RESEARCH ARTICLE

The effects of PMS/PMDD on attention and short-term memory in adolescent girls

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ABSTRACT

Objective: There are few studies of premenstrual syndrome (PMS)/premenstrual dysphoric disorder (PMDD) in adolescents. The research conducted to date generally consists of prevalence studies that did not evaluate neuropsychological parameters. This study was designed to assess neurocognitive functions, such as attention and memory, in adolescent girls diagnosed with PMS or PMDD during different phases of the menstrual cycle.

Method: A total of 86 adolescents aged 14-18 years completed the Premenstrual Assessment Form (PAF). Of that initial group, 56 who had a score of ≥1.7, indicating the presence of PMS, were enrolled; 20 were subsequently excluded. A final group of 36 with PMS/PMDD and 30 controls (PAF <1.7) cases were used for the statistical analysis. The participants were assessed in different phases of the menstrual cycle: once in the follicular phase and once in the luteal phase. The Edinburgh Depression Scale, the Visual Aural Digit Span (VADS) Test-Form B, the Stroop Color and Word Test-TBAG Form, the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version, and the Child Behavior Checklist were also administered to evaluate other parameters.

Results: The subjects with PMS/PMDD demonstrated weaker performance than the control group on the Stroop test (Section 5), which presents incongruence and measures the interference effect, and the results of the PMS/PMDD group were also significantly lower in the luteal phase compared with the follicular phase. No significant difference was found between the groups in the VADS-B test subparameters; however, the results of the PMS/PMDD group were weaker in the luteal period, while there was no significant difference seen in the control group according to phase of the menstrual cycle.

Conclusion: To the best of our knowledge, this is the first published study to evaluate neurocognitive function in adolescent girls who have been diagnosed with PMS/PMDD in 2 phases of the menstrual cycle. The results of this study identified some neurocognitive difficulty with attention maintenance, disruptive effect, and short-term memory in those with PMS/PMDD. Furthermore, the menstrual phase had a significant impact on test scores.

Keywords: Adolescence, attention, premenstrual dysphoric disorder, premenstrual syndrome, short-term memory

INTRODUCTION

Premenstrual symptoms may start at any age after menarche (1). Premenstrual syndrome (PMS) is a cyclical pattern of symptoms that begins during the luteal phase of the menstrual cycle and can include somatic, emotional, behavioral, and cognitive changes (2). The symptoms diminish with the onset of the menstrual cycle. Premenstrual dysphoric disorder (PMDD) is a severe form of PMS. The symptoms can have a variety of negative effects in adolescents, including diminished self-confidence, social relationships, and academic performance (3). Emotional and behavioral problems are common; the most frequent psychiatric symptoms are irritability, feeling low or tense, restlessness, indecision, forgetfulness, sleep disorders, and reduced concentration. In some cases, work capacity and academic performance may be seriously affected (3).

Previous studies have evaluated the neurocognitive function of adult women diagnosed with PMS/PMDD (4-6). However, there are very few studies of PMS/PMDD in adolescents, and those conducted to date have generally been studies to determine prevalence. To the best of our knowledge, there has been no study that has evaluated attention, memory, and other neuropsychological parameters of adolescents with PMS/PMDD.

Studies of adults with PMDD have revealed that comorbid psychiatric disorders are common (7,8). A significant proportion of women with PMS/PMDD have been reported to demonstrate cognitive impairment, such as poor concentration, decreased verbal and working memory, and impaired motor coordination, as well as negative effects on visual-spatial skills, and reaction time, especially in the luteal phase (4-6,9-11). However, a review of the scientific literature did not reveal research related to attention-deficit hyperactivity disorder (ADHD) in adolescents diagnosed with PMS/PMDD.

The aim of this study was to evaluate neurocognitive functions, such as attention and short-term memory, of adolescent girls diagnosed with PMS or PMDD during different phases of the menstrual cycle. This is an understudied area of research, and since PMS is very common, greater knowledge of the factors that could affect cognitive performance in adolescent girls experiencing premenstrual symptoms would be extremely valuable, especially with respect to general functionality home/school/social relationships.

METHOD

Participants and Study Design

Approval for this study was granted by the Clinical Research Ethics Committee of Ondokuz Mayis University (IRB: 08/06/2017-B.30.2.ODM.0.20.08/999-103). Informed consent was provided by all of the participants and their parents.
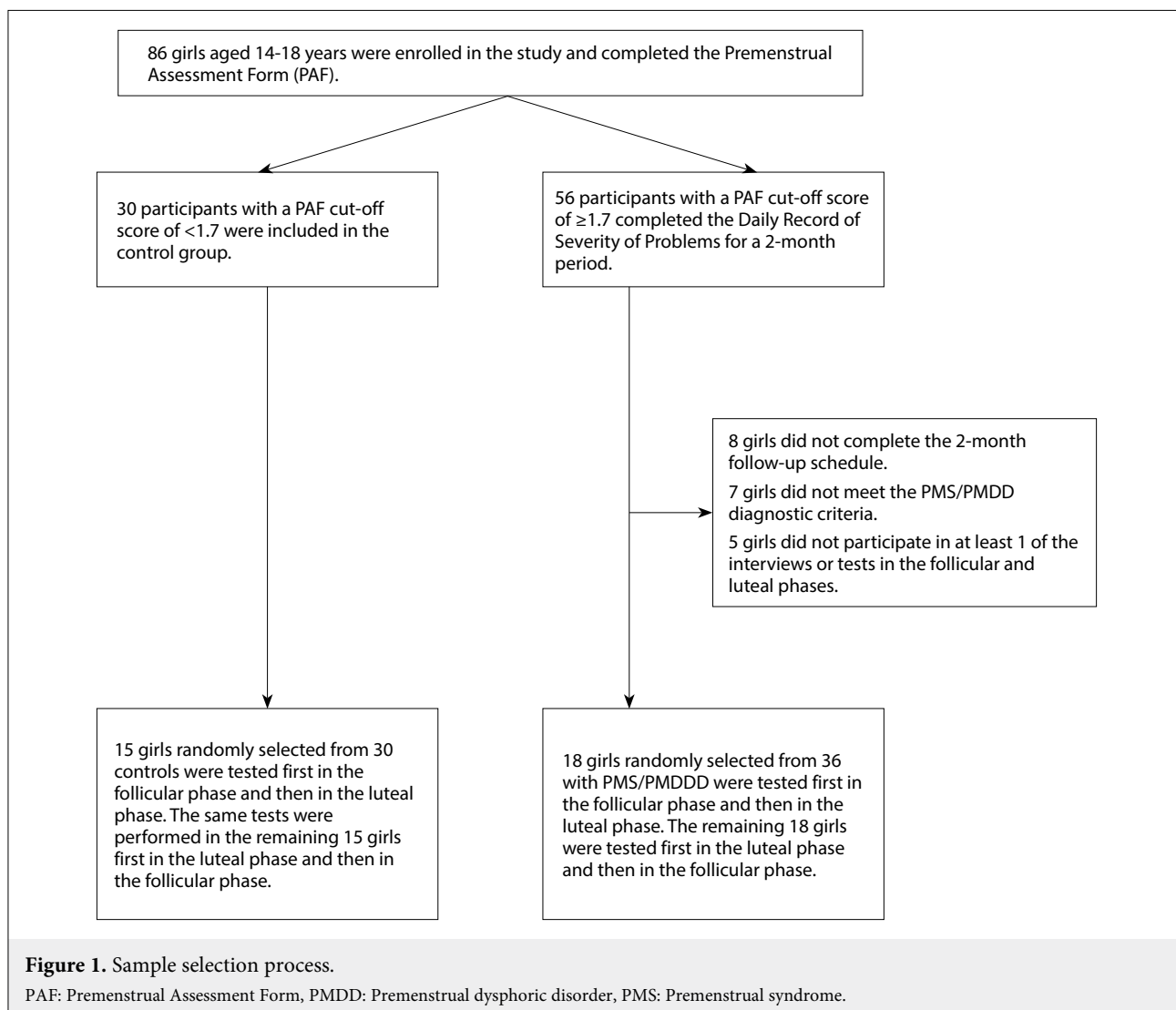
This was a single-center, prospective, controlled study. Patients presenting at the Mental Health Clinic for Children and Adolescents and the pediatric outpatient clinic of Ondokuz Mayis University Faculty of Medicine Training and Research Hospital and daughters of hospital employees or their relatives 14-18 years of age were evaluated for inclusion in the study. A total of 86 adolescents completed the Premenstrual Assessment Form (PAF).

Exclusion criteria were a diagnosis of autism spectrum disorder, bipolar affective disorder, or psychotic disorder (in the patient, a parent, or a sibling), a major physical (diabetes, cancer), or neurological (neurodegenerative disease, epilepsy) disease, a history of trauma with loss of consciousness of more than 1 hour, a history of premature/hypoxic birth, visual and/or hearing disability, current or previous use of an oral contraceptive, any known organic gynecological/obstetric pathology, irregular menstrual cycle in the last 2 years, consumption of alcohol or drugs in the previous month, corticosteroid treatment in the previous 6 months, and pregnancy.

Based on the PAF results, 56 were initially enrolled in the PMS/PMDD group, and 36 completed the study requirements and were used in the analysis. Another 30 participants with a PAF score that did not meet the threshold for PMS were included as the control group. Individuals with a Porteus Maze Test (PMT) score of <100, a non-verbal measure of intelligence, were not included in the study. The study and control groups were of a similar mean age and had a similar mean PMT score, which eliminated the potential effects of age and basic cognitive ability.

The control and PMS/PMDD groups were divided according to menstrual cycle status in order to evaluate 2 phases (PMS/PMDD group: n=18 in follicular and luteal phase subgroups; control group: n=15 in follicular and luteal phase subgroups. A research process flowchart of the sample selection is provided in Figure 1.

Additional psychiatric disorders were diagnosed using the Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version (K-SADS-PL). The Turgay DSM-IV-

Figure 1. Sample selection process.
PAF: Premenstrual Assessment Form, PMDD: Premenstrual dysphoric disorder, PMS: Premenstrual syndrome.

Based Child and Adolescent Behavioral Disorders Screening and Rating Scale (T-DSM-IV-S), which uses Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria, was used to evaluate hyperactivity, impulsivity, and disruptive behavioral problems. The Child Behavior Checklist (CBCL) was used to assess internalized and externalized disorders. Each participant completed the PAF and was asked about the calendar of her menstrual cycle.

The members of the PMS/PMDD group were instructed to complete the Daily Record of Severity of Problems (DRSP) for 2 consecutive months. Participants who did not comply, who no longer met the PMS diagnostic criteria, or who did not attend at least 1 of the interviews and tests in the 2 phases (luteal and follicular) were excluded from the statistical analyses of the study (n=20). Two appointments were made according to the menstrual cycle: 1 in the follicular phase and 1 in the luteal phase.

Half of the control group subjects were selected at random, and the Edinburgh Postnatal Depression Scale (EPDS), Stroop Color-Word Test-TBAG Form, and the Visual Aural Digit Span Test-B Form (VADS-B) instruments were administered first in the follicular phase and then in the luteal phase. The remainder of the group took the tests in the same order, but first in the luteal phase and then in the follicular phase. The same procedure was applied in the PMS/PMDD group. The results of the 2 groups were compared.

Evaluation Instruments
Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version
The Turkish version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL-T) is a structured diagnostic assessment schedule

based on the DSM-IV criteria for major psychiatric disorders. The validity of the K-SADS-PL-T has been found to be excellent for elimination disorders, good for ADHD and tic disorders, and fair for affective disorders, anxiety disorders, and oppositional defiant disorder (12,13). Inter-rater reliability has been observed to be excellent for elimination disorders and tic disorders, and good for ADHD and anxiety disorders (12).

Porteus Maze Test

The PMT was created in 1914 and the form in current use was developed in 1958 (14,15). This test is used as a non-verbal measure of intelligence for children aged 7-14 years and assesses areas such as mental planning, ability to adapt to new situations, and general capability. The quantitative test age score was proposed as an index related to chronological age and was used to compute an intellectual quotient score (16).

Riddle and Roberts (17) reported that the test was generally valid as a measurement of foresight, planning, impulsivity, and judgement, and the ability to delay gratification. They also found that it had inter-operator reliability. In a study that examined the validity of the PMT and the ability to evaluate social adaptation, maze ratings were examined alongside Stanford-Binet performance. The rank order correlations were 0.57 for the Binet and 0.77 for the maze test (18). The PMT was adapted to Turkish by Togrol (19).

Edinburgh Postnatal Depression Scale

Engindeniz et al. (20) performed a validity and reliability study of a Turkish version of the EPDS originally developed by Cox (21). The instrument consists of 10 items scored 0-3 using a Likert-type scale. A score of 12-13 indicates a fairly high possibility of depression (22). Since the scale focuses on mental health, rather than physical symptoms, it was considered an appropriate tool to screen for depressive symptoms in the current study.

DSM-IV Disruptive Behavior Disorders Rating Scale

Turgay developed the T-DSM-IV-S, a Turkish scaled based on the work of Swanson, Nolan and Pelham (23). The instrument is designed to identify symptoms of ADHD, oppositional defiant disorder, and conduct disorder in children and adolescents. There are 9 items associated with attention, 9 with hyperactivity and impulsivity, 8 with oppositional defiance disorder, and 12 with behavioral disorder. Each item is rated on a 4-point scale ranging from not at all (0 points) to very

much (3 points). Validity and reliability studies for the scale in Turkish were performed by Ercan et al (24).

Child Behavior Checklist

The CBCL was developed to evaluate information obtained from parents and caregivers about the behavior of children and adolescents in the age group of 4-18 years (25). The scale comprises 118 items that probe the presence of behavioral and emotional problems. The frequency of behavior in the previous 6 months is graded 0-2, and the items are evaluated using a number of syndrome subscales. A broad scale of internalized behavior includes anxious/depressed, withdrawn-depressed, and somatic complaints syndrome scores; externalized behavior combines the rule-breaking and aggressive behavior scores. A total problems score is the sum of the scores of all of the syndrome subscales, which adds attention problems, social problems, and thought problems.

Premenstrual Assessment Form

The PAF was developed to measure premenstrual changes and symptoms. The scale comprises 95 items scored 1-6 based on symptom severity and includes summary scales of dysphoric changes: low mood, endogenous depressive features, lability, atypical depressive features, hysteroid features, anxiety, and hostility/anger; behavioral changes of social withdrawal, impulsivity, impaired social functioning, and organic mental features; and physical changes of water retention, general physical discomfort, autonomic physical changes, and fatigue (26).

Validity and reliability studies of a Turkish version of the scale were performed in 1994 by Dereboy et al. (27). Scoring is based on the total score divided by the total number of items. A value of <1.7 is considered no PMS, values of 1.7-2.8 are regarded as mild PMS, 2.8-3.7 are classified as moderate PMS, and >3.7 are graded as severe PMS. A Chronbach alpha coefficient of 0.97 was determined for the entire PAF, and 0.46-0.90 for the domains, which indicated sufficient internal consistency (27).

Daily Record of Severity of Problems

The DRSP is an 11-item self-evaluation tool used to track symptoms daily using a severity scale of 1-6 for 2 months. The evaluation is helpful in determining the timing and severity of premenstrual symptoms and the effect on functionality. Prospective daily monitoring of symptoms for 2 consecutive menstrual cycles is a clinical requirement to meet DSM-IV criteria of

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PMDD. The diagnosis of PMDD is made based on a score of ≥4 points related to depression, anxiety, affective lability, or anger/irritability on at least 2 or more days in the week before menstruation (late luteal phase) in 2 consecutive cycles, ≥4 points on a minimum of 5 of the 11 items for at least 2 days, and ≥4 points for 1 of 3 items evaluating functionality for a period of at least 2 days (28). The scale was developed by Endicott and Harrison in 1990 (29).

Stroop Color-Word Interference Test

The Stroop test first developed in 1935 has been modified into various forms. The Stroop Test-TBAG (Scientific and Technological Research Council of Turkey [TUBITAK] Basic Sciences Research Group) Form was created by combining the original Stroop test with the Victoria form (30,31). Standardization studies have been made of the Stroop test-TBAG Form for a Turkish population (32) This instrument was designed to evaluate the ability to direct and maintain attention, and particularly, the ability to inhibit cognitive interference. The measurement of disruption, or delay in reaction time between congruent and incongruent stimuli is the finding most used (Section 5, in which the participants are asked to reply with the color of the ink of a word provided in an inconsistent color, rather than what the word says. For example, the word "red" presented in blue ink). The Stroop effect upon encountering dissonance is a reliable behavior phenomenon (33). The test is also used to measure other cognitive functions, such as attention, processing speed, cognitive flexibility, and working memory using consistent color-word and simple color patch identification prior to introducing inconsistencies.

The Visual Aural Digit Span Test-B Form

The VADS-B neuropsychological test measures short-term memory, sequencing, and sensory-motor integration. The test subject is presented with increasing sequences of numbers in an oral or visual format and asked to recall the string orally or in writing. Calculations of 4 basic scores (aural-oral, aural-written, visual-oral, visual-written), 6 combined scores, and a total score.

The original VADS Test created by Koppitz to assess basic aspects of memory was revised and adapted for a Turkish population by Karakas and Yalın (34). The B Form includes longer sequences, standardization of the form, and presentation of the subtests, and standard guidelines, with instructions specifying that mnemonic or other assistive strategies were not to be used.

Data Analysis

It was determined that a minimum of 27 patients in each group was necessary to achieve statistical power of 90% and an alpha level of 0.05. The researchers elected to include at least 30 in each group. The statistical analysis of the study data was conducted using IBM SPSS Statistics for Windows, Version 21.0 software (IBM Corp., Armonk, NY, USA). Normal distribution was assessed using the Shapiro-Wilk test. The Student t-test was used to compare the mean values of 2 independent groups showing normal distribution, and a paired t-test was applied for 2 dependent groups. Repeated measures analysis of variance was used on a general linear model to observe changes over time. The Mann-Whitney U test was applied in comparisons of median values of 2 dependent groups not showing normal distribution. The Pearson correlation coefficient was calculated to examine the direct relationship between 2 continuous variables. Descriptive statistics calculated were the mean, SD, median, minimum, and maximum values. A chi-squared test was used to analyze categorical variables. The Fisher exact test was applied to 2x2 tables when >20% of the cells had <5 observations. Descriptive statistics of frequency and percentage were computed. In order to determine the risk factors affecting the PMS/PMDD group, logistic regression analysis was performed and odds ratios and confidence intervals were provided. A value of $p < 0.05$ was accepted as statistically significant.

RESULTS

All of the study participants were in the age group of 14-18 years; the mean age was 16.14 years in the PMS/PMDD group and 16.13 years in the control group. No significant difference was determined between the groups in terms of age or PMT score. In addition, there was no significant difference between the groups in the number of years of education, maternal education level, maternal employment status, paternal education level, paternal employment status, number of siblings, parents living together, or parental consanguinity.

The diagnoses of mental disorder determined with the K-SADS-PL and the evaluations according to the CBCL scores are shown in Table 1. At least 1 comorbid psychiatric disorder was diagnosed in 63.9% of the participants diagnosed with PMS/PMDD. In a

Table 1: The diagnosis of mental disorder and evaluation according to the CBCL score

Diagnosis	PMS (n=36)	Control (n=30)	Statistics	p
Attention deficit hyperactivity disorder	22.2% (n=8)	10.0% (n=3)	χ^2:1.761	0.320
Specific phobia	8.3% (n=3)	0.0% (n=0)	χ^2:1.020	0.245
Major depressive disorder	27.8% (n=10)	3.3% (n=1)	χ^2:32.124	0.009*
Social phobia	5.6% (n=2)	10.0% (n=3)	χ^2:0.461	0.653
Generalized anxiety disorder	8.3% (n=3)	13.3% (n=4)	χ^2:0.431	0.693
Panic disorder	5.6% (n=2)	0.0% (n=0)	χ^2:0.687	0.497
Obsessive compulsive disorder	2.8% (n=1)	0.0% (n=0)	χ^2:0.182	1.000
More than one diagnosis	63.9% (n=23)	36.7% (n=11)	χ^2:4.855	0.028*
Psychiatric treatment	47.2% (n=17)	23.3% (n=7)	χ^2:4.036	0.045*
Child Behavior Checklist	**PMS (n=36)**	**Control (n=30)**	**Statistics**	**p**
Social withdrawal	4.69±3.38	3.86±3.54	T:0.948	0.347
Somatic complaints	2.97±3.14	1.64±2.18	T:1.901	0.062
Anxiety/depression	8.71±4.86	6.25±4.61	T:2.046	0.045*
Social problems	1.97±1.77	1.21±1.45	T:1.823	0.073
Attitude problems	2.80±2.55	1.26±1.10	T:2.931	0.005*
Attention problems	6.37±4.02	4.04±3.10	T:2.533	0.014*
Criminal behavior	1.37±1.50	1.07±1.88	T:0.705	0.484
Aggressive behavior	9.14±5.67	5.86±5.91	T:2.243	0.029*
Internalizing problems	13.66±8.80	9.11±6.51	T:2.281	0.026*
Externalizing problems	10.51±6.89	6.93±7.55	T:1.967	0.054
Total problems	41.80±23.54	28.39±18.28	T:2.474	0.016*

T: Student t-test, χ^2: Chi-squared test and Fisher exact test. *p<0.05. CBCL: Child Behavior Checklist, PMS: Premenstrual syndrome

comparison of the PMS/PMDD group and the control group, a statistically significant difference was determined in the presence of major depressive disorder (MDD) (p=0.009), a concomitant diagnosis of mental disorder (p=0.028), and medical treatment (p=0.045). Evaluation of the CBCL scores indicated that the externalizing, internalizing, and total problem scores were higher in the PMS/PMDD group.

The rate of MDD was 11.2-fold higher in the PMS/PMDD group (p=0.026). Psychiatric disorder was present about 3.5 times more often in the PMS/PMDD group compared with the control group (p=0.015). The EDS results from testing both the luteal and follicular phases and the difference between the phases (mean change over time) of the PMS/PMDD and control groups was found to be statistically significant (p=0.004). In the PMS/PMDD group, the difference between the mean EDS score in the follicular and luteal phases was statistically significant (p=0.003), while it was not statistically significant in the control group.

Evaluation according to the mean T-DSM-IV-S score revealed no significant difference between the PMS/PMDD and control groups in any of the subtests.

The evaluation of the Stroop test is shown in Table 2. In the PMS/PMDD group, a statistically significant difference was observed between the follicular and luteal phases in the mean score for time 4 (p=0.017), time 5 (p=0.004), error 5 (p=0.011) and correction 5 (p=0.010), as presented in Table 3. In the control group, a statistically significant difference was observed between the follicular and luteal phases only in the mean score for time 1 (p=0.006). No significant difference was seen between the groups in the change over time of any other scores.

The PMS/PMDD severity points recorded using the PAF were evaluated in the 2 phases in comparison with Stroop test performance, and the results are shown in Table 4. A weak, positive, linear correlation was determined between the PMS score and Stroop time 1 (follicular phase) (r=0.244, p=0.048). Similarly, a weak, positive, linear correlation was determined between the PMS score and Stroop time 1 (luteal phase) (r=0.252,

Table 2: Stroop Test scores in the study groups

	PMS (n=36)	Control (n=30)	T	p
Follicular phase				
Time 1	8.59±0.98	8.22±0.97	1.500	0.139
Error 1	0.00±0.00	0.00±0.00	-	-
Correction 1	0.00±0.00	0.00±0.00	-	-
Time 2	10.20±2.35	8.87±1.32	2.741	0.008*
Error 2	0.19±0.40	0.17±0.38	0.287	0.775
Correction 2	0.19±0.40	0.13±0.35	0.655	0.515
Time 3	11.37±1.94	11.75±2.00	-0.772	0.443
Error 3	0.28±0.45	0.40±0.77	-0.800	0.426
Error 2	0.19±0.40	0.17±0.38	0.287	0.775
Correction 3	0.28±0.45	0.40±0.77	-0.800	0.426
Correction 2	0.19±0.40	0.13±0.35	0.655	0.515
Time 4	14.01±2.54	14.36±2.66	-0.548	0.585
Time 5	20.25±4.52	20.52±5.85	-0.213	0.832
Error 5	1.08±1.16	1.13±1.22	-0.170	0.865
Correction 5	0.86±1.02	1.10±1.24	-0.859	0.394
Luteal phase				
Time 1	8.82±1.26	8.69±1.16	0.447	0.656
Error 1	0.08±0.28	0.07±0.37	0.210	0.835
Correction 1	0.08±0.28	0.07±0.37	0.210	0.835
Time 2	9.96±2.08	9.26±1.54	1.540	0.129
Error 2	0.22±0.54	0.13±0.43	0.726	0.470
Correction 2	0.17±0.45	0.13±0.43	0.306	0.761
Time 3	11.81±2.10	11.97±1.90	0.389	0.699
Error 3	0.47±0.81	0.40±0.67	-0.318	0.751
Correction 3	0.44±0.81	0.37±0.61	0.433	0.667
Time 4	15.13±2.84	14.74±3.39	0.508	0.613
Error 4	0.58±0.69	0.40±0.62	1.122	0.266
Correction 4	0.56±0.69	0.33±0.55	1.423	0.160
Time 5	22.44±5.15	20.19±4.19	1.921	0.059
Error 5	1.61±1.29	1.30±1.12	1.034	0.305
Correction 5	1.36±1.17	1.17±1.02	0.710	0.480

T: Student t-test. *p<0.05. PMS: Premenstrual syndrome

p=0.041). A weak, positive, linear correlation was also determined between the PMS score and Stroop time 2 (luteal phase) (r=0.309, p=0.011).

A statistically significant difference was determined between the PMS/PMDD and control groups in the luteal phase VADS-B auditory verbal (p=0.015), auditory written (p=0.040), auditory stimulus (p=0.009), verbal response (p=0.010), written response (p=0.049), internal sense (p=0.046), intrasensory (p=0.025), and luteal mean total scores (p=0.013) (Table 5). No significant difference was observed between the groups in the mean luteal visual-oral, luteal visual-written, luteal visual stimulus, or follicular VADS-B scores.

In the PMS/PMDD group, a statistically significant difference was determined between the follicular and luteal phases in the VADS-B aural-oral (p=0.032), visual-oral (p=0.005), visual-written (p=0.005), aural stimulus (p=0.025), visual stimulus (p<0.001), verbal response (p<0.001), written response (p=0.002), intersensory (p<0.001), intrasensory (p=0.003), and

Table 3: Stroop Test scores in the PMS/PMDD group by phase of menstrual cycle

	Follicular (n=36)	Luteal (n=36)	T	p
Time 1	8.59±0.98	8.82±1.26	0.982	0.333
Error 1	0.00±0.00	0.08±0.28	-1.784	0.083
Correction 1	0.00±0.00	0.08±0.28	-1.784	0.083
Time 2	10.20±2.35	9.96±2.08	0.606	0.548
Error 2	0.19±0.40	0.22±0.54	-0.255	0.800
Correction 2	0.19±0.40	0.17±0.45	0.274	0.786
Time 3	11.37±1.94	11.81±2.10	-1.252	0.219
Error 3	0.28±0.45	0.47±0.81	-1.363	0.182
Correction 3	0.28±0.45	0.44±0.81	-1.183	0.245
Time 4	14.01±2.54	15.13±2.84	-2.501	0.017*
Error 4	0.42±0.60	0.58±0.69	-1.435	0.160
Correction 4	0.42±0.60	0.56±0.69	-1.152	0.257
Time 5	20.25±4.52	22.44±5.15	-3.087	0.004*
Error 5	1.08±1.16	1.61±1.29	-2.677	0.011*
Correction 5	0.86±1.02	1.36±1.17	-2.707	0.010*

T: Paired t-test. *p<0.05. PMDD: Premenstrual dysphoric disorder, PMS: Premenstrual syndrome

Table 4: Effect of premenstrual syndrome on Stroop Test by phase of menstrual cycle

Stroop Test scores and PMS	Follicular (n=36)		Luteal (n=36)	
	r	p	r	p
Time 1	0.244	0.048*	0.252	0.041*
Error 1	N/A	N/A	0.050	0.687
Correction 1	N/A	N/A	0.050	0.687
Time 2	0.225	0.069	0.309	0.011*
Error 2	-0.130	0.299	0.143	0.252
Correction 2	-0.098	0.432	0.088	0.481
Time 3	-0.064	0.612	-0.071	0.570
Error 3	-0.009	0.940	-0.122	0.331
Correction 3	-0.009	0.940	-0.146	0.243
Time 4	-0.114	0.364	-0.019	0.882
Error 4	0.025	0.843	-0.027	0.831
Correction 4	0.025	0.843	-0.011	0.930
Time 5	-0.013	0.914	0.128	0.305
Error 5	0.039	0.754	0.068	0.588
Correction 5	-0.092	0.465	0.009	0.944

Pearson correlation test used for analysis. *p<0.05. PMS: Premenstrual syndrome

mean total scores (p<0.001), which are shown in Table 6. In the control group, no significant difference was found between the follicular and luteal phases in any of the VADS-B scores.

No significant difference was observed in the analyses performed examining those without an ADHD comorbidity (PMS group n=28, control group n=27) or without any psychiatric comorbidity (PMS group n=13, control group n=20).

DISCUSSION

High rates of concomitant mental disorders have been reported in studies of adult women diagnosed with PMS or PMDD (7,8). Consistent with the literature, we also found that there was a significantly higher rate of accompanying mental disease in the PMS/PMDD group. The presence of psychiatric disease was 3.5-fold higher in the PMS/PMDD group than in the control group. The CBCL score was also higher in the PMS/PMDD group. A statistically significant difference was also determined between the PMS/PMDD group and the control group in the anxiety/depression, attitude, attention problems, and aggressive behavior scales, and the internalizing problems and mean total problems scores. It has been reported that the rates of internalizing and impulsive behavior are high in girls with PMS/PMDD (35). The findings of the current study were consistent. A significant proportion of young women with PMS/PMDD are known to have cognitive impairments, such as poor concentration, memory, and motor coordination (9,10). PMS/PMDD cases have also been shown to have a significantly high rate of attention problems and experience difficulties in this respect. We did not determine a significant difference in terms of social withdrawal, somatic complaints, social problems, or criminal behavior scores.

In a previous study of adult females with PMS/PMDD, a positive correlation between a PMS score and trait anxiety and depression levels was reported and it was determined that women with PMS experienced significantly more emotional problems than women without PMS (36). Increasing evidence has been presented to indicate that women with PMDD could be at risk of developing MDD in the future (37). One study found that women with PMDD have a 14-fold higher risk of developing MDD, and it was concluded that PMDD could be a risk factor or a prodromal sign of MDD (38). In the current study, a significant relationship was determined between MDD and the PMS/PMDD group, and the diagnosis of MDD in this group was seen to be 11.1-fold higher than that of the control group. The EDS, which is primarily used to determine depressive symptoms in women with postpartum depression, has been shown to be

Table 5: The Visual Aural Digit Span Test scores in the premenstrual syndrome and control groups

	PMS (n=36)	Control (n=30)	T	p
Follicular phase				
Aural-oral	5.94±0.89	6.17±1.05	-0.928	0.357
Visual-oral	6.11±1.06	6.10±1.24	0.039	0.969
Aural-written	6.03±0.94	6.43±1.17	-1.565	0.123
Visual-written	6.75±1.23	7.00±1.20	-0.831	0.409
Aural stimulus	11.97±1.63	12.60±1.99	-1.408	0.164
Visual stimulus	12.86±1.84	13.10±1.94	-0.513	0.610
Oral response	12.06±1.62	12.27±1.96	-0.479	0.634
Written response	12.78±1.77	13.43±2.03	-1.400	0.166
Intersensory	12.69±1.64	13.17±1.95	1.070	0.288
Intrasensory	12.14±1.61	12.53±2.13	0.857	0.395
Total	24.83±2.90	25.70±3.62	1.079	0.285
Luteal phase				
Aural-oral	5.64±0.90	6.17±0.79	-2.505	0.015*
Visual-oral	5.58±0.87	6.03±1.03	-1.917	0.060
Aural-written	5.86±0.83	6.33±0.99	-2.100	0.040*
Visual-written	6.33±1.01	6.60±1.00	-1.069	0.289
Aural stimulus	11.50±1.40	12.50±1.59	-2.711	0.009*
Visual stimulus	11.92±1.40	12.63±1.77	-1.835	0.071
Oral response	11.22±1.31	12.20±1.67	-2.665	0.010*
Written response	12.19±1.39	12.93±1.60	-2.010	0.049*
Intersensory	11.97±1.63	12.77±1.52	-2.030	0.046*
Intrasensory	11.44±1.42	12.37±1.83	2.304	0.025*
Total	23.42±2.38	25.13±3.05	-2.567	0.013*

T: Student t-test. *p<0.05. PMS: Premenstrual syndrome

Table 6: Evaluation of the Visual Aural Digit Span Test scores in the premenstrual syndrome group by phase of menstrual cycle

	Follicular (n=36)	Luteal (n=36)	T	p
Aural-oral	5.94±0.89	5.64±0.90	2.231	0.032*
Visual-oral	6.11±1.06	5.58±0.87	3.001	0.005*
Aural-written	6.03±0.94	5.86±0.83	1.291	0.205
Visual-written	6.75±1.23	6.33±1.01	2.973	0.005*
Aural stimulus	11.97±1.63	11.50±1.40	2.348	0.025*
Visual stimulus	12.86±1.84	11.92±1.40	4.130	0.001*
Oral response	12.06±1.62	11.22±1.31	3.918	0.001*
Written response	12.78±1.77	12.19±1.39	3.416	0.002*
Intersensory	12.69±1.64	11.97±1.63	3.993	0.001*
Intrasensory	12.14±1.61	11.44±1.42	3.247	0.003*
Total	24.83±2.90	23.42±2.38	5.222	0.001*

T: Paired t-test. *p<0.05

significantly sensitive in women with PMS/PMDD. The results suggest that PMS/PMDD could produce similar hormonal events and symptoms to those experienced in the postpartum period.

Analysis of the current study data indicated that the incidence of ADHD was greater in the PMS/PMDD group than in the control group, but not to a level that reached statistical significance. This may have been due to the relatively small number of cases in the sample. According to the DSM diagnostic criteria, the symptoms must have started before puberty for the diagnosis of ADHD. While no significant difference was found in the T-DSM-IV-S scores of the groups in this study, there was a difference in concentration, attention and short-term memory according to the phase of the menstrual cycle, specifically the luteal phase, which could go unnoticed. We observed no significant difference in the diagnosis of ADHD based on semi-structured interviews and

clinical evaluations between the 2 groups, which was consistent with the scale results.

It has been reported that women diagnosed with PMS/PMDD experienced effects on visual-spatial and motor skills, attention and concentration, verbal memory, working memory and reaction times, especially in the luteal phase (4-6,11). In the current study, the results of the neuropsychological tests administered in the luteal phase to the girls in the PMS/PMDD group were significantly lower in that phase than in the follicular phase, which was consistent with findings in literature. Studies have not reported change in other neuropsychological functions of visual memory, cognitive flexibility, planning capability, or verbal fluency (39-42).

The Stroop test essentially evaluates the susceptibility to cognitive interference and the ability to sustain attention. Concepts that can be measured include the ability to pursue processing despite a disruptive effect, cognitive flexibility, selective and divided attention, and the speed of information processing (33,43). When the 2 groups in the current study were examined, the only statistically significant difference seen was between the follicular and luteal phases in the mean points for time 1 (p=0.006) in the control group; no significant difference was observed in any other Stroop scores.

Variability in cognitive and motor test performance during different phases of the menstrual cycle among healthy women with a normal cycle has previously been reported (44). In a study that compared 50 males with 50 healthy females with regular menstrual cycles, it was observed that women in the luteal phase demonstrated significantly lower performance on the Stroop test compared with the men (45). In the current study, although the time 1 results in the luteal phase were longer than those recorded in the follicular phase in the PMS/PMDD group, the difference was not statistically significant. The Stroop effect, the delay in reaction time between congruent and incongruent stimuli, is thought to be related to the left orbitofrontal cortex and the anterior singular cortex (43). Consistent with the literature, the results of the current study showed a statistically significant difference between the PMS/PMDD group and the control group in the results measuring reaction to interference. In addition, the difference in the findings of the same test between the follicular and luteal phases in the PMS/PMDD group was significant, with more difficulty successfully completing the task seen in the luteal phase. This was also valid for time 4, error 5 and correction 5 scores.

The change over time (difference between the follicular and luteal phases) in the oral response elements of the VADS-B test was found to be statistically significant in a comparison of the PMS/PMDD and control groups, but no significant difference was found in the other scores. Some studies in literature have stated that estrogen influences memory processes and increases working memory and brain activity (46,47). The drop in estrogen before menstruation could affect working memory. Previous studies have shown that serotonin is also related to working memory and that a deficiency in serotonin is related to PMDD (48,49). It has also been reported that a reduction in tryptophan impairs working memory and increases PMS symptoms (50-52). Therefore, hormonal changes occurring in the luteal phase may be related to performance in women with PMS/PMDD. The difference in function we observed between the luteal phase and the follicular phase in the PMS/PMDD cases that was not seen in the control group is a strength of this study. Comorbid psychiatric disorder, such as ADHD or MDD, was considered as a possible influence on neuropsychological test results; however, the assessment of the participants in this study revealed no significant change in the results when this was taken into account.

In conclusion, PMS/PMDD appeared to have a significant effect on short-term memory, sensory-motor integration, series learning, sequencing, and attention in the luteal phase, independent of ADHD or any other mental disorder, but when compared with the control group, the impairment remained within normal limits for the age group.

The neurocognition of the girls in the current study was examined twice during the menstrual cycle. Further studies of this type conducted with a larger number of cases would be useful to further examine the effect of comorbid psychiatric diseases and medication use. Although patients using methylphenidate for ADHD did not take the medication just before the application of the tests, any type of routine psychotropic drug treatment could have an effect on neurocognitive function. Therefore, we repeated the analyses excluding cases with a comorbid psychiatric diagnosis. Nevertheless, additional data from a larger group with no comorbid psychiatric disease and who are not receiving any treatment would be valuable. In addition, while participants were excluded from this study if they had not had a regular menstrual cycle for at least 2 years prior to the study in order to exclude irregular, non-

productive cycles, non-productive menstrual cycles can be associated with periods of stress. Periodic ultrasonography examinations in future research could be useful in this respect.

Appointments in the follicular and luteal phases made in this study were based on the patients' DRSP data. Though it has been said in the literature that hormone tests are not a definitive measurement, this information could be helpful in a more precise determination of the phase. The application of brain imaging methods could have provided clearer information related to brain regions and functions as a supplement to the neuropsychological tests used in this study. It would also have been extremely useful to have extensively examined the levels of gonadal steroid hormones, as this could be responsible for fluctuations.

The effects and results of treatment given to the patients after the diagnosis of PMS/PMDD were not examined in this study. There is a need for further research on this aspect. The formal diagnosis of PMS/PMDD requires a confirmed daily record maintained for several months. Early screening tools would both facilitate diagnosis and prevent cases being left untreated.

A review of the research in the literature suggests that the current study may be the first to examine neurocognitive function in adolescent girls aged 14-18 years diagnosed with PMS/PMDD. Previous studies have been more focused on cognitive and memory problems in participants diagnosed with PMS/PMDD in early adulthood. Our research was designed to be a comprehensive study of problems associated with hormonal processes in adolescent girls diagnosed with PMS/PMDD. The results demonstrated that PMS/PMDD had a negative effect on cognitive action in the face of disruption, cognitive flexibility, selective and divided attention, and information processing.

Healthy adolescent girls demonstrated poorer cognitive function in the luteal phase. One of the most significant results of the current study is that the PMS/PMDD patients had lower performance in the areas of disruptive effect, and information processing and attention. Within the PMS/PMDD group, performance in the luteal phase was significantly lower than that recorded in the follicular phase. The fact that this significant difference continued after the exclusion of concomitant psychiatric diseases suggests that the PMS/PMDD diagnosis alone may have been the cause. In addition, within the PMS/PMDD group, significantly lower performance was observed in short-term memory functions in the luteal phase,

which was not apparent in the control group. There was no significant difference between the PMS/PMDD group and the control group in the VADS-B subparameters, suggesting that even if there was an effect in the PMS/PMDD group, it was within normal limits.

Examination of the relationship between PMS severity and Stroop-effect attention problems and short-term memory function indicated that there was a correlation with time 1 and 2 in the Stroop test, but this significance was not seen in other subparameters or in the VADS-B test results. This suggested that these cognitive functions may be related to the diagnosis of PMS/PMDD rather than the severity of PMS.

Contribution Categories		Author Initials
Category 1	Concept/Design	K.K., C.C., M.B.U.
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	Data analysis/Interpretation	C.C., M.B.U., B.S.
Category 2	Drafting manuscript	K.K., C.C., B.S.
	Critical revision of manuscript	M.B.U., K.K.
Category 3	Final approval and accountability	K.K., M.B.U., C.C., A.B., B.S., T.K.
Other	Technical or material support	A.B., B.S., T.K.
	Supervision	K.K.

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