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

Background: Female sex hormones, specifically estradiol, have progressively demonstrated significance in motor function and neuromodulation of cortical excitability. Both estradiol (E2) and progesterone (P4) receptors are found within central and peripheral neuromuscular complexes, thus tying in sensorimotor execution with the menstrual cycle hormonal variations. Our data suggests that E2 can impact the neuronal control of distal lower limb muscles, such as the tibialis anterior (TA) only with the presence of progesterone (P4), by modulating intracortical inhibition and facilitation. Consequently, exploration on how these dynamics may influence the quadriceps muscle has not yet been fully elucidated.

Objectives: Investigation of how estradiol influences the quadriceps poses importance as this muscle group plays a paramount role in preventing injury and motor control. Interpretation of how hormone-related fluctuations within cortical excitability may provide a crucial understanding sex-specific motor injury and neuromuscular accommodation.

Methods: Eight young eumenorrheic female participants were assessed at two marked hormonal states: menses (2 sessions) and peak E2 (1 session), which were confirmed via the concentration within serum. The cortical excitability of quadriceps muscle was evaluated using transcranial magnetic stimulation (TMS), in the vastus lateralis with rectus femoris and vastus medialis responses simultaneously recorded. During experimentation, participants retained an isometric contraction of the quadriceps at 10% of maximum torque of voluntary knee extension. The lowest stimulation intensity that elicited a detectable motor evoked potential (MEP) above baseline muscle activity was defined as active motor threshold (AMT). The paired pulse paradigm consisted of a conditioning stimulus (CS) at 90% of AMT and a test stimulus (TS) at the intensity inducing peak-to-peak MEP amplitude of an 0.5-1.5 mV with inter-stimulus intervals (ISIs) from 2-30 ms. The quantification of intracortical inhibition and facilitation was calculated as the ratio of conditioned MEP amplitudes at each ISI to unconditioned MEP amplitudes. Both short interval intracortical inhibition (SICI) and intracortical facilitation (ICF) were evaluated at specific inter-stimulus intervals. The differences of SICI and ICF between two E2 states were examined using univariate general linear model for each ISI.

Results: The averaged E2 concentration of the menses and peak E2 sessions was 39.13±11.29 and 314.44±107.03 pg/mL. Although we observed a trend that ICF at 10 ms ISI reduced at peak E2 compared to the 1st menses session, the difference did not exceed the inter-session variance between the 2 menses sessions. We did not observe a significant E2 effect on SICI.

Discussion: Our preliminary results suggest that during the follicular phase, E2 level does not modulate intracortical inhibition and facilitation for vastus lateralis. This result is consistent with our finding in tibialis anterior. The next step is to further examine the E2 effect on rectus femoris and vastus medialis muscles.