



Personalized Gamma Center Frequency Derived from Natural Conversation Enhances Neural Entrainment Beyond Fixed 40 Hz Stimulation

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Personalized conversation gamma frequency (CGF) successfully captures task-embedded, endogenous network dynamics under active cognitive load. It achieves significantly stronger neural entrainment, broader cortical network synchronization, and enhanced cross-frequency coupling compared to conventional fixed 40 Hz protocols.

Introduction

Gamma-band (40 Hz) sensory stimulation has emerged as a promising non-invasive intervention to modulate neural circuits and mitigate connectivity impairments implicated in Alzheimer's disease (AD). Traditional protocols uniformly apply a fixed 40 Hz stimulation across all individuals, assuming uniform gamma dynamics and overlooking critical inter-individual neural variability. However, endogenous gamma oscillations vary substantially across individuals and are strongly shaped by active cognitive and task engagement. This study introduces Conversation Gamma Frequency (CGF), a personalized, task-informed digital biomarker estimated during naturalistic verbal interaction involving linguistic, cognitive, and social processing. We hypothesized that CGF would better capture functionally relevant network dynamics and optimize neuromodulation targets compared to either fixed 40 Hz or a passive sensory-driven individual gamma frequency (IGF).

Methods

Participants: 48 cognitively unimpaired adults (27 females, 21 males; age range: 21–70 years; mean age: 43.0 ± 19.1 years) participated in a within-subject crossover design.

Experiment 1 (Estimation): 64-channel EEG was recorded continuously during resting state, reading aloud (5 min), and a semi-structured autobiographical conversation task (10 min). CGF was defined as the dominant gamma peak slope within 30–50 Hz during conversational engagement. Separately, IGF was derived from envelope-following responses (EFR) to 300 auditory click trains (30–50 Hz) representing bottom-up sensory resonance.

Experiment 2 (Entrainment): Participants received 3-minute blocks of synchronous audiovisual stimulation (10 kHz square-wave auditory clicks at 68 dB and white light flicker) tuned to three randomized conditions: fixed 40 Hz, personalized CGF, and sensory IGF.

Analysis: Neural metrics included power spectral density (PSD) ratios, source-level projection (Desikan-Killiany Atlas via MNE-Python), functional coherence among 68 regions of interest, and phase-amplitude coupling (PAC) quantified by the Modulation Index (MI).

Results

• **CGF Characteristics:** Gamma peak frequencies significantly deviated from 40 Hz across most cortical regions ($p < 0.01$), yielding a mean CGF of 36.7 ± 4.6 Hz and a mean IGF of 38.0 ± 5.7 Hz. The conversation task elicited significantly higher gamma spectral power in the temporal cortex and overall average compared to reading aloud ($p < 0.05$).

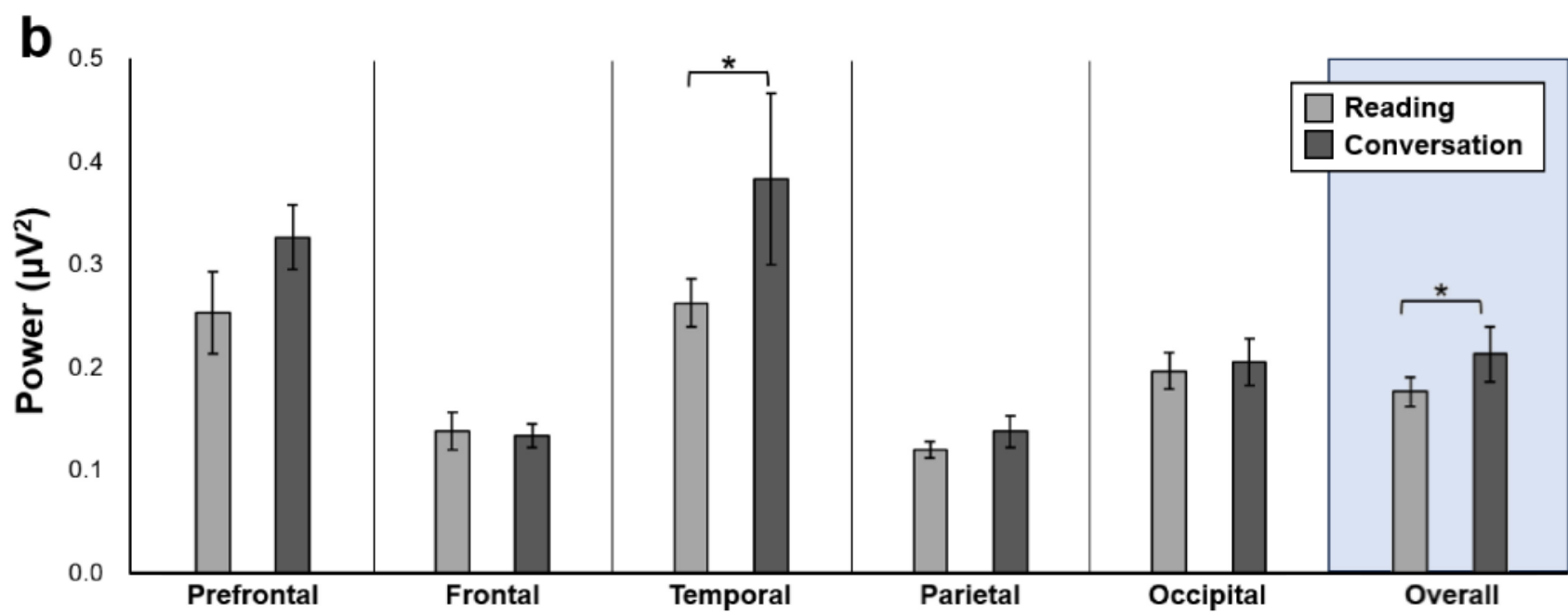


Figure 1. Regional differences in gamma spectral power between reading and conversation tasks

Results

- **PSD Entrainment:** Repeated measures ANOVA revealed significant regional variations across stimulation conditions: Prefrontal (PF: $F=4.50$, $p=0.014$), Temporal ($F=5.88$, $p=0.004$), and Occipital ($F=3.95$, $p=0.022$). CGF elicited significantly higher normalized PSD ratios in the PF cortex (1.75 ± 0.12) and occipital cortex (1.44) compared to fixed 40 Hz (PF: 1.58, Occipital: 1.32; $p < 0.05$). In the temporal cortex, both CGF (1.58) and IGF (1.55) significantly outperformed 40 Hz (1.44; $p < 0.05$).
- **Source-Level Connectivity:** Source mapping showed that CGF successfully engaged 49 out of 68 brain regions compared to 40 Hz (27/68) and IGF (13/68), showing the strongest activation in frontal and temporal networks ($p < 0.001$). CGF achieved the highest global coherence (0.381) compared to IGF (0.374) and 40 Hz (0.369), significantly enhancing interhemispheric and fronto-posterior connectivity.
- **Cross-Frequency Interactions:** Theta-gamma coupling (TGC) analysis demonstrated that CGF significantly enhanced phase-amplitude coupling over 40 Hz within the low-theta phase (3–5 Hz) and mid-gamma amplitude (32–42 Hz) bands. Furthermore, absolute frequency mismatches between CGF and 40 Hz negatively correlated with temporal cortex entrainment ($r = -0.39$, $p < 0.01$), proving that fixed 40 Hz protocols provide suboptimal entrainment for individuals with large intrinsic deviations.

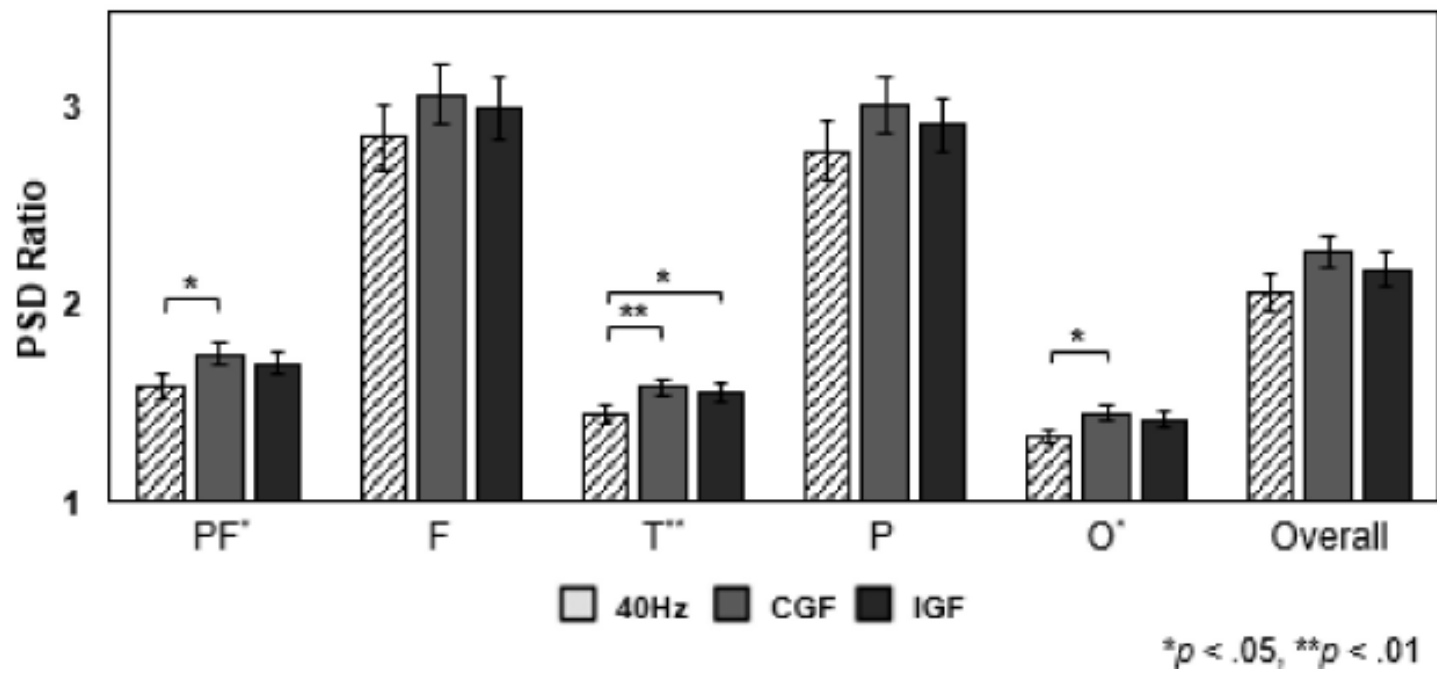


Figure 2. Power spectral density (PSD) ratio comparisons across stimulation conditions.

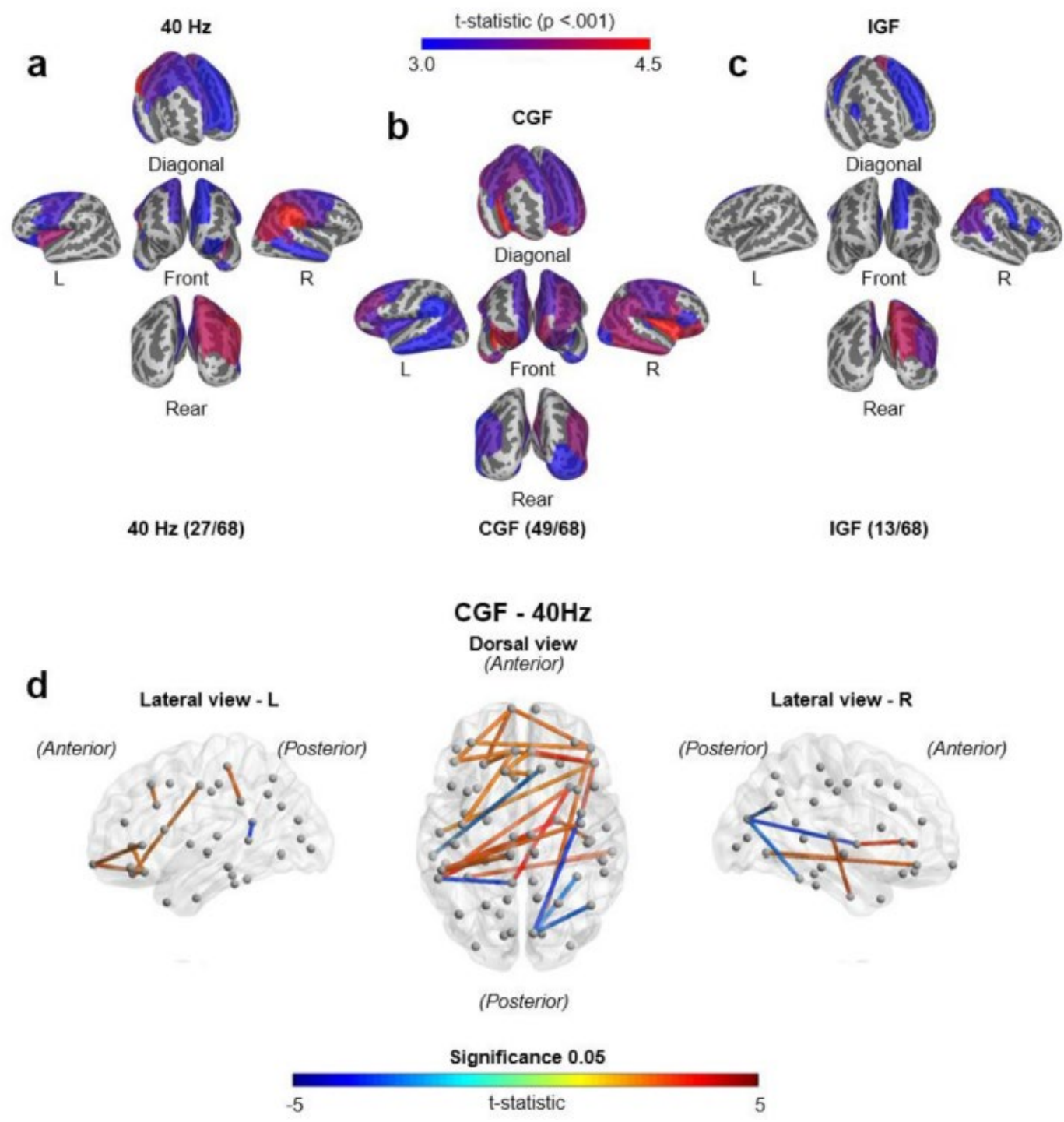


Figure 3. Brain activation and source-level connectivity comparisons across gamma stimulation conditions

Conclusion

Gamma oscillations relevant to high-order cognitive processing are most effectively captured during active, naturalistic tasks like conversation rather than passive sensory or resting states. CGF represents a novel, task-embedded personalized digital biomarker reflecting endogenous neural coordination and network alignment. Personalizing stimulation frequency based on CGF optimizes large-scale cortical synchronization, global functional connectivity, and theta-gamma cross-frequency coupling, significantly outperforming uniform 40 Hz selection. This framework offers a rigorous translational foundation for early, non-pharmacological interventions in preclinical Alzheimer's disease where network dysregulation precedes clinical cognitive decline

References

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