HEBBIAN ASSOCIATIVE PLASTICITY DRIVES THE EMERGENCE OF MOTOR RESONANCE:

a novel Paired Associative Stimulation protocol

Guidali Giacomo[1,2], Carneiro S. I. Maíra[1] & Bolognini Nadia[1,3]

[1] Department of Psychology, University of Milano-Bicocca & Milan Center for Neuroscience – NeuroMI, Milan, Italy.
[2] PhD program in Neuroscience, School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy.
[3] Laboratory of Neuropsychology, IRCCS Istituto Auxologico Italiano, Milan, Italy.

1 – BACKGROUND

The human brain is endowed with an action-observation network, the **Mirror Neuron System (MNS)** which implements a 'mirror' mechanism matching sensory and motor representations of actions. Even if the anatomo-functional properties of this network are been widely investigated, less is know about the plasticity mechanisms that rule mirror neurons and shape visuo-motor associations. One of the hypothesis put forward suggest that **mirror neurons develop their characteristics as a result of experience** and, in details, **Hebbian learning and Hebbian associative plasticity have been hypothesized as the neurophysiological substrate[1]**.

2 – AIM

Trying to deepen the nature of the plasticity mechanisms that rule the MNS, we test whether **atypical visuo-motor associations can be induced in the human MNS by directly targeting Hebbian associative plasticity using an ad-hoc developed non-invasive Paired Associative Stimulation (PAS) protocol[2]**, in turn re-shaping the resonance mechanisms of the human MNS.

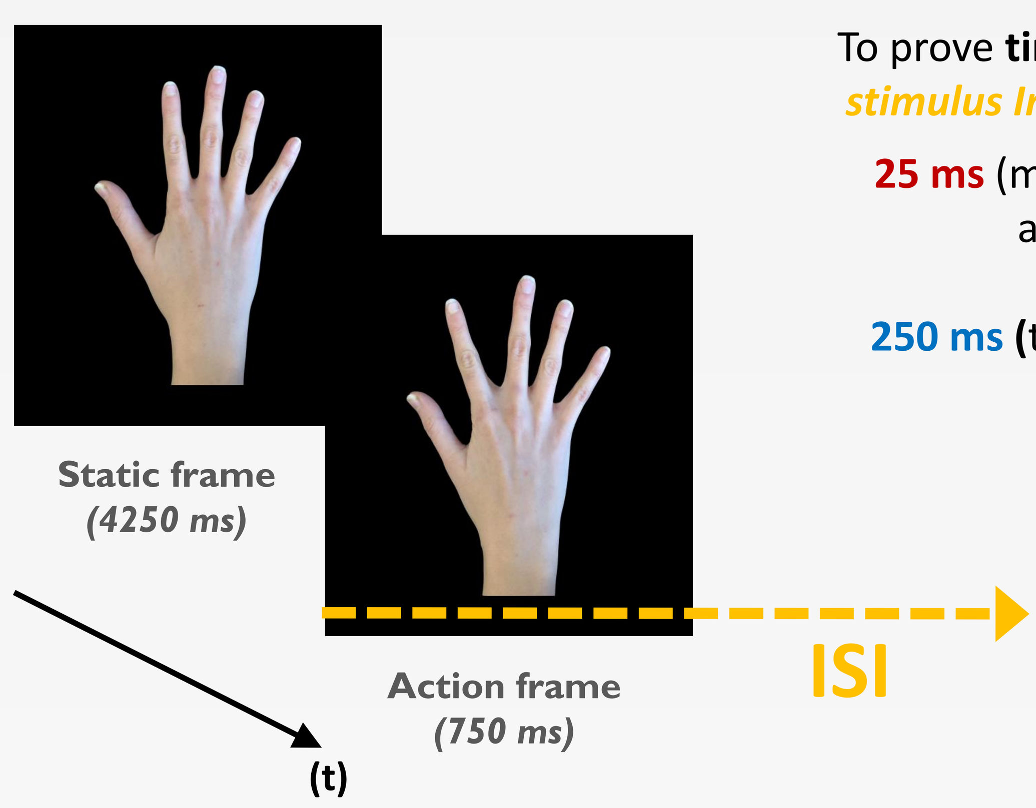
3 – METHODS and MATERIALS

3.1 mirror PAS (m-PAS)

The m-PAS repeatedly paired *(a)* **TMS pulses over the right primary motor cortex** with *(b)* **visual stimuli depicting a right-hand index finger abduction movement**

!! *unilateral movements are not associated to motor resonance in the ipsilateral hemisphere[3]*

Visual stimulus of movement + **TMS pulse (over right M1)**



To prove **timing-dependency** of the m-PAS, *Inter-stimulus Interval (ISI)* from onset 'action frame':

25 ms (mimic the reafferent M1 activation by action execution – m-PAS$_{25ms}$)

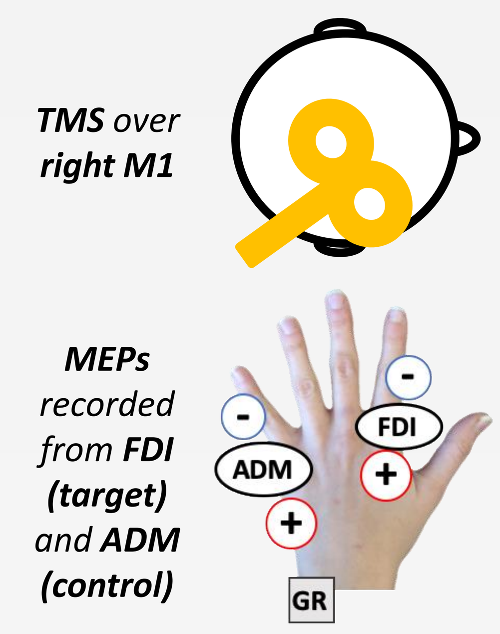
or

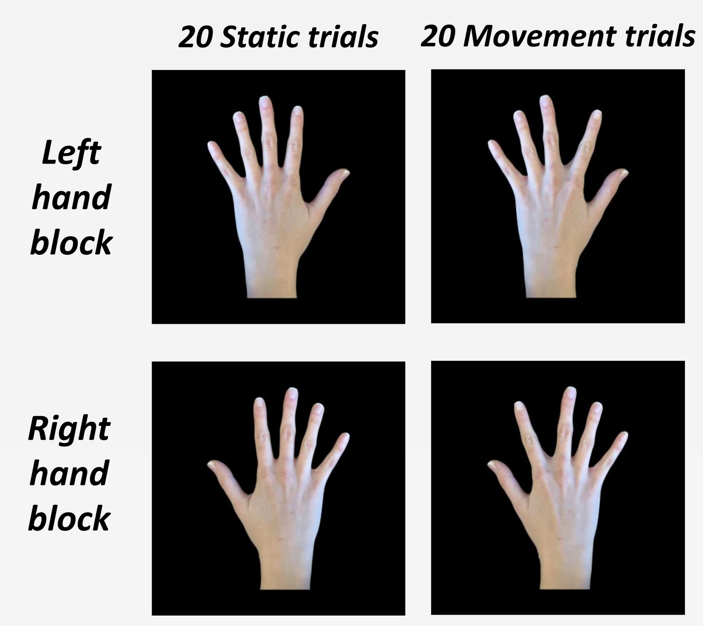
250 ms (time course of M1 activation by MNS recruitment – m-PAS$_{250ms}$)

180 paired stimulations (TMS @ 120% rMT) **at 0.2 Hz** (duration: 15 minutes)

3.2 Action observation task

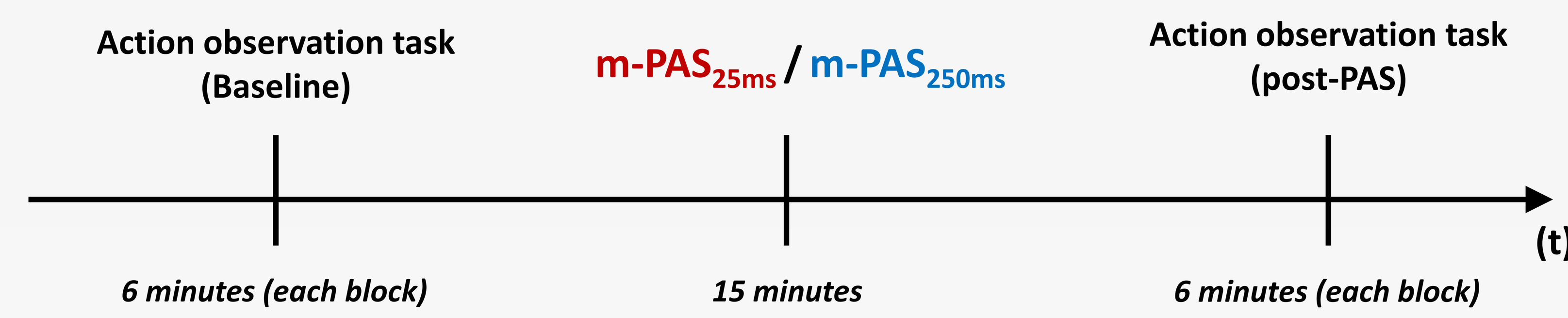
Motor resonance (i.e., effects of m-PAS) was assessed using a standard **action observation task[4]** divided in two blocks according to the side of the observed hand (left hand or right hand)





3.3 Experimental procedure

20 healthy participants tested in a two sessions within-subjects experiment

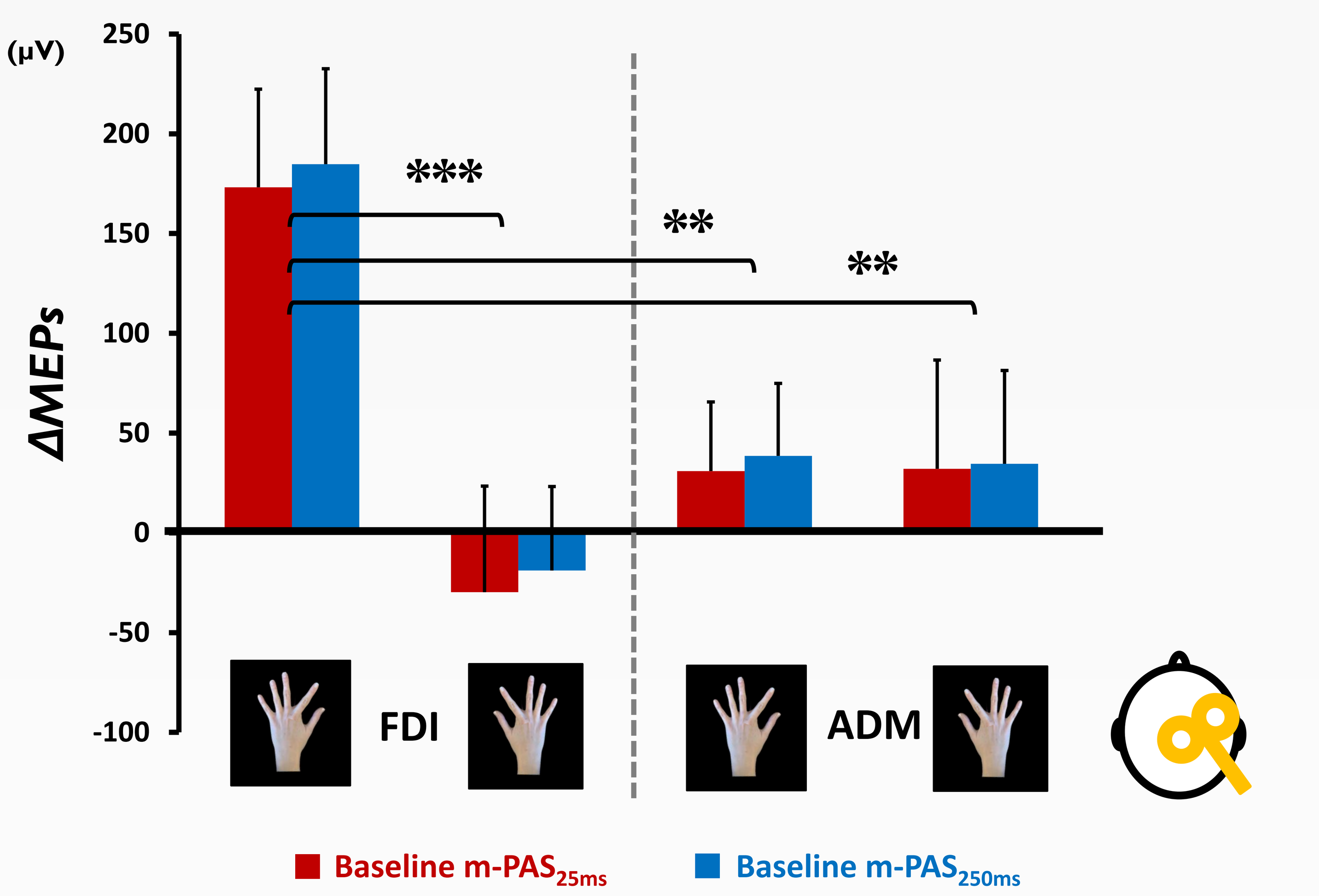


4 - RESULTS

* p < 0.05 ** p < 0.01 *** p < 0.001 *(Bonferroni corrected)*

4.1 Motor resonance before m-PAS

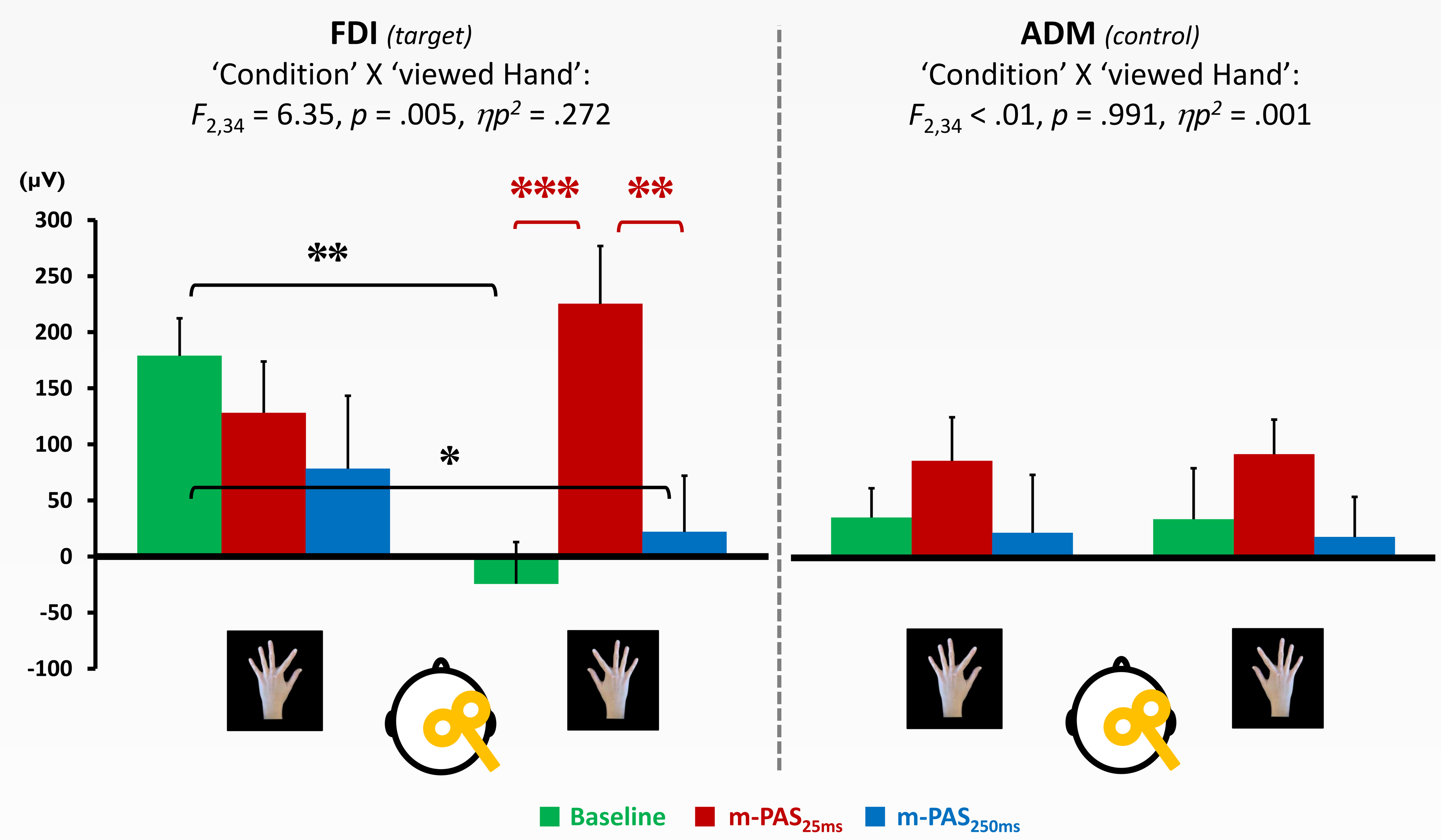
Preliminary, a rmANOVA was conducted to test whether **typical motor resonance phenomena is recorded before the administration of the m-PAS protocols.** A significant 'viewed hand' X 'muscle' interaction is found ($F_{1,17}$ = 22.148, p < .001, ηp^2 = .566)



MEPs facilitation in baseline only **during the observation of left hands** (ipsilateral to TMS) and only **in the muscle involved in the observed movement** (FDI)

4.2 Effects of m-PAS

m-PAS effects were assessed through a 2 "Muscle" X 3 "Condition" X 2 "viewed Hand" rm-ANOVA. A significant triple interaction was found ($F_{2,34}$ = 4.31, p = .021, ηp^2 = .202) and it was further investigate in separate rmANOVAs for each muscle.



5 - CONCLUSIONS

The results of the present study show the efficacy of the m-PAS protocol, documenting that **it is possible to promote novel visuo-motor associations in the human MNS through the induction of plastic mechanisms that rely on Hebbian associative plasticity[1]**. Hebbian learning driven by the m-PAS is therefore a bottom-up, plastic process that starts with the **induction of associative plasticity only if we are exposed to visuo-motor association dealing with the time course of action execution** (25 ms), rather than that of its visual input (250 ms)[4]. Further studies have to be conducted to better explore, e.g., the role of other MNS cortical areas or the nature of the biological movements depicted (e.g., goal vs. non-goal movements; possible vs. impossible movements).

6 – REFERENCES

1) Keysers, C., & Gazzola, V. (2014). Hebbian learning and predictive mirror neurons for actions, sensations and emotions. *Philosophical Transactions of the Royal Society B*, *369*, 20130175.
2) Suppa, A. et al.(2017). The associative brain at work: Evidence from paired associative stimulation studies in humans. *Clinical Neurophysiology*, *128*(11), 2140–2164.
3) Aziz-Zadeh et al. (2002). Lateralization in motor facilitation during action observation: A TMS study. *Experimental Brain Research*, *144*(1), 127–131
4) Naish, K. R. et al. (2014). Effects of action observation on corticospinal excitability: Muscle specificity, direction, and timing of the mirror response. *Neuropsychologia*, *64*, 331–348.

CORRESPONDING AUTHOR:
g.guidali@campus.unimib.it