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Novel methods for clarifying the psychiatric effects of ovarian steroids across the female lifespan

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Ovarian steroid hormone fluctuations can influence mood and cognition in susceptible females during reproductive transitions, including the perimenstrual phase of the menstrual cycle (as in premenstrual dysphoric disorder and perimenstrual worsening of depression), the perinatal period, and the perimenopause. The development of effective treatments for these susceptible individuals requires a clearer understanding of the pathophysiology of steroid-related risk for psychological symptoms. Several statistical and experimental advancements may be useful for this purpose. First, several notable developments in statistics and measurement can help to untangle the effects of steroids on mood and cognition, including (1) the development of various steroid fluctuation metrics to determine how different types of flux precipitate symptoms in susceptible females, (2) the use of multilevel models to parse between- and within-person effects of steroid levels and changes on symptoms, (3) the use of standardized, reliable protocols to improve the reliability of time-locked steroid-related diagnoses such as premenstrual dysphoric disorder, and (4) the use of latent trajectory models to identify subgroups of normal and abnormal responses to steroid fluctuations across the perimenopause and perimenstrual transitions. Second, several rigorous experimental approaches to studying reproductive steroid influences in clinical populations will be discussed, including (1) the use of GNRH agonist baselines and steroid addback to model the causes of psychological risk and resilience in females during various reproductive transitions, (2) the use of carefully-timed luteal steroid administration to explore the steroid withdrawal mechanisms of perimenstrual worsening of depression and suicidality, and (3) the use of prophylactic perimenopausal estrogen stabilization trials to determine the role of steroid flux in perimenopausal-onset depression. The presenter will briefly describe examples of each of these statistical and experimental approaches, and will discuss how their use can help to clarify the steroid mechanisms of emotional and cognitive dysfunction during female reproductive transitions.

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