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Alpha sensory entrainment modulations of brain oscillations and visual detection in hemianopic patients

Theoretical Background

Brain electrophysiological activity is characterized by rhythmic fluctuations. Among all spontaneous brain rhythms, neural oscillations in the frequency range of alpha (~7–13 Hz) are consistently linked to various aspects of visual processing and represent a reliable hallmark of the functionality of posterior brain areas, and hence of the visual system[1]. Variations in alpha activity, accompanied by changes in visual performance, are typically observed under different task demands, suggesting that alpha-band activity relies on dynamic processes that can be externally modulated to shape visual perception[2]. In this perspective, converging research showed that applying a rhythmical external force (e.g., sensory stimulation) at an alpha-band frequency induces a synchronization of ongoing alpha and perceptual activity, a mechanism known as neural entrainment[2]. Namely, trains (~2 seconds) of alpha-band sensory entrainments induce transient enhancements in task-related alpha activity (e.g., power increase and frequency shift) in posterior areas contralateral to the stimulation and in visual performance, that outlast the entrainment offset for several alpha cycles (~350 ms)[3-5], suggesting that sensory stimulations effectively promote resonance phenomena in the underlying oscillating networks in healthy participants. In addition, prolonged trains (~1 minute) of alpha entrainment were shown to induce also long-lasting modulations (>1 minute) on alpha parameters (i.e., power increase) at rest[6], suggesting effectiveness of entrainment in inducing long-term modulations of resting oscillatory activity.
These promising results are of great relevance within the context of possible clinical applications of sensory stimulations, based on well-documented reports of impaired alpha parameters in patients with posterior brain lesions. Indeed, a residual but dysfunctional alpha activity, at rest[7] and during task[8], was consistently documented in brain-damaged patients with visual field defects (hemianopia), characterized by a slower individual alpha frequency and reduced alpha power[7]. Noteworthy, these altered alpha parameters predict impaired visual performance in the blind field[7], suggesting that alpha dynamics can represent a valuable biomarker of postlesional functional and structural integrity of the visual system.

Aims and Hypotheses

Since hemianopics show altered alpha parameters associated to their visual defects, both at rest and during visual tasks, we can hypothesize that they may substantially benefit from alpha-band sensory entrainment in modulating impaired alpha activity. Indeed, alpha-band sensory entrainment may effectively act on their alpha dynamics, inducing a synchronization of the residual alpha to the sensory rhythmic stimulation. In this perspective, sensory (e.g. audio-visual) entrainment administered at their Individual Alpha Frequency (IAF) in their blind field should induce an increase of alpha power in the contralateral lesioned hemisphere, while entrainment administered at IAF+1Hz should speed-up their alpha frequency. This will result in an improvement of temporal structuring within this frequency band, with related beneficial effects on alpha parameters and increasing in visual performance in the blind field.

Methods

Participants
Patients (N=35; age: 18-80 years) with acquired cerebrovascular damage to posterior brain areas (i.e., occipital cortex and/or optic radiations) and documented visual field defects will participate to the

study. Patients' selection will be based on available neuroradiological reports and neuropsychological assessments of visual functions. History of psychiatric disorders or cognitive deterioration represent exclusion criteria.
Sample size was calculated using Gpower 3.1.9.6, based on effect sizes observed in previous similar studies[4-6] (Cohen $f = 0.55$). To investigate the effect of interest with a power of 80% at the 5% level of significance, for a within subject design (1 within factor, 3 levels), a sample of 34 participants is required.

Tools

- Neuropsychological standardized tests to assess visual functions
- Computerized visual detection tasks
- Electroencephalography (EEG) recording (ActiCHamp Plus, Brain Products)
- Eye movements recoding (ASL 6000 eye tracker)

Procedure

Patients will undergo two separate sessions (EXP) in separate days (~2 hours/each).
EXP1: Hemianopics will be asked to rest, with their eyes closed and EEG signal during resting-state will be recorded in multiple experimental blocks (1 minute each) before and after entrainment stimulations. Entrainment consists in sensory audio-visual rhythmic sequences of stimuli (duration: ~1 minute) administered at various frequencies within the alpha range (i.e., IAF and IAF+1Hz) and, as a control, at an arhythmic frequency in their blind visual field (9 repetitions per condition). During presentation of the entrainment, patients will maintain their gaze on a central fixation and eye movements will be monitored with eye-tracking.
EXP2: Hemianopics will perform a visual detection task of visual targets (Gabor patches) presented to the blind field. Each target will follow the administration of trains of audio-visual entrainments (see above; duration: ~2 seconds), at various frequency (IAF, IAF+1Hz and arhythmic; 200 trials per condition). EEG signal and eye movements will be recorded throughout the entire task.

Statistical analyses

EXP1: The resting-state oscillatory activity will be analyzed in terms of alpha power and frequency and alpha parameters before and after the entrainment will be compared, as a function of the entrainment administered, with repeated measures ANOVAs.
EXP2: Task-related EEG signal will be analyzed as in EXP1. Visual performance will be assessed via Signal Detection Theory[9], in terms of perceptual sensitivity and willingness to response with repeated measures ANOVAs.

Declaration of commitment to request ethical approval

Formal request for the ethical approval has been already submitted to the Committee.

Expected results and implications

In EXP1, enhancements in alpha power (following IAF stimulation) and speeding up of the IAF (exclusively after IAF+1Hz stimulation) are expected in the post-, relative to the pre-entrainment EEG resting activity. No change is expected in alpha activity after the control arythmic stimulation.
In EXP2, task-related alpha activity is expected to be modulated as mentioned in EXP1. Moreover, an increase in terms of perceptual sensitivity, especially after IAF+1Hz condition, linked to entrainment-induced enhancements in task-related alpha activity, is expected.
Overall, the demonstration that residual alpha activity in hemianopics retains susceptibility to plastic changes, both at rest and during visual task, would represent an important precondition to adopt rehabilitative protocols based on alpha-band sensory entrainment.

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Plan of activities

The candidate will review the literature on the topic and validate the procedure, piloting the experimental design. The candidate will also select patients participating to the study, based on available neuroimaging documentation and neuropsychological assessment. Moreover, she/he will perform data collection, EEG and behavioral data processing and statistical analyses. The results will be presented at scientific national/international conferences. Finally, the candidate will draft a scientific manuscript on the findings. Trainings to increase technical skills on EEG analyses will be provided, through participation to selected workshops.

The supervisor will schedule weekly project meetings to monitor the progress and to discuss possible issues.

Timeline:

Months 1-2: Validation and piloting of the experimental design, participants' selection and recruitment.

Months 2-10: Data collection, EEG and behavioral data processing.

Months 7-10: Statistical analyses.

Months 10-12: Manuscript preparation and presentation at conferences.

Feasibility of the project

The equipment and software (EEG system, Eye-tracking, Neuropsychological standardized tests) required for the project are available at the Center for Studies and Research in Cognitive Neuroscience (CNC). Participants will be recruited among the patients admitted to the CNC for clinical assessments and rehabilitation. In case of methodological issues with the entrainment paradigm, expert advice will be provided by the collaborators to the project (Prof. Luca Ronconi – San Raffaele).