

Neuropsychological performance and menstrual cycle: a literature review

Desempenho neuropsicológico e ciclo menstrual: revisão da literatura

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Abstract

Approximately 80% of all women of reproductive age experience psychological and physical changes associated with the premenstrual phase. Cognitive alterations are among the most common complaints. In this context, studies have assessed cognitive performance across the menstrual cycle in healthy women and also in women with premenstrual syndrome (PMS). The main objective of the present study was to review the literature on cognitive function in different phases of the menstrual cycle in women of reproductive age, both healthy and with PMS, in particular premenstrual dysphoric disorder (PMDD). We searched MEDLINE and LILACS databases. A total of 27 studies were selected. The studies used heterogeneous methodologies. Most studies suggested that healthy women show small fluctuations in cognitive performance across the menstrual cycle, with low performance scores in the luteal phase for visuospatial and motor skills, attention and concentration, verbal memory, visual memory, working memory, and reaction time. Among women with PMS or PMDD, low performance scores for visuospatial and motor skills, attention and concentration, verbal memory, working memory, reaction time and impulsivity were also detected in the luteal phase. Symptoms observed in PMS/PMDD patients showed low intensity, but greater when compared with healthy women. Evidence indicates fluctuations in cognitive performance in the different phases of the menstrual cycle in healthy and PMS women, with worse performance for women with PMS/PMDD in the luteal phase. However, methodological limitations prevent us from drawing solid conclusions. Further studies are needed to investigate the impact of these cognitive fluctuations on patients' daily activities.

Keywords: Premenstrual syndrome, premenstrual dysphoric disorder, cognitive functioning, impulsivity, attention, executive functions.

Resumo

Cerca de 80% das mulheres em idade fértil apresentam alterações psicológicas e físicas associadas à fase pré-menstrual. Dentre as queixas mais comuns estão as alterações cognitivas. Nesse contexto, tem-se estudado o desempenho cognitivo ao longo do ciclo menstrual de mulheres com e sem síndrome pré-menstrual (SPM). O objetivo principal deste estudo foi revisar a literatura acerca do desempenho das funções cognitivas nas diferentes fases do ciclo menstrual de mulheres em idade reprodutiva, sadias ou portadoras de SPM, em particular o transtorno disfórico pré-menstrual (TDPM). Foram revisadas as bases de dados MEDLINE e LILACS. Um total de 27 estudos foram selecionados. Os estudos eram heterogêneos em suas metodologias. Em sua maioria, os trabalhos evidenciaram que mulheres sadias apresentam variações leves no desempenho cognitivo ao longo do ciclo menstrual, obtendo menor pontuação, durante a fase lútea, nas habilidades visuoespaciais e motoras, atenção e concentração, memória verbal, memória visual, memória de trabalho e tempo de reação. Entre as mulheres com SPM ou TDPM, foi identificada, na fase lútea, redução no desempenho das habilidades visuoespaciais e motoras, atenção e concentração, memória verbal, memória de trabalho, tempo de reação e impulsividade. Tais sintomas apresentaram intensidade leve, porém superior à observada em mulheres sadias. As evidências indicam a existência de variações no desempenho cognitivo ao longo das diferentes fases do ciclo menstrual de mulheres sadias ou com SPM, com desempenho cognitivo pior em mulheres com SPM/TDPM na fase lútea. Entretanto, limitações metodológicas impedem conclusões sólidas. Novos estudos são necessários para investigar o impacto dessas oscilações cognitivas nas atividades cotidianas dos pacientes.

Descritores: Síndrome pré-menstrual, transtorno disfórico pré-menstrual, funcionamento cognitivo, impulsividade, atenção, funções executivas.

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Introduction

Physical and psychological symptoms associated with the premenstrual phase are reported by about 80% of women of reproductive age.¹ The spectrum of symptoms may range from mild discomfort up to multiple symptoms of moderate to severe intensity, including functional impairment. In the latter case, women may be diagnosed with premenstrual syndrome (PMS) or, in more severe cases, with premenstrual dysphoric disorder (PMDD).^{1,2}

According to the International Classification of Diseases (ICD-10),³ PMS is characterized by a collection of physical, mood, cognitive, and behavioral symptoms that follow a cyclic pattern, starting between 1 to 2 weeks before menstruation (luteal phase) and vanishing on the first days of menstrual flow (follicular phase).⁴ The prevalence of PMS in international studies varies from 20 to 40%.⁵ PMDD is a severe subtype of PMS in which mood symptoms predominate in the premenstrual phase (e.g. sadness, reduced ability to experience pleasure, mood lability, anxiety, irritability, anger, self-depreciation, reduced pain threshold, reduced impulse control, and sleep disorders).^{6,7} PMDD affects 3 to 8% of women.¹

Cognitive complaints, including difficulty concentrating, memory impairment, distractibility, lack of self-confidence when making decisions, or even indecision, in addition to motor insufficiency, comprise the spectrum of symptoms associated with the premenstrual phase. In PMDD, these complaints are even more frequent and intense.^{1,2} However, the results reported by studies focusing on the influence of the menstrual cycle on cognitive function are conflictive.⁸

The main aim of the present study was to review the literature on neuropsychological performance in the different phases of the menstrual cycle of women of reproductive age, both healthy and with PMS/PMDD.

Method

The literature was browsed for studies focusing on cognitive performance in women of reproductive age across the different phases of the menstrual cycle. The databases and periods assessed were as follows: MEDLINE, studies from 1976 to December 2010, and Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS), studies from 1982 to December 2010. The following keywords were used: menstrual cycle, premenstrual syndrome, premenstrual dysphoric disorder, neuropsychology, cognitive functioning, impulsivity, attention, and executive functions. Studies published in Portuguese and English were reviewed. The reference lists of the selected studies were also searched. A total of 155 articles were read to

select those assessing neuropsychological functioning with the use of psychometric tests in women of reproductive age, either healthy or with PMS/PMDD.

Results and discussion

Of the 155 articles retrieved, 27 were found to use psychometric tests for the assessment of neuropsychological functioning across the menstrual cycle of women of reproductive age (18 to 45 years), either healthy or with PMS/PMDD. Seventeen articles assessed cognitive changes in the different phases of the menstrual cycle in healthy women,⁸⁻²⁴ six assessed women with PMS,²⁵⁻³⁰ and four articles assessed women with PMDD.³¹⁻³⁴ The neuropsychological functions assessed were different across studies and included verbal and non-verbal memory, working memory, attention and concentration, reasoning, language, executive functions (planning, impulse control, and cognitive flexibility), reaction time, motor and visuospatial skills.

The main neuropsychological tests used in the reviewed studies were: Stroop Test, Digit Span, Digit Symbol, Trail Making A and B, California Verbal Learning Test (CVLT), Wechsler Adult Intelligence Scale – Revised (WAIS-R), Wechsler Memory Scale – Revised (WMS-R), Verbal Fluency (FAS), and the Grooved Pegboard test. The designs and results of the 27 studies included in the review are described in Tables 1 and 2.

Studies involving healthy women showed mild fluctuations in visuospatial, fine motor, and articulatory skills, attention and concentration, verbal memory, visual memory, working memory, and reaction time across the menstrual cycle, with a trend towards worse performance scores in the luteal phase (Table 1). However, findings were not consensual. No changes were observed in impulsivity and deductive logical reasoning. The results reported suggest that hormonal changes have an impact on the cognitive performance of healthy women.^{9,12-18,20,24}

In women with PMS and PMDD, cognitive complaints associated with the premenstrual phase point to the presence of abnormalities in the different phases of the menstrual cycle and suggest that systematic evaluations would reveal additional details of such abnormalities. However, studies employing neuropsychological functioning tests have reported only mild changes, with conflictive findings. Evidence points to the presence of mild impacts on visuospatial and motor skills, attention and concentration, verbal memory, working memory, reaction time, and impulsivity, with worse performance scores in the luteal phase (Table 2). No changes were observed in visual memory, cognitive flexibility, ability to plan, and verbal fluency. When women with PMS or

Table 1 – Studies assessing neuropsychological functioning across the menstrual cycle in healthy women

Study	n	Mean age (age group)	Neuropsychological functions	Results (follicular vs. luteal phase)	Tests	Notes
Golub, 1976 ²¹	50	NI (30-45)	a) Visuospatial and motor skills b) Attention and concentration c) Verbal memory	a) NS b) NS c) NS	Hidden patterns, Nearer point, Gestalt, Anagrams, Inference, Picture number, Utility (fluency), Utility (flexibility), Associational fluency, Plot titles (fluency), Plot titles (cleverness), Possible jobs, Expressional fluency, Hidden figures, Figure classification	Confirmation of menstrual phase by counting the days since the first day of the last menstrual period
Slade & Jenner, 1980 ²⁰	13	NI (19-22)	Reaction time	Worse performance in the luteal phase	Primary task, Secondary task	Confirmation of menstrual phase by counting the days since the first day of the last menstrual period
Broverman et al., 1981 ¹⁹	87	19.2	a) Visuospatial and motor skills b) Attention and concentration c) Impulsivity	a) NS b) NS c) NS	Speed of reading repeated color names, Speed of naming repeated colors, Embedded figures test, WAIS block design subtest	Confirmation of menstrual phase by the basal body temperature method: 21/87 (24%) probably did not ovulate
Hartley et al., 1987 ¹⁸	30	34.6	a) Verbal memory b) Verbal logical reasoning	a) Worse performance in memory tests using semantically similar word lists in the follicular phase and worse performance in memory tests using acoustically similar word lists in the luteal phase b) Improved verbal reasoning speed in complex sentences in the luteal phase	Logical reasoning, Recall of acoustically or semantically similar word lists, Immediate and delayed retention of prose	Confirmation of menstrual phase by the basal body temperature method
Hampson, 1990 ¹⁷	50	26.4 (20-43)	a) Visuospatial and motor skills b) Deductive logical reasoning c) Verbal fluency	a) Worse performance in spatial skills and improved performance in manual and articulatory skills in the late follicular phase compared with the menstrual phase b) NS between the menstrual and late follicular phases c) NS between the menstrual and late follicular phases	Portable Rod-and-Frame Test, Hidden Figures, Space Relations, Number Comparisons, Identical Pictures, Subtraction and Multiplication, Oral Fluency, Expressional Fluency, Speeded Counting, Color Reading and Naming, Syllable Repetition, Manual Sequence Box, Purdue Pegboard, Finger Tapping, Inference Test	Hormonal confirmation of menstrual phase
Lord & Taylor, 1991 ¹⁴	50	NI	Attention and concentration	Worse performance in the luteal phase	Stroop color-word test	Confirmation of menstrual phase by counting the days since the first day of the last menstrual period Control group: 50 men
Phillips & Sherwin, 1992 ¹⁶	25	24 (18-35)	a) Attention and concentration b) Verbal memory c) Visual memory d) Working memory	a) NS b) NS c) Worse performance in the follicular phase d) NS	WMS	Hormonal confirmation of menstrual phase
Gordon & Lee, 1993 ¹³	82	NI (18-36)	a) Visuospatial and motor skills b) Attention and concentration c) Verbal memory d) Visual memory	a) NS b) NS c) NS d) NS	Symbol digit modalities, Cognitive laterality battery, Verbosequential tests, Visuospatial tests	Hormonal confirmation of menstrual phase Inclusion of oral contraceptive users (34/82)

(cont.)

Table 1 – Studies assessing neuropsychological functioning across the menstrual cycle in healthy women (cont.)

Study	n	Mean age (age group)	Neuropsychological functions	Results (follicular vs. luteal phase)	Tests	Notes
Brugger et al., 1993 ¹⁵	20	30.4	a) Attention and concentration b) Working memory	a) Worse performance in the luteal phase b) Worse performance in the luteal phase	Mental Dice Task	Confirmation of menstrual phase by counting the days since the first day of the last menstrual period
Matthews & Ryan, 1994 ¹²	28	21 (19-26)	a) Visuospatial and motor skills b) Attention and concentration c) Reaction time	a) NS b) NS c) Worse performance in the luteal phase	Sustained attention tasks	Confirmation of menstrual phase by counting the days since the first day of the last menstrual period Inclusion of oral contraceptive users (16/28)
Cockerill et al., 1994 ¹¹	27	22.6	Visuospatial and motor skills	NS	Perceptual motor task	Confirmation of menstrual phase by counting the days since the first day of the last menstrual period, basal body temperature method Control group: 27 men
Epting & Overman, 1998 ¹⁰	27	19.1 (17-22)	Visuospatial and motor skills	NS	Mental rotations, Rod and Frame, Finger Tap, Spatial Array, Water Level, Purdue Pegboard	Confirmation of menstrual phase by ovulation prediction test (urinary luteinizing hormone) Control group: 20 men
Maki et al., 2002 ⁹	16	20.1 (18-28)	a) Visuospatial and motor skills b) Verbal memory c) Verbal fluency	a) Worse performance in visuospatial skills and improved performance in fine motor skills in the luteal phase b) Improved performance in implicit memory test in the luteal phase c) Improved performance in the luteal phase	Attention/vigilance task, FOI study task, Fluency tasks, Category exemplar generation test, FOI test, Mental Rotations, Grooved Pegboard	Hormonal confirmation of menstrual phase
Halari et al., 2005 ²⁴	42	27.6 (19-35)	a) Visuospatial and motor skills b) Working memory c) Verbal fluency	a) NS b) NS c) NS	Vocabulary subtest of the WAIS-R, Working memory task, Mental rotation, CBJOLO, MJOLO, Phonological fluency, Category fluency, Inhibition task	Hormonal confirmation of menstrual phase Control group: 42 men
Solís-Ortiz & Corsi-Cabrera, 2008 ⁸	9	25.7 (19-34)	a) Visuospatial and motor skills b) Attention and concentration c) Visual memory d) Verbal fluency	a) NS b) Improved performance in the early luteal phase c) Worse performance in the luteal phase d) Improved performance in the luteal phase	Hidden Figures, Purdue Pegboard, Word fluency, Localization, Continuous Performance, Wisconsin Card Sorting	Confirmation of menstrual phase by counting the days since the first day of the last menstrual period, basal body temperature method
Mordecai et al., 2008 ²²	36	25.7 (18-40) 24.2 (18-40) oral contraceptive users	a) Visuospatial and motor skills b) Attention and concentration c) Verbal memory d) Visual memory e) Verbal fluency	a) NS b) NS c) NS d) NS e) NS	CVLT, Phonemic, Rhyme, Ideational, Brief visuospatial memory test revised, Mental rotations, Brief test of attention	Hormonal confirmation of menstrual phase Inclusion of oral contraceptive users (20/36)
Hatta & Nagaya, 2009 ²³	30	25.6 (20-34)	a) Attention and concentration b) Verbal memory	a) NS b) NS	WMS-R, Stroop test	Hormonal confirmation of menstrual phase

CVLT = California Verbal Learning Test; FOI = Fragmented Object Identification; NI = not informed; NS = non-significant differences; WAIS = Wechsler Adult Intelligence Scale; WMS = Wechsler Memory Scale.

Table 2 – Studies assessing neuropsychological functioning across the menstrual cycle in women with PMS/PMDD

Study	n	Mean age (age group)	Neuropsychological functions	Results (follicular vs. luteal phase)	Tests	Notes
Posthuma et al., 1987 ³⁰	12 PMS 9 C	NI (28-40)	Visuospatial and motor skills	Women with PMS showed psychomotor slowness in the luteal phase	MacQuarrie test for mechanical ability, Revised Minnesota Paper Form Board, Crawford small parts dexterity, Minnesota rate of manipulation	Confirmation of menstrual phase by the basal body temperature method PMS confirmation by completing a daily questionnaire for two menstrual cycles
Rapkin et al., 1989 ²⁹	10 PMS 9 C	NI (18-40)	a) Attention and concentration b) Verbal memory	a) NS b) NS	Selective recall, Incidental recall, Perceptual speed	Confirmation of menstrual phase by the basal body temperature method PMS confirmation by completing a daily questionnaire for two menstrual cycles
Diener et al., 1992 ²⁵	16 PMS	37.6 (27-43)	a) Attention and concentration b) Working memory c) Reaction time	a) Worse performance in the luteal phase b) Worse performance in the luteal phase c) Worse performance, regardless of phase	Digit span task, Letter detection, Combined task	Confirmation of menstrual phase by counting the days since the first day of the last menstrual period PMS confirmation by interview
Keenan et al., 1992 ²⁶	14 PMS 10 C	34 PMS 31 C	a) Visuospatial and motor skills b) Attention and concentration c) Verbal memory d) Working memory e) Cognitive flexibility f) Impulsivity g) Verbal fluency	a) NS b) NS c) Women with PMS showed worse performance, regardless of phase d) Women with PMS showed worse performance in the luteal phase e) NS f) PMS and healthy women showed worse performance in the luteal phase g) NS	CVLT, Stroop Color Interference Test, Trail making test, FAS, Finger Tapping and Grip Strength, Grooved Pegboard, Digit Symbol, Digit Span	Confirmation of menstrual phase by counting the days since the first day of the last menstrual period PMS confirmation by completing the PRISM questionnaire for two menstrual cycles + NIMH criteria
Keenan et al., 1995 ²⁸	19 PMS 17 C	32.2 (20-44) 33.1 (19-44)	a) Visuospatial and motor skills b) Attention and concentration c) Verbal memory d) Visual memory e) Working memory f) Verbal fluency	a) NS b) NS c) NS d) NS e) NS f) NS	CVLT, WMS-R, 10/36 Visuospatial learning, Benton visual retention, Benton visual recognition, Numerical attention task, Symbol digit modalities, Trail making, Paced auditory serial addition, Digit span, Stroop, Grip strength, Grooved pegboard, FAS, Vocabulary WAIS-R, Block design WAIS-R	Hormonal confirmation of menstrual phase PMS confirmation by completing the PADRF questionnaire for three menstrual cycles + NIMH criteria
Morgan et al., 1996 ²⁷	30 PMS 31 C	29.6 (18-45) 27.1 (18-45)	a) Visuospatial and motor skills b) Attention and concentration c) Verbal memory d) Visual memory e) Working memory f) Reaction time g) Cognitive flexibility	a) NS b) NS c) NS d) NS e) NS f) NS g) NS	Color trails I and II, Color figure maze I, II, and III, Block design, Figure memory, Logical memory I and II, Visual memory, Digit symbol, Digit span	Confirmation of menstrual phase by the basal body temperature method, ovulation prediction test (urinary luteinizing hormone) PMS confirmation: DSM-IV criteria

(cont.)

Table 2 – Studies assessing neuropsychological functioning across the menstrual cycle in women with PMS/PMDD (cont.)

Study	Mean age (age group)	n	Neuropsychological functions	Results (follicular vs. luteal phase)	Tests	Notes
Resnick et al., 1998 ³³	38.3 (29-45)	19 PMDD 18 C	a) Visuospatial and motor skills b) Attention and concentration c) Verbal memory d) Working memory	a) Women with PMDD showed psychomotor slowness in the luteal phase b) NS c) NS d) NS	Digit symbol WAIS-R, Grooved pegboard, Digit vigilance, Trail making A and B, Stroop color and word, CVLT	Confirmation of menstrual phase by counting the days since the first day of the last menstrual period PMDD confirmation: DSM-IV criteria
Man et al., 1999 ³²	NI (19-44) NI (22-45)	10 PMDD 10 C	a) Working memory b) Ability to plan	a) NS b) NS	CANTAB	Confirmation of menstrual phase by counting the days since the first day of the last menstrual period PMDD confirmation: DSM-IV criteria
Morgan & Rapkin, 2002 ³¹	NI	37 PMDD 32 C	a) Attention and concentration b) Reaction time c) Cognitive flexibility	a) NS b) NS c) NS	Neurocognitive tasks	Confirmation of menstrual phase: NI PMDD confirmation: DSM-IV criteria
Reed et al., 2008 ³⁴	30 30	14 PMDD 15 C	a) Visuospatial and motor skills b) Attention and concentration c) Verbal memory	a) Women with PMDD showed psychomotor slowness in the luteal phase b) Women with PMDD showed worse performance in the luteal phase c) Women with PMDD showed worse performance in the luteal phase	Word recall/recognition, Digit-recall, Digit symbol substitution, Divided-attention, Repeated acquisition of response sequences, Balance	Confirmation of menstrual phase by ovulation prediction test (urinary luteinizing hormone), hormonal confirmation PMDD confirmation: DSM-IV criteria

C = controls; CANTAB = Cambridge Neuropsychological Test Automated Batteries; CVLT = California Verbal Learning Test; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders; NI = not informed; NIMH = National Institute of Mental Health; NS = non-significant differences; PADRF = Premenstrual Assessment Form-Daily Rating Form; PMDD = premenstrual dysphoric disorder; PMS = premenstrual syndrome; PRISM = Prospective Record of the Impact and Severity of Menstrual Symptomatology.

PMDD were compared with healthy women, the former showed a tendency towards worse cognitive performance in the luteal phase.

The lack of consensus in the results reported may be explained, at least in part, by heterogeneous samples, variations in age, educational levels, use of oral contraceptives, diagnosis (PMS or PMDD), and severity of symptoms.

Studies with young women should investigate the occurrence of anovulatory cycles, since only 62% of women in the 20-24 age group ovulate in all menstrual cycles.^{10,16} Because anovulatory cycles have been associated with absence of progesterone increases in the luteal phase, failing to detect these data (or eliminating them from the analyses) would decrease the probability of detecting cognitive abnormalities across the menstrual cycle.¹⁹

With regard to education, an improved knowledge of symptoms associated with the premenstrual phase seems to overestimate complaints, especially those related to the last cycle.²

Most studies focusing on neuropsychological functioning across the menstrual cycle have excluded women using oral contraceptives.¹² Although extremely popular, little is known about the effect of contraceptive pills on cognitive functioning.²² In the few studies that included oral contraceptive users, several potential biases were observed, e.g. the so-called survivor effect (excluding women that did not tolerate contraceptives), which causes a selection bias. The irregular use of oral contraceptives also provides grounds for concern, once it is known that nearly 25% of women stop taking oral contraceptives within 1 year. One further problem is the commercial availability of several different brands of contraceptives in the market, each one with different doses of estradiol and different types of progestinic agents.

In the studies included in the present review, diagnostic confirmation of PMS or PMDD was performed prospectively. This is a methodological strength of these studies, once only a minority of the women who believe they have PMS or PMDD actually meet diagnostic

criteria.³⁵ An additional difficulty in the comparison of results is the diversity of neuropsychological tests and batteries used to measure different cognitive functions. It is possible that at least some of the psychometric tests employed have been inadequate, i.e., not sensitive enough to detect menstrual influences on cognition.³⁶

Another relevant problem is related to the determination of the menstrual cycle phase in the different studies. Most studies used one of the following methods to confirm the menstrual phase: counting the days since the first day of the last menstrual period, basal body temperature method, or hormonal confirmation. The latter method is the most reliable, but also the most costly.^{10,16,23} Studies that base menstrual cycle phase confirmation on counting days use different criteria to define the luteal phase (e.g. days 20-25 or days 15-22).¹⁶ Finally, the absence of control for anxiety and depression symptoms may affect women's performance on tests, hindering a consistent comparative analysis across studies.³⁶

As already mentioned, there is no consensus in the literature on the relationship between hormones and cognitive performance. Even when positive results were reported, they were either not replicated or inconsistent.¹³ It is also necessary to consider the possibility that a larger number of studies with positive results have been published (publication bias). Finally, the poor understanding currently available of the effects of hormones and other neurobiological substances on cognitive performance, as well as the influence of environmental variables (e.g. stress, sleep deprivation, diet), should be taken into consideration.¹³

Conclusion

Although complaints are frequent, there is no unequivocal evidence of the influence of the menstrual cycle on neuropsychological abnormalities in healthy women. Conversely, there appears to be some influence on visuospatial and motor skills, attention and concentration, verbal memory, visual memory, working memory, and reaction time, with a tendency toward worse performance scores in the luteal phase.

In women with PMS or PMDD, unequivocal evidence of such influence has not been found either. There is only little evidence of reduced performance on visuospatial and motor skills, attention and concentration, verbal memory, working memory, reaction time, and impulsivity in the luteal phase; symptoms in PMS/PMDD patients show low intensity, but greater when compared with healthy women. The fluctuations found can be considered mild if compared with those observed in other psychiatric or neurological disorders.

Differences in study designs and methodological limitations are factors that prevent us from drawing solid conclusions. Further studies are necessary to investigate the impact of such cognitive fluctuations on clinical practice and patients' daily activities. It is also necessary to try to correlate patients' complaints with abnormalities found on cognitive tests, in order to determine the clinical relevance of the results found in neuropsychological evaluations.

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