Neuropsychologia, Vol. 27, No. 6, pp. 871–880, 1989.
Printed in Great Britain.

0028-3932/89 $3.00+0.00

SHIFT OF FUNCTIONAL CEREBRAL ASYMMETRY DURING THE MENSTRUAL CYCLE

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(*Received* 21 *January* 1988; *accepted* 19 *November* 1988)

Abstract—This study investigated whether for females, who are said to be less strongly lateralized for cognitive functions than men, hemispheric superiority might depend on the phase of the menstrual cycle. The results show that while asymmetry in lexical decisions did not change throughout the menstrual cycle, asymmetry in face perception decreased linearly from a large right hemisphere superiority during menstruation to a small left hemisphere superiority during the premenstrual phase. This is seen as being relevant not only for the discussion of sex differences in cerebral asymmetry but also for the concept of cerebral organization in general.

INTRODUCTION

DURING THE last decade the question of whether sex differences exist in functional cerebral asymmetry has attracted increasing attention. Many investigations showed that hemispheric specialization was larger for men than for women or that the female groups differed more with respect to direction of asymmetry [10, 25, 37]. But experimental data on this point varied [15, 24, 37] and the investigation of cerebral asymmetry seems to be complicated by intraindividual fluctuations in hemispheric activity [20, 25, 26, 31, 32]. If there were cyclic hormonal influences on functional cerebral asymmetry, this could be responsible for divergent experimental results concerning sex differences in lateralization (with unclear hormonal status of the subjects) and would support a more dynamic concept of cerebral dominance.

It is well established that there are influences of sex hormones on the brain, for example on the sexually dimorphic nucleus in the medial preoptic area (see [19]; or for other effects [13, 14, 39, 41] for reviews). Furthermore there are animal studies [11, 12, 38], clinical studies [17, 36] and developmental studies [43, 44, 48, 49] which support the hypothesis of asymmetrical effects of sex hormones on the brain. HINES and SHIPLEY [30], for example, could not find an effect on verbal or spatial abilities but found an influence of prenatal exposure to DES, a synthetic oestrogen, on the lateralization that subjects demonstrated as adults in a dichotic listening task. While the above mentioned studies are concerned with *permanent* effects of hormones on brain structure and behaviour, other recent research has revealed effects of gonadal or pituitary hormones on *fluctuations* in the level of performance

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of sensory and cognitive functions [e.g. 9, 16, 18, 40] but were not concerned with cerebral asymmetry. That gonadal steroids can modify brain activity was also demonstrated in electrophysiological studies [6, 8, 50]. Cognitive functions were investigated mainly under the aspect of generally activating effects of gonadal hormones and showed variable results (for reviews see [7, 9]). HAMPSON and KIMURA [23] detected performance changes across the menstrual cycle on a speeded manual and a nonverbal spatial task. It seems that high levels of female sex hormones facilitate tasks known usually to favour women and affect skills which usually favour men. Also, GORDON and LEE [18] investigated the relation between hormonal status and performance in a battery of cognitive tasks. For women the results were less clear than for men, but FSH (follicle stimulating hormone) was negatively correlated with the visuospatial test and positively correlated with word fluency (the latter was also true for LHC [luteinizing hormone]), which also fits with HAMPSON and KIMURA'S [23] thesis. In a similar study GORDON *et al.* [16] tried to investigate this hormone/behaviour relationship in a within-subject design, but no hormone-related fluctuations in cognitive function were observed in the women. This may depend among other things on the fact that such behaviour is rather stable and that hormones probably do not influence the general level of performance but rather the speed of processing or hemispheric superiority, both of which were not investigated in this study.

In conclusion: there are already results suggesting that hormones may permanently or temporarily influence brain activity and performance on cognitive tasks, in particular on spatial processing. None of the previous studies, however, investigated a possible influence of hormones on *fluctuations in cerebral asymmetry*. Therefore the main question addressed by the present experiments was whether, with lateralized stimulus input, a systematic change in asymmetry of processing would occur during the menstrual cycle— suggesting the influence of female sex hormones on hemispheric activation. In the menstrual phase both steroid and pituitary hormone levels are low, so that—if female sex hormones influence hemispheric activation—one would expect a rather "male" pattern of hemispheric asymmetry, i.e. a larger field difference during menstration than during the other phases of the cycle.

METHOD

Subjects

Twelve normally menstruating females aged 22 to 39 participated four times each in our experiments. Two additional subjects were tested but had to be excluded from the data analysis, one because of irregular menses (too early onset of menstruation) and one because of a technical defect of the machinery during one experimental session. They were recruited through advertisement or personal contact and were paid 30 Swiss Franks for participating in the study. Most of the participants were students or hospital employees. Only women with regular menstrual cycles who had not taken oral contraceptives or hormonal medication within at least 6 months prior to the test sessions were accepted. Eleven of the 12 subjects had taken contraceptive medication at some time previously. During the period of testing they also did not take any medication which might influence cognitive performance. All were clearly right-handed according to the handedness questionnaire of SALMASO and LONGONI [46] and had no close left-handed relatives. All were native speakers of German without a history of dyslexia or neurological problems, and had normal or corrected-to-normal eyesight. The subjects were naive as to the purpose of the experiment but were—because of all the necessary inquiries about their menstrual cycle—told that the visual perception of women who are not taking contraceptives was to be investigated.

Procedure and materials

Every subject attended four experimental sessions, each in a different phase within one menstrual cycle. There is a lack of agreement in definitions of cycle phases. In our study we divided the cycle into four phases (as e.g. [45]) which should differ in terms of the natural variation of steroid and pituitary hormones: (I) menstrual phase (day 1, 2 or 3 from the beginning of menstruation); (II) follicular-phase (days 8 to 14); (III) luteal phase (days 15 to 22); and (IV) premenstrual phase (days 23 to 28). The menstrual phase is characterized by the fact that levels of pituitary and gonadal hormones are low; in the follicular phase especially the oestrogen levels are high (as are LH and FSH); during the luteal phase progesterone is high in combination with high oestrogen levels; and during the premenstrual phase progesterone is still high but declining, oestrogen should have declined compared to phases II and III, and LH and FSH are low. There were 4 women with cycles longer than 28 days. For the one subject with a 30 day cycle only 1 day was added to the upper limit of the follicular phase, for the two subjects with 31 day cycles 1 day each was added to phases II and III and for the subject with 35 days 3 days were added to phase II, and two to phases III and IV. Testing during the premenstrual phase was generally arranged to take place early in the phase to avoid the risk that the onset of menstruation might occur earlier than expected. For subjects with average cycle lengths of less than 28 days the above mentioned phases were simply used, but testing took place somewhat closer to the lower limits of the intervals, especially for phase II. The individual average cycle length was determined with the help of the records of the subjects who, since they declined to take the pill, all had menstruation calendars.

The menstrual phase, in which we are most interested because of the expected larger asymmetry, is exactly determined through the onset of bleeding; the other phases are rather roughly defined. The hormonal levels of the different phases were not measured. To determine the hormone levels is not only not common in behavioural studies [e.g. 2, 3, 47] but is even of questionable value if used to define cycle phases or to exclude subjects. This is demonstrated, for example, by the problems of GORDON and LEE [18], who excluded half of their female group because of hormonal cutoffs (e.g. subjects, whose progesterone level was "too high" during menstruation). It is still unclear how various hormones interact, how peripheral measures of circulating hormones are related to hormone levels in the brain (there are reports of hormones accumulating in certain parts of the brain), and whether absolute differences in levels of hormones between individuals show any relation to relative changes in levels within individuals [9]. Therefore we consider our method of classification as justified for detecting any menstruation-related change in cerebral asymmetry.

When the subjects were contacted, they were asked the date of the first day of their last menstruation, and the average cycle length was determined. Then the dates for test sessions were fixed according to the phases mentioned above. The first session started with a detailed handedness and personality questionnaire, inquiring about any history of dyslexia or hormonal treatment, familial handedness, year of menarche, etc.

In order to exclude a confounding of cycle phases with the order of experimental sessions (practice effect), three subjects started during phase I, three during phase II, three during phase III and three during phase IV. As was confirmed by *post hoc* analyses of the data, there was no significant change in field asymmetry depending on the time order of test sessions, that is, in relation to the practice effect (neither for the lexical decision nor for the face decision task, all $P > 0.5$).

In each of the four experimental sessions two experiments were conducted: a tachistoscopic verbal experiment (lexical decision) and an analogously constructed non-verbal one (face decision). These tasks were chosen because lexical decisions with visual half-field presentation were shown to reliably demonstrate a right-field (left hemisphere) superiority [5] and face decisions a left-field (right hemisphere) superiority [51].

Experiment I: the verbal task consisted of German four-letter function words and four-letter meaningless syllables presented horizontally to the right or to the left of a fixation point. The stimuli were printed in black lower-case letters on white ground and subtended a visual angle of 0.5° vertically and 1.8° horizontally.

Experiment II: the stimuli for the non-verbal task consisted of photographically produced composites of normal and "scrambled" faces. The normal composite faces had an identical frame of hair and ears, but otherwise varying features. The scrambled faces had the same frame: however, the position of the nose and forehead was transposed (see Fig. 1). They subtended a visual angle of 4.5° vertically and 3.2° horizontally.

FIG. 1. Examples of normal and scrambled faces in the face decision task (Experiment II).

In both experiments stimuli were presented tachistoscopically for 130 msec in the right or left visual field with a luminance of about 29 lux for the verbal and 27 lux for the face stimuli. The centre of the stimuli was positioned at 3° of visual angle to the right or left of a fixation point. The viewing distance was 63 cm. The verbal task and the non-verbal task each consisted of 96 items, with 48 presentations in the right visual field and 48 in the left one. In every experimental session, 16 practice trials were presented at the beginning of each task, which were similar but not identical to the experimental trials.

The reaction was given bimanually with two buttons mounted one behind the other in the midsaggital plane. This was in order to exclude possible additional spatial S-R compatibility effects [see 27, 28]. Half of the subjects pressed the farther button for a yes-decision (word or face) and the nearer button for a no-decision (non-word, or non-face), half of them with the right and the other half with the left hand. The other half of the subjects used the farther button for no and the nearer one for yes, and so on. Alternating between sessions, subjects started either with the verbal experiment or with the non-verbal one. In the first session subjects received written instructions stressing the importance of fixation and asking them to react as quickly and as correctly as possible. Reaction times and errors were recorded for both experiments.

RESULTS

For both the lexical decision and the face decision task medians of the reaction times were subjected to a three-way analysis of variance with phases of menstrual cycle (I, II, III, IV), field of stimulus presentation (right, left) and stimulus category (word/non-word or face/non-face) as factors with repeated measures. In cases without compound symmetry, multivariate tests based on the Hotelling T^2 statistics were performed. The cell means and standard deviations are presented in Table 1.

TABLE 1. Means of the median response times and corresponding standard deviations (in parentheses) for Experiment I (lexical decisions) and Experiment II (face decisions).

Phase of menstrual cycle	Experiment I				Experiment II			
	Right visual field		Left visual field		Right visual field		Left visual field	
	Word	Non-word	Word	Non-word	Face	Non-face	Face	Non-face
I	685	722	707	771	719	691	683	653
	(115)	(142)	(140)	(187)	(145)	(136)	(182)	(121)
II	635	691	650	730	691	653	636	656
	(110)	(94)	(103)	(119)	(108)	(152)	(93)	(165)
III	688	713	673	779	678	643	667	616
	(212)	(113)	(169)	(220)	(118)	(106)	(130)	(89)
IV	637	678	665	712	786	669	805	675
	(177)	(178)	(154)	(171)	(264)	(176)	(302)	(165)

Experiment I

Response times and errors of the lexical decision task revealed the usual left hemisphere (right field) advantage for verbal processing and showed that this asymmetry did not change throughout the menstrual cycle (see Fig. 2). The analysis of the response times showed two significant main effects: reactions were 30 msec faster with right field presentation than with left field presentation ($F(1, 11)=7.62$, $P<0.05$), and reactions were 57 msec faster with words than with non-words ($F(1, 11)=13.84$, $P<0.01$). There were no reliable differences in overall speed of reaction between cycle phases ($F(3, 33)=0.92$, $P>0.4$) and no changes in asymmetry during the cycle ($T^2=1.27$, $F(3, 9)=0.35$, $P>0.7$). No other main effects or interactions were significant.

Errors were few (about 4%) but showed a result similar to that of the reaction times, i.e. no change in asymmetry and overall a right field superiority. An analysis of variance for errors with field of stimulation and cycle phase as factors also showed the significant field effect ($F(1, 11)=4.65$, $P=0.05$).

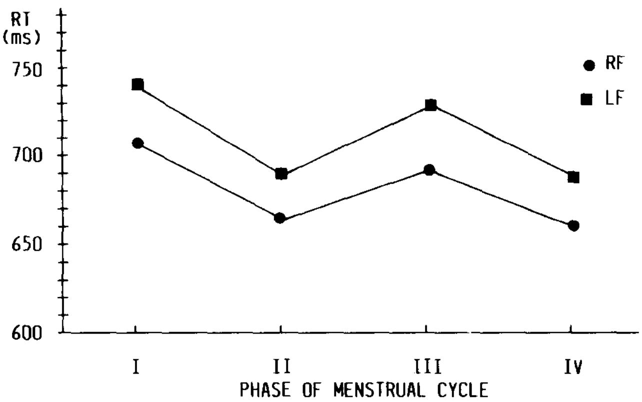

FIG. 2. Means of the median response times for Experiment I with verbal stimuli presented in the right (RF) or left (LF) visual field in cycle phases I to IV.

Experiment II

The results of the face decision task demonstrate a shift in cerebral asymmetry, or, more precisely, a decrease of right hemisphere (left field) superiority from menstruation to the premenstrual phase (see Fig. 3). Ten of the 12 subjects showed a smaller or even a reversed field difference during the premenstrual than during the menstrual phase.

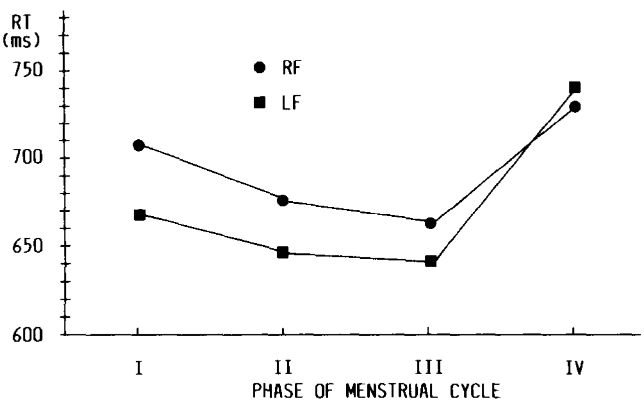

FIG. 3. Means of the median response times for Experiment II with face stimuli presented in the right (RF) or left (LF) visual field in cycle phases I to IV.

In the analysis of variance a significant interaction between phase of menstrual cycle and field of stimulus presentation was obtained ($T^2 = 13.69, F\ (3, 9) = 3.73, P = 0.05$), indicating a shift in field superiority. Most important for the question of the present study was the significant result for the linear orthogonal polynomial for the interaction between phase of menstrual cycle and field of stimulus presentation ($F\ (1, 11) = 6.20, P < 0.05$). This shows that the asymmetry shift for face perception consists in a linear decrease of asymmetry from the menstrual phase (I) to the premenstrual phase (IV) (reaction time difference between right and left field, phase I: 37 msec; phase II: 26 msec; phase III: 19 msec; phase IV: −12 msec). The shift depends especially on a change of asymmetry between the menstrual and premenstrual phases (see Fig. 3), which is confirmed by a subanalysis comparing these two phases: there was a significant interaction between phase of menstrual cycle (I vs IV) and field of stimulation ($F(1, 11)=7.18$, $P<0.05$). In order to demonstrate the statistical robustness of this important result, a non-parametric test, the Friedman two-way analysis of variance, was conducted in addition. Here also the change in asymmetry (field difference scores) between the menstrual and premenstrual phases was significant ($\chi^2=5.33$, $df=1$, $P<0.05$). Separate analyses of variance for each menstrual phase showed that the field difference was only significant for the menstrual phase ($F(1, 11)=10.50$, $P<0.01$), in which the asymmetry was largest.

In addition a significant main effect for stimulus category was obtained: reactions were 51 msec faster with scrambled faces (no-decisions) than with normal faces (yes-decisions, $F(1, 11)=6.00$, $P<0.05$). Also the interaction between stimulus category and phase of menstrual cycle was significant ($T^2=21.54$, $F(3, 9)=5.87$, $P<0.05$), thus demonstrating that the processing of normal faces (yes-decisions) is extremely slow in the premenstrual phase. As the significant result for the linear orthogonal polynomial for the interaction between phase of menstrual cycle and stimulus category shows ($F(1, 11)=8.70$, $P=0.01$), the difference in processing time between faces and non-faces increased linearly from phase I to phase IV.

The overall speed of processing changed systematically throughout the menstrual cycle. Reactions towards normal and scrambled faces were faster in the two middle cycle phases (II: 659 msec and III: 651 msec) than in the menstrual (I: 687 msec) and premenstrual phases (IV: 734 msec). This is expressed in the significant result for the quadratic orthogonal polynomial for the main effect for cycle phase ($F(1, 11)=5.02$, $P<0.05$). No other main effects or interactions were significant in the three-way analysis of variance.

Although errors were few (about 9%), a pattern of results was obtained for them similar to that which had been found for reaction times, especially with respect to the shift of asymmetry in phase IV (though here non-significant). As for reaction times, the analysis of errors showed a significant result for the quadratic orthogonal polynomial for the main effect of cycle phase ($F(1, 11)=4.80$, $P=0.05$), thus indicating that more errors were made in the premenstrual and menstrual phases than in the middle of the cycle.

In order to investigate the question whether reactions might be overall faster in one of the cycle phases (because of a probably generally activating effect of hormones) a comparison of experiments I and II was performed in a common four-way analysis of variance for reaction times. The results showed no significant main effect for cycle phase ($F(3, 33)=0.65$, $P>0.5$), so there was no reliable difference in overall speed of processing between the four phases of the menstrual cycle. In the verbal experiment yes-decisions were faster than no-decisions (word vs non-word) while in the non-verbal experiment no-decisions were faster than yes-decisions (non-face vs face) which is indicated by the significant interaction between experiment and stimulus category ($F(1, 11)=15.70$, $P<0.01$). In cycle phases I, II and III responses were faster with non-verbal stimuli than with verbal ones while in phase IV the reverse took place (see Figs 2 and 3). This was confirmed by a significant interaction between experiment and cycle phase ($F(3, 33)=3.69$, $P<0.05$).

DISCUSSION

In general the two experiments express the well-known left hemisphere superiority for verbal processing and right hemisphere superiority for face perception. However, while the right field advantage for lexical decisions did not change throughout the menstrual cycle, the significant left field advantage for face perception in the menstrual phase disappeared during the menstrual cycle and even shifted in the premenstrual phase, suggesting that hormones may influence the balance of hemispheric activation. Such influences might at least in part be responsible for more variable results with female than with male subject groups and for contradictions between different experimental studies. That the asymmetry for lexical decisions did not change might depend on the verbal stimuli employed. Function words are known to be processed almost exclusively by the left hemisphere [42]. However, we do not want to place much emphasis on explaining the absence of a shift in asymmetry in this task. It might be that verbal processing is more stable than face processing during the menstrual cycle, but on the other hand perhaps fluctuations in asymmetry could be detected with other verbal stimuli.

With respect to overall speed of processing the results for face decisions indicate that during menstruation and especially during the premenstrual phase, the processing of such stimuli seems to be more difficult than in the middle of the cycle, where reactions were faster and fewer errors were made (see Fig. 3). This fits rather well with reports in the literature demonstrating better performance (and lower visual thresholds [40]) in midcycle, probably due to the activating effects of oestrogen [see 1, 2, 9, 23, 34, 47]. However, it is difficult to compare results because of the many different ways of defining cycle phases, and the various measures and tasks employed in the literature. Our finding of faster and more correct responses in midcycle is also in certain agreement with HAMPSON'S [22] and HAMPSON and KIMURA'S [23] result that speed and accuracy on nonverbal tasks were better during the luteal than during the menstrual phase. If one compares the results of Experiments I and II one realizes that during the menstrual, follicular and luteal phases face decisions tended to be faster overall than lexical decisions, while during the premenstrual phase face decisions were much slower than the verbal ones. The premenstrual phase showed at the same time the fastest verbal and the slowest non-verbal responses of all phases of the menstrual cycle. (Other studies not concerned with cerebral asymmetry have also previously found changes in various measures just during the premenstrual phase [1].) These results of our study are unexpected but demonstrate that here variation in overall speed of reaction during the menstrual cycle cannot simply be explained by a *general* activating effect of gonadal hormone levels on the CNS [for discussion see 7, 33]; rather, such an effect seems to be tied to *specific* types of stimuli and cognitive processing, which is also in agreement with HAMPSON and KIMURA'S [23] reciprocal effects of hormones. This may explain heterogeneous findings with respect to reaction time changes during the menstrual cycle, since the speed of processing depends on the kind of tasks employed.

The main result of our study is the linear decrease of left field superiority for face decisions, as measured from menstruation (during which pituitary and gonadal hormones are low) to what we here call the premenstrual phase, where—compared with the other phases—in particular the progesterone level should be high. That is, even with respect to asymmetry a change takes place in the premenstrual phase. Our hypothesis that the largest asymmetry, a relatively "male pattern" of lateralization, should be found during menstruation when female sex hormones are extremely low, was supported. As compared to the menstrual phase, during the premenstrual phase 10 of the 12 subjects showed a smaller or even reversed asymmetry for this task. The reliability of our findings is also supported by the analysis of errors, which yielded the same pattern of results as reaction times, that is, a shift of asymmetry in the premenstrual phase. Since the main difference was obtained between the menstrual and premenstrual phases and not between the menstrual and follicular phases, one may speculate that the result is related to progesterone, since oestrogen has one peak during the follicular phase and one during the luteal phase and should be lower during the premenstrual phase. The phase which we call premenstrual probably included the peak level of progesterone because subjects were not tested immediately before the onset of menstruation (when a sudden decrease of progesterone takes place) but closer to the lower limit of this phase (see Method). This hypothesis would agree with results of electrophysiological studies which found that the time course of changes in alpha frequency and reaction times best fits the changes in progesterone level [6, 8] and with other electrophysiological and psychological studies reporting progesterone-associated changes [4, 6, 8, 9, 21, 29, 35, 50]. The present study is a first attempt to detect asymmetry shifts mediated by the menstrual cycle. Which hormonal reasons finally affected the shift cannot be determined here. The fact is that menstrual cycle-related changes of asymmetry did take place, while the same data, when grouped according to time order of test sessions, did not show any changes in field difference. This result not only seems to reflect *hemisphere-specific* influences of gonadal hormones but also demonstrates a possibility of natural fluctuations in hemispheric superiority and, in turn, has consequences for theories of functional cerebral organization, since it supports a dynamic, rather than a classical static concept of cerebral dominance.

Acknowledgements—This study was supported by a research grant from the Deutsche Forschungsgemeinschaft to the first author. The results were presented in part at the 30. Tagung experimentell arbeitender Psychologen (Marburg, 28–31 March 1988) and at the 20th EBBS Annual Meeting (Zürich, 7–9 September 1988). Thanks are due to Jules Davidoff for permitting us to use his stimulus material for the production of our face stimuli, Willi Nagl for statistical advice, the referees for helpful comments and suggestions, David Emmans and Vivien Kitteringham for revising the English manuscript, and especially our subjects for their co-operation.

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