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Depressive Symptoms do not Affect Lipids and Haemostasis throughout the Menstrual Cycle in Apparently Healthy Young Women

Ioannis Syros [1-3]*, Kolaitis G[2], Papageorgiou C[4], Gourna C[1], Chrousos GP[5] and Liapi C[1]

[1]*Department of Pharmacology, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece*
[2]*Department of Child Psychiatry, School of Medicine, National and Kapodistrian University of Athens, "Aghia Sophia" Children's Hospital, Athens, Greece*
[3]*Child and Adolescent Psychiatry Unit, "Sotiria" General Hospital, Athens, Greece*
[4]*Psychophysiology Laboratory, 1st Department of Psychiatry, School of Medicine, National and Kapodistrian University of Athens, Aiginiteion Hospital, Athens, Greece*
[5]*1st Department of Pediatrics, , School of Medicine, National and Kapodistrian University of Athens, "Aghia Sophia" Children's Hospital, Athens, Greece*

Abstract

Background: According to evidence, association between lipids, haemostatis, depressive symptoms and hostility is cloudy. In order to examine these relations in depth, menstrual cycle could serve as a natural model.

Objective: In the present study, we examined the association between lipids, haemostasis, symptoms of hostility and depression at 3 phases of the menstrual cycle in 59 healthy young women (23.0 ± 2.8 mean age ± SD).

Methods: Blood was drawn at follicular (FL), mid luteal (ML) and late luteal (LL) phase. At each visit, students completed the Zung Depression and Hostility and Direction of Hostility scales; following variables were measured: a) Total cholesterol, LDL-cholesterol, HDL-cholesterol, VLDL-cholesterol, Triglycerides b) PT, APTT, AT III, Proteins C and S, Plasminogen and Fibrinogen. Pearson´s and Spearman s rank correlation were used to determine the relation between variables. P<0.05 was considered significant.

Results: Data indicate that hormonal changes during premenstrual phase might interfere in the connection between haemostasis and lipid profile, as well as in the inverse relation between extroverted forms of hostility and atherogenic lipid ingredients. Hostility might enhance haemostasis in luteal phase, though it might weakens it before the ovulation. Finally, depressive symptoms do not influence lipids and haemostasis across all phases of the cycle.

Conclusion: Relations between hostility, and lipids and haemostasis in the young female population appear to differ markedly across the cycle, while this is not the case regarding depressive symptoms. In order to evaluate the relation between depression and the above biological markers, the menstrual cycle effect probably should not be taken into consideration.

Keywords: Menstrual cycle; Depressive symptoms; Hostility; Lipids; Haemostasis

Introduction

The literature, so far, has detected an interaction between haemostatic variables and lipid metabolism [1-3]. Furthermore, depressive symptoms and hostility seem to be associated with lipidemic and haemostatic variables, as well, suggesting a complex pathway, which has a biological and a behavioural dimension responsible for this link [4,5]. More specifically, a large number of reports so far describe an association between hostile behaviour and depressive mood with impaired lipid levels [6-12], while a correlation between depression, increased procoagulant [13,14] as well as decreased fibrinolytic activity [15,16] has been also shown, indicating that haemostasis could be also influenced by this emotional state [5]. However, a considerable number of studies contradict the above findings, especially in sample groups comprising healthy and younger individuals [4,13-15,17-22].

Some studies have detected that the variations of sex hormones across the cycle are associated with serum lipids and clotting factors [23-26], but the research regarding the specific relation between haemostasis and lipid metabolism at each phase of the cycle is more diminished [3]. Therefore, we thought it would be interesting to investigate the effect of hostile behaviour or depressive symptoms on these biochemical factors throughout the cycle. In addition, it has been postulated that the variations of these biological and psychological factors across the menstrual cycle could serve as a natural model in order to test the effect of menstrual cycle on these relations, and thus to increase our understanding about the normal biology that possibly underlie these links. In the present study, we examined the relation between haemostatic activity, lipidemic profile and symptoms of hostility and depression at each phase of the menstrual cycle in apparently healthy young women.

Subjects and Methods

Fifty-nine young students (mean age 23.0 ± 2.8 years) were participated, after exclusion from the analysis of women with missed data, (n=10). The women received written information on the purpose and procedures of the study and gave informed consent. All of them were interviewed and examined by an internist. All women were physically healthy, free of clinical evidence of cardiovascular disease and were not using medication (i.e. birth control pills or Selective Serotonin Reuptake Inhibitors); they reported regular menses ranging between 27-33 days and had no signs of acnea or hirsutism. Clinical examinations included weight, height, blood pressure and

***Corresponding author:** Ioannis Syros, MD, PHDc, Department of Child Psychiatry, School of Medicine, National and Kapodistrian University of Athens, "Aghia Sophia" Children's Hospital, Athens, Greece, Tel: +306972735958; E-mail: jonsir9975@yahoo.com

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electrocardiogram. The Body Mass Index (BMI) was calculated as weight/height (kg/m^2). Furthermore, the women reported no signs of major symptomatology (clinical depression or any other mental disorder), and were also questioned about premenstrual symptoms.

Lipids and clotting factors measurement

Venous blood samples were drawn between 8-10 am, after overnight fasting for at least 12 hours, three times at each cycle: at the follicular phase (FL), mid luteal phase (ML) and late luteal phase (LL), the latter corresponding to the premenstrual phase. The following lipidemic factors, haemostatic factors and clotting time tests were determined at each sample as follows.

Lipidemic factors

Total Cholesterol, LDL-Cholesterol, HDL-Cholesterol, Triglycerides, VLDL.

Factors of haemostasis

- Coagulant factor: Fibrinogen
- Fibrinolytic factor: Plasminogen
- Anticoagulant factors: Protein S, Protein C, ATIII
- Clotting time tests: APTT, PT.

Serum lipid concentrations were measured using biochemical analyzer ILAB 350 of company Instrumentation Laboratory. LDL cholesterol was calculated with the Friedewald equation [27].

Fibrinogen, plasminogen, ATIII, APTT, and PT were analyzed on a DADE-Behring analyzer (with reagents from the same company); protein S and protein C were measured using Eliza. Normal range of Protein S activity is 60-150% and that of Protein C activity is 65-140%.

Assessment of depression and hostility

Depressive symptomatology was assessed by the Zung Self-Rating Depression Scale, a 20-item self-report questionnaire, which is widely used as a screening tool encompassing affective, psychological and somatic symptoms associated with depression [28]. The Questionnaire takes about 10 minutes to complete, and items are framed in terms of positive and negative statements. Each item is scored on a Likert scale ranging from 1 to 4. A total score is derived by summing the individual item scores and ranges from 25 to 80. The scores provide indicative ranges for depression severity that can be useful for clinical and research purposes.

Individuals also completed the Hostility and Direction of Hostility Questionnaire (HDHQ) [29]. This assessment instrument represents a measure of hostility and anger, and consists of five subscales: (a) the urge to act out hostility (AH), (b) criticism of others (CO), (c) projected delusional or paranoid hostility (PH), (d) self-criticism (SC), and (e) delusional guilt (DG). The first three subscales are summed to form an Extrapunitive score, and the other two are summed to yield an Intropunitive score. The direction of hostility was obtained from the following formula: [2x self-criticism+delusional guilt–(urge to act out hostility+criticism of others+projected delusional or paranoid hostility)]. Each subscale score is ranged from 0 to 11, so the total Hostility score ranges from 0 to 55 by summing the five subscale scores. The women completed these questionnaires immediately before blood sampling at each phase of the cycle.

Statistical Analysis

Data are presented as mean ± SD. The relations between variables at each phase of the menstrual cycle were determined using the Pearson correlation coefficient (R). The Spearman rank correlation coefficient (RS) was also computed when normality assumption was not satisfied. Comparisons within cycle phases were performed by the one-way analysis of variance (ANOVA) for repeated measures followed by Bonferroni correction for multiple comparisons. When data were not normally distributed, the non-parametric Friedman test was used for comparisons within phases and the Wilcoxon Signed Ranks test for paired comparisons. All reported p-values were considered significant when less than 0.05.

Results

The clinical features of the women are shown in Table 1. Mean values ± SD of lipidemic and haemostatic factors, as well as of the psychometric scores evaluated in FL, ML, LL phases of the menstrual cycle are shown in Table 2. Tables 3-5 show the statistically significant correlations between lipids, haemostatic factors, hostility, and depressive symptoms respectively. There were no statistically significant correlations between the tested lipids, the haemostatic factors and the Zung scores throughout the menstrual cycle phases.

Discussion

Haemostatic variables and lipids

A significant correlation between any haemostatic variable and lipids was detected at the LL phase only. Specifically, HDL-C levels might be implicated in the reduction of the coagulation process while they are positively related to APTT. In addition, a positive association between fibrinogen and triglycerides, as well as between protein C and cholesterol/LDL was determined, while plasminogen, the only fibrinolysis-related parameter examined, was positively correlated with VLDL and triglycerides. Regarding the data so far, V. Giardiva et al. [3] focused on the relation between lipids and clotting factors at each phase of the menstrual cycle in 20 young women; in contrast to our results, no selective correlation was determined at specific time points across the cycle, although the averaged concentrations of total cholesterol and fibrinogen were positively associated.

Among the studies concerning female subjects only, several detected an inverse association between HDL and fibrinogen in various sample groups, while a positive correlation was reported between fibrinogen and total cholesterol, LDL and triglycerides [1,2]. The dissimilar results, in comparison to our work, could be justified by the discrepancies with regard to the study samples and design. On the contrary, in ARIC study, authors reported a positive relation between proteins C with many elements of the lipid profile, paralleling our results concerning the LL phase [30]. As mentioned before, our findings concern the premenstrual phase only. These data indicate that probably the specific hormonal changes during this phase of the cycle might interfere in the connection between haemostasis and lipid profile.

Clinical characteristics of subjects (n=59)	
Age	23.0 ± 2.8 (years)
Weight	60.1 ± 8.0 (kg)
Height	164.9 ± 6.2 (cm)
BMI	22.1 ± 2.7 (kg/m^2)
Menstrual cycle duration (range)	27-33 (days)
Menstrual cycle duration	29 (days)

Table 1: Clinical characteristics of the individuals.

	Phase FL	PHASE ML	PHASE LL
Lipids			
Total cholesterol (mg/dL)	184.96 ± 30.94	183.90 ± 29.68	185.27 ± 24.78
Triglycerides (mg/dL)	65.52 ± 28.31	66.15 ± 19.28	61.47 ± 16.82
HDL-C (mg/dL)	54.66 ± 9.30	57.27 ± 9.49	60.00 ± 8.99
LDL-C (mg/dL)	117.40 ± 29.47	113.45 ± 29.60	113.08 ± 25.59
VLDL (mg/dL)	13.06 ± 5.62	13.22 ± 3.80	12.27 ± 3.37
Haemostatic factors			
PT (sec)	13.80 ± 1.29	13.88 ±1.72	13.92 ± 1.18
APTT (sec)	42.04 ± 4.91	44.81 ± 12.58	40.58 ± 5.93
Fibrinogen (mg/dL)	2.67 ± 0.76	3.12 ± 1.34	3.11 ± 1.39
AT III (mg/dL)	99.07 ± 13.97	100.91 ± 9.46	101.48 ± 10.11
PRC (mg/dL)	96.66 ± 17.95	95.07 ± 17.79	92.24 ± 18.05
PRS (mg/dL)	46.30 ± 14.88	53.60 ± 9.38	48.75 ± 12.01
Plasminogen (mg/dL)	91.78 ± 13.37	96.23 ± 14.06	91.48 ± 12.21
Depression (Zung self-rating scale scores)			
	47.69 ± 8.28	46.57 ± 8.96	46.16 ± 9.68
Hostility (Hostility and direction of hostility questionnaire scores)			
Urgue to act out Hostility (AH)	4.30 ± 1.90	4.06 ± 1.92	4.02 ± 2.14
Critisism of others (CO)	5.41 ± 2.06	5.48 ± 2.26	5.58 ± 2.70
Projected delusional or Paranoid Hostility (PH)	1.76 ± 1.37	1.93 ± 1.35	1.58 ± 1.42
Self Critisism (SC)	3.65 ± 1.96	3.57 ± 2.11	3.94 ± 2.19
Delusional Guilt (DG)	1.78 ± 1.27	1.71 ± 1.40	1.55 ± 1.22
Intropunitive Hostility	11.01 ± 5.74	10.53 ± 6.18	11.05 ± 5.98
Extrapunitive Hostility	11.33 ± 4.17	11.48 ± 4.34	11.16 ± 4.97
Direction of Hostility	-0.55 ± 5.25	-1.04 ± 5.26	0.28 ± 5.11
Total Hostility	16.93 ± 5.90	16.78 ± 6.57	16.69 ± 7.08

Notes: For the variables Triglycerides, Total Cholesterol, VLDL, HDL-C and LDL-C, a statistically significant difference was found only for HDL-C between phases FL and LL (p=0.009, Bonferroni correction). For the variables PT, APTT, Fibrinogen, ATIII, Pr C, Pr S and plasminogen, a statistically significant difference was found only for Pr C between phases FL and LL (p= 0.043 by the non-parametric Wilcoxon Signed Ranks test).

Table 2: Mean values± SD of the biological and psychometric parameters measured. Total Chol, Trigl, HDL-C, LDL-C, VLDL: mg/dL, PT, APTT: sec, Fibrinogen, PrC, PrS, Plasminogen: mg/dL.

Haemostatic Factors	Lipidemic Factors	Cycle Phase			R (p-value)	Rs°(p-value)
		FL	ML	LL		
APTT	HDL-C			+	0.57 (0.022)	
Fibrinogen	Triglycerides			+	0.75 (-0.001)	
	VLDL			+	0.73 (-0.001)	
PR C	T Cholesterol			+	0.61 (-0.012)	
	LDL-C			+		0.51 (0.044)
Plasminogen	Triglycerides			+		0.57 (0.026)
	VLDL			+		0.51 (0.054)

Notes: A statistically significant correlation was found between many haemostatic components and the lipids in LL phase: a) APTT was positively correlated with HDL-C (R= 0.57, p=0.022), b) Triglycerides and VLDL were positively correlated with fibrinogen (R=0.75, p=0.001, and R=0.73, p=0.001, respectively) and plasminogen (Rs=0.57, p=0.026, and Rs=0.51, p=0.054, respectively). Finally, Pr C was positively correlated with Cholesterol (R=0.61, p=0.012) and LDL-C (Rs= 0.51, p=0.044).

Table 3. Statistically significant correlations between haemostatic factors and lipidemic factors in the various phases of cycle. The phase marked by gray denotes the significant correlation. The (+) and the (-) sign indicate the positive and the negative correlation respectively. R: Pearson rank correlation coefficient; RS: Spearman rank correlation coefficient; P< 0.05 was considered significant.

Lipids and hostility

Several authors so far showed an association between low lipid levels or lipid lowering and hostility, however, this relation was not confirmed by other studies. In the present study, some elements of extrapunitive hostility (criticism of others and paranoid hostility) were negatively correlated to atherogenic elements such as LDL cholesterol and total cholesterol levels in the luteal phase only. No correlation was found between triglycerides, VLDL and HDL-C levels, with hostility, throughout the menstrual cycle.

Focusing on the data concerning female subjects, in a large cohort of Taiwanese women [8] as well as in healthy primiparous women [31], a negative correlation between total cholesterol and hostility was detected, while Rutledge et al. [11] showed a positive correlation between LDL cholesterol and 'anger out scores' in a sample group comprising middle aged women. However, a considerable number of reports do not support a consistent relation between these lipid elements and hostility [19,21]. The studies so far vary with regard to the sex and physical condition of the individuals, the examined lipidemic factors as well as the psychometric scales and the statistical methods the authors used. In contrast to these reports, the negative correlation between extroverted forms of hostility and atherogenic igriedents like LDL cholesterol and serum total cholesterol, observed in our study, shows selectivity for the luteal phase of the cycle.

Although various CHD risk behaviours have been determined in hostile persons [32], it has been proposed that hostility might directly

Psychometric Parameter	Lipidemic Factors	Cycle Phase			R[a] (p-value)	Rs (p- value)
		FL	ML	LL		
HDHQ CO	T Cholesterol			-		-0.35 (0.048)
HDHQ PH	T Cholesterol		-			-0.31 (0.044)
	LDL-C		-			-0.32 (0.041)

Notes: In ML phase, HDHQ PH was negatively correlated with total cholesterol (Rs=-0.31, p=0.045) as well as with LDL-C (Rs=-0.32, p=0.041). In LL phase, total cholesterol was negatively correlated with HDHQ CO (Rs=-0.35, p=0.048). In FL phase no significant correlation was determined.

Table 4: Statistically significant correlations between hostility and lipidemic factors in the various phases of cycle. The phase marked by gray denotes the significant correlation. The (+) and the (-) sign indicate the positive and the negative correlation respectively. R: Pearson rank correlation coefficient; RS: Spearman rank correlation coefficient; P< 0.05 was considered significant.

Psychometric Parameter	Haemostatic Variables	Cycle Phase			R[a] (p-value)	Rs (p-value)
		FL	ML	LL		
HDQ DG	Fibrinogen	-				-0.49 (0.048)
	PT		-			-0.79 (0.001)
	APTT		-			-0.67 (0.004)
HDHQ AH	PT	+				0.54 (0.024)
HDHQ PH	PT	+				0.59 (0.013)
HDHQ Intropunitive	Fibrinogen	-				-0.51 (0.037)
	PR C			-	-0.60 (0.014)	
	ATIII			-	-0.52 (0.038)	
HDHQ SC	PR C			-	-0.55 (0.027)	
HDHQ Extrapunitive	PR C			-	-0.52 (0.040)	
HDHQ Direction	PT		-		-0.61 (0.012)	
	APTT		-			-0.52 (0.039)
	PR S		+		0.66 (0.037)	
				-	-0.83 (0.043)	
HDHQ Total	PT	+			0.52 (0.033)	
	PR C			-	-0.59 (0.017)	

Notes: In FL phase: a) negative correlation between fibrinogen and HDHQ DG (Rs=-0.49, p=0.048) and intropunitive Hostility (Rs=-0.51, p=0.037), b) PT was positively correlated with HDHQ AH (Rs=0.54, p=0.024), with HDHQ PH (Rs=0.59, p=0.013) and with HDHQ total (R=0.52, p=0.033). In ML phase: a) PT and APTT were negatively correlated with HDHQ DG (Rs=-0.79, p=0.001 and Rs=-0.67, p=0.004), b) Pr S was positively correlated with direction of Hostility (R=0.66, p=0.037). In LL phase: a) Pr C was negatively correlated with HDHQ SC (R=-0.55, p=0.027), with intropunitive hostility (R=-0.60, p=0.014), with extrapunitive hostility (R=-0.52, p=0.04) and with the HDHQ total (R= -0.59, p=0.017), b) AT III was negatively correlated with intropunitive hostility (R=-0.52, p=0.038), c) Pr S was negatively correlated with direction of hostility (R=-0.83, p=0.043). Plasminogen was not significantly correlated with any of the components of hostility.

Table 5: Statistically significant correlations between hostility and coagulant/anticoagulant/fibrinolytic factors in the various phases of the cycle. The phase marked by gray denotes the significant correlation. The (+) and the (-) sign indicate the positive and the negative correlation respectively) R: Pearson rank correlation coefficient; RS: Spearman rank correlation coefficient; P < 0.05 was considered significant.

influence lipid metabolism, probably through the modification of serotonergic neurotransmission. This was based on the observation of an association between measures of aggression and hostility, and changes in 5-HT function [6,33] and low lipid levels and alterations in 5-HT activity [6].

Haemostatic variables and hostility

Our findings indicate that introverted aspects of hostility might decrease coagulation activity through an inverse effect on fibrinogen levels in the FL phase. Moreover, the positive correlation between the PT test and some overt forms, as well as the total hostility scores support the hypothesis that hostility might weaken haemostasis in the particular cycle phase. In ML phase, it seems that hostility promotes a hypercoagulable state, while the clotting time tests were negatively correlated to some ingredients of hostility (i.e., delusional guilt as well as the Directionality of Hostility). Finally, in the premenstrual phase (LL), many elements of hostility were inversely correlated to the anticoagulant variables AT III, Pr C and Pr S. This might suggest a potential mechanism through which hostility enhance haemostasis in the specific cycle phase.

In various reports concerning female groups, no statistically significant correlation between fibrinogen and hostility was detected, particularly when cardiovascular risk factors were taken into account [4,13,20]. Although these studies referred to healthy individuals, there were essential discrepancies in comparison to the present study, in the size and the age range of the sample, as well as the different statistical analysis the authors used. In addition, to the authors' knowledge, no investigation concerning the association of clotting time tests PT and APTT with hostility has been published so far.

As for the mechanism which underlies the link between hostility and haemostasis, it has been speculated that not only unhealthy lifestyle behaviours [32] but also neuroendocrine pathways are involved to this association [5]. Several authors investigate the involvement of hostile behaviour to the hyper activation of sympathetic nervous system [32,34] and the hypothalamic-pituitary-adrenocortical HPA axis [35] in order to provide insight into this relation. With respect to future research, these biological mechanisms could mediate the association between hostility and haemostatic alterations.

Lipids and depressive symptoms

In the present study, no statistically significant correlation was detected between the tested lipids and the Zung scores throughout the menstrual cycle phases, suggesting that the cycle effect does not seem to influence this relation.

The literature until now has revealed contradictory results, probably due to different study samples, and techniques employed by the authors. In agreement with our study, two reports concerning young and healthy individuals found no correlation between total Cholesterol and depression scores [17,19]. Similar results were shown in hospitalized depressed patients [36] as well as in postmenopausal women [8]. On the contrary, there is a paucity of studies which support a relation between low cholesterol levels and depression; in a study group comprised of healthy middle aged Swedish women, authors detected an inverse relation between plasma cholesterol and severity of depressive symptoms. A main discrepancy with our study was the use of a different depression measure scale, as well as the different age range, and ethnicity of the study sample [37]. An inverse association between depression and total cholesterol, as well as the ratio total cholesterol/ HDL- cholesterol, was also reported concerning healthy young adult women. Likewise, the author used a different depression scale which, in comparison to the Zung questionnaire, could be characterized as a trait, rather a state indicator of depression [12]. A similar negative correlation has been shown in other study samples, comprising healthy women in the initial puerperal period [38], as well as in the postpartum period [31], healthy and obese postmenopausal women [39] and subjects with major depression [9]. Regarding HDL-C, some studies have revealed an inverse association with depression, focusing on healthy young [19] and middle aged women [37] as well as on subjects diagnosed with major depression [9]. The different age range, the unlike psychometric assessment, as well as the different mental condition of the above sample groups, could justify the dissimilar results. In accordance with our work, many other studies, including various study groups, have not concluded to a consistent relation between HDL-C and depression, either as a personality trait, or as a psychological state at the given moment [12,17,36]. With respect to the association between LDL-C or triglycerides and depression, the majority of the studies are consistent with a lack of an association, paralleling our results [9,17,19,36,37]. The hypothesis of a direct biological link between low lipid levels and depression remains unclear; parameters like the age, the poor physical health and the preexisting medical conditions of the study group possibly influence the relations between these factors [12,40]. Additionally, relevant psychological variables like anxiety and hostility should be taken into consideration, while it is well known that depression often co-occurs with these statuses [12]. Serotonin alterations have been involved in the interrelation between depressive symptoms and lipid changes; it was reported that low lipid levels may lead to reduction of central serotonergic activity [6]. Additionally, low serotonin concentrations have been detected in depressed subjects [41]. It is speculated that low serum lipid levels and, thus, a reduction in the lipid content of brain cells could possibly affect serotonergic function, which has been implicated in depressive symptomatology.

Haemostatic variables and depressive symptoms

With respect to the association between haemostatic variables and depressive symptoms, our study indicates no interrelation across the menstrual cycle.

In contrast to the data regarding hostility, there is abundant, albeit conflicting evidence, about the relation between haemostasis and depression. However, the studies varied widely as concerns the size and the characteristics of the sample, the questionnaire the investigators used as well as the kind of the haematological markers examined. Regarding fibrinogen, various studies failed to detect a significant association with depression in middle-aged healthy females [14,22] as well as in females above 40 years. [20]. Doulalas et al. [17], in young and healthy females, produced results comparable to ours, since a relation between depression and a hypercoagulant profile was found, but no significant correlation was determined concerning fibrinogen, while depression was assessed by a different psychometric instrument. The lack of a significant correlation between these parameters was also found in two reports where healthy middle aged males participated [15,18]. On the contrary, an association between depressive symptoms and fibrinogen was observed in healthy women of a wide range of age [13], a study group during the menopausal transition [42], as well as non-medicated subjects with major depression [9]. The information concerning the association between the clotting time tests with depression is scant, though similar with our results; Maes et al. [43], compared the PT and APTT tests between 4 groups of non-medicated individuals with different severity of depression showing no statistically significant difference.

Like hostility, depression is associated with traditional cardiovascular risk factors, some of them known to influence haemostasis, such as smoking, physical inactivity and poor patient compliance [44]. Apart from that, some authors postulate a possible link between depression and hyper secretion of hormones such as epinephrine, norepinephrine [45], cortisol [46] and ADH [47]. Serotonergic dysfunction in depression has been also proposed as a possible pathway which leads to impaired haemostasis [48]. Moreover, major depression has been associated with increased levels of acute phase proteins, such as fibrinogen [49,50]. All these behavioural and neuroendocrine factors, relevant to depression could promote a hypercoagulable state [16,51].

Limitations

The conclusions of this study should be interpreted with caution because of several limitations. Hostility and Depressive symptoms are difficult to measure and may change over time. Thus, measurement error (plus the fact that our measures refer to a single point in time) may have resulted in important bias toward the null. Another limitation is the reliance on a self-report test to assess the presence of hostile behaviour and depression. Nevertheless, self-reports are widely used in epidemiological studies and are generally considered satisfactory tools to detect and assess depressive symptoms, as well as hostility feelings. Furthermore, while the Zung Scale cannot substitute a comprehensive clinical interview, no formal structured interview was used to establish the absence of a psychiatric disorder (e.g., through the MINI-plus, CIDI or SCID). In contrast, psychiatric assessment of participants was based on their personal reference as well as on the brief psychiatric history taken by the internist. Finally, due to the cross-sectional design of this research, we can simply no causal relation between the parameters examined. However, we speculate that the hormonal fluctuations throughout the menstrual cycle might mediate the association among these psychometric and biochemical parameters.

Further investigation which would include extended study periods, as well as larger size sample groups is required.

Conclusion

The literature for the association between depression, hostility and the selected biological markers we measured appears controversial. Based on our research, changes of depressive mood throughout the cycle appear not to relate with lipid or haemostatic fluctuations. On the contrary, a selective relationship was showed between lipids and some aspects of extrapunitive hostility, as well as the haemostatic activity, in the luteal phase of the cycle, Additionally, data showed that hostile

behaviour interfere with haemostatic activity: across the cycle in a non-consistent manner• hostility might promote haemostasis process in the L phase, while weaken it in the FL phase. It is obvious difficult to evaluate clinically the significance of our findings but it seems that in order to determine the interaction between lipid profile, haemostatic activity and depression in apparently healthy young women, the influence of the menstrual cycle may not have to be taken into consideration.

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