



**Università  
degli Studi  
di Ferrara**

XXIX Congresso Nazionale SIPF 2021



# **Neurophysiological correlates of ventral premotor cortex to primary motor cortex cortico-cortical paired associative stimulation**

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## PMv-M1 circuit

- ❖ This neural circuit is crucial in the transformation process of an object' geometrical properties into a specific motor command suitable for grasp (Murata et al., 1997; 2000; Davare et al., 2010).

### dual-sites TMS protocol



- ❖ PMv could both exert an inhibitory (or facilitatory!) influence on M1 at rest (Bäumer et al., 2006; Davare et al., 2008; Beukelaar et al., 2016).
- ❖ PMv exerts a facilitatory influence on M1 during the action preparation and the action observation (Davare et al., 2009; Koch et al., 2013; Beukelaar et al., 2016).

### cortico-cortical paired associative stimulation (cc-PAS)



PMv-M1 cc-PAS seems to increase the inhibitory influence of PMv at rest and the facilitatory influence during the action preparation (Buch et al., 2010).

cc-PAS



pre-PAS

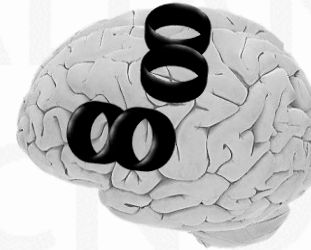
- ❖ 100 couple of pulses with 6 ms ISI
- ❖ Frequency: 0.25 Hz (about ~ 6 min)
- ❖ left PMv was stimulated at 90% RMT
- ❖ left M1 was stimulated at 120% RMT

post-10

*Experiment 1*

post-30

*Experiment 1*  
*Experiment 2*  
*Experiment 3*  
*Experiment 4*



**Exp 1: effect of PMv-M1 cc-PAS on M1 intracortical circuits**

**N = 14**

- ❖ MEP \*
- ❖ SICF - ISI 2.5 ms \*
- ❖ ICF - ISI 15 ms
- ❖ SICI - ISIs 1 and 3 ms
- ❖ LICI - ISI 100 ms \*

**Exp 2: Is the SICF modulation specific?**

**N = 21**

- ❖ SICF (ISIs):
  - 1.3 ms
  - 2.1 ms
  - 2.5 ms \*
  - 3.3 ms
  - 4.1 ms

**Exp 3: PMv-M1 connectivity modulation**

**N = 18**

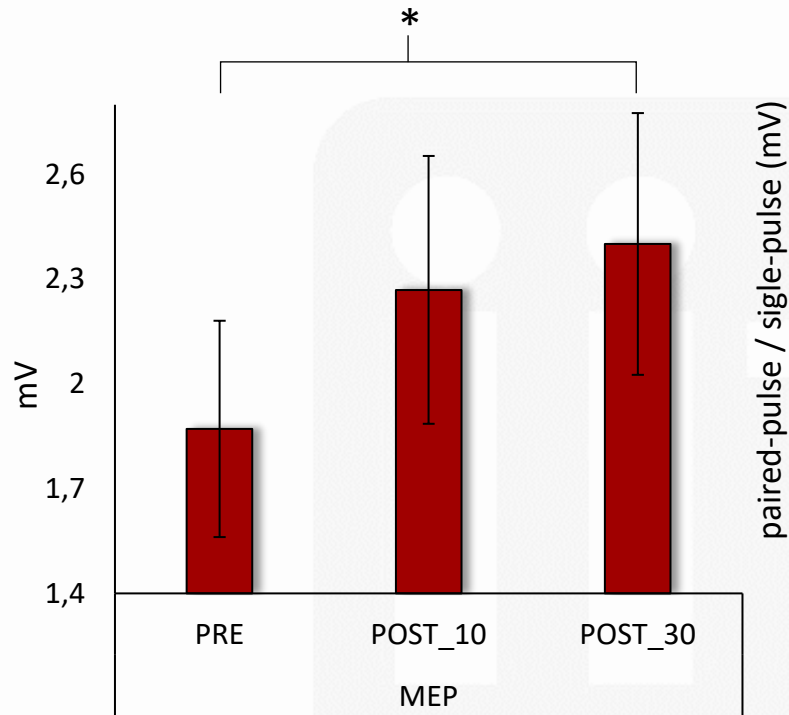
- ❖ Connectivity:
  - CS intensity (% of RMT)
    - 30%,
    - 50%,
    - 70% \*
    - 90%
  - TS intensity at 120% of RMT

**Exp 4: cc-PAS with anterior-posterior (AP) M1 coil orientation**

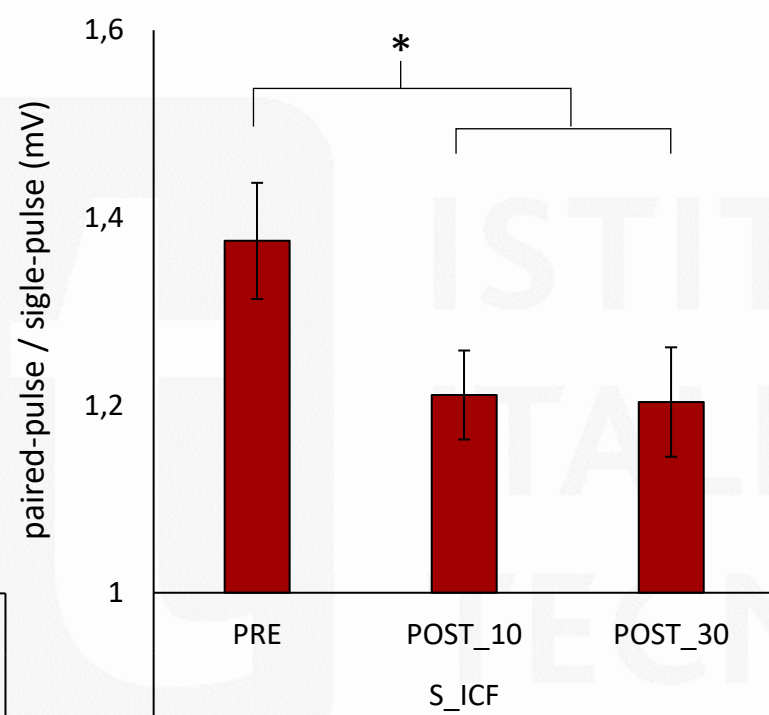
**N = 17**

- ❖ MEP (PA orientation) \*
- ❖ MEP (AP orientation)
- ❖ SICF 2.5 ms
- ❖ Connectivity
  - CS intensity (% of RMT)
    - 30%
    - 70% \*
  - TS intensity at 120% of RMT

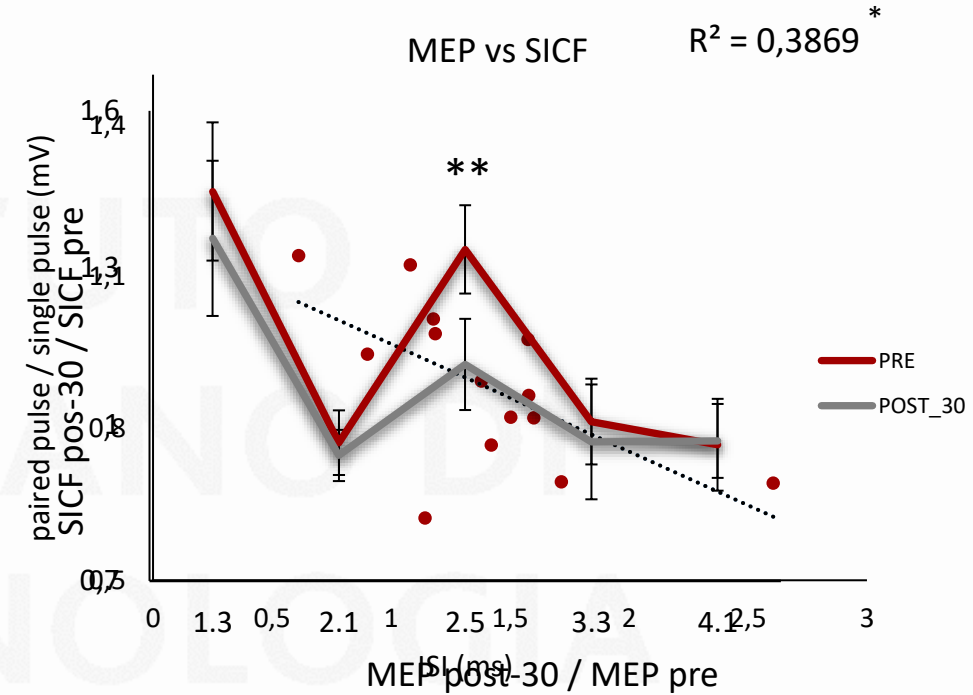
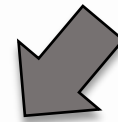
- ❖ Corticospinal Excitability (MEP)
- ❖ Short Intracortical Facilitation (SICF)
- ❖ Intracortical Facilitation (ICF)
- ❖ Short Intracortical Inhibition (SICI)
- ❖ Long Intracortical Inhibition (LICI)



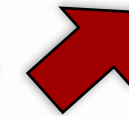
corticospinal excitability



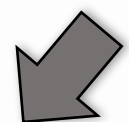
SICF 2.5 ms ISI



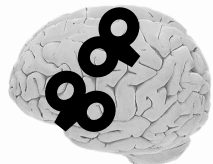
MEP



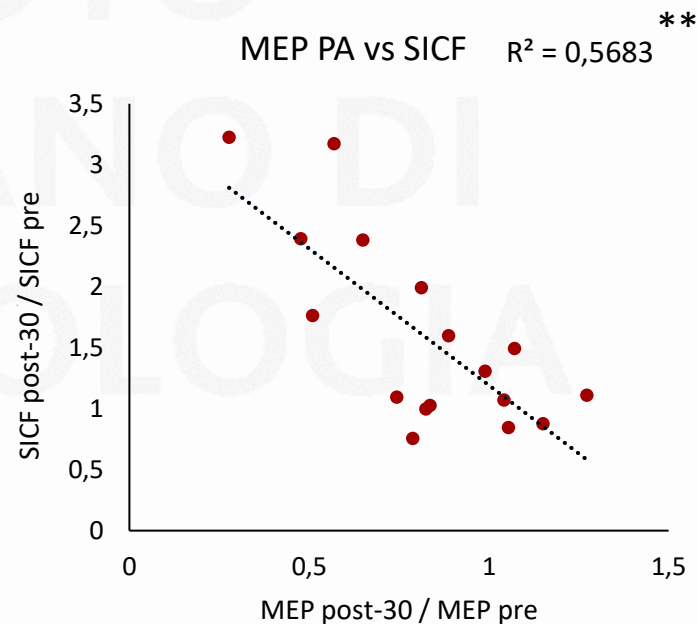
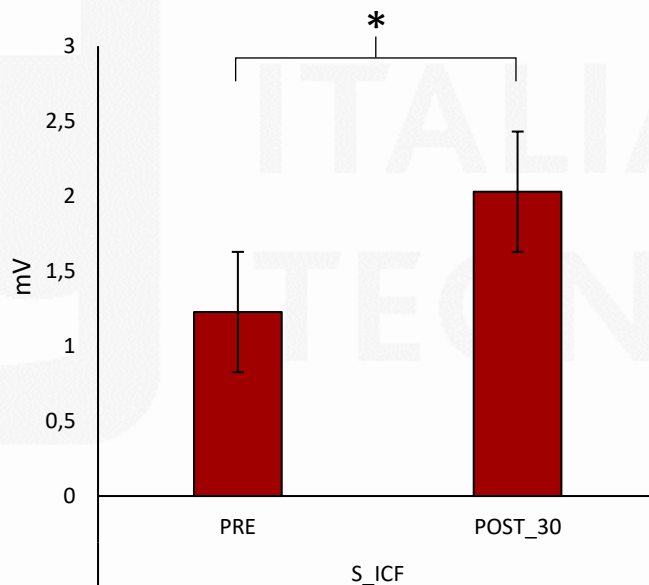
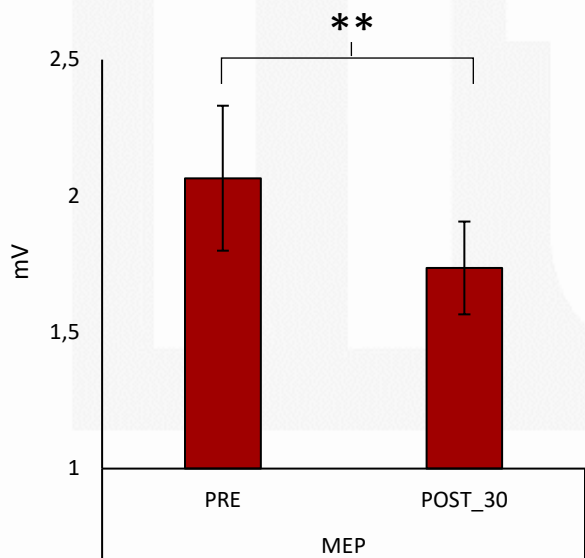
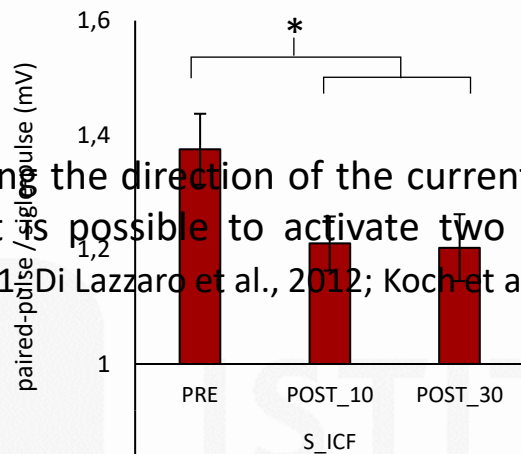
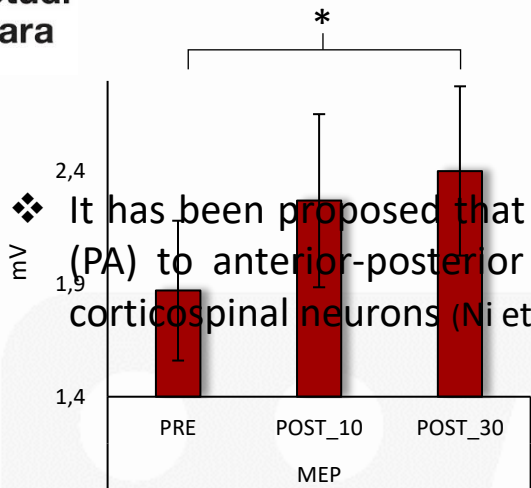
SICF



\* =  $p < 0.05$   
 \*\* =  $p < 0.01$



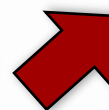
It has been proposed that changing the direction of the current induced in M1 from posterior-anterior (PA) to anterior-posterior (AP) it is possible to activate two different sets of synaptic input to the corticospinal neurons (Ni et al., 2011; Di Lazzaro et al., 2012; Koch et al., 2013)



corticospinal excitability

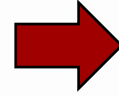


SICF 2.5 ms ISI



\*= p < 0.05  
\*\* = p < 0.01

PMv-to-M1 cc-PAS lead to



- ❖ PMv-M1 connectivity modulation
- ❖ M1 local circuitry modification

- ❖ The strengthening of the PMv-M1 connections could lead to an increment of the pyramidal neurons activity.  
of the inhibitory activity.
- ❖ The increment of the gabaergic inhibitory activity could lead to the reduction of the SICF (Ziemann et al., 2015).
- ❖ SICF and MEP might be mediated by, at least in part, by distinct circuits.



These circuits seem to influence each other.

MEP



SICF



- ❖ The results are specific for the cc-PAS protocol applied in postero-anterior (PA) orientation.

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**Thanks to...**



Elisa Dolfini



Pasquale Cardellicchio



Alessandro D'Ausilio



Giacomo Koch



Luciano Fadiga

**Thank you all for your attention!**