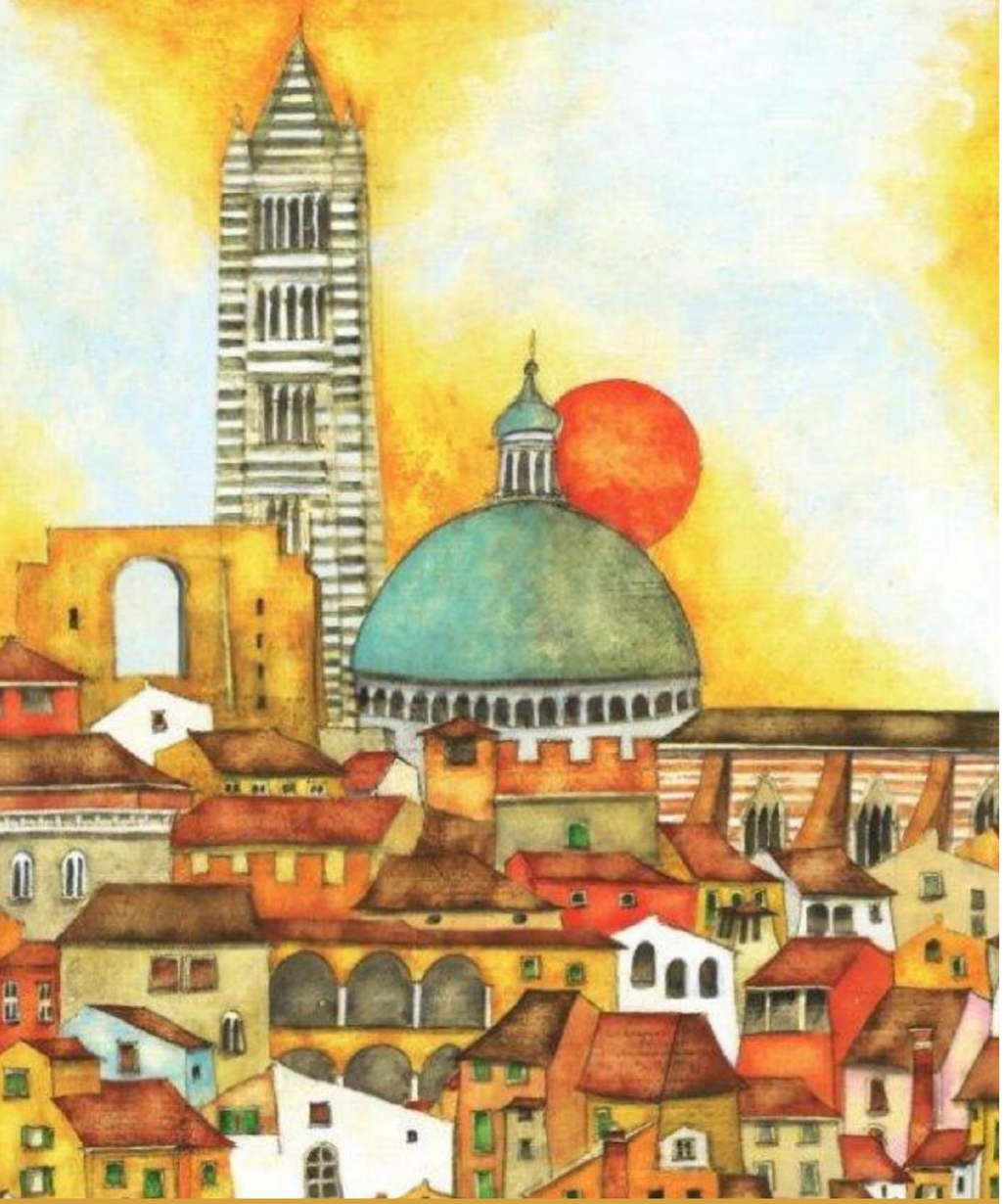

NEUROMODULATION OF GAMMA OSCILLATIONS: FROM BASIC RESEARCH TO CLINICAL APPLICATIONS

Effects of transcranial Alternating Current Stimulation (tACS) on visual perception

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Neural oscillations

*"Neuronal oscillations are not independent events that impose timing on neuronal spikes, but rather are **a reflection of self-organized interactions of those same neurons that detect, transfer, and store information**"*

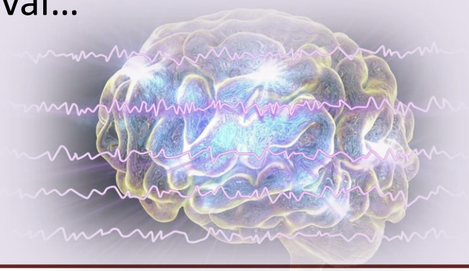
A reflection of self-organized interactions among neurons

- Follow a sinusoidal pattern, with alternating and temporally coexisting high and low levels of activity
- Have been clustered into canonical frequency bands (δ, θ, α, β, γ)
- Hold functional significance for cognitive and perceptual processes

Gamma-band activity

30-90 Hz

Involved in visual and auditory perception, attentional selection, information encoding, maintenance, retrieval…



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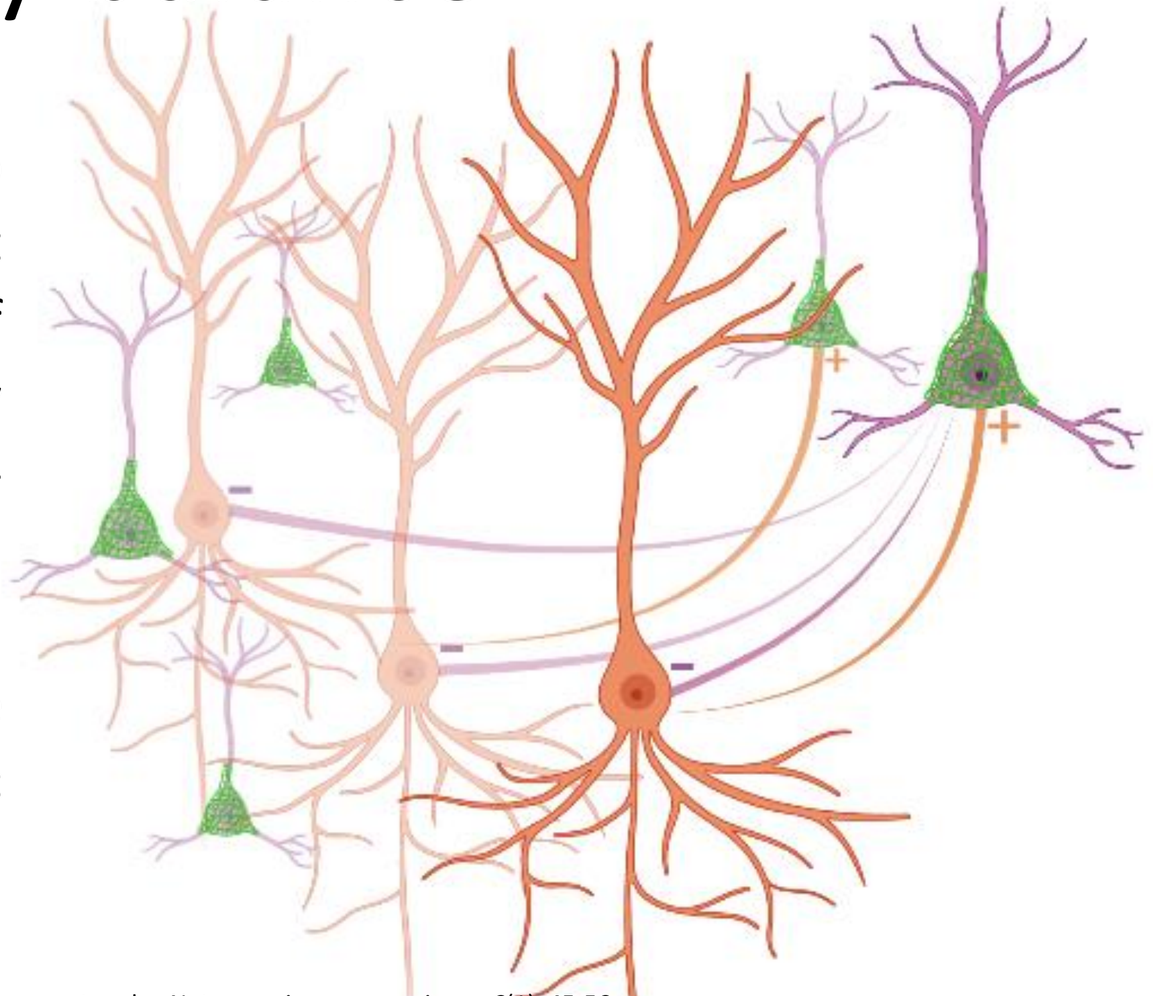
The excitatory-Inhibitory balance

- Pyramidal cells-perisomatic inhibitory neurons loop is thought to be the dominant source of fast oscillations at the network level, as propagation of fast oscillation is mainly mediated by excitatory connections (+) onto interneurons (-) displaying long-range projections targeting other interneurons

- **Gamma oscillations** are mainly attributed to the activity of *Parvalbumin*-expressing GABAergic interneurons, which exhibit fast-spiking properties



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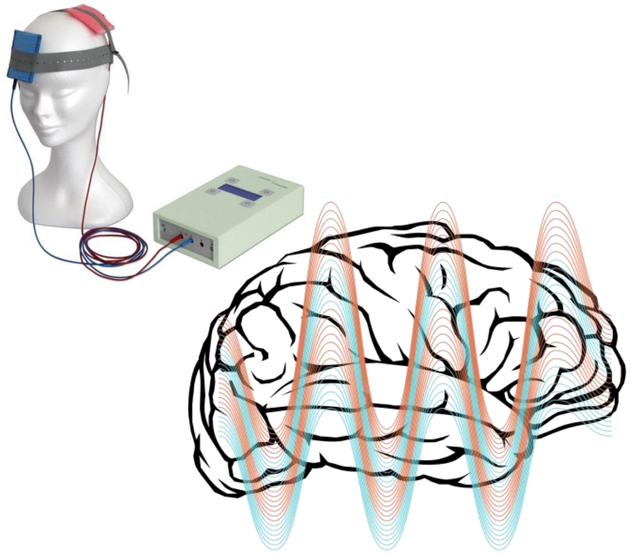
Non-invasive brain stimulation (NIBS): **transcranial Alternating Current Stimulation (tACS)**

Non-invasive **entrainment** of rhythmic endogenous patterns via externally-driven sinusoidal currents, with potential long-lasting **plasticity** effects

Parameters

- Frequency (Hz)
- Montage (traditional vs. High-Density)
- Electrode location
- Duration
- Timing (online vs. offline)



Side effects

- Tingling
- Itching
- Skin redness
- Dizziness
- Nausea

- Antal, A., & Paulus, W. (2013). Transcranial alternating current stimulation (tACS). *Frontiers in human neuroscience, 7*, 317.
- Helfrich, R. F., Schneider, T. R., Rach, S., Trautmann-Lengsfeld, S. A., Engel, A. K., & Herrmann, C. S. (2014). Entrainment of brain oscillations by transcranial alternating current stimulation. *Current biology, 24*(3), 333-339.

i. Neuromodulation of gamma-band activity in basic research

- Investigating the neurophysiological correlates of perception and cognition
- Modeling reversible functional alterations

ii. Neuromodulation of gamma-band oscillations an interventional avenue

- Restoration of brain activity patterns and the underlying neuropathology
- Identification of abnormalities with diagnostic and prognostic value

- Antal, A., & Paulus, W. (2013). Transcranial alternating current stimulation (tACS). *Frontiers in human neuroscience, 7,* 317.
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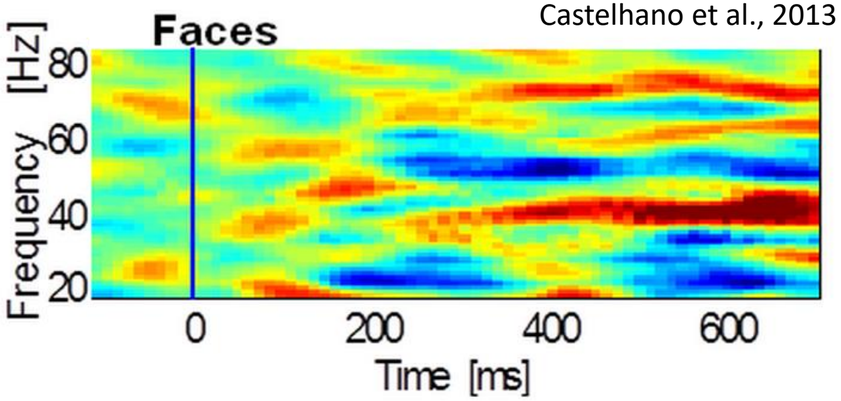
Gamma-tACS to modulate illusory face perception

- Gamma activity subserve holistic face perception via processes of **feature-binding** and **perceptual integration**

Castelhano et al., 2013



- Studies adopting **Mooney stimuli** in patients with **Schizophrenia** report **impaired performances** associated with abnormal gamma spectral power

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- Haxby, J. V., Hoffman, E. A., & Gobbini, M. I. (2000). The distributed human neural system for face perception. *Trends in cognitive sciences, 4*(6), 223-233.
- Rivolta, D., Castellanos, N. P., Stawowsky, C., Helbling, S., Wibral, M., Grützner, C., ... & Uhlhaas, P. J. (2014). Source-reconstruction of event-related fields reveals hyperfunction and hypofunction of cortical circuits in antipsychotic-naive, first-episode schizophrenia patients during Mooney face processing. *Journal of Neuroscience, 34*(17), 5909-5917.
- Schwiedrzik, C. M., Melloni, L., & Schurger, A. (2018). Mooney face stimuli for visual perception research. *PLoS One, 13*(7), e0200106.

Gamma-tACS to modulate illusory face perception

Can we modulate illusory face perception in healthy individuals via gamma-tACS?

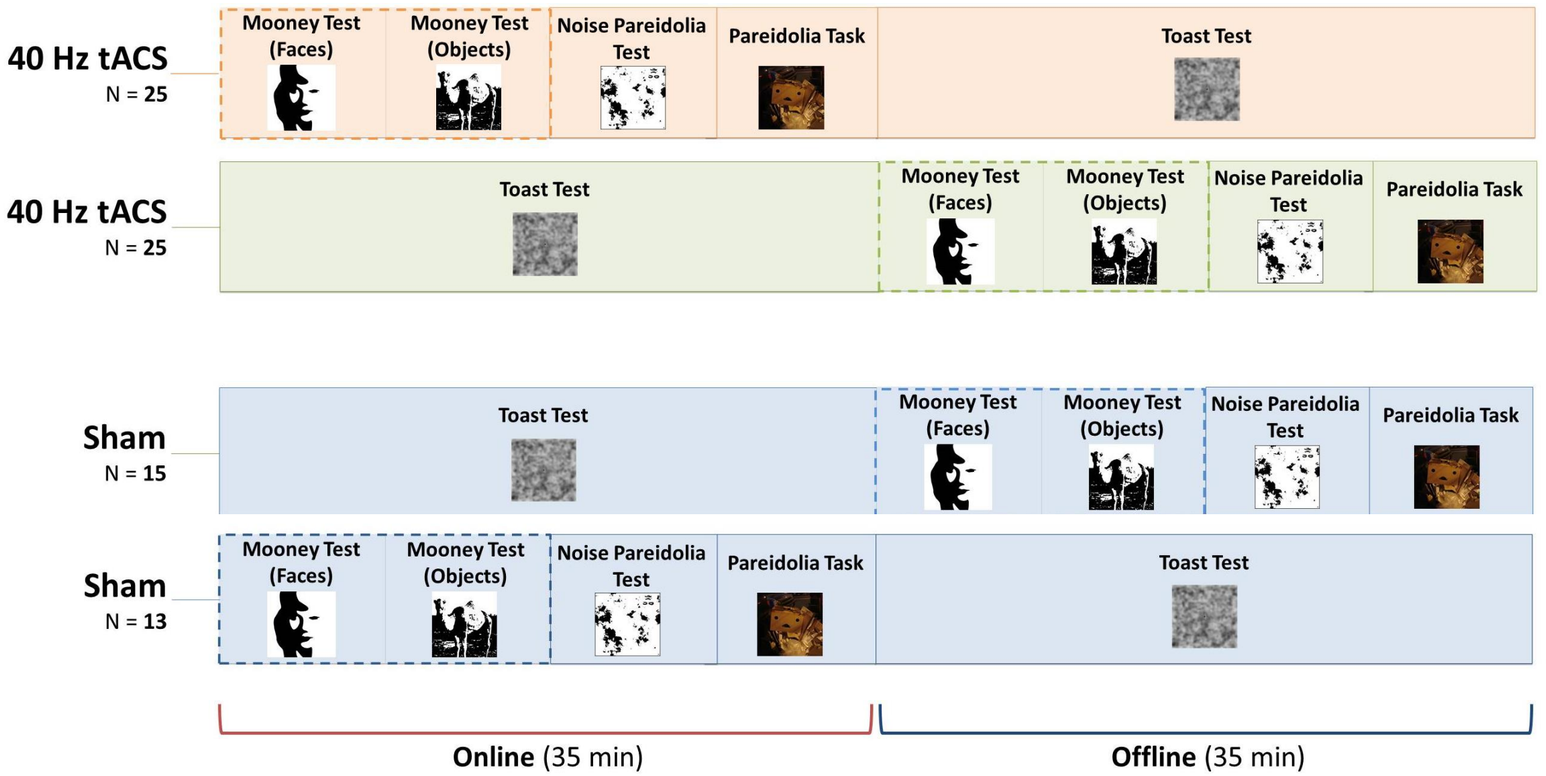
This study investigates whether *real* and *illusory* face perception can be modulated via tACS (vs. **placebo**) in the **gamma** (40 Hz) and **theta** (5 Hz) bands over the **right occipito-temporal** (i.e., face-selective regions) and **left prefrontal** cortices.

- Performance: face vs. no face
- Analyses: Mixed-effects generalized linear models (GLMMs)

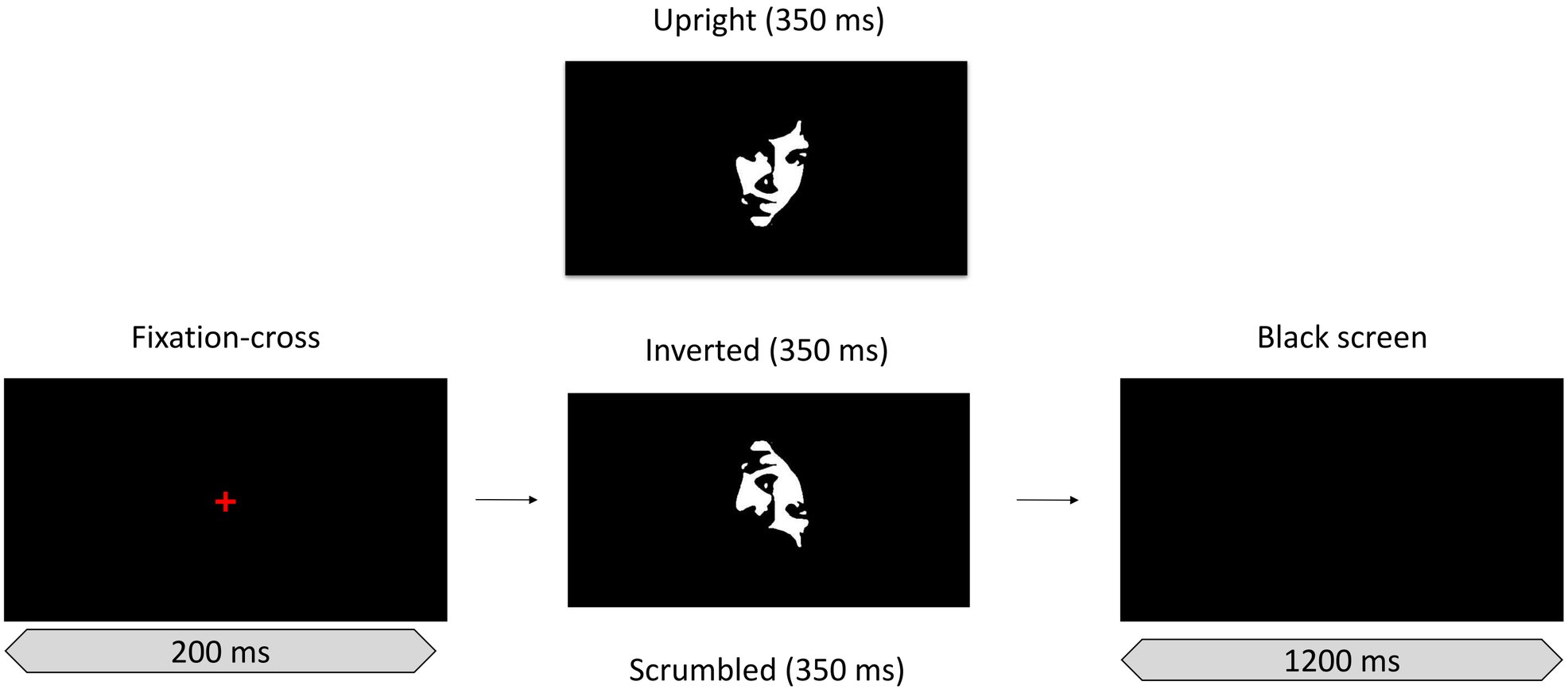
Face pareidolia is enhanced by 40 Hz transcranial alternating current stimulation (tACS) of the face perception network

Annalisa Palmisano, Giulio Chiarantoni, Francesco Bossi, Alessio Conti, Vitiana D'Elia, Serena Tagliente, Michael A. Nitsche & Davide Rivolta

Scientific Reports **13**, Article number: 2035 (2023)

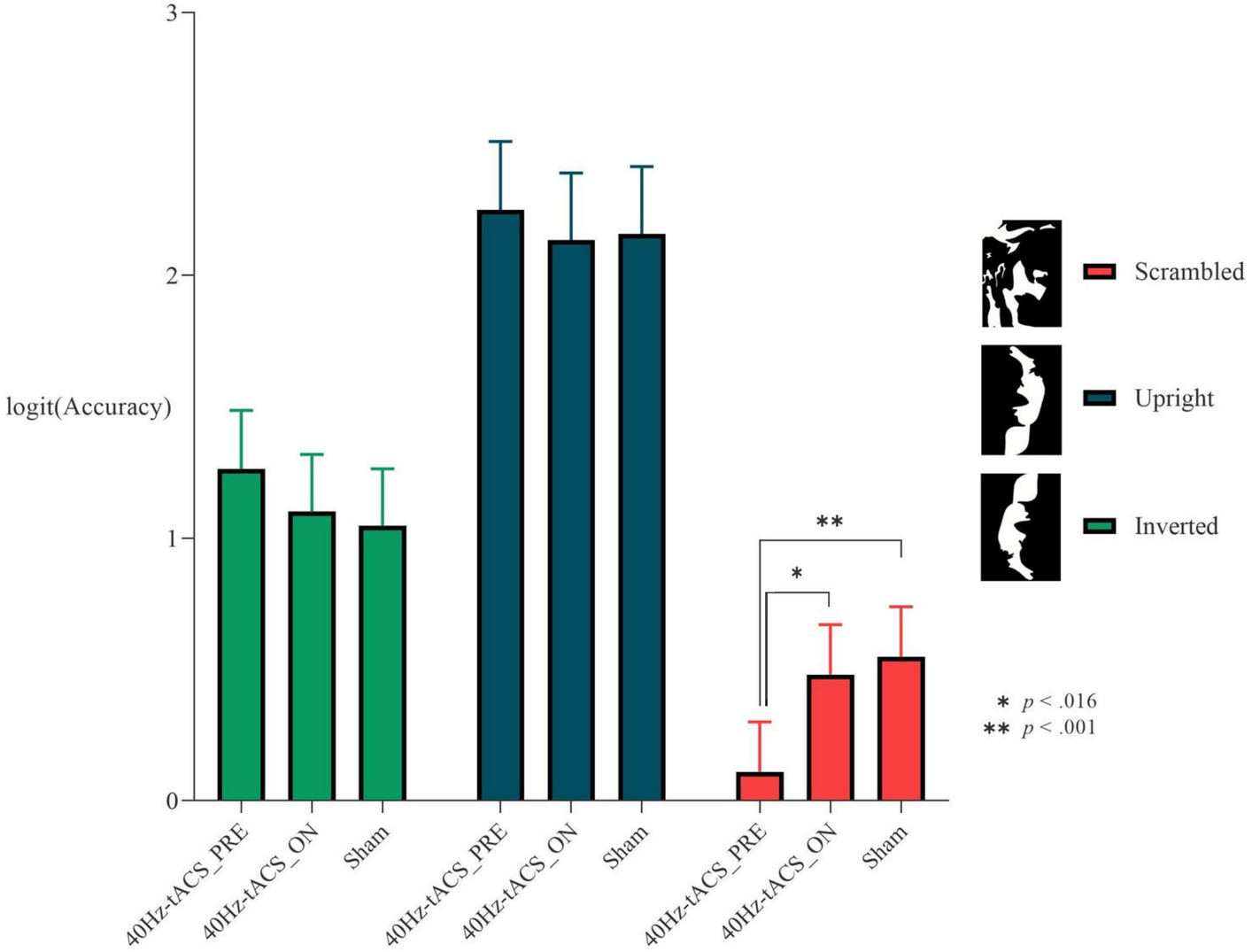


Gamma-tACS to modulate illusory face perception



Results: accuracy

Ref: Palmisano, A., Chiarantoni, G., Bossi, F., Conti, A., D'Elia, V., Tagliente, S., ... & Rivolta, D. (2023). Face pareidolia is enhanced by 40 Hz transcranial alternating current stimulation (tACS) of the face perception network. *Scientific Reports, 13*(1), 2035.



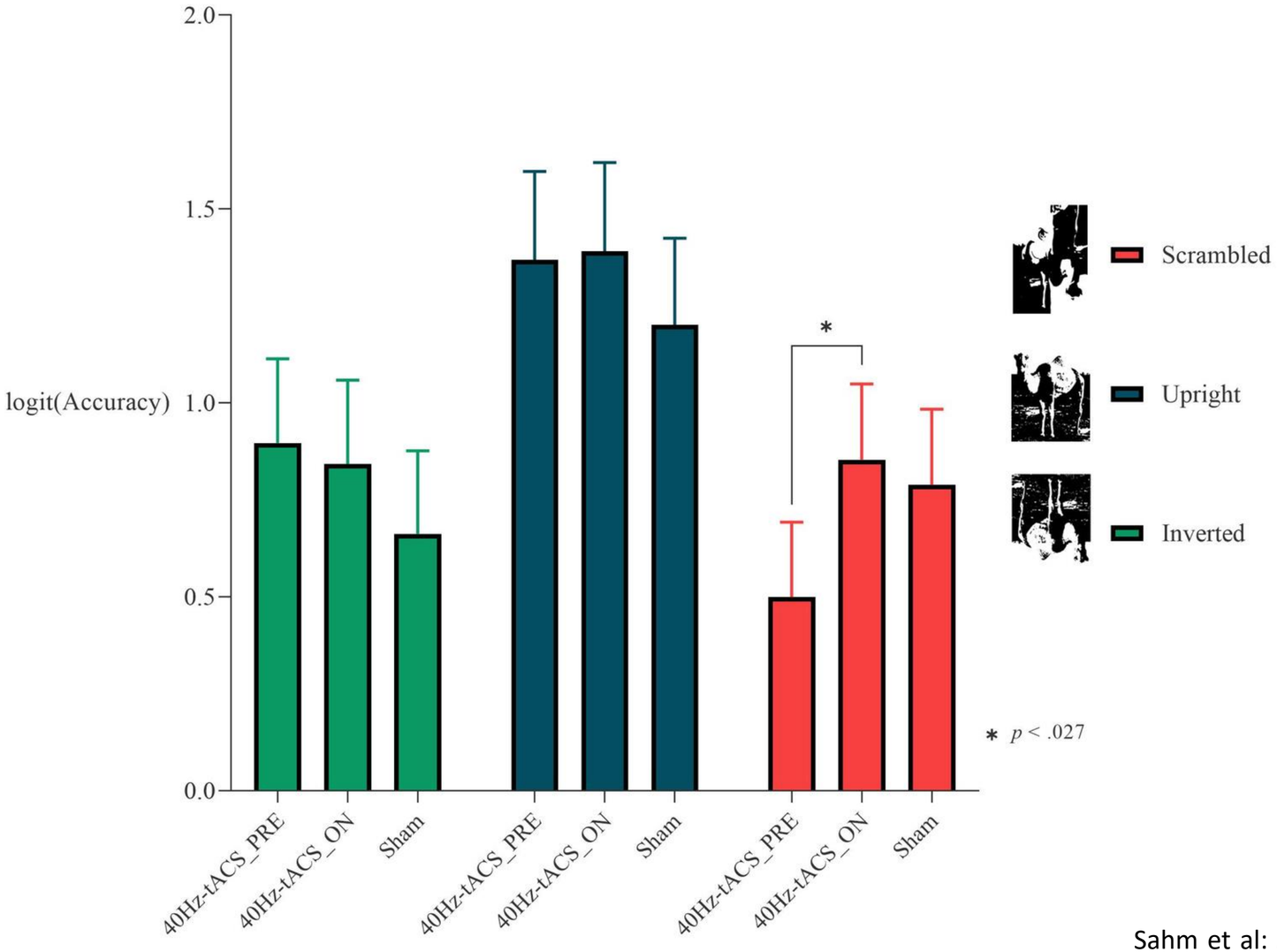
Group*Response interaction for the Mooney test for faces

Induced pareidolia proneness

The Mooney test for faces: Participants in the offline (40Hz-tACS_PRE) group exhibited worse performance in terms of accuracy for **Mooney scrambled stimuli**, which **were more often misperceived as faces** than in the Sham and online (40Hz-tACS_ON) groups

Results: accuracy

Ref: Palmisano, A., Chiarantoni, G., Bossi, F., Conti, A., D'Elia, V., Tagliente, S., ... & Rivolta, D. (2023). Face pareidolia is enhanced by 40 Hz transcranial alternating current stimulation (tACS) of the face perception network. *Scientific Reports, 13*(1), 2035.



Group*Response interaction for the Mooney test for objects

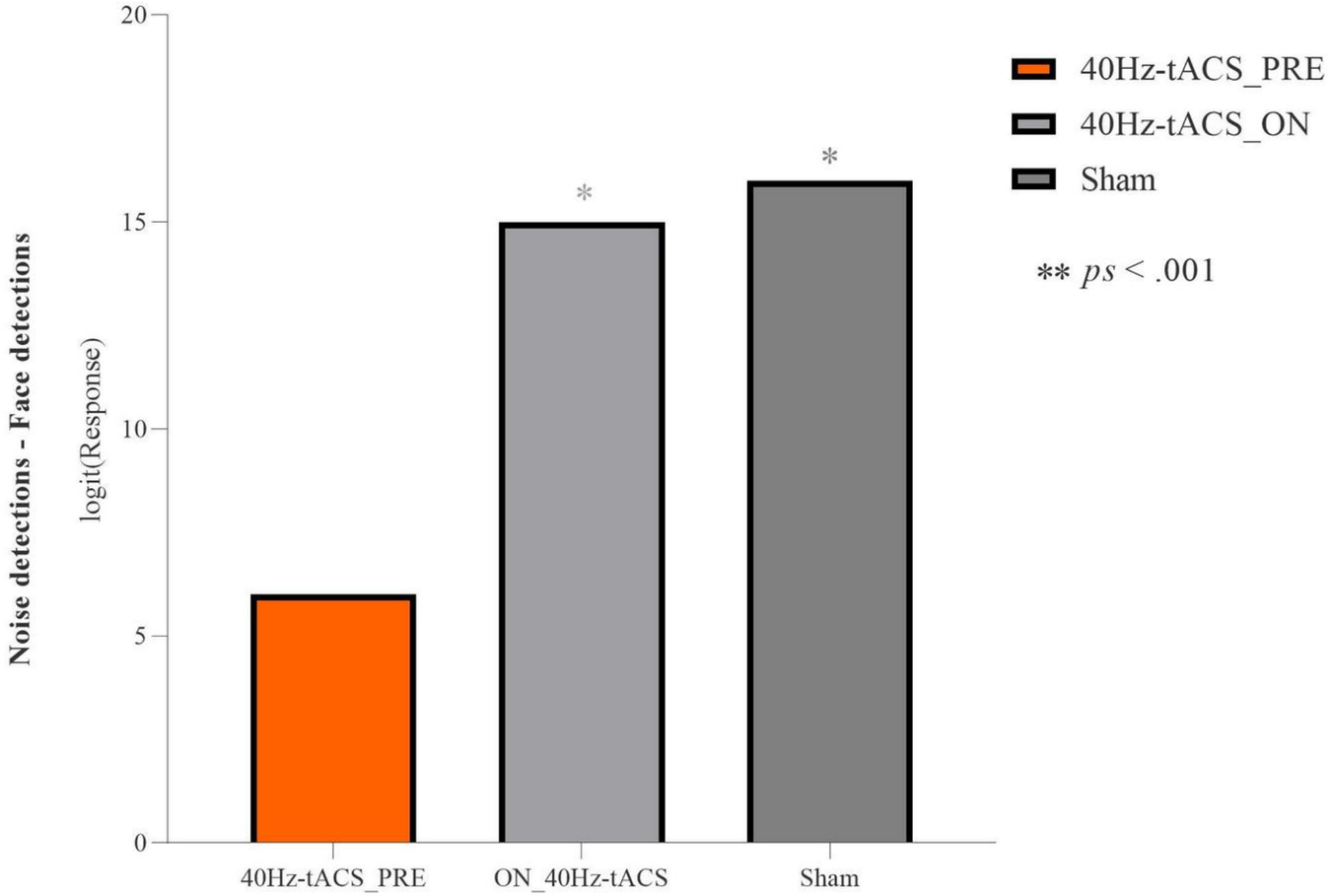
Effect specificity

The Mooney test for objects: Participants in the offline (40Hz-tACS_PRE) group were significantly less accurate at recognizing scrambled Mooney stimuli than those in the online (40Hz-tACS_ON) group. **No differences emerged by comparing performances in the 40Hz-tACS_PRE and the Sham groups**

Sahm et al: *Face Off: A Comparison of Face and Object Recognition in Patients with Psychosis, Individuals at Risk of Psychosis, and Healthy Controls Using Mooney-Type Stimuli* (https://osf.io/vm639)

Results: reaction times

Ref: Palmisano, A., Chiarantoni, G., Bossi, F., Conti, A., D'Elia, V., Tagliente, S., ... & Rivolta, D. (2023). Face pareidolia is enhanced by 40 Hz transcranial alternating current stimulation (tACS) of the face perception network. *Scientific Reports, 13*(1), 2035.



Group*Response interaction for the Toast test (differences in absolute value)

Induced pareidolia proneness

The Toast test: **No significant differences emerged in RTs of pareidolia responses vs. noise detections in the offline (40Hz-tACS_PRE) group**, while participants in the Sham and online (40Hz-tACS_ON groups) were slower for face detections than noise detections

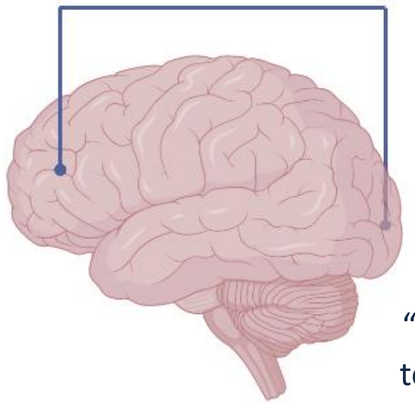
Liu, J., Li, J., Feng, L., Li, L., Tian, J., & Lee, K. (2014). Seeing Jesus in toast: neural and behavioral correlates of face pareidolia. *Cortex*, *53*, 60-77.

Modeling illusory face perception

- Strengthening of perceptual grouping and visual integration via gamma-tACS
- Gamma tACS-driven enhancement of top-down processes
- Stimulation-based behavioral model of “psychotic-like” visual experiences
- Frequency-specific effects?

Palmisano, A., Chiarantoni, G., Bossi, F., Conti, A., D’Elia, V., Tagliente, S., ... & Rivolta, D. (2023). Face pareidolia is enhanced by 40 Hz transcranial alternating current stimulation (tACS) of the face perception network. *Scientific Reports, 13*(1), 2035.

Face-Perception Network



Left Prefrontal Cortex

“Core” right occipito-temporal areas (Face Fusiform area)

Illusory perception

Typical subjects

Hallucinations

Schizophrenia
Parkinson's disease
Lewy Body Dementia

- Gonzalez-Perez, M., Wakui, E., Thoma, V., Nitsche, M. A., & Rivolta, D. (2019). Transcranial alternating current stimulation (tACS) at 40 Hz enhances face and object perception. *Neuropsychologia, 135,* 107237.
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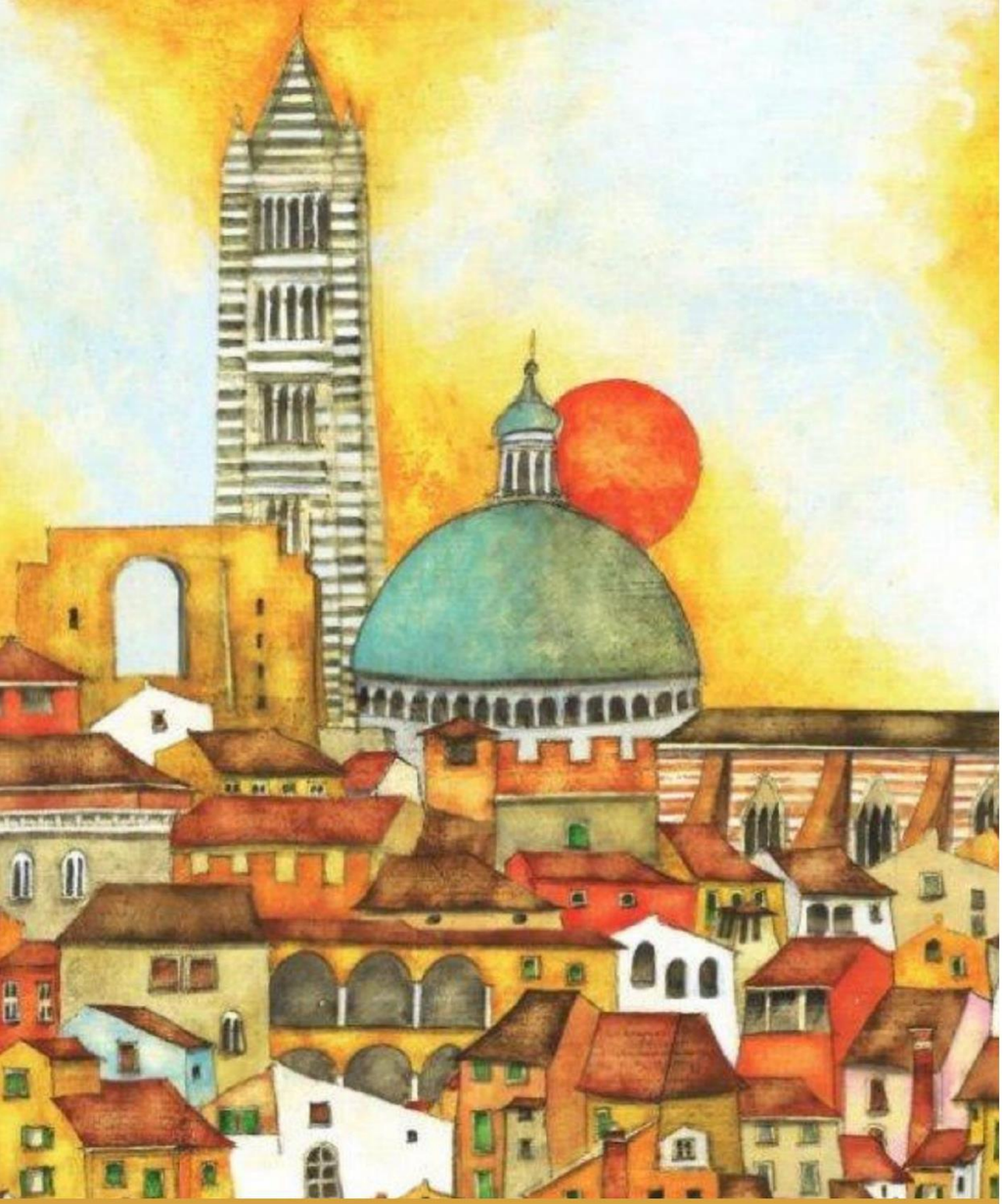


XXXI CONGRESSO NAZIONALE SIPF

Siena 9-11 novembre 2023

Museo Santa Maria della Scala

Thank You

Beth Israel Deaconess Medical Center

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

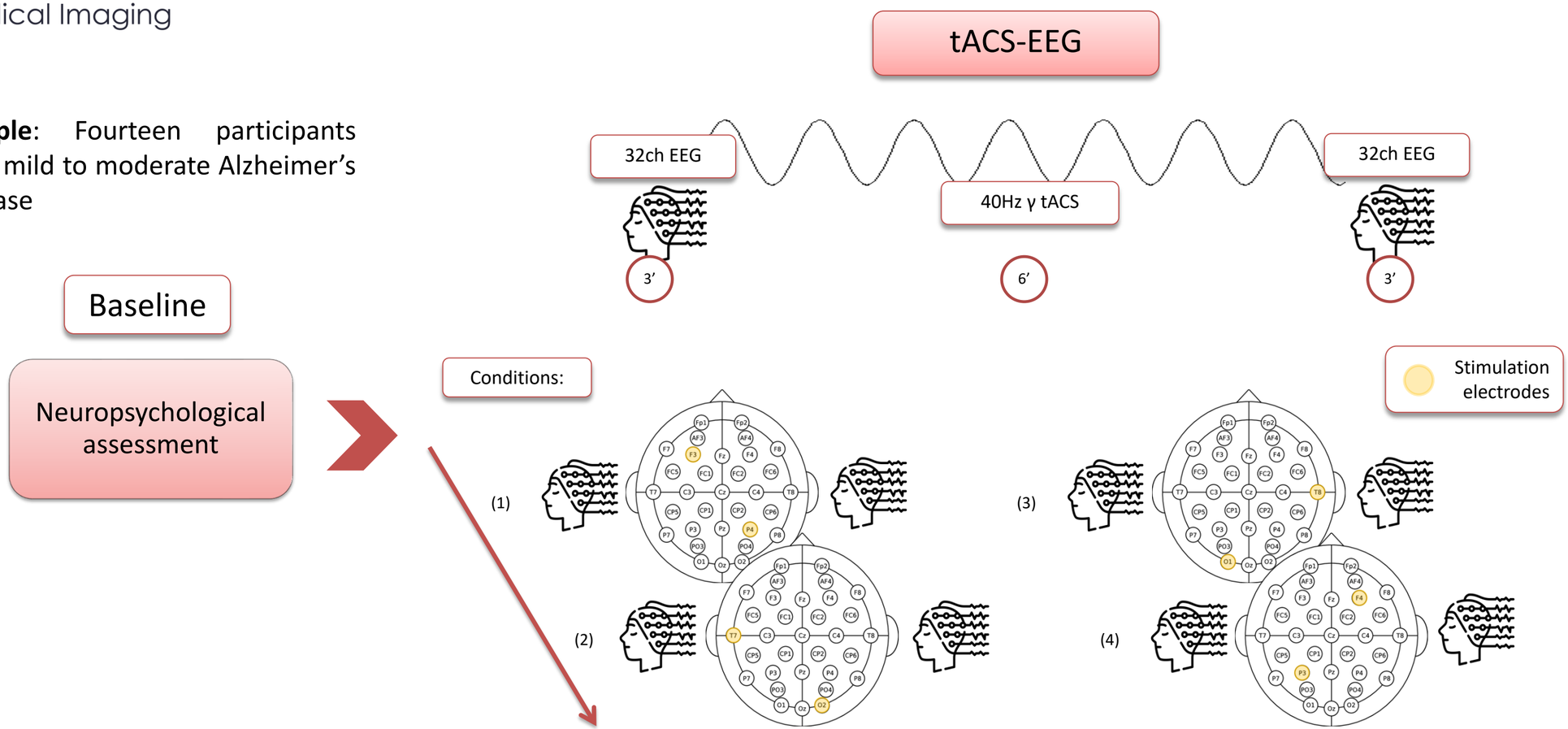
Gordon Center for Medical Imaging

Preliminary Evidence for Perturbation-based tACS-EEG Biomarkers of Gamma Activity in Alzheimer's Disease

P.I. Prof. E. Santarncchi

BA CNBS Berenson-Allen Center For Noninvasive Brain Stimulation

Sample: Fourteen participants with mild to moderate Alzheimer's Disease



Starstim 32 (Neuroelectrics®)

Palmisano A, Pezanko L., Cappon D., Tatti E., Macome J., Koch G., Smeralda C. L., Romanella S. M., Ruffini G., Rivolta D., Press D., Pascual-Leone A., El-Fakhri G., Santarnecchi E., *Preliminary Evidence for Perturbation-based tACS-EEG Biomarkers of Gamma Activity in Alzheimer's Disease* – Submitted as short research report to the International Journal of Geriatric Psychiatry

Beth Israel Deaconess Medical Center

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

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Preliminary Evidence for Perturbation-based tACS-EEG Biomarkers of Gamma Activity in Alzheimer's Disease

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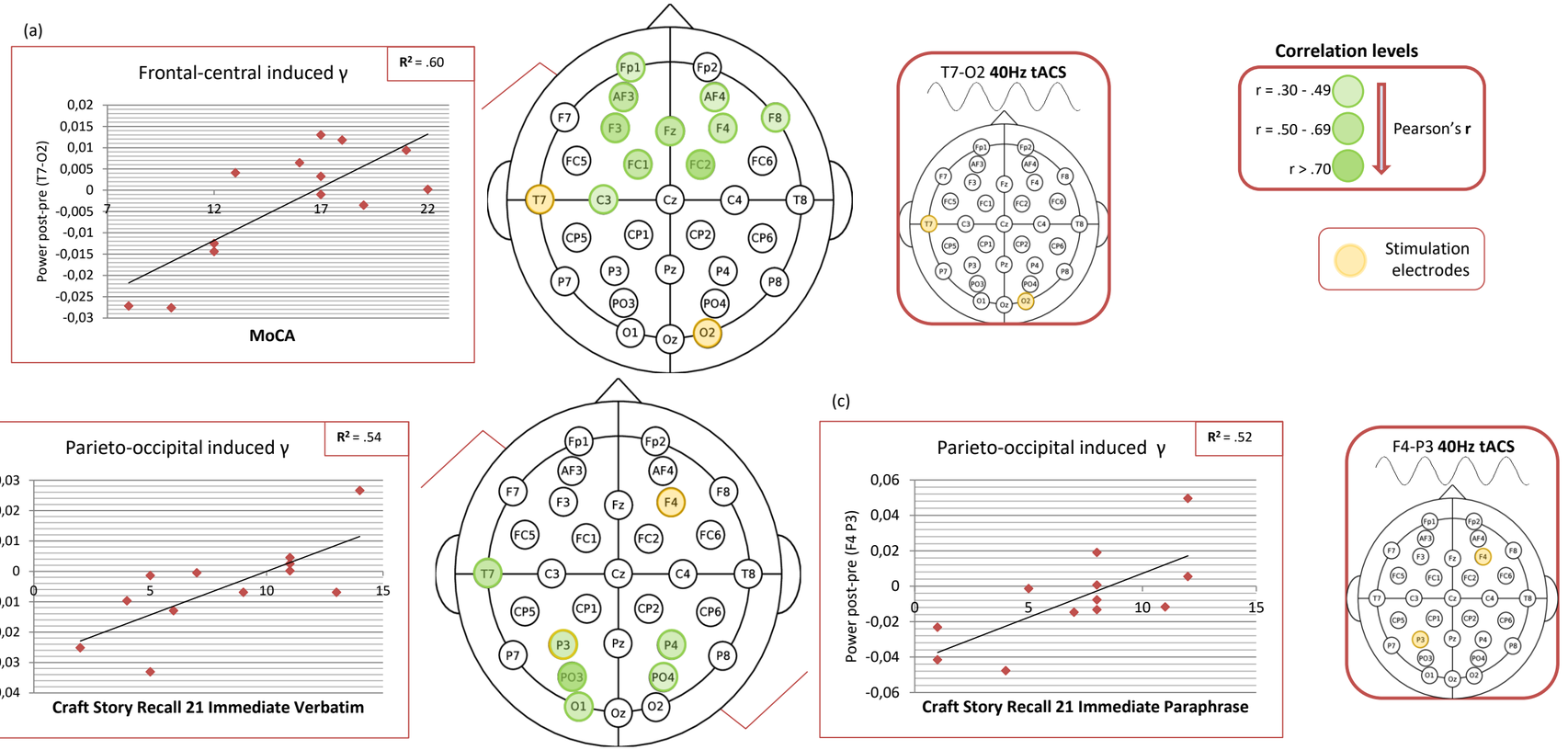

Results. Positive correlation between 40Hz-induced fronto-central γ power and MoCA (a); positive correlation between 40Hz-induced parieto-occipital γ power and Craft Story Recall Immediate Verbatim (b) and Craft Story Recall Immediate Paraphrase (c) (*ps* < .0125)

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