the time-window of **MMN** ($p = .066$; 131-161 ms) and **P3a** ($p = .01$; 186-253 ms and $p = .054$; 319-461 ms).

Global Deviance: high-level prediction error (PE) only

Healthy controls: Effect of global deviance from 380-715ms, **P3b** (pos. cluster at posterior electrodes, $p = .01$). No significant differences between the two groups.

4. Conclusions

The processing of tones deviating in pitch (i.e., PE to stimuli that are unpredicted at the **local level**) generates low-level PE response indexed by a **typical MMN** followed by a **P3a**.

The processing of tones, which deviate in pitch and are unpredicted by the global rule (i.e., PE to stimuli that are unpredicted at both the **local and global level**), evokes patterns of brain activity comprised of a **biphasic and long-lasting MMN** followed by a **P3a/P3b complex**.

OFC damage impacts local level deviance processing as indicated by the **attenuated MMN**.

OFC damage impacts combined local+global level deviance processing as suggested by the **reduced and later in latency MMN** and **P3a**.

