Motor cortex plasticity and the influence of menstrual phase

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Neuroplasticity is a fundamental process both for the acquisition and maintenance of motor skills, and for the capacity for recovery from neurological insult such as stroke. As such there is a growing interest in the mechanisms and factors that influence cortical plasticity within the human motor system and attempts to develop techniques to drive plasticity for therapeutic purposes (Ridding & Ziemann, 2010). Recent transcranial magnetic stimulation (TMS)-based research suggests that fluctuations in the levels of certain hormones, for example cortisol, can influence the induction of neuroplasticity (Sale *et al.*, 2007; 2009). Further, animal-based research has revealed powerful sex and hormonal influences on the mechanisms of plasticity that underlie learning and memory (Andreano & Cahill, 2009) and evidence is accumulating that these hormones are also potent mediators of neuroplasticity and its underlying mechanisms in humans (Chaieb *et al.*, 2008; Kuo *et al.*, 2006; Smith *et al.*, 1999; Smith *et al.*, 2002; Tecchio *et al.*, 2008). Surprisingly, however, there has been little research explicitly addressing the role of ovarian hormones on neuroplasticity and motor control and learning in humans. Indeed, some of the research that has been conducted has emphasised the potential *confounding* influence of ovarian hormones (Smith *et al.*, 1999; Smith *et al.*, 2002), something that could lead to the explicit exclusion of females. A result of this exclusion is that a potential modulatory role of ovarian hormones on neuroplasticity and motor learning that could *benefit* recovery from stroke in women, could go unrecognised. In an attempt to address this we have recently begun a program of research investigating the influence of menstrual phase, and the associated fluctuations of ovarian hormones, on motor learning and neuroplasticity.

In six studies, four investigating motor learning using a novel serial reaction time pegboard task, and two investigating neuroplasticity (paired-associative stimulation, PAS) and intracortical inhibition using TMS, females participated in two sessions, one during the menses phase (days 1-3) of the menstrual cycle, when both oestrogen and progesterone levels are low, and the other during either (depending on the study) the late-follicular phase (day 14) when oestrogen levels are high or the luteal phase (day 21) when both oestrogen and progesterone levels are high (Farage *et al.*, 2008). Results from the motor learning studies yielded mixed results, though the most parsimonious conclusion is that there are minimal effects on motor learning across the menstrual cycle. The results from the TMS studies are also suggestive of little influence of menstrual phase on the induction of neuroplasticity using PAS, or on intracortical inhibition. The latter finding is surprising as it fails to replicate the results of Smith *et al.* (1999, 2002), suggesting that fluctuations in ovarian hormones may not have the potential to confound research on intracortical inhibition that they suggested. On the other hand, the current findings suggest that ovarian hormones have little influence on the neural processes that underlie neuroplasticity.

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