Paired Associative Stimulation for visual cortical plasticity: timing-dependency and hemispheric lateralization

Francesca Crespi[1,2], Giacomo Guidali[2], Eleonora Arrigoni[2] & Nadia Bolognini[2,3]

1) Ph.D. Program in Neuroscience, School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy
2) Department of Psychology, University of Milano-Bicocca, Milan, Italy
3) Neuropsychological Laboratory, IRCSS Istituto Auxologico Italiano, Milan, Italy

1) Background & Aim

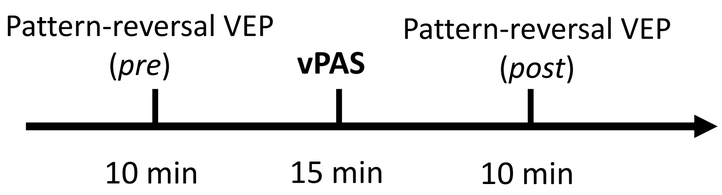
Paired associative stimulation (PAS), a non-invasive brain stimulation protocol based on time-locked cortical stimulation via transcranial magnetic (TMS) and peripheral stimulations (1,2), can affect cortical excitability and induce Hebbian associative plasticity. To date, only one study has investigated the effects of a PAS protocol targeting the primary visual cortex (V1), consisting in the repeated pairings of TMS pulses over V1 and visual stimuli, the last consisting in a black-and-white checkboard with contrast-reversing (v-PAS, 3), showing its effectiveness in modulating visual-evoked potentials (VEPs).

Starting from this premise and looking for a clinical translation of this protocol, this study **aims** to further explore the potential effectiveness of the v-PAS, testing three different inter-stimulus intervals (ISIs) between paired stimulations and assessing the hemispheric specificity of the induced modulations

2) Methods

2.1 Experimental procedure

25 healthy subjects tested (7 M)

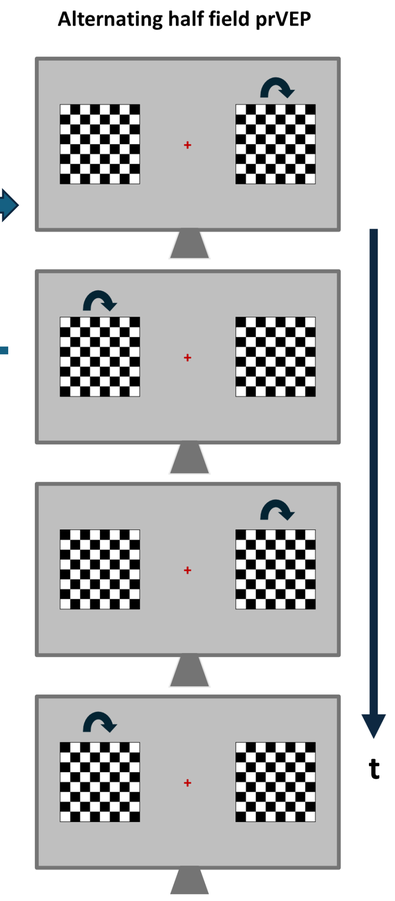


2.2 VEP assessment

Pre and Post vPAS:
- **200** right-lateralized
- **200** left-lateralized

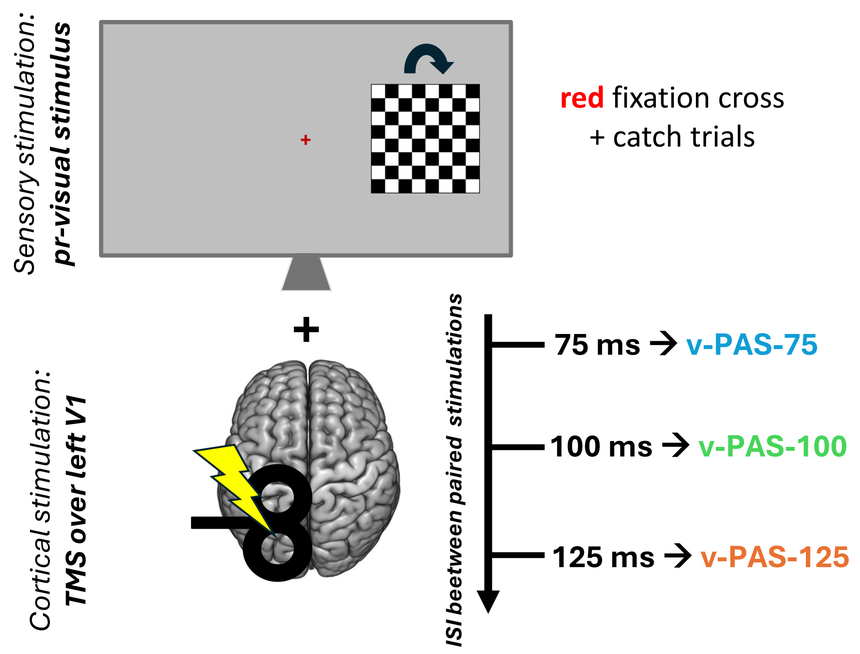
alternating black-and-white checkboards with contrast reversing

EEG recorded from 60 channels



2.3 v-PAS

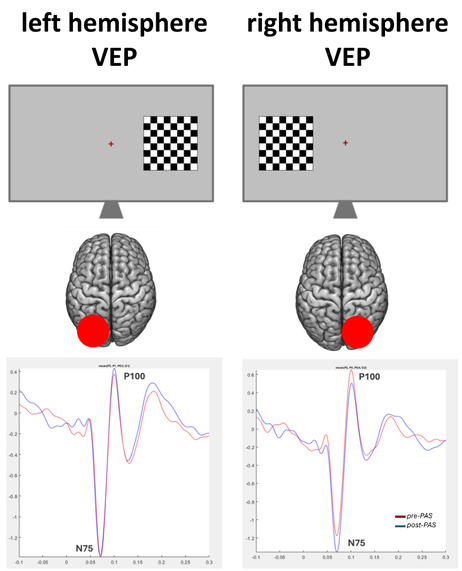
- **Peripheral visual stimulus**: black-and-white checkboard with contrast-reversing every 5 s presented in the right VF
- **Cortical stimulus**: TMS pulses over left V1 @ 120% rMT
- **180 paired pulses @ 0.2 Hz** (duration: 15 min)



2.4 Data extraction

- Clusters for component extraction:
  - P3, P1, PO3, O1 for left VEP
  - P2, P4, PO4, O2 for right VEP
- VEP components extracted and analyzed:
  - **N75** (amplitude and latency)
  - **P100** (amplitude and latency)

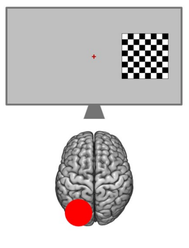
Additional analyses:
- Spearman correlation between PAS effect (i.e, $\Delta amplitude_{post-pre}$) and baseline VEP component amplitude
- N75 inter-hemispheric transfer time (**IHTT,** i.e., delta post – pre VEP component's latency)



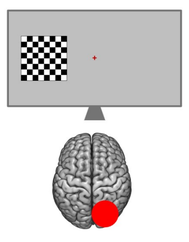
3) Results

3.1 VEP amplitude (N75 and P100)

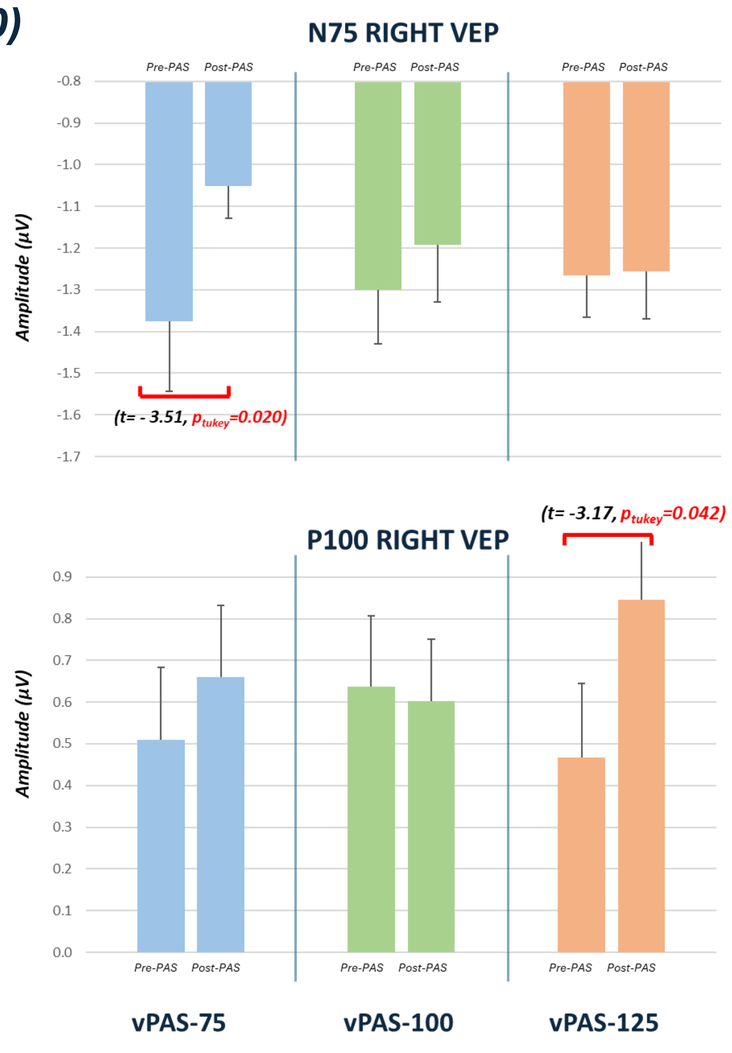
v-PAS effects on VEPs amplitudes (N75, P100) were assessed through a series of 3 'Condition' *(vPAS-75, vPAS-100, vPAS-125)* X 2 'Time' *(pre-PAS, post-PAS)* rmANOVA. Post-hoc comparisons corrected with Tukey HSD



For ***left hemisphere VEP***:
- **N75**: 3 X 2 interaction: $F_{2,48}$ = 0.594, p = 0.556, η_p^2 = 0.024
- **P100**: 3 X 2 interaction: $F_{2,48}$ = 0.833, p = 0.441, η_p^2 = 0.034



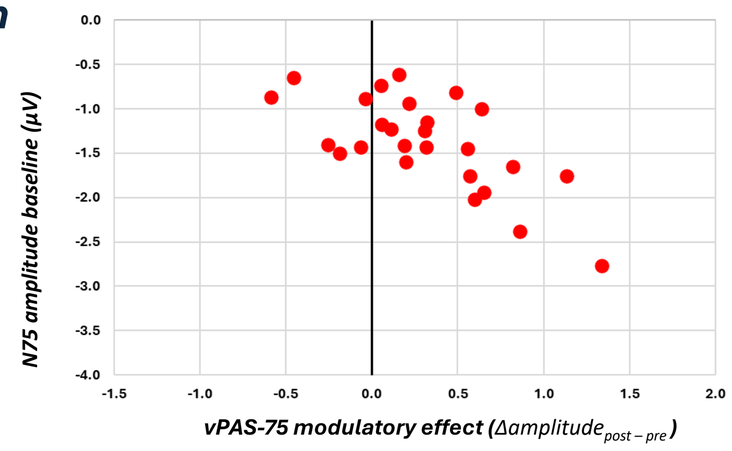
For ***right hemisphere VEP***:
- **N75**: 3 X 2 interaction: $F_{2,48}$ = 4.501, **p = .016**, η_p^2 = .158
- **P100**: 3 X 2 interaction: $F_{2,48}$ = 4.517, **p = .016**, η_p^2 = .158



3.2 Correlation

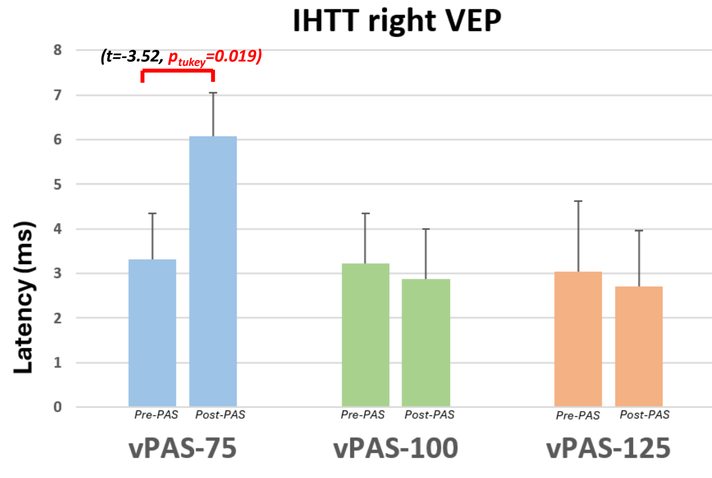
N75 $\Delta amplitude_{post-pre}$ (i.e., PAS effect) correlates **negatively** with its baseline amplitude **(**rho = -.679, **p < .001)**

n.s. for the other conditions and others VEP components



3.3 Inter-hemispheric transfer time (IHTT)

rmANOVA: 3 'Condition' *(vPAS-75, vPAS-100, vPAS-125)* X 2 'Time' *(pre-PAS, post-PAS)*
→ $F_{2,48}$ = 3.7, **p = .031**, η_p^2 = .13



4) Conclusion & Discussion

Significant modulation effects emerged only for **VEPs recorded from the visual cortex not stimulated during the vPAS** (i.e., right hemisphere VEP). Following **vPAS-75, the N75 amplitude was reduced and its IHTT significantly increased**, indicating longer inter-hemispheric time for signal propagation from the right to the left visual cortex. The **magnitude of vPAS-75 modulations correlated with N75 baseline amplitude:** the greater the amplitude of N75 at baseline, the more substantial is the inhibitory effects. In contrast, **vPAS-125 selectively enhanced the P100 amplitude,** while **vPAS-100 did not modulate either component**.
These results confirm that associative plasticity can be induced in the visual cortex through vPAS, with time- and hemisphere-specific effects. Importantly, vPAS plastic modulations are induced at the interhemispheric level, influencing the reactivity of the contralateral V1, not directly stimulated during vPAS.

f.crespi5@campus.unimib.it

References

1) Guidali, G., Roncoroni, C., & Bolognini, N. (2021). Paired associative stimulations: Novel tools for interacting with sensory and motor cortical plasticity. Behav Brain Res, 414, 113484.
2) Stefan, K., Kunesch, E., Cohen, L. G., Benecke, R., & Classen, J. (2000). Induction of plasticity in the human motor cortex by paired associative stimulation. Brain, 123 Pt 3, 572–584.
3) Ranieri, F., Coppola, G., Musumeci, G., Capone, F., Di Pino, G., Parisi, V., & Di Lazzaro, V. (2019). Evidence for associative plasticity in the human visual cortex. Brain Stimulation, 12(3), 705–713.