Etiologic studies of premenstrual disorders require prospective confirmation of affective cyclicity.

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To the editor,

We are writing in response to the article by Jaholkowski et al.[1], which reports an association between "premenstrual disorder symptoms" and polygenic susceptibility to common psychiatric disorders. The study's methodology, which consisted of retrospectively assessing premenstrual disorder symptoms via a single question about depression and irritability before menstruation, raises some concerns.

We emphasize that these findings do not imply or support any conclusion about premenstrual disorders. Retrospective self-report assessment has poor validity[2] being grossly biased towards false positives and impacted by the participant's beliefs about premenstrual syndrome[3]. Therefore, the diagnosis of premenstrual dysphoric disorder in the Diagnostic and Statistical Manual of Mental Disorders requires prospective daily ratings during at least two symptomatic cycles. Clinical[4] and research guidelines[3] also recommend prospective ratings for the assessment and diagnosis of circa-menstrual disorders.

The research design of Jaholkowski et al.[1] highlights the unique and substantial challenges in the study of cyclical conditions in people who menstruate. The necessary prospective daily ratings are, in fact, difficult and time-consuming to obtain. They are, however, of paramount importance for etiological studies such as those investigating the role of genetic markers. Only with prospective symptom ratings in a within-subject design is it possible to reliably distinguish between cyclical and non-cyclical symptoms. Between-subject, cross-sectional studies tend to conflate variance attributable to non-cyclical symptoms (i.e., liability to

common psychiatric disorders) with that of cyclical symptoms limited, for example, to the luteal phase[3].

Prospective longitudinal ratings are also necessary to distinguish between the different neurobehavioral phenomena that may occur across the menstrual cycle. Premenstrual disorders are heterogenous disease entities. Research has, for example, suggested that there are different temporal subtypes of premenstrual dysphoric disorders, which are likely to be underpinned by different disease mechanisms[5].Similarly, distinct symptoms can all be exacerbated by the hormonal fluctuations of the menstrual cycle, through both shared and unique pathways.

Therefore, we urge greater caution when evaluating and undertaking studies on the pathophysiology of premenstrual disorders—longitudinal data are a necessity, not a luxury.

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