Functional and behavioral correlates of the mirror *Paired Associative Stimulation* protocol

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1 – BACKGROUND

Hebbian associative plasticity has been implied in the formation of the association between sensory and motor representations of actions in the Mirror Neuron System (MNS)[1]. Recently, our research group developed a novel *Paired Associative Stimulation* (PAS) protocol[2] targeting the MNS: the mirror PAS (m-PAS)[3]. The m-PAS repeatedly pairs transcranial magnetic stimulation (TMS) pulse over the right primary motor cortex (M1) with visual stimuli depicting abduction movements made with the index finger of the right hand (ipsilateral to TMS cortical site). The **m-PAS successfully induced new ipsilateral motor resonance responses, indexed by an atypical facilitation of cortico-spinal excitability by the view of ipsilateral (right) hand movements** – i.e., the ones conditioned during the protocol.

2 – AIM

To deepen the functional and the behavioral correlates of the m-PAS, we run an experiment exploring:

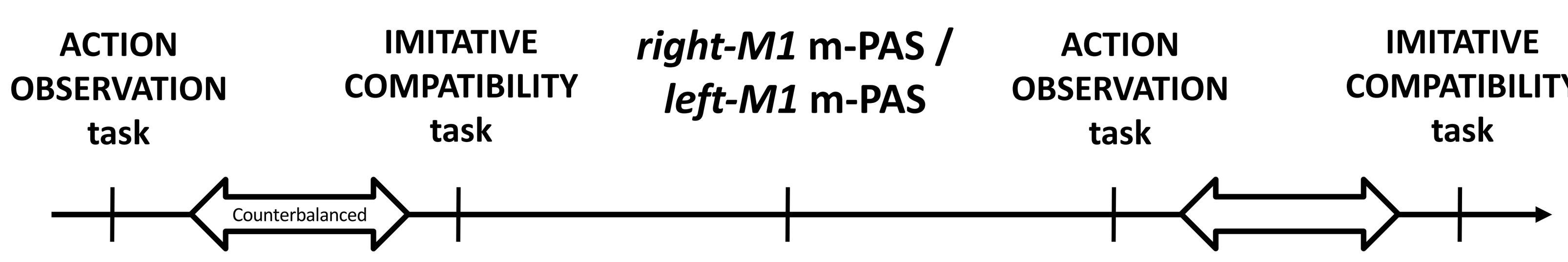
(a) its **cortical specificity**, hence modulating the site of TMS administration during the protocol (stimulating the left M1);

(b) the **possible effects on behavior**, exploiting an imitative compatibility task assessing *automatic imitation*[4].

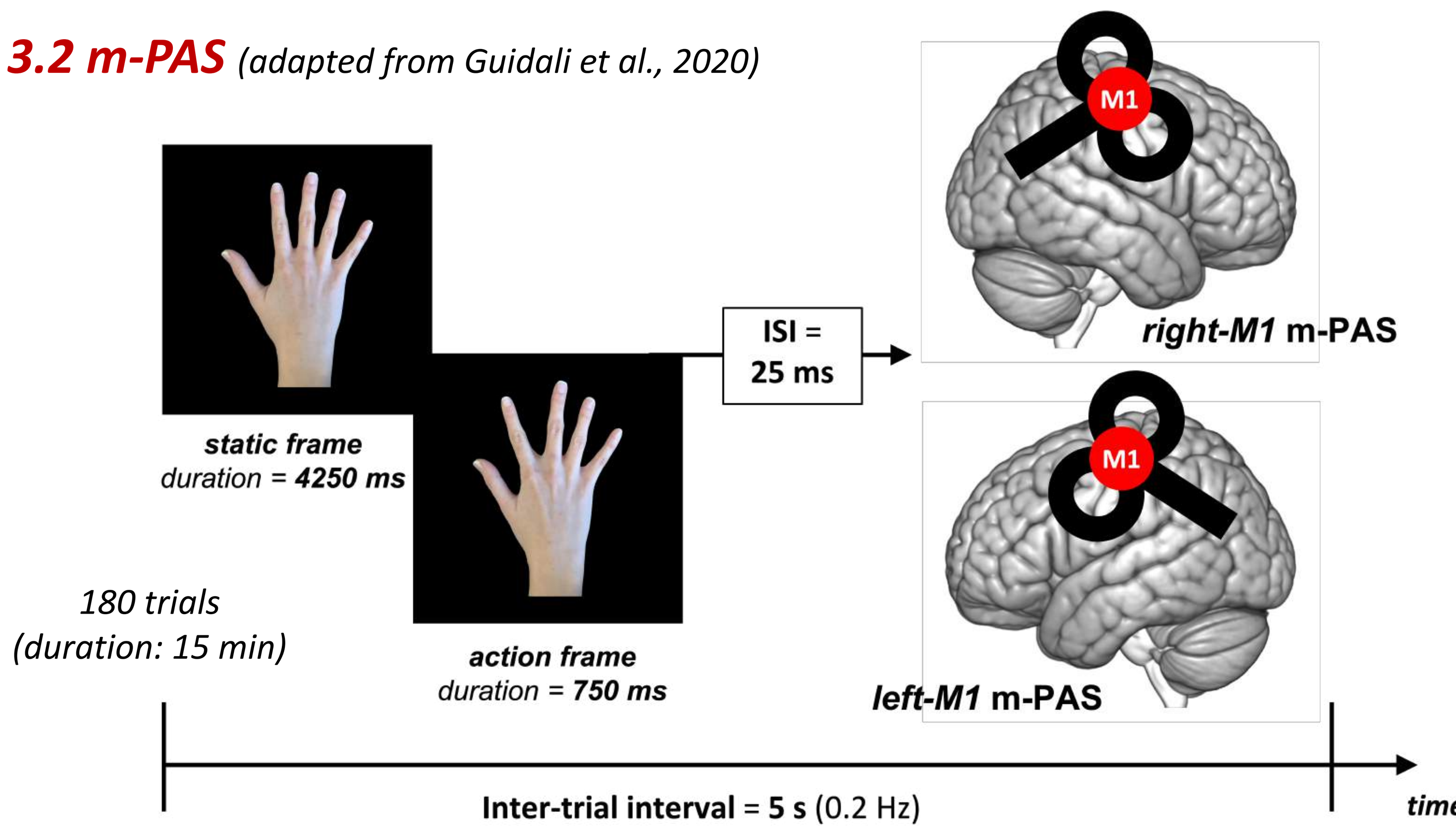
3 – METHODS and MATERIALS

3.1 Experimental procedure

- **15** participants (6 males, age ± S.D. = 25 ± 3.3 years; education ± S.D. = 16.5 ± 1.4 years), all righthanded, all naïve to experimental purpose
- **2** within-subject sessions, according to the m-PAS protocol

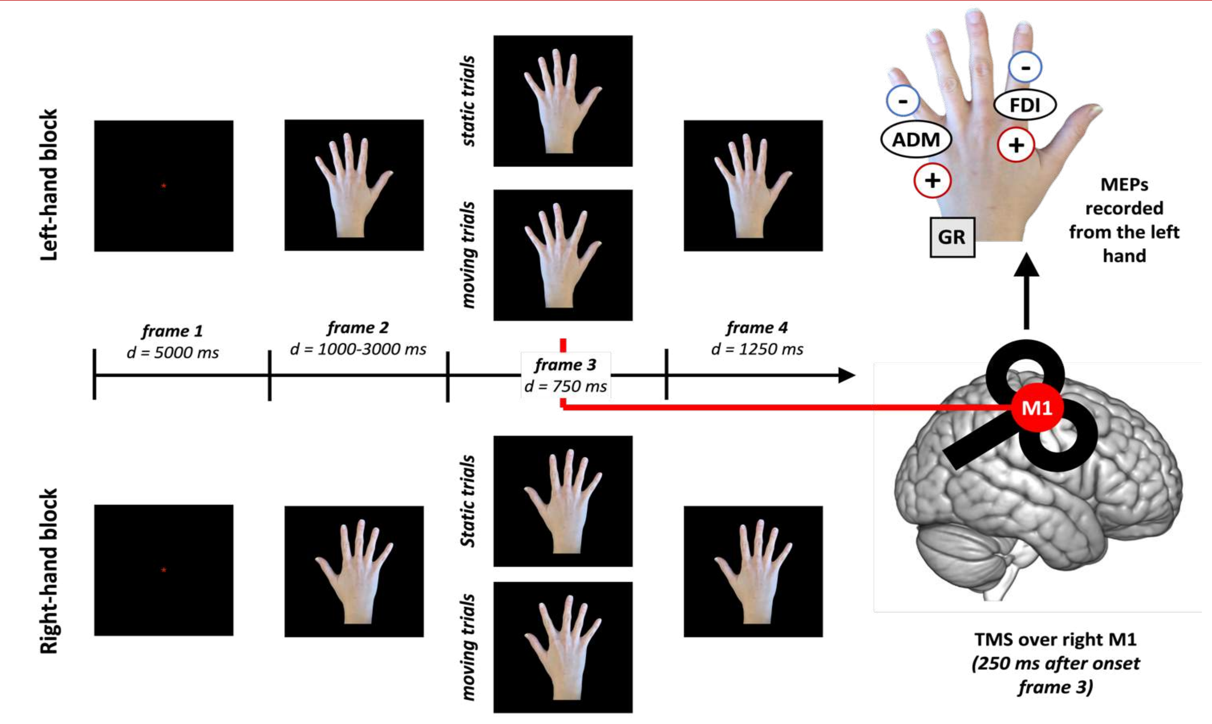


3.2 m-PAS *(adapted from Guidali et al., 2020)*



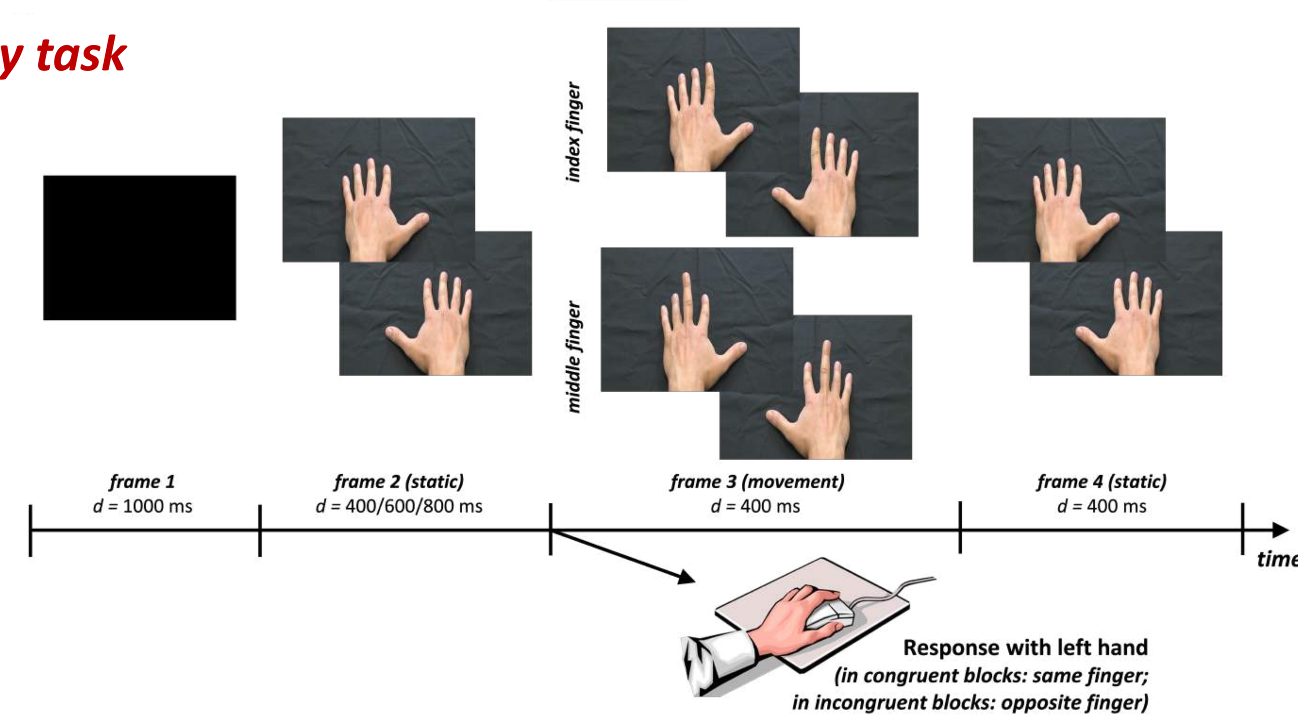
3.3 Action observation task

Motor resonance (i.e., neurophysiological effects of m-PAS) was assessed using a standard **action observation task** [3] divided in two blocks according to the side of the observed hand (left hand or right hand). Regardless of the m-PAS (right- or left-hemisphere), **TMS was always delivered over right M1.**



3.4 Imitative compatibility task

Behavioral correlates was assessed using an **imitative compatibility task** adapted from previous literature[4] with **2 blocks** according to the instruction gave to participant: ***congruent*** (to respond with the same finger observed moving on screen); ***incongruent*** (to respond with the opposite finger).



4 - RESULTS

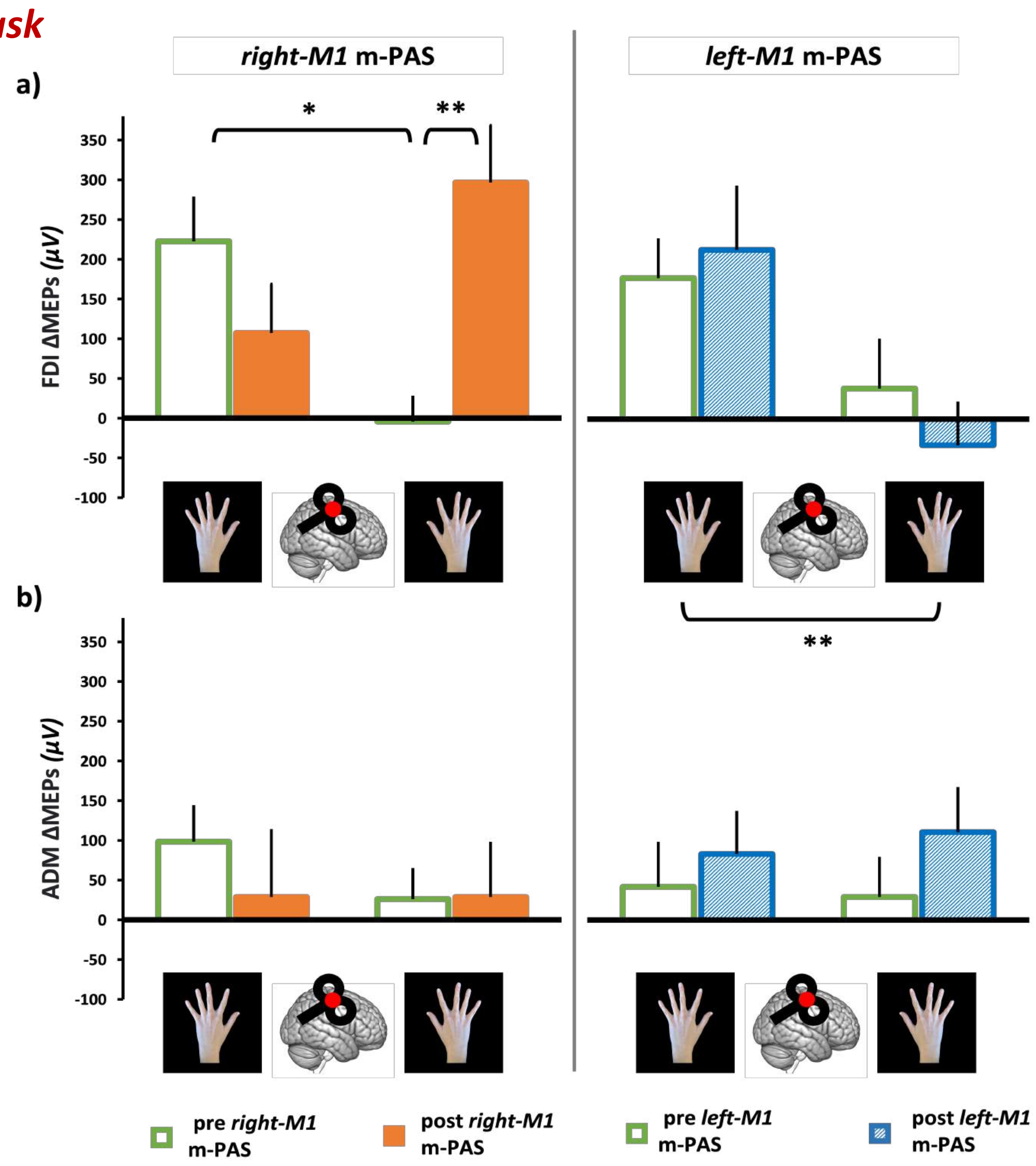
* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$ *(Bonferroni corrected)*

4.1 Action observation task

Differences in MEP amplitude between moving and static trials (MEPs) were used as index of motor resonance.

m-PAS effects were assessed through a 2 "Session" X 2 "Time" X 2 "viewed Hand" x 2 "Muscle" rm-ANOVA. A significant quadruple interaction was found ($F_{1,14}$ = 4.83, p = .045, ηp^2 = .257)

Further analyses show that only after the *right-M1* PAS, and only for FDI (target muscle), motor resonance emerges during the observation of ipsilateral (to TMS) moving stimuli, as expected from our previous study[3].

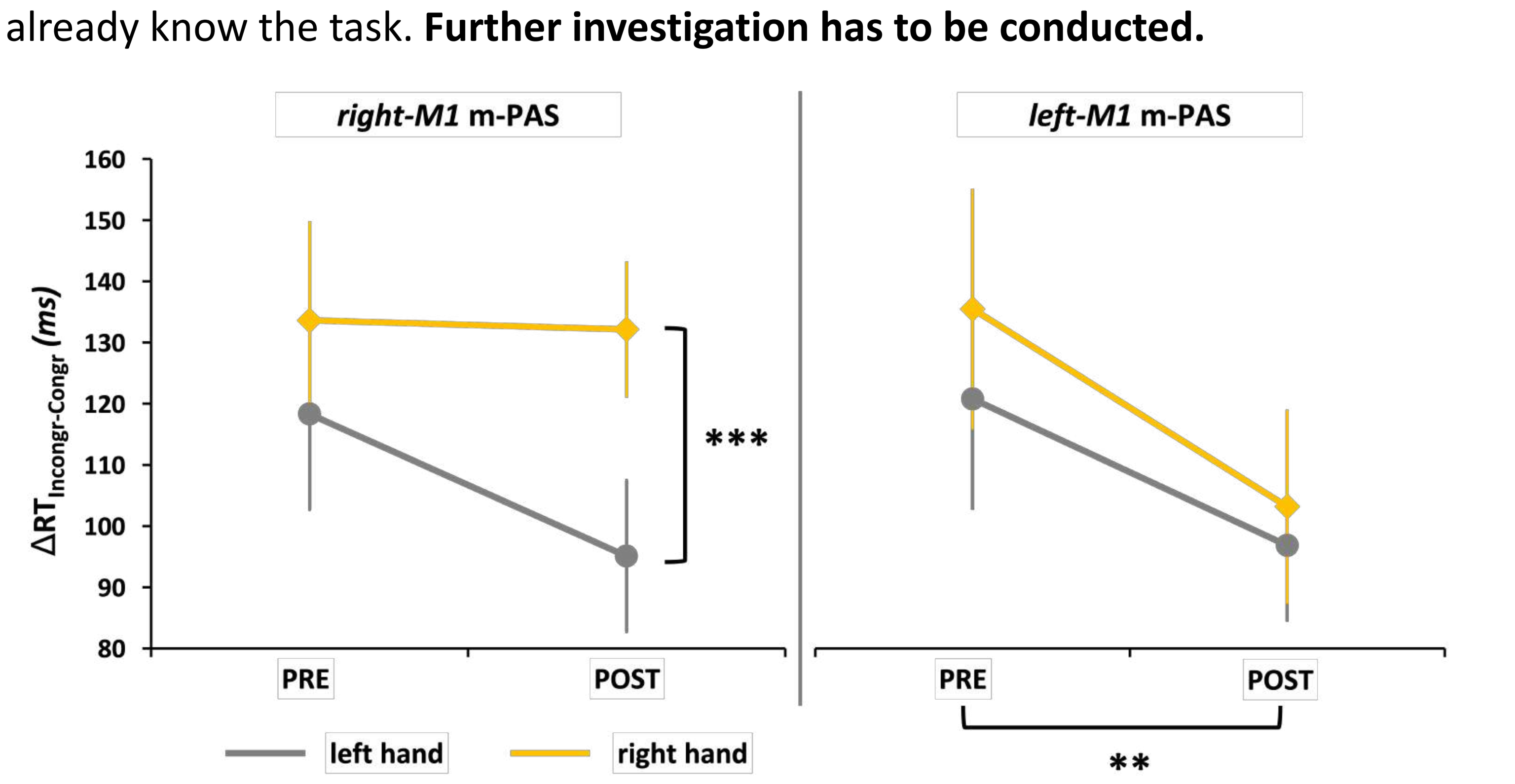


4.2 Imitative compatibility task

Differences in reaction times (RT) in incongruent and congruent trials – split according to the observed hand – were used as behavioral marker of *automatic imitation*.

m-PAS effects were assessed through a 2 "Session" X 2 "Time" X 2 "viewed Hand" rm-ANOVA. A significant triple interaction was found ($F_{1,14}$ = 6.15, p = .026, ηp^2 = .305).

Only after the *right-M1* PAS, and only during the observation of right moving hand (i.e., same hand conditioned during the m-PAS), ***automatic imitation* seems to be somehow 'blocked' while in the other conditions a fastening of RTs is always observed.** This latter evidence can be interpreted as a learning effect: namely, participants become faster in incongruent trials, which are the difficult ones, because they already know the task. **Further investigation has to be conducted.**



5 - CONCLUSIONS

Results showed the efficacy of the standard m-PAS in inducing the emergence of motor resonance for the conditioned, ipsilateral (to TMS), index-finger movement. Crucially, this effect is not present when TMS is delivered over the contralateral (to the observed movement) hemisphere. Importantly, m-PAS also affects behavior, modulating *automatic imitation* (indexed as the difference between reaction times in incongruent and congruent trials of the imitative compatibility task) selectively when a right hand is observed. **Our results corroborate the evidence that the visual-motor matching properties of the MNS can be shaped by the m-PAS protocol, suggesting possible modulations also at a behavioral level.**

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.
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