Effect of individual dietary fatty acids on postprandial activation of blood coagulation factor VII and fibrinolysis in healthy young men[1–4]

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ABSTRACT

Background: Hypertriglyceridemia may represent a procoagulant state involving disturbances to the hemostatic system. Plasminogen activator inhibitor type 1 (PAI-1) is increased in the presence of hypertriglyceridemia. Free fatty acids (FFAs) in plasma may promote factor VII (FVII) activation.

Objective: We tested the hypothesis that FVII activation would be less after consumption of saturated fatty acids than after other fatty acids.

Design: The effects of 6 matching dietary test fats, rich in stearic (S), palmitic (P), palmitic + myristic (M), oleic (O), *trans* 18:1 (T), and linoleic (L) acid, respectively, on the postprandial lipid and hemostatic profile (after 2, 4, 6, and 8 h) were investigated in 16 young men. High-fat meals (1 g fat/kg body wt; 43% from the test fatty acid) were served in the morning on 6 separate days.

Results: All fats increased FVII activation. The S fat resulted in a lower increase in activated FVII (FVIIa) than did the T fat and in a lower FVII coagulant activity (FVII:c) than did the O fat ($P < 0.02$, diet × time interaction). When the data were pooled, the saturated (S, P, and M) test fats resulted in a smaller postprandial increase in FVIIa ($P = 0.036$, diet effect), a smaller increase in FVII:c ($P < 0.001$, diet × time interaction), a greater rise in tissue plasminogen activator concentrations ($P = 0.028$, diet effect), and a tendency to a greater postprandial decline in PAI-1 ($P = 0.06$, diet effect) compared with the unsaturated test fats (O, T, and L). The increase in FVIIa was not significantly associated with the level of lipemia, plasma FFAs, or plasma lipoprotein lipase activity.

Conclusion: Our results indicate a lesser increase in FVIIa after the consumption of saturated fats, especially the S fat, than after unsaturated test fats. *Am J Clin Nutr* 2003;77:1125–32.

KEY WORDS Factor VII, plasminogen activator inhibitor type 1, PAI-1, tissue plasminogen activator, stearic acid, saturated fatty acids, unsaturated fatty acids, postprandial lipemia, men

INTRODUCTION

Humans are typically in a nonfasting state and consume between 30 and 150 g fat/d with meals. Total fat intake is an important determinant of the plasma concentration of triacylglycerol-rich lipoproteins (1), and the degree of alimentary lipemia is reported to have effects on hemostatic status (2–4), which may be relevant for risk of coronary heart disease. However, the significance of the fatty acid composition of ingested fat for postprandial lipid concentrations and hemostatic factors is unclear.

After early reports that, unlike unsaturated fatty acids, long-chain saturated fatty acids may have thrombogenic properties (5–7), attention has focused on possible relations between dietary fatty acid composition and postprandial changes in coagulation and fibrinolytic and platelet characteristics. Alimentary lipemia is reported to be associated in a dose-response manner with activation of factor VII (FVII) (8), and there is conflicting evidence to suggest that stearic acid–rich fats may induce less lipemia than dietary fats of other composition (9–15). On the other hand, once absorbed, stearic acid may be a more potent activator of factor XII (16) and FVII (17) than are unsaturated fatty acids. Plasma FVII coagulant activity (FVII:c) has been reported to be strongly and independently associated with risk of coronary heart disease in middle-aged men (18), although this relation was not observed in several more recent prospective studies (19–22). Nevertheless, the possibility cannot be discounted that a high peak FVII:c in the postprandial period, due to activation of FVII (2), may temporarily raise the risk of serious coronary thrombosis in the event of rupture of an atheromatous plaque.

The thrombogenic state arises when an imbalance exists between procoagulant and profibrinolytic activity (23, 24). FVII appears to play a major role in basal thrombin generation (25), whereas the generation of the fibrinolytic enzyme plasmin is regulated by plasminogen activator inhibitor type 1 (PAI-1) (26). High PAI-1 concentrations have been associated with coronary heart disease (27–29). Hence, reports of postprandial increases in PAI-1 antigen and activity (3) and the demonstration that triacylglycerol-rich VLDLs stimulate the expression and secretion of PAI-1 by endothelial cells in vitro (30) may have clinical significance for this disorder. The discovery that linoleic acid enhances the secretion of PAI-1 by HepG2 cells

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TABLE 1
Major fatty acids in the test fat triacylglycerols (TGs) and 2-monoacylglycerols (2MGs)[1]

	M		P		S		O		T		L	
Fatty acid	TG	2MG	TG	2MG	TG	2MG	TG	2MG	TG	2MG	TG	2MG
	% by wt of total fatty acids											
14:0	21.5	21.2	0.5	0.5	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
16:0	23.9	24.7	44.2	44.6	2.6	2.8	3.9	4.3	3.6	3.8	5.2	5.6
18:0	3.5	5.6	4.6	4.6	47.0	43.3	4.8	5.0	4.7	5.0	4.5	4.8
trans 18:1[2]	Tr	Tr	Tr	Tr	Tr	0.1	Tr	0.1	44.7	45.8	Tr	0.1
cis 18:1[3]	43.2	42.1	45.9	44.3	45.4	46.8	82.5	81.4	43.1	41.0	45.2	44.9
18:2n−6	6.7	6.4	3.4	3.2	3.4	3.5	6.3	6.0	1.8	1.7	42.9	41.7

[1] M, test fat high in myristic and palmitic acids; P, test fat high in palmitic acid; S, test fat high in stearic acid; O, test fat high in oleic acid; T, test fat high in *trans* fatty acids; L, test fat high in linoleic acid; Tr, trace amounts.
[2] The sum of *trans* 18:1 isomers.
[3] The sum of *cis* 18:1 isomers.

(31) and a recent report of an association between linoleic acid intake and PAI-1 concentrations in the absence of any association between PAI-1 and saturated fatty acid consumption (32) suggest that the fatty acid composition of dietary fat may influence PAI-1 concentrations in the postprandial state.

The present study sought effects of dietary fatty acid composition on key postprandial variables of coagulation and fibrinolysis in healthy subjects. Results on lipoprotein, lipid concentrations, free fatty acid (FFA) concentrations, and preheparin lipoprotein lipase and cholesteryl ester transfer protein activities are published elsewhere (33).

SUBJECTS AND METHODS

Subjects

Sixteen men with a mean (± SD) age of 23.4 ± 2.4 y (range: 21–28 y) were recruited for study. The men had a mean body mass index (in kg/m^2) of 23 ± 2 (range: 19.5–28.1), fasting plasma cholesterol concentration of 4.0 ± 0.5 mmol/L (range: 3.1–5.1 mmol/L), and mean fasting plasma triacylglycerol concentration of 0.8 ± 0.3 mmol/L (range: 0.4–1.32 mmol/L). None had a history of atherosclerotic disease and all were apparently healthy as judged by their responses to a standardized medical questionnaire. None of the subjects had hypertension or were taking medication of any kind. Fifteen subjects were nonsmokers and one smoked < 10 cigarettes/d. Most had a moderate level of physical activity, either cycling regularly to work or training for a maximum of 1–2 h twice weekly.

The protocol and the aim of the study were fully explained to the subjects, who gave their written consent. The Scientific Ethics Committee of the municipalities of Copenhagen and Frederiksberg (01274/95) approved the research protocol.

Study design

The test meals were consumed in randomized order. Sixteen subjects received the test meals rich in stearic acid (S), palmitic acid (P), oleic acid (O), and linoleic acid (L), respectively. Fifteen subjects also received a test meal high in *trans* 18:1 (T), and 8 subjects consumed a test meal rich in myristic and palmitic acids (M). All test days were separated by ≥ 3 wk of consumption of the subjects' habitual diet. The test meals were served in the morning after the men had fasted for 12 h and were eaten within 15 min.

Preparatory phase

To reduce any effect of the diet eaten before the study days, standardized food items were delivered to the subjects for them to consume during the 48 h before each test meal. The fatty acid composition of this pretest diet approximated the mean of the current Danish diet (34): 40% saturated fatty acids, 41% monounsaturated fatty acids, and 19% polyunsaturated fatty acids. The foods consisted of ready-made dinners, bread, cakes, and margarine. Subjects were instructed *1*) to refrain from consuming high-fat products (cheese, potato chips, ice cream, chocolate, sausage, etc); *2*) to record the type, quantity, and time of day of all food items eaten during the 48-h preparatory period before the first test meal, so that this pattern could be replicated before subsequent test meals; *3*) to standardize and record physical activities performed during the 72-h period before each study day; and *4*) to refrain from heavy physical activity and alcohol for ≥ 24 h and to fast for ≥ 12 h before each test meal.

Test meals

The test meals were prepared and weighed in individual servings at the experimental kitchen of the Research Department of Human Nutrition. The meals consisted of mashed potatoes in which the test fats were incorporated and juice. The fat intake of each test meal was fixed at 1 g/kg body wt. The energy content was ≈7 MJ for a person with a body weight of 75 kg. The test meals contained 50.6% of energy from fat, 43.0% of energy from carbohydrates, and 6.4% of energy from protein. Aarhus Olie (Oils and Fats Division, R and D, Aarhus, Denmark) supplied 6 matching dietary fats. The fat rich in oleic acid was a high–oleic acid sunflower oil (TRISUN 80) obtained from SVO Enterprises (Eastlake, OH).

To optimize the matching of the test fats with regard to their fatty acid composition and the positional distribution of the fatty acids on the glycerol backbone of the triacylglycerols, the fats were produced by interesterification of commercially available pure triacylglycerol (as tristearin, tripalmitin, or trimyristin; Hüls, Marl, Germany), as high–linoleic acid sunflower oil or high–oleic acid sunflower oil, or as a fat rich in *trans* 18:1 produced by hydrogenation of the high–oleic acid sunflower oil with a single batch of high–oleic acid sunflower oil. The interesterification resulted in a random distribution with an equal amount of test fatty acids in the 3 positions of the triacylglycerol molecules, as verified by finding the same proportion of fatty acid in the 2-position of the triacylglycerol molecule as the one of total triacylglycerol (**Table 1**). The melting points of the test fats were as follows: S, 58–59 °C;

TABLE 2
Fasting hemostatic variables and blood lipids at baseline[1]

Variable	L (n = 16)	M (n = 8)	O (n = 16)	P (n = 16)	S (n = 16)	T (n = 15)
FVIIa (μg/L)	1.16 ± 0.54	1.00 ± 0.34	1.09 ± 0.46	1.10 ± 0.44	1.20 ± 0.52	1.09 ± 0.39
FVII:c (%)	81.31 ± 9.6	77.5 ± 6.7	79.44 ± 9.9	78.00 ± 12.5	82.56 ± 12.3	80.20 ± 11.1
PAI-1 (μg/L)	9.79 ± 6.54	10.1 ± 4.72	10.0 ± 6.60	9.63 ± 5.62	9.99 ± 8.17	7.21 ± 4.46
tPA (IU/mL)	0.72 ± 0.41	0.53 ± 0.16	0.63 ± 0.27	0.66 ± 0.24	0.73 ± 0.29	0.77 ± 0.25
FFAs (mmol/L)	0.46 ± 0.26	0.34 ± 0.14	0.33 ± 0.15	0.39 ± 0.24	0.42 ± 0.23	0.44 ± 0.26
TG (mmol/L)	0.83 ± 0.26	0.68 ± 0.10	0.74 ± 0.30	0.69 ± 0.22	0.78 ± 0.26	0.72 ± 0.22

[1] $\bar{x}$ ± SD. L, test fat high in linoleic acid; M, test fat high in myristic and palmitic acids; O, test fat high in oleic acid; P, test fat high in palmitic acid; S, test fat high in stearic acid; T, test fat high in *trans* fatty acids. FVIIa, activated factor VII; FVII:c, factor VII coagulant activity; PAI-1, plasminogen activator inhibitor; tPA, tissue plasminogen activator; FFAs, free fatty acids; TG, triacylglycerol. There were no significant differences between baseline values.

P, 47–48 °C; M, 42–44 °C; and T, 31–32 °C. The melting points for O and L were < 20 °C. The specified fatty acid characterizing each test fat made up 41–47% of total fatty acids (by wt). The purpose of using triacylglycerol (tristearin, tripalmitin, and trimyristin) was to keep nonglyceride constituents to a minimum. Furthermore, a single batch of TRISUN 80 was used for interesterification to balance the nonglyceride content of the dietary fats. The fatty acid composition of the test fats is presented in Table 1.

Blood sampling and analysis

Blood samples were taken by venipuncture with minimal stasis and collected into siliconized evacuated tubes. Subjects rested supine for 15 min beforehand. Samples were taken while subjects were fasting and 2, 4, 6, and 8 h after the beginning of the meal. Between blood drawings, subjects pursued their usual study activities or walked within the department.

Blood for the measurement of FVII:c and activated factor VII (FVIIa) was collected in citrated tubes (kept at room temperature for not more than 1 h), and aliquots for fibrinolytic variables were drawn into precooled tubes containing strong acidic citrate (Stabilyte; Biopool, Umea, Sweden). All samples were centrifuged for 15 min at 3000 × *g* (samples for fibrinolysis at 4 °C, the others at room temperature). Plasma was pipetted into plastic vials, rapidly frozen, and stored at −80 °C. Additional details were described previously (35).

Plasma FVII:c (% of standard) was assessed in a one-stage clotting assay as described (36). After incubation of 100 μL diluted test plasma (1:10 in tris buffer) and 100 μL human FVII-deficient plasma (Biopool, Umea, Sweden) at 37 °C for 3 min, clotting was initiated by the addition of 200 μL of a 1:1 mixture of a 25-mmol CaCl/L solution and human thromboplastin. The clotting time was recorded on a coagulometer (Schnitger-Gross, Amelung, Germany), and FVII:c was expressed relative to a commercial reference plasma (Hemostasis Reference Plasma: assayed value, 106 ± 16%; Biopool).

Plasma FVIIa was measured in a one-stage clotting assay by using a soluble mutant recombinant tissue factor that possesses cofactor activity for FVIIa but fails to support activation of FVII (37). Clotting times were converted to FVIIa concentration (ng/mL) by comparison with a standard curve given by a freeze-dried preparation of purified recombinant FVIIa (code labeled 89/688; National Institute of Biological Standards and Control, Potters Bar, United Kingdom) serially diluted with a commercial FVII-deficient human plasma (George King Biomedical, Overland Park, KS). The within-run CVs for FVII:c and FVIIa were 2.2% and 11.1%, respectively.

Plasma tissue plasminogen activator (tPA) activity (mIU/mL) and PAI-1 antigen concentration (ng/mL) were assessed by commercial enzyme-linked immunosorbent assays (Biopool). Plasma PAI-1 antigen was estimated by a chromogenic assay (Spectrolyse/pL PAI; Biopool). Plasma lipids, FVII:c, and FVIIa were measured for all samples drawn, whereas tPA and PAI-1 were measured only at baseline, 4 h, and 8 h.

Blood for lipid analysis was collected in tubes containing EDTA, which were immediately placed on ice and centrifuged at 3000 × *g* for 15 min at 4 °C. Triacylglycerol concentrations were assessed in plasma by enzymatic procedures (Boehringer Mannheim GmbH, Mannheim, Germany) on a Cobas Mira analyzer (Roche, Basel, Switzerland). FFAs were determined by a test kit based on an in vitro colorimetric method (Wako NEFA C; Wako Chemicals GmbH, Neuss, Germany).

Statistical analysis

When necessary, values were logarithmically transformed to normalize the distributions. To compare the effect of the 6 meals, a two-way repeated-measures analysis of variance (ANOVA) was carried out with diet and subject as main effects and the baseline values used as the covariates. When the analysis indicated that the levels for diets were significantly different, pairwise comparisons were carried out by repeated-measures ANOVA or two-way ANOVA by using the SAS general linear model procedure (version 8.2; SAS Institute Inc, Cary, NC) to assess the effects of time and type of experimental fat during the first 8 h postprandially and to study the interaction between time and type of fat. Because of the many comparisons, a Bonferroni adjustment was applied. A significant interaction indicated that the effects of the experimental fats on the variable of interest differed with time. Least-squares means were used instead of means because not all 16 subjects received 6 test fats, as described under "Study design."

RESULTS

Baseline (fasting) hemostatic variables and blood lipids are presented in **Table 2**. There were no significant differences in fasting values.

Comparison of individual test fats

Fasting and postprandial values for FVIIa, FVII:c, PAI-1 antigen, and tPA activity after consumption of the S, P, M, O, T, and L test fats are shown in **Figure 1**. Graphs showing the effect on postprandial plasma FFAs and plasma total triacylglycerol are included for comparison. [The data on plasma triacylglycerol and FFAs are also presented elsewhere (33).] All test fats resulted in an increase in FVIIa and in FVII:c. When the overall repeated-measures ANOVA indicated differences, we performed pair-wise

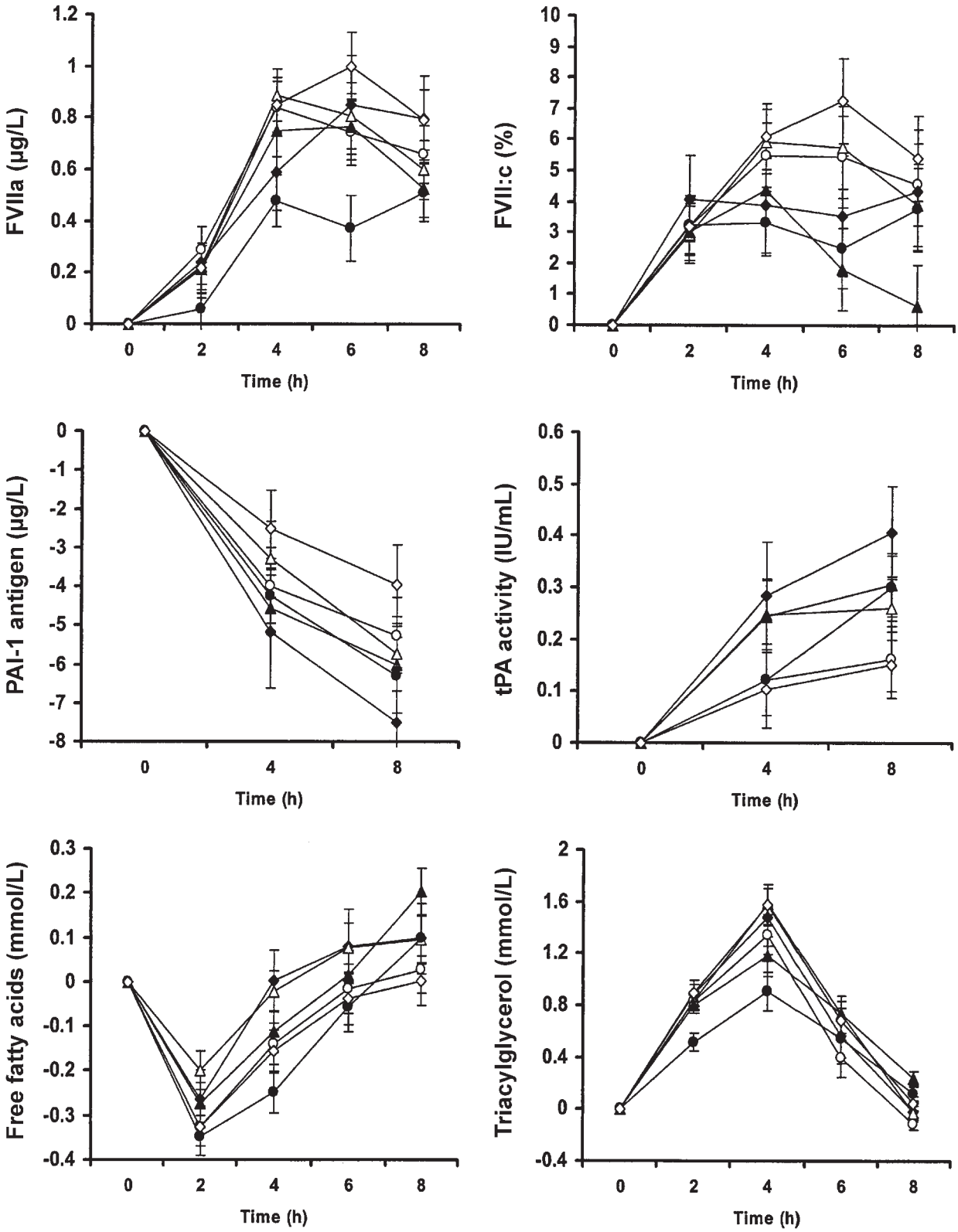

FIGURE 1. Least-squares mean (± SE) changes in activated factor VII (FVIIa) and factor VII coagulant activity (FVII:c) 2, 4, 6, and 8 h after intake and in plasminogen activator inhibitor 1 (PAI-1) antigen and tissue plasminogen activator (tPA) activity 4 and 8 h after intake of test meals rich in palmitic + myristic acid (M, ◆; $n = 8$), palmitic acid (P, ▲; $n = 16$), stearic acid (S, ●; $n = 16$), oleic acid (O, △; $n = 16$), *trans* fatty acids (T, ◇; $n = 15$), and linoleic acid (L, ○; $n = 16$). For comparison, we include data for the change in free fatty acids and plasma triacylglycerol 2, 4, 6, and 8 h after intake of test meals rich in the same fats. Data for 0 h are fasting values; other values are postprandial. For details of the fatty acid composition of the test fats, *see* Table 1. The overall repeated-measures ANOVA for FVIIa was $P = 0.053$; that for S versus T was $P = 0.017$. The overall repeated-measures ANOVA for FVII:c was $P = 0.018$; that for S versus O was $P = 0.012$ and that for S versus P was $P = 0.021$. Values for FFA and triacylglycerol are reported elsewhere (33).

comparisons when there was a diet × time interaction. As confirmed by the graphs, FVIIa was lower after the S than the T test fat ($P = 0.017$) and FVII:c was lower after the S than the O test fat ($P = 0.012$). The time course of FVII:c also differed significantly between the P and S test fats ($P = 0.021$). Overall, there was a strikingly different effect on FVIIa after the S diet compared with the other 5 diets. The S test fat resulted in a relatively lower response at 2–6 h but, unlike the responses to the other test meals, showed no decline between 6 and 8 h. Plasma PAI-1 antigen decreased and tPA activity increased postprandially (Figure 1). No significant differences in PAI-1 antigen and tPA activity were observed between test meals.

Comparison of pooled data

There was no statistical contraindication to pooling the results for test fats rich in saturated fatty acids (S, P, and M test fats) and those rich in unsaturated fatty acids (O, T, and L test fats). In other words, no statistical reason was found to believe that the chain length of the saturated fatty acids or the form of unsaturation of the unsaturated fatty acids influenced the postprandial responses measured. Even though *trans* fatty acids share certain chemical (eg, melting point) and functional (eg, effects on blood cholesterol) properties with saturated fatty acids, the effects of *trans* fatty acids on the postprandial responses in this study resembled those of other unsaturated fatty acids more than those of saturated fatty acids. Thus, our classification was based on the chemical property of saturation. These 2 pooled groups were therefore compared, and the results are presented in **Figure 2**. The saturated fatty acids resulted in lower FVIIa ($P = 0.036$, diet effect) and a lower FVII:c ($P < 0.001$, diet × time interaction), a tendency to a greater postprandial decline in PAI-1 antigen ($P = 0.06$, diet effect), and a higher tPA activity ($P = 0.028$, diet effect) than did the unsaturated fatty acids when analyzed by repeated-measures ANOVA. There were significant diet × time interactions in the responses of FFAs ($P = 0.006$) and plasma triacylglycerol ($P < 0.001$), with slightly lower FFA and triacylglycerol concentrations after the saturated fatty acids than after the unsaturated fatty acids at 2 and 4 h and higher values at 8 h.

DISCUSSION

As expected, the test fats resulted in increased postprandial FVII:c and FVIIa, as shown by us and others (11, 38–40). There was a distinctive response in FVIIa with the fat high in stearic acid: a lesser and slower increase between 2 and 6 h compared with the response to the fat high in *trans* fatty acid (and with the same tendency with respect to some of the other test fats). The pronounced difference in the response of FVII to the stearic acid test fat compared with the other fatty acids is in contrast with the results of most studies, which did not find that alimentary FVII activation was dependent on fatty acid composition (12, 39, 41, 42). However, consistent with our observations, a study that included a stearic acid test fat (15) reported a lower lipemic response with a correspondingly lower factor VIIa after stearic acid than after oleic acid. One reason for the discrepancy in results may be that our own study and that of Sanders et al (15) tested synthetic fats produced by random esterification, whereas others tested natural fats (39, 42, 43). The synthetic stearic fat in this study and the study of Sanders et al (15) was produced from tristearin, which was interesterified randomly with high–oleic acid sunflower oil. Thus, a distinctive distribution of the fatty acids on the triacylglycerol molecules may have caused an impaired absorption in both studies. This may also have been true in a recent study, in which meals containing a structured triacylglycerol with stearate (16% of fatty acids) present predominantly as randomly distributed monostearoyl triacylglycerol generated less FVIIa postprandially than did cocoa butter (11% stearate) (44). Mennen et al (12) did not observe a distinctively different effect of the stearic acid test fat compared with other test fats. In that study, no information was provided as to the source of the stearic acid in the margarine. Another reason for the apparent disagreement may be related to the level of stearic acid intake. Mennen et al (12) served 20 g stearic acid, compared with 36 g in the study of Sanders et al (15) and 30–38 g in our study (intake standardized for body weight). The capacity to absorb stearic acid may be somewhat impaired or delayed when large amounts are eaten.

The lipemic responses to *cis* and *trans* monounsaturated fatty acids did not differ significantly, even though in some other respects such as melting point and effects on blood cholesterol *trans* monounsaturated fatty acids resemble *cis* unsaturation more closely. Thus, for present purposes, the results for the saturated and unsaturated fatty acids were pooled into 2 groups.

Interestingly, in the present study, the graphs for the pooled saturated fatty acids versus the unsaturated fatty acids showed a lower FVIIa after 4 h and the same tendency after 6 h, indicating that long-chain saturated fatty acids in general probably tend to activate FVIIa less than do unsaturated fatty acids within this time. The lower rise in FVIIa after the saturated fatty acids accorded with the slower and less marked rise in total plasma triacylglycerol and FFAs. Because postprandial lipolysis was found to be less marked after the S test fat, as previously reported (33), we believe that this fat resulted in lower activation of FVII as the result of an impaired absorption of stearic acid, as reported also by Sanders et al (15). This agrees with the weaker although not significantly different response of FVII:c to stearic acid than to the myristic acid test fat, as was previously shown by our group (11).

The mechanism by which FVII is activated during lipemia after fatty meals is not fully understood, and several hypotheses (16, 45–48) have been refuted over the years (32, 45, 49, 50). Recently, evidence was presented for a link between FVII activation and stimulation of reverse cholesterol transport postprandially (51). Whatever the mechanism of FVII activation in the postprandial state, the results of the present study indicate that in some way it is linked to the strength of the lipemic response to a fatty meal, which itself is partly determined by the composition of the fat consumed. An observation of potential significance made in this study and reported elsewhere (33) is the relatively weak response of lipoprotein lipase activity to stearic acid– and palmitic acid–rich test meals as compared with the responses to meals of other fatty acid composition.

PAI-1 antigen concentrations decreased during the day, in agreement with the findings of others showing a strong diurnal variation (52). Although the effects of the individual test fats on PAI-1 did not differ significantly, as also found by Sanders et al (44), the time curves of the pooled data for the saturated and unsaturated fatty acids indicated a tendency for lower PAI-1 antigen 8 h after the intake of saturated fatty acids than after unsaturated fatty acids. Although it has been reported that PAI-1 is not affected postprandially by dietary changes (52), we and others have found that PAI-1 is affected by lipemia (3, 11). An in vitro increase in PAI-1 secretion after incubation with linoleic acid was reported (31), together with a positive association of

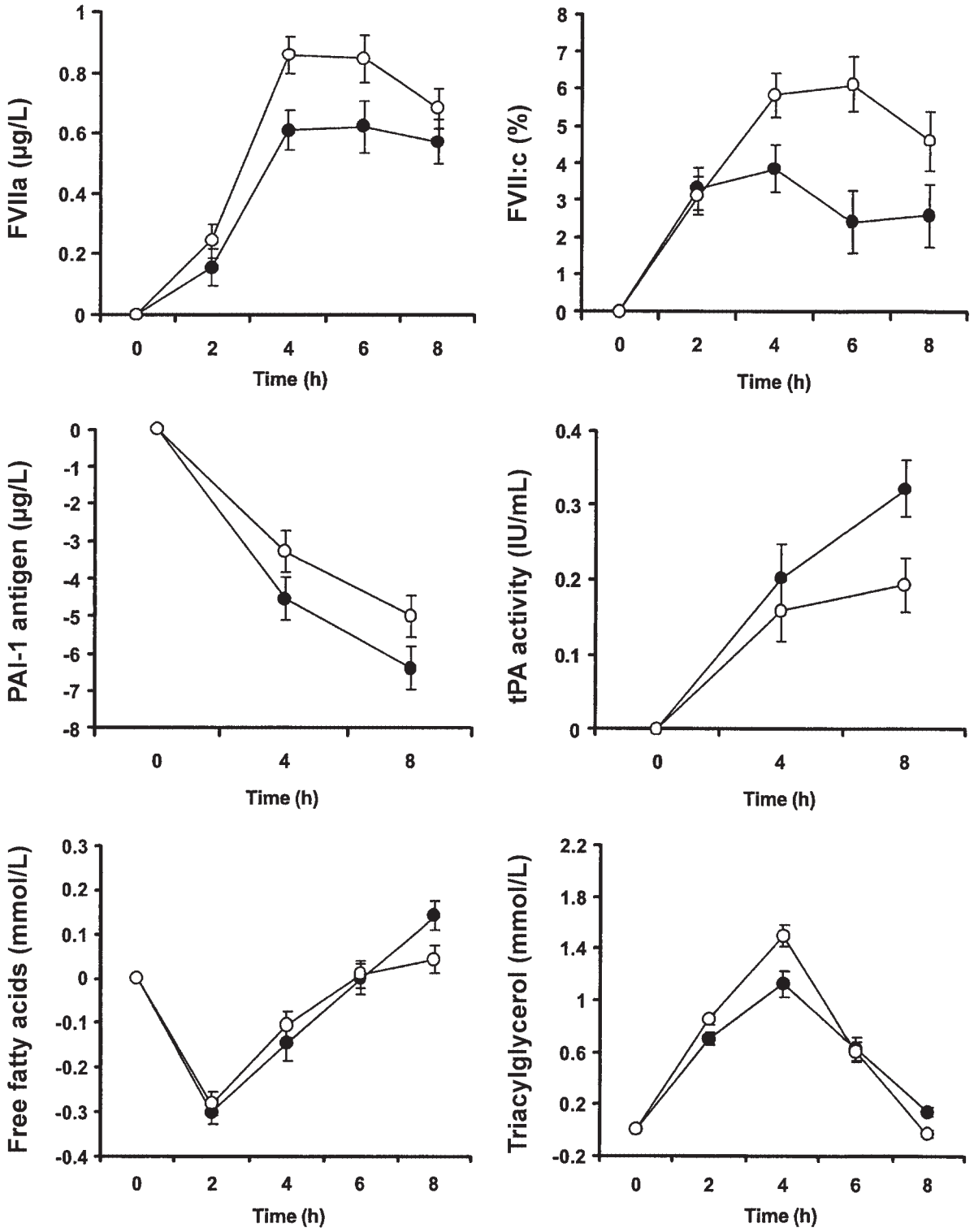

FIGURE 2. Least-squares mean (±SE) changes in activated factor VII (FVIIa) and factor VII coagulant activity (FVII:c) 2, 4, 6, and 8 h after intake and in plasminogen activator inhibitor 1 (PAI-1) antigen and tissue plasminogen activator (tPA) activity 4 and 8 h after intake of test meals rich in saturated fatty acids (●; n = 40) or unsaturated fatty acids (○; n = 47). For comparison, we include data for the change in free fatty acids and plasma triacylglycerol 2, 4, 6, and 8 h after intake of test meals rich in the same fats. Data for 0 h are fasting values; other values are postprandial. For details of the fatty acid composition of the test fats, see Table 1. The data are summarized as least-squares means for ease of presentation only; this is not appropriate for statistical analysis, which was performed by repeated-measures ANOVA and two-way ANOVA. For FVIIa, repeated-measured ANOVA resulted in a significant difference between the pooled groups ($P = 0.036$, diet effect) and no interactions; for FVII:c, there was a diet × time interaction ($P < 0.001$); for tPA activity, a diet effect ($P = 0.028$); and for free fatty acids and triacylglycerol, a diet × time interaction ($P = 0.006$ and $P < 0.001$, respectively). Two-way ANOVA showed a lower FVII:c after saturated fatty acids than after unsaturated fatty acids at 6 h ($P = 0.030$); for FFAs, responses were lower after saturated fatty acids at 2 h ($P = 0.005$) and 4 h ($P = 0.039$) and higher at 8 h ($P = 0.005$). The same pattern was seen for triacylglycerol at 2 h ($P = 0.034$), 4 h ($P = 0.012$), and 8 h ($P < 0.001$).

PAI-1 and linoleic acid intake (53) and of PAI-1 and unsaturated fatty acids (both monounsaturated and polyunsaturated; 54). By contrast, no association of PAI-1 and saturated fatty acids was reported in the 2 studies (53, 54). These observations agree with our results. Altogether, these results speak for moderate differences in the effect of specific dietary fatty acids on PAI-1, plasma VLDL (55), and remnant-like particles (H Shige, T Ishikawa, M Nishiwaki, et al, unpublished observations, 1994). With regard to tPA activity, the data suggested a higher tPA activity 8 h after the intake of saturated than after unsaturated test fats, which agrees with the tendency to a higher postprandial tPA activity after palmitic acid than after polyunsaturated fatty acids as shown recently (56). However, most studies have not observed a modulation of postprandial tPA activity by dietary fat composition (11, 43, 44, 57).

In conclusion, the results of the present study indicate a lesser increase in FVIIa after the consumption of fats high in saturated acid, especially stearic acid, than after fats high in unsaturated fatty acids, probably because of a lower postprandial lipemia associated with relatively poor absorption of stearic acid. Saturated fatty acids seem to result in a slightly more favorable effect on fibrinolysis than do unsaturated fatty acids in the late postprandial phase. Overall, therefore, and in agreement with the results of other studies (11), we did not find dietary stearic acid to be more thrombogenic in its acute effects on coagulation and fibrinolysis than are dietary unsaturated fatty acids, including *trans* monounsaturated fatty acids.

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TT was the daily project leader and was responsible for the study scheme, statistical calculations, interpretation of the data, and writing of the manuscript. GJM was responsible for analyses of factor VIIa, statistical calculations, data interpretation, and providing significant advice. AB was responsible for fatty acid analyses and interpretation. BS was responsible for study design, data interpretation, and providing consultation. None of the authors had any financial or personal interest in any organization sponsoring the research, including advisory board affiliations.

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