Premenstrual dysphoric disorder and changes in frontal alpha asymmetry

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Abstract

Objective: Since the clinical picture of premenstrual dysphoric disorder (PMDD) in the Luteal phase of the menstrual cycle is characterized by extreme negative affect, we predicted and obtained a change in frontal cortical EEG alpha asymmetry, which has been shown to be an index of affect. Method: We observed two monthly cycles for five women diagnosed as having PMDD and one monthly cycle for five non-PMDD control subjects. Results: Asymmetry percent scores for the five PMDD women, and for the five control subjects before and after the Luteal phase were typically within the normal non-depressed range, however the asymmetry scores for the PMDD group fell into the negative range during the Luteal period while the control subjects remained stable. Discussion: We predicted alpha asymmetry scores would be affected by the luteal phase in PMDD cases. This hypothesis was clearly confirmed.

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1. Introduction

Premenstrual dysphoric disorder (PMDD) is defined in DSM IV-TM (American Psychiatric Association, 2000) as a disorder which occurs during the last week of the luteal phase of the menstrual cycle (days 15–28 of a 28-day cycle). It is characterized by moderate to severe symptoms such as depressed mood, self depreciating thoughts, marked anxiety and tension, affective lability, anger and irritability, difficulties in concentration, lack of interest in activities, lethargy, a sense of being overwhelmed, and suicidal ideation. It is differentiated from premenstrual syndrome (PMS), which produces milder physical and emotional symptoms. Approximately 75% of the women with regular menstrual cycles experience PMS as compared to 3 to 15% of women who experience the more extreme dysphoric disorder. (Steiner and Born, 2000; Bronson, 2000; Dalton, 1990,
The PMDD affective symptoms disappear after the luteal phase, in the beginning of the follicular period, and are distinguished from premenstrual exacerbation of Axis 1 psychiatric disorders (PME). This latter category includes mood disorders, anxiety disorders, personality disorders, somatoform disorders, bulimia and substance abuse disorder, where the symptoms persist throughout the entire menstrual cycle (American Psychiatric Association, 1994). In addition to emotional changes, there are neurobiological changes that occur in women who suffer with PMDD. While the symptoms of PMDD may be superimposed on the above-mentioned disorders, the DSM-IV-TM clearly states that they are not merely an exacerbation of these disorders. The cyclic pattern of symptoms must be documented for a period of at least two months. (American Psychiatric Association, 2000).

It is known that in non-PMDD women, the neurotransmitters Gamma-Aminobutyric Acid (GABA) and serotonin peak premenstrually and decline during the follicular phase of the cycle (Blum et al., 1992; Hindberg and Naesh, 1992). In contrast, the normal premenstrual peak serum levels of these substances are absent or blunted during the late luteal phase of the cycle of women with PMDD (Miller, 2002; Kouri and Halbreich, 1997; Halbreich et al., 1996). Both serotonin and GABA mediate inhibitory input to the amygdala (Weiss et al., 2000), a structure frequently implicated in affective phenomena (File, 2000; Nemeroff, 1998; Owens and Nemeroff, 1994), and known to connect to frontal cortical areas whose EEG asymmetry we may have been recording in relation to affect (see next paragraph and Rosenfeld, 2000). In this study we present data for five depressed women who also met the criteria for PMDD. Comparison data from four previously depressed but non-PMDD women, and one non-depressed and non-PMDD control subject are also presented.

Recent studies have shown that asymmetry in the activity of neurons in frontal cortical areas is a correlate of affect (see review by Davidson, 2000). To briefly oversimplify, we note that Davidson (2000) has theorized that affect is mediated by a conjoint action of a positive emotion/avoidance system in the left frontal cortex, and a negative emotion/avoidance system in the right frontal cortex. Thus if right frontal activity exceeds left frontal activity, a depressed affect results, whereas positive affect correlates with relatively greater left frontal cortical activity. Henriques and Davidson (1990) showed that currently depressed persons have left frontal hypoactivation in comparison with never depressed persons. They also demonstrated in Henriques and Davidson (1991), that previously depressed persons in remission, still showed left frontal hypoactivation in comparison with never depressed persons. This finding suggested that a brainwave trait for depression was identified. The finding was replicated and extended by Gotlib et al. (1998) and Baehr et al. (1999) and Baehr et al. (2001). Since the alpha frequency in the brain indexes cortical idling (Hughes, 1994), alpha may be used as an inverse index of cortical activation. The relative amounts of left and right frontal alpha should thus correlate with affect, and indeed, asymmetry indices have been reliably used as metrics of affect (Rosenfeld, 2000; Baehr et al., 1998).

Since the clinical picture of PMDD in the luteal phase of the menstrual cycle is characterized by extreme negative affect, we predicted a drastic change in frontal cortical EEG alpha asymmetry of PMDD cases during the luteal phase, in the direction of greater right than left cortical activation, i.e. more left than right alpha activity.

### 2. Method

EEG was passed through a computer driven amplification system, which calculated EEG asymmetry from F3 and F4 electrodes. The asymmetry score is defined on a moment-to-moment basis as \( \frac{(F4 - F3)}{(F4 + F3)} \). F4 and F3 represent alpha magnitude at those two sites in the 10–20 system, respectively. Cz was reference and the left earlobe was grounded. We are aware that use of the Cz reference is controversial (Reid et al., 1998; Haggemann et al., 1998; Davidson, 1998). We use it here as it is the reference initially used by the Davidson group to demonstrate correlation of frontal EEG asymmetry and affect, and which we too have used in obtaining the best diagnostic and
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