PERSONAL AND FAMILY HISTORY OF DEPRESSION MAY PUT WOMEN AT RISK FOR PREMENSTRUAL DYSPHORIC SYMPTOMATOLOGY

Eynav E. Accortt[1]& John J.B. Allen[2]

[1]Miami University, [2]University of Arizona

Abstract

The present study characterized the co-occurrence of Premenstrual Dysphoric Disorder (PMDD) and Major Depressive Disorder (MDD) and assessed whether PMDD relates to increased family history of depression. Co-occurrence of MDD and PMDD existed and promising evidence of a relationship between family history of MDD and likelihood of PMDD was found.

Introduction

- Depression is twice as common in women as in men, however, rates are similar in girls and boys before puberty. Higher depression rates in adolescent girls suggest that the maturational processes may differentially promote depression in post-pubertal girls.
- Premenstrual dysphoric disorder (PMDD) involves complex, chronic, psychoneuroendocrine factors that affect emotional functioning throughout the reproductive years.
- PMDD is included as a diagnosis for further study in the DSM-IV-TR. Symptomatology is linked to menstrual cycle phases, with pronounced symptoms in the late luteal phase, symptom remission during menstrual flow, and no symptoms in the follicular phase (Freeman, 2003). The prevalence is 6% and 19% more are 'near-threshold' (Witchen, 2002).
- Women with PMDD are more likely to have had a history of depression (Endicott & Halbreich, 1988) and are more likely to develop a subsequent Major Depressive Disorder (MDD) (Yonkers, 1997). The comorbidity between the two disorders is significant, ranging from 30 to 70% (Endicott, 1994). MacQueen (2004) reports that the likelihood of past depression in women with PMDD is 30% to 97% (Yonkers, 1997; Cohen et al, 2002; Pearlstein et al., 1990).
- The similarities in symptoms between PMDD and MDD are evident; in fact, a severe case of PMDD can resemble a full depressive episode. Some of the overlapping symptomatic criteria include: depressed mood, irritability, decreased interest, difficulty concentrating, fatigue, changes in appetite, and changes in sleep (Yonkers, 1997).
- Genetic contributions to both MDD (Merikangas et al, 1988; Winokur et al 1982; Kendler et. al., 2006) and menstrual cycle-related symptoms (Parry & Rausch, 1995) have been identified. Whether common or distinct genetic factors contribute to MDD and PMDD remains an empirical question.

Methods

• This sample was obtained in the context of a larger study on EEG asymmetry and risk for depression that included both males and females. Across 6 semesters, 164 women with a broad range of depressive symptoms and history were enrolled and had complete data. All participants were university undergraduates with an age range of 18 to 25 years, and an average age of 18.9 years (± 1.2 s.d.).

• A face-to-face intake interview by an advanced graduate student interviewer consisted of the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1967) and the Structured Clinical Interview for the DSM-IV (SCID; First et al., 1994) as well as a custom interview covering PMDD symptoms.

•Family history of depression was obtained by a proxy interview (cf. Burnam et al., 1985) using a version of the Family History method (Andreasen, Endicott, Spitzer, & Winokur, 1977). If any of their first degree relatives met criteria for MDD, the participants would be classified as being family history positive. One of the 164 participants in the present study was adopted, therefore results for a total of 163 participants are included in the family history analyses.

Participant Classification:

• **PMDD Classifications:**

- **Strict PMDD**: Of the 25 PMDD interview identified participants, 13 were classified as Strict PMDD because they met DSM-IV-TR criteria by self report during the interview, endorsing five or more of the DSM-IV-TR items with symptoms that lasted four or more days.
- **Spectrum PMDD**: The other 12 participants endorsed five or more of the DSM-IV-TR items during interview, however symptoms lasted less than four days, but did result in impairment. These 12 women, together with the women meeting the strict criteria (totaling 25 participants), were classified as Spectrum PMDD.

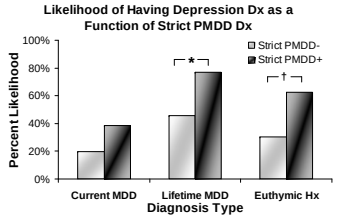
•**MDD Classification:** Participants were categorized into the following non-mutually exclusive groupings:

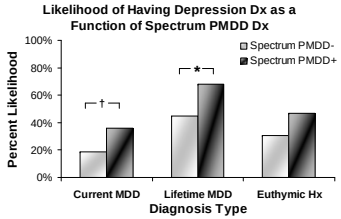
- Current Major Depressive Disorder (MDD).
- Currently Euthymic, MDD Hx + referring to participants with past MDD only and no current MDD diagnosis.
- Lifetime MDD for participants with either past or current MDD diagnosis.
- Dysthymic Disorder.

Results

Question: Did Co-occurrence of MDD and PMDD exist in this sample?

Answer: Yes

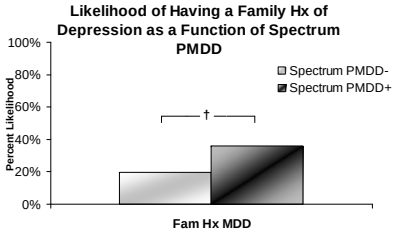




Co-occurrence of PMDD and MDD, assessed for strict and spectrum PMDD, and for three MDD classifications. Lifetime MDD=current or past MDD. Euthymic Hx = Currently Euthymic, no current depression or dysthymia, but positive for history of MDD. Significance * is $p<0.05$ and † is $p<0.065$ via chi-square tests

Question: Was a relationship between family history of MDD and likelihood of PMDD found?

Answer: Yes.



For Spectrum PMDD, there was a trend for a relationship (X2 (1, N=163) = 3.32, p=0.068) between Family History and this PMDD classification. Spectrum PMDD+ women had a higher rate (36.0 %) of Family History of MDD than Spectrum PMDD- women (19.6 %).

Discussion

Despite a generally consistent pattern across different depression diagnoses (Current, Lifetime, & Euthymic Hx+), the present study findings of co-occurrence of MDD and PMDD were only statistically significant when considering Lifetime MDD for both Strict and Spectrum PMDD classifications. Importantly, these findings refute the possibility that currently depressed women are simply endorsing pre-menstrual symptoms due solely to current depressive symptoms (I feel depressed, so 'everything' is wrong with me). In such a scenario, a comorbid current MDD diagnosis would have been most strongly related to PMDD.

Additionally, the present study provided promising but non-definitive evidence of a relationship between family history of MDD and a likelihood of PMDD, as only a trend was discovered. This trend was found only for Spectrum PMDD women who had a higher rate of Family History of MDD (36%) than non PMDD women (19.6%), which could be due to the high comorbidity with MDD in the PMDD group. Both Strict and Spectrum PMDD groups had similar rates of comorbid MDD: 38% of Strict PMDD & 36% of Spectrum PMDD women also met criteria for MDD. Future work might profitably gather family history of premenstrual symptoms to see if there exists a higher rate of familial risk for PMDD as well as MDD among female relatives of participants with PMDD.

Together, the present study results are consistent with the notion that a similar biological predisposition to hormonal related depression likely exists in women with a lifetime and/or family history of depression. Repeated episodes of depression may sensitize depressed women to Pre-Menstrual Exacerbation of their symptoms. For example, past depressive episodes may act as a "kindling" mechanism in which increasingly severe depression occurs with little provocation (Post and Ballenger, 1981). The provocation, in this case, may be fluctuations of hormones and neurotransmitters related to the menstrual cycle (Breaux et al., 2000; Kendler et al., 2001).

The age range of our cohort is 18-25, so these women have not had a long period of risk for either MDD or PMDD. Hartlage et al (2004) and Steiner (2000) also reported premenstrual symptoms worsening over time and added that the average age of onset is around 26 years of age. Therefore, it is important to be aware that the present study is an early onset sample, both in terms of PMDD and in terms of MDD, the latter with a median age of onset of 30 years of age (Kessler et al., 2005).

To some extent mood instability may be a feature in common among depressed women and women meeting criteria for PMDD. The mood instability characteristics of PMDD may also place women at greater risk for MDD (Endicott & Halbreich, 1988; Yonkers, 1997; Endicott, 1994). For these reasons it is imperative to begin investigating symptomatology, course and risk for PMDD (and other mood disorders) prospectively, and at a young age.

The authors wish to thank Jamie Velo, Dara Halpern, Eliza Ferguson, Craig Santerre, Jay Hegde, and a myriad of research assistants for their efforts in recruiting and testing participants, and to thank Jim Coan for his invaluable contributions leading to the receipt of NIMH R01-MH066902, which funded portions of the collection of these data. This work was also funded, in part, by a grant from the NARSAD foundation. **Reprints available from** www.psychofizz.org

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