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BRIEF COMMUNICATION

Mood, neuropsychological function and cognitions in premenstrual dysphoric disorder

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ABSTRACT

Background. Neuropsychological function and cognitive correlates of depression have not previously been examined in a rigorously defined population of patients suffering from premenstrual dysphoric disorder (PMDD).

Method. Mood, neuropsychological function and cognition were measured in 10 PMDD patients and 10 age-matched controls in both phases of the menstrual cycle in a random order, counterbalanced design.

Results. The BDI was significantly elevated in the luteal phase of PMDD patients only while other cognitive measures showed no significant differences. Working memory was impaired in the luteal phase of the menstrual cycle with no significant differences between PMDD and control subjects.

Conclusion. Despite the small sample size, these results show that the BDI is sensitive to the mood fluctuations of PMDD patients. An impairment in working memory was also found although this is a general menstrual cycle effect.

INTRODUCTION

Premenstrual mood changes encompassing a variety of symptoms varying in frequency and severity but of unknown pathophysiology are well recognized (Frank, 1931). The American Psychiatric Association has suggested specific criteria for premenstrual dysphoric disorder (PMDD), a more severe form of premenstrual mood disorder, which emphasizes psychological symptoms such as depression, anxiety, mood swings and irritability. These symptoms are of sufficient severity to impair normal social or occupational functioning, and only occur in the late luteal phase of the menstrual cycle but are otherwise absent (DSM-IV; APA, 1994). Most previous research has investigated a poorly-defined group of women suffering from premenstrual syndrome (PMS). With the availability of operational criteria, it is important to apply these to premenstrual disorder research.

Given the DSM-IV definition, it is not surprising that PMDD symptoms are similar to those of depression. Women seeking treatment for severe premenstrual symptoms often exhibit an ongoing mood disorder, most commonly major depression or dysthymia (Steiner, 1992). Premenstrual exacerbation of an existing depressive disorder has also been shown (Endicott, 1993). In addition, antidepressant treatments, especially the SSRIs are efficacious in treating PMDD (Menkes *et al*. 1992; Steiner *et al*. 1995).

Changes in both cognition and neuropsychological function are well established in depression (Coyne & Gotlib, 1983). Given the parallels that exist between PMDD and depression, these abnormalities may also be present in women vulnerable to developing PMDD.

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It has often been suggested that women at risk of premenstrual mood disorders show pre-morbid psychological or personality vulnerability. Coppen & Kessel (1963) noted an association between high levels of pre-morbid neuroticism and presentation of premenstrual syndrome. The relationship of cognitive vulnerability to premenstrual syndrome has not been extensively explored although Christensen & Oei (1995) suggested a positive response to cognitive therapy in a heterogeneous group of women with premenstrual symptoms recruited through advertisement.

The purpose of this study was to examine mood, cognition and neuropsychological function in PMDD patients. Cognitive vulnerability to depression, measured by levels of dysfunctional attitudes and attributional style was assessed and central executive function was investigated using tests from a computer-automated test battery. Attempts were made to correlate any changes in cognition or neuropsychological function to fluctuations in mood.

METHOD

Subjects

Patients meeting DSM-IV criteria for PMDD (American Psychiatric Association, 1994) and aged-matched control subjects were studied. Patients were recruited from a regional liaison clinic and completed a prospective daily rating scale during two consecutive menstrual cycles. Patients were not receiving oral contraceptive pills or any other medication, were not pregnant or lactating, had a regular menstrual cycle between 24–32 days and were not suffering from any underlying gynaecological or psychiatric disorder. Control subjects were recruited on a voluntary basis by the use of poster advertisements and asking friends of staff and patients. These individuals conformed to the same inclusion criteria but did not fulfil criteria for PMDD. Subjects were randomized into two groups and tested in random order. Investigators were blind to the menstrual status of all subjects.

Questionnaire measures

National Adult Reading Test (*NART*)

The NART gives an estimate of pre-morbid verbal IQ and hence full scale IQ can be predicted (Nelson, 1982).

Beck's Depression Inventory (*BDI*)

Mood was assessed using the BDI self-rating scale (Beck *et al.* 1961). Scores above 10 indicated increasingly severe degrees of depression.

Pre-morbid Neuroticism (*N score*)

This is a 21-item, modified version of the Eysenck Personality Inventory N-scale, with an additional statement in accordance with Kendell & DiScipio (1968).

Locus of Control (*LOC*)

Derived from Rosenbaum (1980), the LOC involves subjects rating 15 statements on a six-point scale (-3 to $+3$). Higher positive scores indicated more internal LOC and greater independence in problem solving, while negative scores are associated with poor outcome in depression.

Sentence Completion Task

This task (Teasdale *et al.* 1995) involves completing 19 incomplete sentences with the first word that popped into mind. Sentence stems were derived from the Dysfunctional Attitude Scale (Weissman, 1979), therefore, positive sentence completions were seen as an endorsement of dysfunctional beliefs.

Dysfunctional Attitudes Scale (*DAS*)

The DAS attempts to quantify dysfunctional beliefs (Weissman, 1979). Total scores ranged from 40 to 280, with higher scores denoting greater dysfunction.

Self-Schema Questionnaire

This test (Teasdale & Dent, 1987) involves a surprise recall of words from a pool of 12 positively and 12 negatively toned adjectives that subjects had previously rated. The number of negative words remembered was taken as a measure of negative self-schema.

Attributional Style Questionnaire (*ASQ*)

The ASQ (Seligman *et al.* 1979; Peterson *et al.* 1982) involves assigning a causal factor to six positive and six negative hypothetical situations. Questions on dimensions of internality, stability and globality were rated on a seven-point scale generating a mean score for the three subscales for total positive and negative events.

Table 1. *Means and S.E.M. of questionnaires and neuropsychological tests assessed*

Questionnaire	PMDD		Control	
	Luteal	Follicular	Luteal	Follicular
BDI*	23·4 ± 2·79	3·1 ± 1·05	5·7 ± 1·98	3·2 ± 1·41
EPI-N	8·0 ± 0·75	11·8 ± 1·70	7·7 ± 1·38	6·8 ± 1·81
Locus of control	17·2 ± 4·74	21·1 ± 3·63	10·9 ± 2·45	9·3 ± 4·04
Sentence completion	6·2 ± 1·36	6·1 ± 1·19	4·4 ± 0·69	4·6 ± 1·01
DAS	119·4 ± 9·44	111·7 ± 9·71	114·5 ± 5·75	112·4 ± 6·75
Self-schema	2·0 ± 0·37	2·7 ± 0·29	2·3 ± 0·56	3·0 ± 0·47
Attributional Style (ASQ)†				
Internality (+)	4·59 ± 0·46	4·81 ± 0·33	4·80 ± 0·25	4·93 ± 0·21
(−)	4·44 ± 0·36	4·28 ± 0·20	3·78 ± 0·24	4·13 ± 0·35
Stability (+)	5·00 ± 0·35	4·52 ± 0·16	5·20 ± 0·20	5·03 ± 0·14
(−)	4·02 ± 0·28	3·96 ± 0·20	4·07 ± 0·22	3·88 ± 0·34
Globality (+)	4·69 ± 0·37	4·20 ± 0·35	4·25 ± 0·28	3·98 ± 0·31
(−)	3·57 ± 0·38	3·63 ± 0·39	2·95 ± 0·29	3·07 ± 0·41
Tower of London				
Number of excess moves	1·03 ± 0·21	0·90 ± 0·15	0·84 ± 0·16	0·76 ± 0·16
Perfect solutions (%)	63·3 ± 5·58	70·8 ± 4·85	70·8 ± 5·59	71·6 ± 4·34
Initial thinking time	3·88 ± 0·06	3·77 ± 0·04	3·80 ± 0·06	3·80 ± 0·03
Subsequent thinking time	3·45 ± 0·04	3·40 ± 0·06	3·35 ± 0·05	3·26 ± 0·06
Motor initiation time	3·80 ± 0·08	3·67 ± 0·06	3·70 ± 0·07	3·71 ± 0·03
Motor execution time	2·98 ± 0·11	2·89 ± 0·11	2·04 ± 0·45	2·12 ± 0·37
Spatial Working Memory (ASQ)‡				
Between errors	4·42 ± 0·68	4·72 ± 0·61	4·22 ± 0·72	4·32 ± 0·64
Within errors	1·41 ± 0·34	0·37 ± 0·20	1·21 ± 0·30	0·61 ± 0·26
Strategy	32·7 ± 1·23	34·9 ± 0·60	34·9 ± 0·95	34·9 ± 1·04

* The BDI showed significant group ($P = 0·002$), cycle ($P < 0·0001$) and group by cycle ($P < 0·0001$) effects. The remaining questionnaires showed no significant group, cycle or interaction effects.

† On the ASQ, the dimension of stability demonstrated a significant event ($P = 0·002$) effect. The dimension of globality also revealed a significant event effect ($P = 0·007$).

‡ On the SWM task, the number of within errors showed a statistically significant cycle effect ($P = 0·003$). No significant effects were noted on any component of the TOL test.

Neuropsychological tests using CANTAB

The Cambridge Neuropsychological Test Automated Batteries (CANTAB) are computer-based cognitive tasks performed using a touch sensitive screen. Two tests used: the Tower of London (TOL) Task and Spatial Working Memory (SWM) are fully described by Owen *et al.* (1990).

Statistical analysis

Data are presented as means ± standard error of means (S.E.M.). Analyses involved two-way analysis of variances (ANOVA; between phase × between group interactions) with covariates and *post-hoc t* tests as necessary. Data involving time (first response latency in the AMT and thinking and motor times in the TOL) were log-base 10 transformed, and errors in SWM were square-root transformed in keeping with previous studies using CANTAB (Park *et al.* 1994). Statistical significance was set at $P = 0·01$. Statistical analyses was conducted using SPSS 7.0 (SPSS, 1996).

RESULTS

Ten PMDD patients (age range 19–44) and 10 age-matched control subjects (age range 22–45) completed the study. Subjects did not differ significantly with respect to parity ($P = 0·29$), but showed statistically significant differences in full scale pre-morbid IQ scores as assessed on the NART (PMDD mean = 102·5 ± 2·7, controls mean = 111·7 ± 2·2; $P = 0·018$). NART score was, therefore, entered as a covariate in the analysis of the neuropsychological tests.

Questionnaire measures

BDI

Two-way ANOVA revealed highly significant group ($F = 17·84$; df = 9; $P = 0·002$), cycle ($F = 41·13$; df = 9; $P < 0·0001$) and group by cycle effects ($F = 34·96$; df = 9; $P < 0·0001$). PMDD patients were moderately to severely depressed when in the luteal phase, but were in the normal range in the follicular phase (see Table 1 and Fig. 1).

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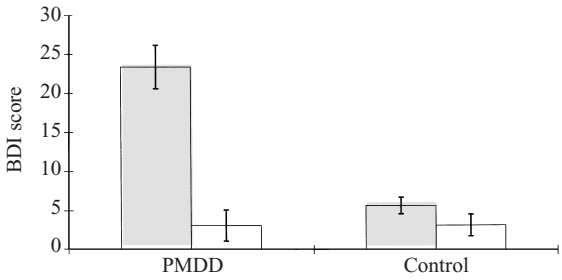

FIG. 1. Comparison of BDI scores in both menstrual phases (▨, luteal; □, follicular) of PMDD and control groups. Error bars represent S.E.M. PMDD luteal phase scores are significantly higher than PMDD follicular phase (cycle effect; $P < 0{\cdot}0001$) and compared with control luteal phase (group effect; $P < 0{\cdot}0001$). PMDD follicular phase BDI scores were not significantly different from controls, and there was no significant cycle effect within the control group.

Personality measures

The N scale score showed mild group by cycle effects ($F = 5{\cdot}78$; df = 9; $P = 0{\cdot}04$) although a large standard deviation caused this to fail to reach stringent statistical significance. No individual group or cycle effects were seen. In the LOC, ANOVA revealed no significant group, cycle or interaction effects.

Beck's cognitive theory of depression

The questionnaires measuring various aspects of Beck's cognitive theory of depression (DAS, self-description and sentence completion task), failed to show any significant differences, see Table 1.

Attributional style

The ASQ demonstrated significant event effects in stable and global dimensions ($F = 20{\cdot}42$; df = 8; $P = 0{\cdot}002$, and $F = 12{\cdot}79$; df = 9; $P = 0{\cdot}007$ respectively), indicating a significantly different response according to whether the hypothetical event was positive or negative; positive events scoring higher. However, in all other measures, no significant group, cycle or interaction effects were found.

Neuropsychological tests

Tower of London

There was no significant group effect for the average number of excess moves ($F = 0{\cdot}45$; df = 9; $P = 0{\cdot}518$). PMDD patients performed at a lower proportion of perfect solutions when in the luteal phase, although no group or cycle effect was demonstrated. No significant differences were observed for thinking or motor times.

Spatial working memory

No group, cycle or interaction effects were found for between errors and strategies in the spatial working memory test. There was however, a strong cycle effect for within errors ($F = 16{\cdot}01$; df = 9; $P = 0{\cdot}003$). Subjects from both groups consistently made more within errors in the luteal phase compared to the follicular phase. Covariate analysis of IQ and BDI score against within errors scores revealed no significant effect of these variables for each group or menstrual phase.

DISCUSSION

The results of this study clearly demonstrate that PMDD patients suffer from a transient mood disorder. Symptoms of depression, as measured by the BDI were present and of greater severity than controls in the luteal phase of the menstrual cycle. The absence of abnormal mood symptoms in the follicular phase confirmed that no underlying persistent depressive disorder was present. The luteal phase BDI score represented a moderate to severe level of clinical depression in PMDD patients (Beck *et al.* 1961).

Previous studies utilizing the short version of the BDI have been demonstrated to be sensitive to premenstrual mood changes in PMS (Keenan *et al.* 1992*a*). In the present study, the full length version of the BDI is also shown to be a sensitive measure, able to differentiate between groups on symptom severity and also able to detect within subject changes over a short time-scale.

No statistically significant changes in neuroticism were demonstrated on the EPI-N scale. This finding differs from previous studies showing higher neuroticism scores in women reporting premenstrual symptoms (Taylor *et al.* 1991), women seeking treatment for PMS (Hallman *et al.* 1987) and women with severe PMDD (Bancroft *et al.* 1993). Levels of neuroticism did not fluctuate with the menstrual cycle, although the small sample size may have obscured changes.

Bains & Slade (1988) noted a particular attributional pattern in women seeking treatment for menstrual complaints – premenstrual

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negative mood was attributed to health problems whereas intermenstrual positive mood was attributed to personality. The ASQ tested whether PMDD patients exhibited a depressive attributional styel but demonstrated no group or cycle effects on any dimension. This is in keeping with Trunnell *et al.* (1988) who also found no difference in ASQ attributional styles between self-diagonosed PMS patients and controls.

The LOC questionnaire also assessed the perception of 'controllability'. Gough (1975) found no correlation of Rotter's LOC with menstrual distress in normal women. O'Boyle *et al.* (1988) showed that locus of control became more external during the premenstrual phase in self-diagnosed PMS suffers. In contrast, the present results for the LOC questionnaire revealed that PMDD patients generally possessed an internal LOC which became more internal during the follicular phase. However, large data variations possibly account for the lack of statistical significance.

Beck's cognitive theory of depression was assessed in PMDD patients using measures shown to be sensitive in depression.

The self-descriptive questionnaire measuring negative self-schema was significantly reduced in depressed patients who recovered after 6 months ($P < 0{\cdot}001$), but not changed if non-recovered (Williams *et al.* 1990). A negative self-schema was unable to predict recovery or relapse, but was demonstrated to be a state-dependent cognitive marker for depression. In the present study, more negative words were endorsed in the follicular compared to luteal phase of both groups. This result would have contradicted the previous study, but the cycle effect failed to reach statistical significance.

The DAS was postulated to be a state-dependent marker for depressed mood in PMDD patients. The present study found no significant group or cycle effects. Since the sentence completion task was developed from the DAS, similar results were predicted. Lack of group or cycle differences shows that both measures are either not specific or sensitive to menstrual cycle/mood changes or that cyclical mood changes have no effect on these measures of dysfunctional beliefs.

The measures of self-schema, dysfunctional attitudes and attributional style in this study suggest that PMDD is an intermittent mood disorder occurring in women who do not demonstrate cognitive vulnerability to depressive disorders. If the women did show such vulnerability, then cognitive theory, particularly Teasdale's (1988) differential activation hypothesis, would predict that transient depressed mood states occurring during the follicular phase would activate negative patterns of thinking leading to events being interpreted as highly aversive and uncontrollable. This would maintain and further worsen the depressed mood and lead to increased accessibility of negative thoughts and memories leading to persistent depressive symptoms. As such, women with premenstrual mood shift and cognitive vulnerability to depression might be expected to develop a persistent major depressive disorder with premenstrual exacerbation of symptoms. Women with PMDD may, therefore, provide a paradigm for exploring biological vulnerability to mood disorders.

Neuropsychological function has previously been shown to be impaired in the luteal phase of PMS subjects (Keenan *et al.* 1992*b*). Impairments in the Stroop colour interference task and trail-making task indicated a deficit in frontal lobe function, especially central executive planning and organization. The Tower of London CANTAB test specifically examined central executive function emphasizing planning ability. On measures of performance accuracy, the number of excess moves and the proportion of perfect solutions were not significantly different between group or menstrual phase. Initial and subsequent thinking times did not differ indicating that mood changes associated with PMDD do not alter planning ability. No differences in motor initiation or execution conforms with other objective measures of motor function (Summer, 1973; Cockerill *et al.* 1994).

On the spatial working memory task, highly significant menstrual cycle effect in within errors was found ($P = 0{\cdot}003$). This did not differ between PMDD patients and controls. Within errors were errors where an individual returned to a previously searched box within the same trial, thus requiring the use of short-term working memory for the duration of each trial within a task. It appears that short-term working memory is affected by menstrual cycle changes rather than PMDD mood changes.

The CANTAB tests have been studied extensively in various patient populations. On the SWM test, significant differences in between search errors but not within search errors were demonstrated in elderly depressed patients (Beats *et al*. 1996) and unipolar depressives (Elliott *et al*. 1996). However, in young unipolar depressed patients of age range 18–52 comparable to the present study, no such differences were found (Purcell *et al*. 1997). Unfortunately, within search errors were not reported in the latter two studies although Beats *et al*. (1996) showed no significant difference in elderly depressives. On the TOL task, the present results of the PMDD group are comparable with the young unipolar depressed patients (Purcell *et al*. 1997) where no significant differences were found. However, in all three studies, the majority of patients were on medication.

This study is limited as the small sample population yielded large data variations and possibly obscured significant changes. In addition, the PMDD and control groups were not IQ matched. This situation is far from ideal and although statistical analyses were covered for pre-morbid IQ, one cannot discount the possibility of an effect. Repetition of the study with a larger sample size and IQ matching would probably provide more meaningful results. The present study has, however, suggested areas where further research can be focused.

In conclusion, the BDI has been demonstrated to be a sensitive measure of depressive mood in PMDD patients. Cognitive measures of depression did not differentiate between PMDD and control subjects. Working memory was found to be impaired during the normal menstrual cycle and not specifically in PMDD. However, due to the small sample size of the study, one must be cautious in interpreting these data. Further studies specifically assessing working memory in PMDD patients is warranted.

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