Characterizing the irreversibility of brain dynamics along the menstrual cycle

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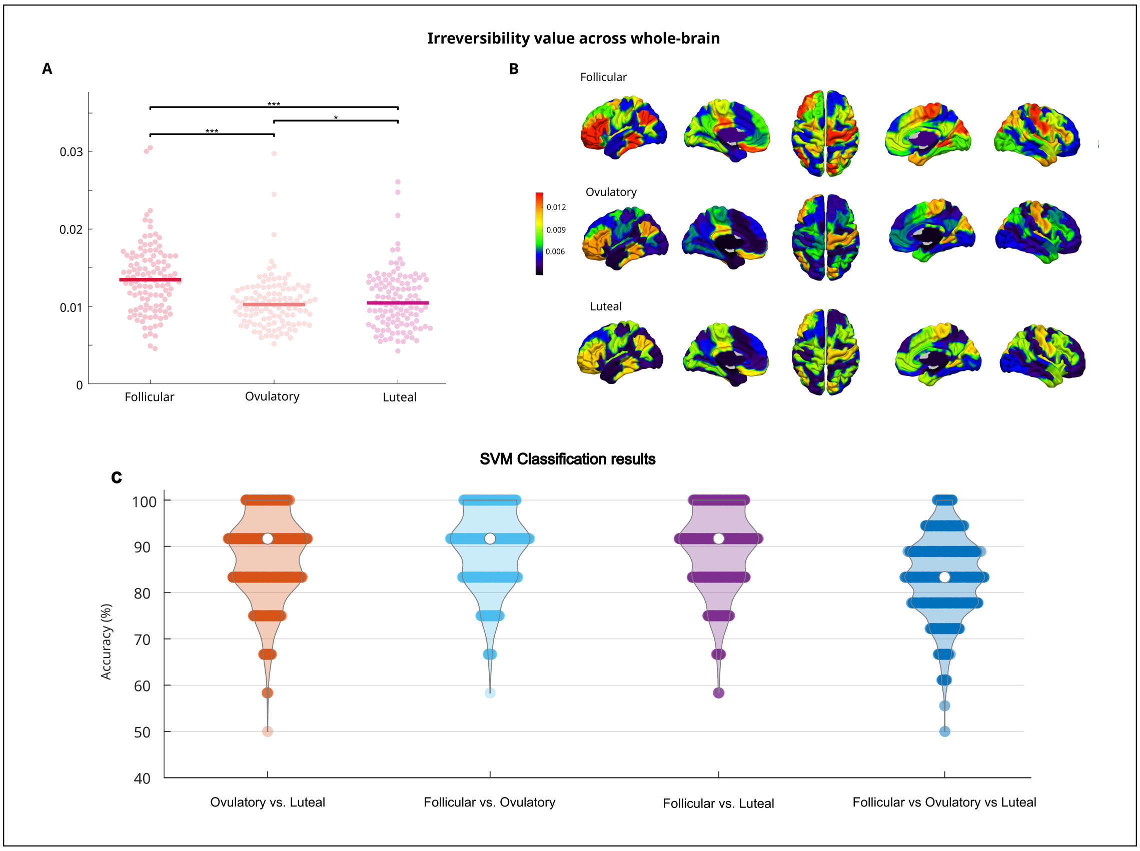
The menstrual cycle is a complex physiological process, typically lasting between 21 to 35 days. It is characterized by three main phases: the follicular, ovulatory, and luteal phases, which are subject to fluctuations in the levels of estradiol and progesterone hormones. These hormonal fluctuations influence the functional reorganization of large-scale brain networks [1, 2, 3]. Nevertheless, the causal mechanisms are still not well understood. Here, we evaluate the underlying signatures of dynamical complexity in the whole-brain network to determine the effect of hormonal fluctuations during the menstrual cycle. We applied a novel theoretical framework to resting-state fMRI data from 60 women scanned longitudinally at each menstrual cycle phase. Our framework quantifies the temporal irreversibility of brain activity by calculating the asymmetry between the forward and reversed flow of events. This provides an indirect measure of the hierarchy of causal interactions in the brain where a weaker hierarchy indicates a more intrinsically driven system [4]. Our results suggest that each menstrual cycle phase is associated with distinct levels of whole-brain irreversibility, where the ovulatory phase exhibits the lowest values compared to the other phases (Fig. A). The irreversibility values per node in each menstrual cycle phase are presented in the rendered brains (Fig. B). These findings suggest that the ovulatory phase is governed by a more democratic system in terms of the balance between intrinsic and extrinsic brain dynamics. Furthermore, to elucidate the underlying mechanisms of the hierarchical organization along the menstrual cycle, we built a whole-brain Hopf model for each woman in each phase to obtain an effective connectivity matrix based on the irreversibility measure [5]. Training a support vector machine model with the effective connectivity matrices as inputs, we achieved an accuracy above 90% when classifying each pair of phases and above 80% when classifying the 3 phases together (Fig. 1C). Overall, these results can be relevant for understanding menstrual cycle-related disorders as well as changes in cognition, emotion, and behavior associated with the menstrual cycle and hormonal fluctuations in healthy women.



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