

Fluctuating Estradiol Modulation of Cortical Activity for Quadriceps: A Paired-Pulse TMS Investigation

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Background

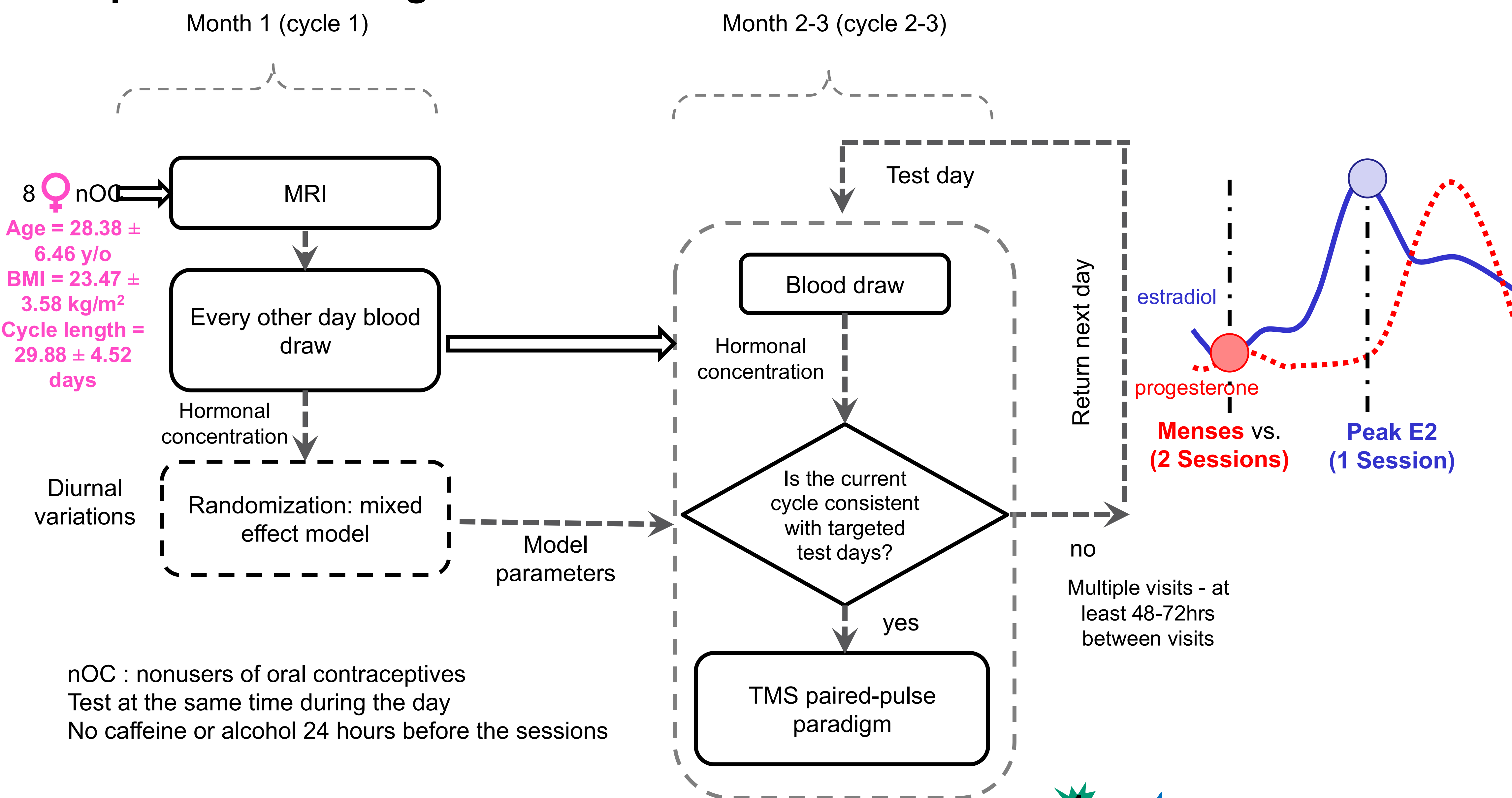
- E2 receptors are distributed throughout the central and peripheral neuromuscular axis, suggesting that hormonal variation can play a role in sensorimotor output and execution¹.
- Estradiol (E2) and progesterone (P4) modulate cortical excitability and neuromuscular control during the menstrual cycle^{2,3}.
- Most previous studies that demonstrate the modulating effect of E2 on cortical excitability were mainly conducted on hand muscles at a resting state⁴.
- The depth to which the hormone-mediated changes in cortical excitability, as manifested in intracortical facilitatory and inhibitory circuits, would exhibit in proximal lower extremity muscles, such as the quadriceps, has not yet been elucidated.

Objective

- To investigate the influence of estradiol (E2) on intracortical facilitation and inhibition of the vastus lateralis throughout menses and peak E2 in pre-menopausal eumenorrheic female participants. The aim is to provide more insight into sex difference in musculoskeletal injury risk.

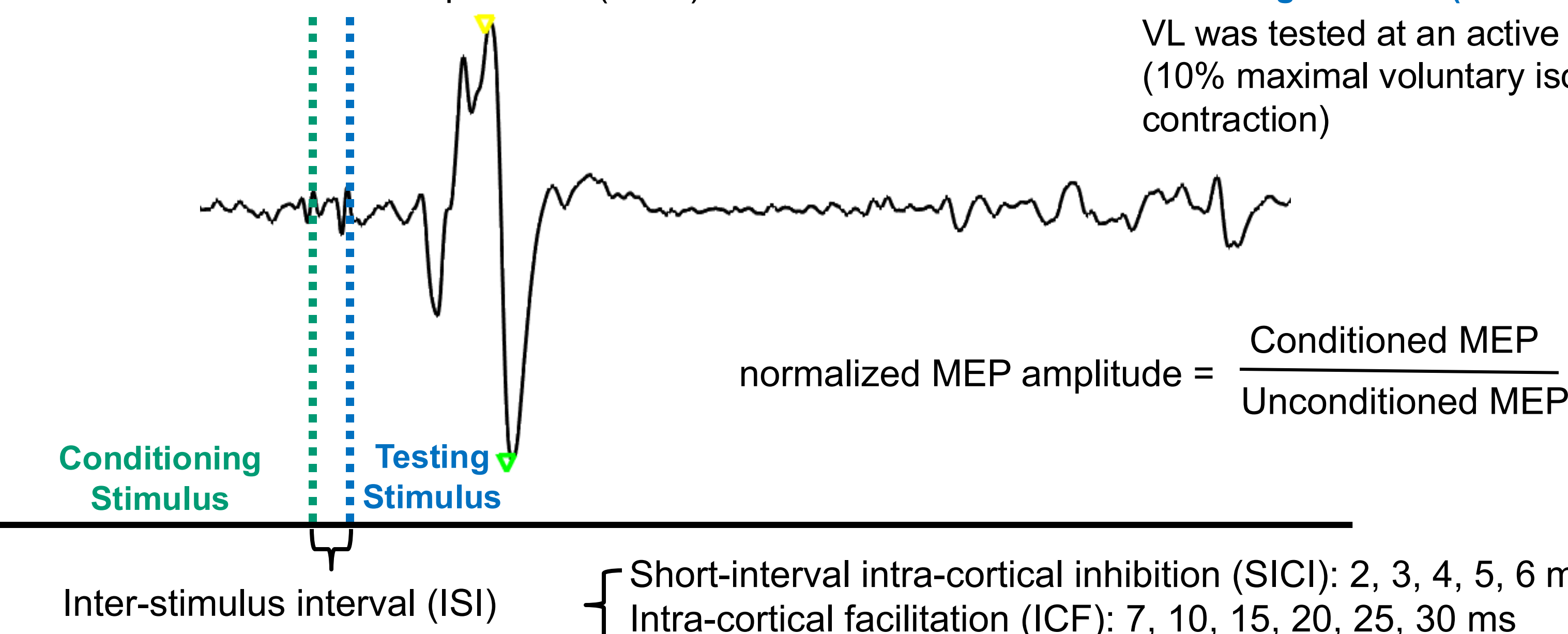
Methods

Experimental Design:

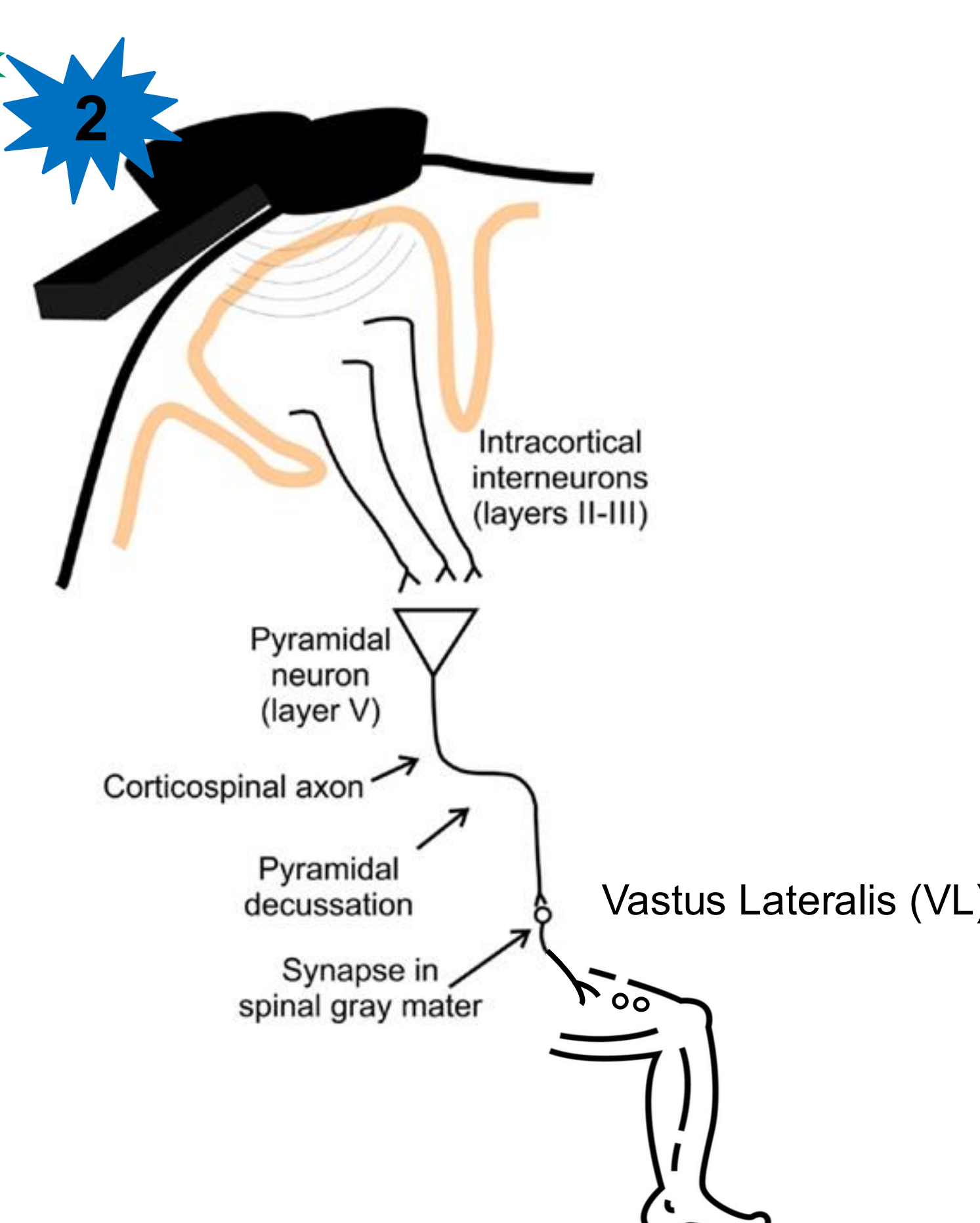


TMS Paired-Pulse Paradigm⁵:

Conditioned motor evoked potential (MEP)



1. Conditioning stimulus (90% active motor threshold)
 2. Testing stimulus (1 mV intensity)
- VL was tested at an active state (10% maximal voluntary isometric contraction)



Results

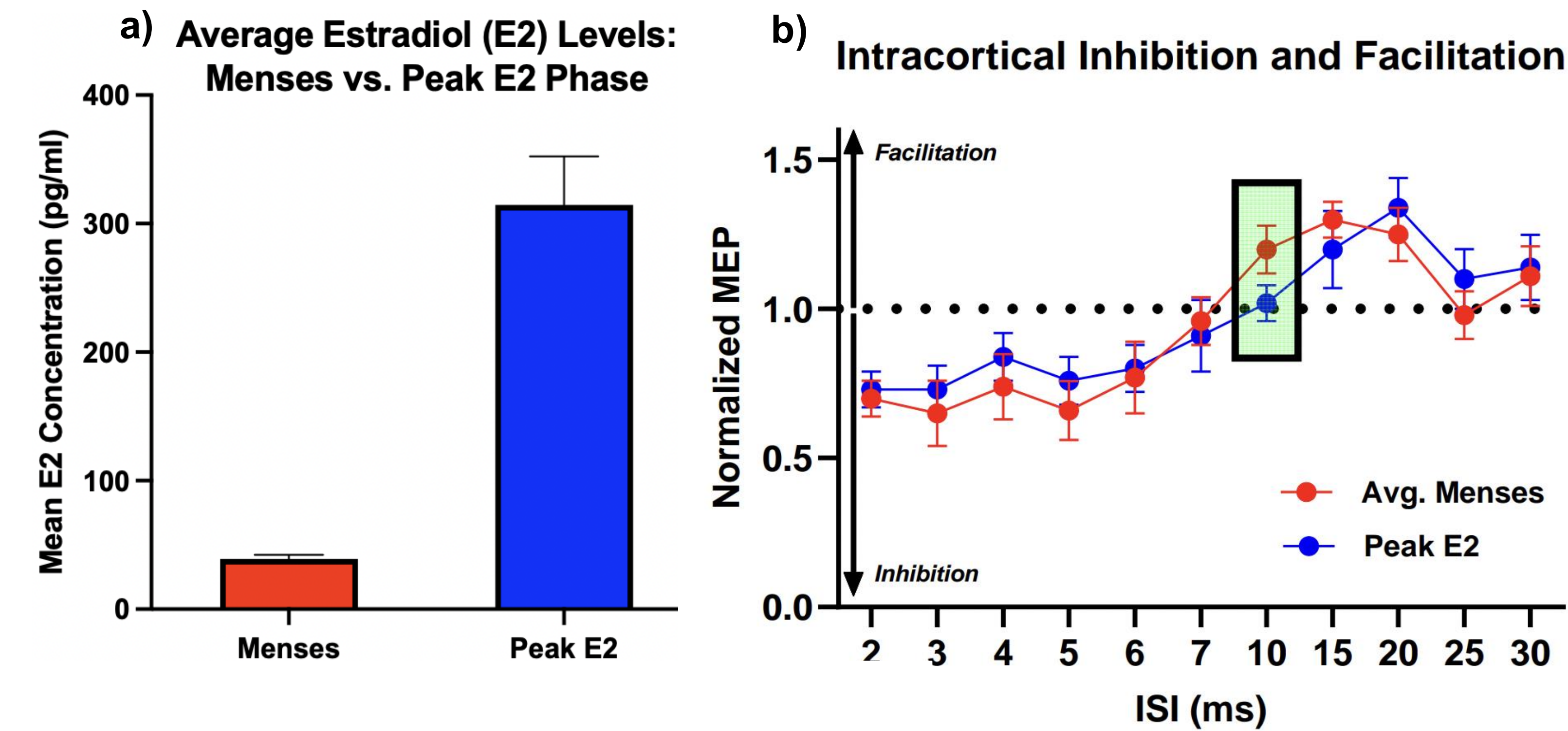


Figure 1. a) Mean serum estradiol (E2) concentrations during menses and peak E2. The E2 concentrations were markedly elevated at peak E2 (314.44 ± 37.84 pg/mL), compared to menses (39.13 ± 3.13 pg/mL), thus demonstrating effective phase dependency in E2 level pertinent to neurophysiological analyses. b) Normalized motor evoked potentials (MEP) across inter-stimulus intervals (ISIs) at menses (averaged across 2 sessions) and peak E2. A significant difference at the 10-ms ISI may suggest hormone-dependent modulation of intracortical facilitation. Values $1.0 >$ indicate facilitation, while values <1.0 demonstrate inhibition.

Participant Normalized MEP at 10 ms ISI

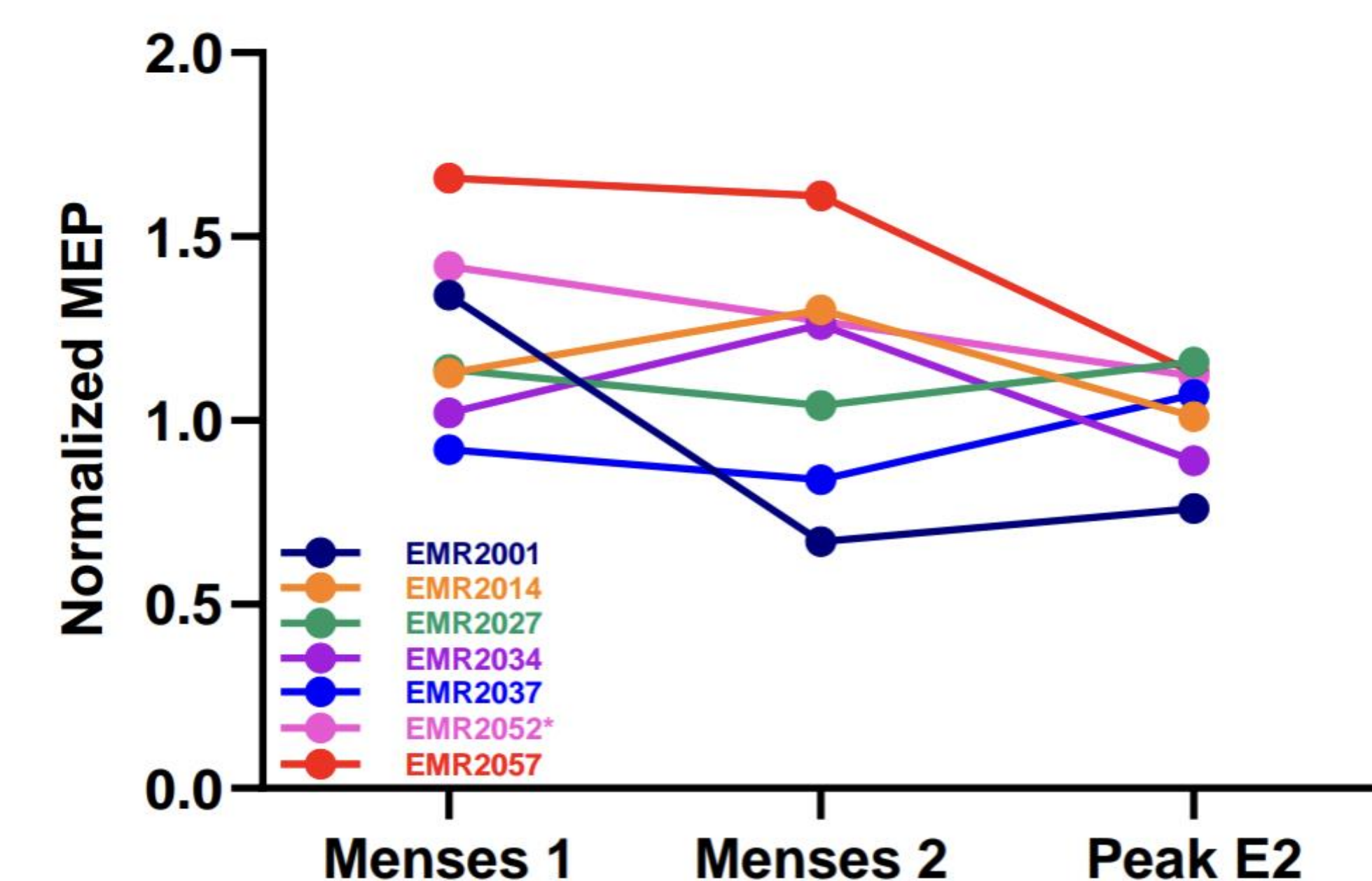


Figure 2. Normalized motor evoked potentials (MEP) at the 10 ms inter-stimulus interval (ISI) across Menses 1, Menses 2, and Peak E2 for individual participants. *Participant EMR2052 only had data values for Menses 1 and Peak E2. In addition, one participant did not exhibit MEP amplitude values at 10 ms ISI after data screening. The individual data showed that the observed difference at the 10-ms ISI between menses and peak E2 may be within the between-session variability.

Discussion

- Our preliminary results suggest that E2 level during the follicular phase does not significantly modulate intracortical inhibition or facilitation of the vastus lateralis.
- This finding aligns with our prior observation in the tibialis anterior, indicating that the non-significant E2-mediated changes on cortical excitability are consistent in both proximal and distal lower extremity muscles.
- Further investigation on other parts of the quadriceps, such as rectus femoris and vastus medialis, is needed.
- In addition, our data collected during the luteal phase could reveal the potential effect of progesterone on cortical excitability of lower limb muscles and is a future aim of investigation.

References

- ¹Hwang et al., *Int J Mol Sci* (2020); ²Dedrick et al., *J Electromyogr Kinesiol* (2008); ³Smith et al., *Ann Neurol* (2002); ⁴Rivas-Grajales et al., *Harv Rev Psychiatry* (2023); ⁵Hallett, *Neuron* (2007)

Acknowledgements: NIH 1R01 AR069176-01