

Intracranial gamma activity tracks human chemosensory processing

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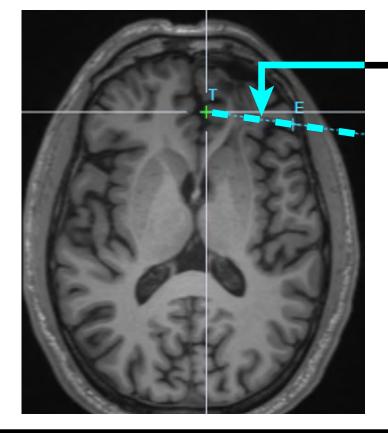
Background: Olfaction and gustation are chemosensory responses that strongly impact both quality of life and safety, yet the neural dynamics from which smell and taste perceptions emerge in humans are largely unknown. Our goal is to create a spatiotemporal map of these processes using intracranial record-

Methods: 15 epilepsy patients implanted with clinical depth electrodes for the purpose of defining their seizure onset zone performed an olfactory task. [Methods 1, Methods 3] Smell wands were used to present 3 different stimuli and a blank, in block-randomized sequences. Participants were instructed to indicate the presence of an odor with a keypress and to identify the stimulus in a multiple-choice question. 13 of these patients performed a similar gustation task using waterless taste strips. [Methods 2]

**Results:** No single olfactory or gustatory stimulus was identified more reliably than the others as assessed by a mixed effects model. Olfactory stimuli reported as "pleasant" were identified more reliably than "neutral" stimuli. Median detection response time was 3.01s (interquartile range 1.96-4.39s) and median percentage of correctly identified stimuli was 71% (55-86%). [Results 1] Electrodes activated by stimuli were located in the piriform cortex (8/41; patients/electrodes), entorhinal cortex (8/48), middle (7/23)and posterior (8/25), insula, frontal operculum (7/25), posterior orbitofrontal cortex (5/18), and rhinal cortex (5/14). Time-frequency analysis of local field potentials demonstrated increased gamma power (60-250 Hz) during olfaction and gustation. Olfactory gamma responses were stronger in the piriform cortex, entorhinal cortex, and orbitofrontal cortex. Gustatory gamma responses were strongest in the insula. [Results 2, Results 3]

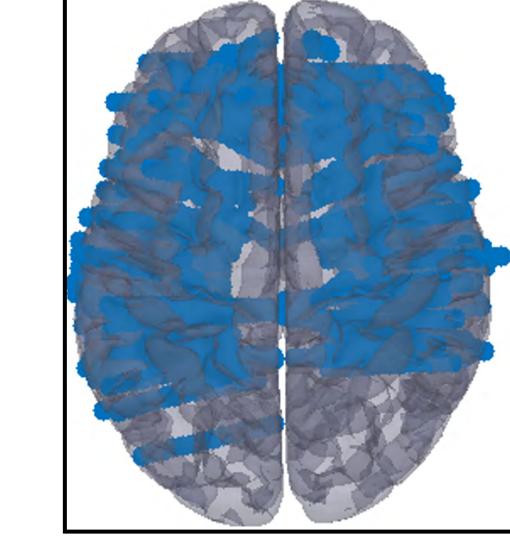
Conclusions: We demonstrated increases in broadband gamma power specific to olfactory and gustatory processing in humans. These results demonstrate that, similar for other perceptions such as sound, gamma activity can be used to track chemosensory processing in the human brain, an important step in understanding network signals that need to be recapitulated to restore function in anosmics.

Methods 1 Olfaction and gustation were studied in patients implanted with SEEG for epilepsy monitoring



Example trajectory to orbitofrontal cortex

Electrode locations all patients



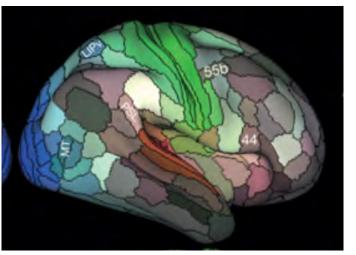
[Methods 2] Olfactory and gustatory stimuli were presented to patients in the Epilepsy Monitoring Unit while collecting neural data



Waterless Taste Strips

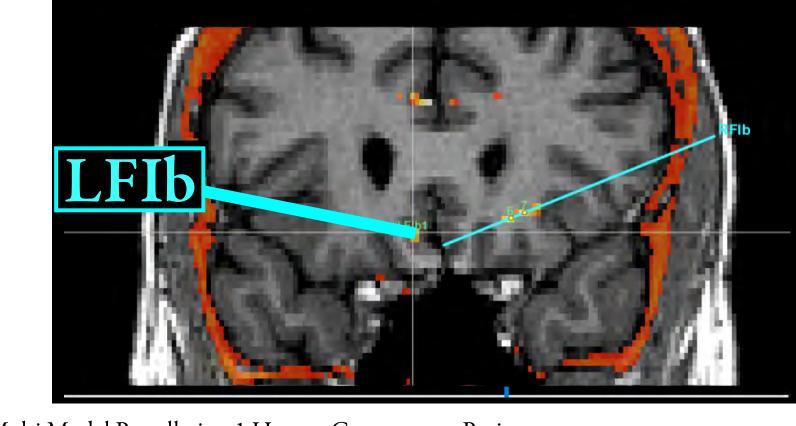


[Methods 3] We used a highly granular multi-modal atlas for precise definition of final electrode location



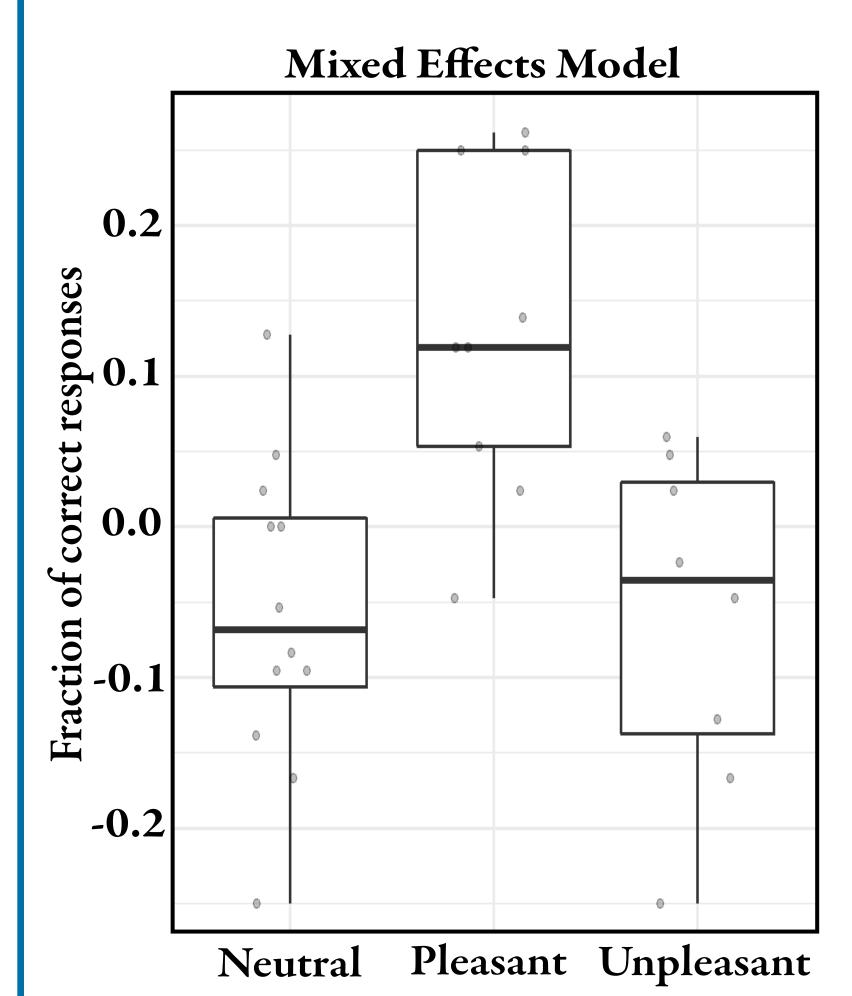
Example of parcellation in multimodal atlas (Glasser et al 2016)

Distant contacts of LFIb below located in orbitofrontal cortex



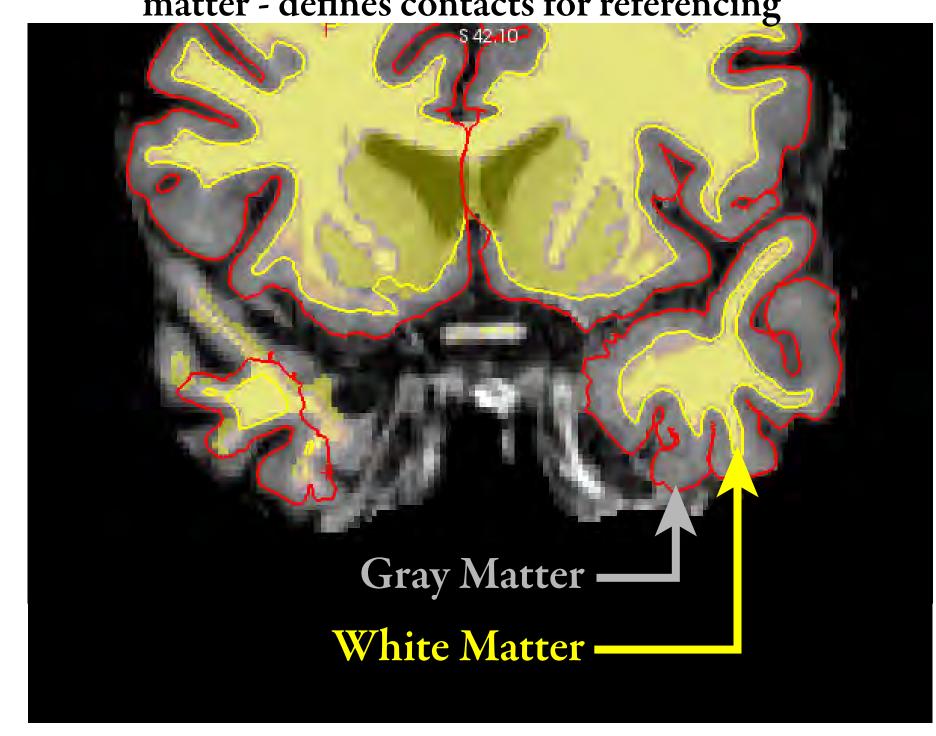
Multi Modal Parcellation 1 Human Connectome Project

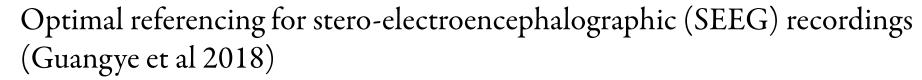
## [Results 1] Behavioral analysis patients identified stimuli they rated as "pleasant" more reliably than others

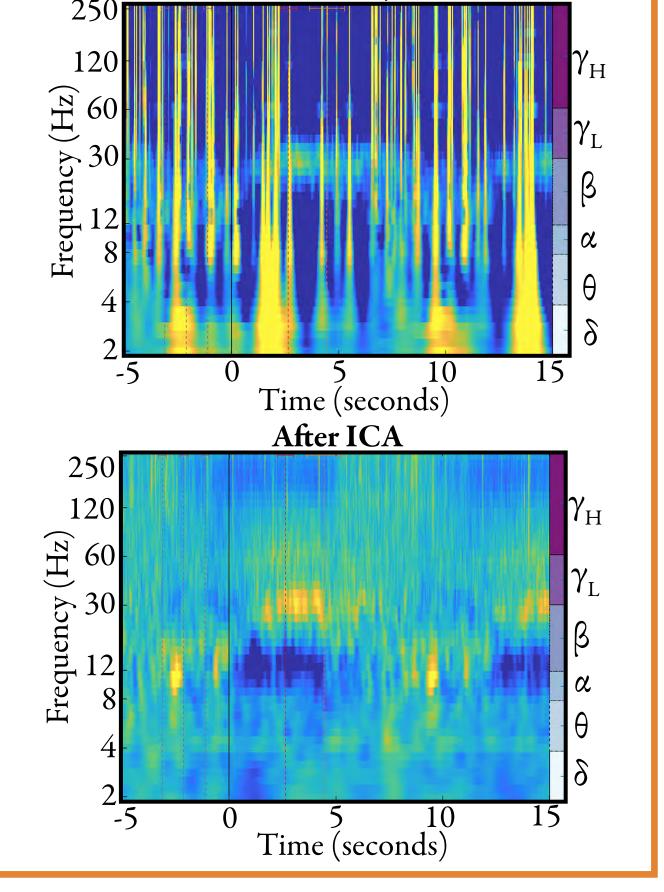


## Results 2 Using ICA for artifact rejection and white matter contact referencing, movement-related artifacts were improved

Using FreeSurfer to determine white matter vs gray matter - defines contacts for referencing







No Artifact Rejection

## References:

Glasser, M. F., Coalson, T. S., Robinson, E. C., Hacker, C. D., Harwell, J., Yacoub, E., ... & Van Essen, D. C. (2016). A multi-modal parcellation of human cerebral cortex. Nature, 536(7615), 171-178. Li G., Jiang S., Paraskevopoulou S.E., Wang M., Xu Y., Wu Z., Chen L., Zhang D., Schalk G. (2018). Optimal referencing for stereo-electroencephalographic (SEEG) recordings. NeuroImage, 183, 327-335. Crone NE, Sinai A, Korzeniewska A. High-frequency gamma oscillations and human brain mapping with electrocorticography. (2006). Prog Brain Res., 159, 275-295. Rojas-Líbano, D., & Kay, L. M. (2008). Olfactory system gamma oscillations: the physiological dissection of a cognitive neural system. Cognitive neurodynamics, 2(3), 179–194.

Olfactory Task - Posterior Orbitofrontal Cortex Results 3 Time frequency analysis 250 demonstrates gamma activation in chemosensory processing. Olfactory  $\cong 60$ y activity activation was stronger in the orbitofrontal cortex and entorhinal cortex, gustatory was stronger in the insula. Gustatory Task - Posterior Insula Time (seconds) y activity Olfactory Task - Entorhinal Cortex Time (seconds)

High-frequency gamma oscillations and human brain mapping with electrocorticography (Crone et al 2006) Olfactory system gamma oscillations: the physiological dissection of a cognitive neural system (Rojas-Líbano et al 2008)