J. biosoc. Sci. (1997) **29**, 129–139 © 1997 Cambridge University Press

SOCIAL NETWORK IN RELATION TO PLASMA FIBRINOGEN

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Summary. Consistent findings about the inverse association of social network level with coronary heart disease mortality and morbidity suggest the importance of investigating biological pathways of association. Differences in plasma fibrinogen level were investigated among middle-aged men with weak and strong structural and functional social network ties. Men with low scores in the adequacy of social participation variable (structural) had higher mean values of plasma fibrinogen than those with high scores. The difference remained after adjustment for age, smoking and cardiovascular health status and after possible modifying factors were taken into account, but did not remain significant after allowing for physical fitness. Men with high scores in overall support (functional) had higher plasma fibrinogen levels compared to the men with low scores. This difference persisted after age and cardiovascular health status were taken into account but was explained by smoking. The data suggest that smoking and cardiorespiratory fitness are important mediating or modifying factors between structural and functional aspects of social network ties and plasma fibrinogen.

Introduction

Rosengren *et al.* (1990) found an inverse correlation between social activity level and plasma fibrinogen concentration among men aged 50, higher scores for social activities being associated with a lower fibrinogen concentration. The activity levels were determined by activities at home, outside the home and by social activities. Although no independent association was found between fibrinogen concentration and occupational class, the authors point out that the activity scores used may well be indicators of social class. Two recent studies have also suggested that low social class associates with increased plasma fibrinogen level (Moller & Kristensen, 1991; Wilson *et al.*, 1993).

Plasma fibrinogen has been repeatedly found to be one major biological factor influencing the development of atherosclerosis (Kannel *et al.*, 1987b; Smith *et al.*, 1990). On the other hand, the inverse association between social network ties and

https://doi.org/10.1017/S0021932097001296 Published online by Cambridge University Press

cardiovascular mortality (Berkman & Syme, 1979; House, Robbins & Metzner, 1982; Orth-Gomer & Johnson, 1987) and morbidity (Seeman & Syme, 1987; Blumenthal *et al.*, 1987; Eriksen, 1994) has also been well documented.

Social relationships may influence the pathogenesis of coronary heart diseases by affecting plasma fibrinogen. Because studies are scarce in this area, it becomes important to reinvestigate whether social network ties relate to plasma fibrinogen. In the present study differences in plasma fibrinogen level among men with weak and strong social network and support ties are examined. Behavioural factors are treated as pathways between social relationships and fibrinogen.

Subjects and methods

Subjects

The cohort was selected as a random sample of men aged 50–60 years ($N = 4850$) from the city of Kuopio and a nearby semiurban community in eastern Finland. The examination was conducted from June to November 1992. Of the 300 men initially invited, 84% participated in the study. The final study cohort comprised 212 men. Complete social network data were obtained from 192 men and data of social support aspects from 195 men. The subjects with missing social network or support data were excluded from the analyses. Of the men, 124 were free from cardiovascular diseases, whereas 82 had a positive history of either cerebro- and/or cardiovascular diseases (CVD). The details of the sampling strategy and the cohort examination procedures have been described previously (Rauramaa *et al.*, 1994).

Procedure

The participants visited the research centre four times within 3 weeks for clinical and biological tests. At the first visit a structured self-administered questionnaire was used to elicit social network and support levels, sociodemographic variables and depressive symptoms. The second data collection for social network and support took place about 3 weeks after the first, to assess the reliability of the index.

Examinations

Participants' social network and support level was measured by 22 items (Appendix 1). The summative index used here is a slightly modified version from the original index with eight subindices based on the validity and reliability analyses (Helminen *et al.*, 1995). Social network as a concept of structural level was assessed with quantitative and qualitative aspects by four summative subindices: social anchorage, contact frequency, social participation, and adequacy of social participation. The beneficial effect of a personal social network is assumed to depend on its ability to supply various resources to the individual. Social support as a function of the individual's interaction within the social network was defined as the resources provided in a supportive exchange among social network. Social support was assessed by three summative subindices: availability of material and informational support, availability of emotional support, and adequacy of emotional support.

The distribution of scores of each item was dichotomised; men above the cut-off

https://doi.org/10.1017/S0021932097001296 Published online by Cambridge University Press

point were given one point and the others zero. The points for each item of a subindex were summed for each individual to form his score for the subindex in question. The distribution of the scores of all the subindices was first divided into tertiles and then dichotomised (weak, strong), except for the adequacy of social participation subindex which was directly dichotomised. The lowest tertile was defined as the weak category. The definitions of the subindices have earlier been presented in detail (Helminen *et al.*, 1995). The summative social network score was low for 26% and the summative social support score low in 21% of the cohort.

Venous blood samples were drawn without stasis between 7.30 and 10.00 am after a 12-hour fast and 30 min rest in the supine position. The men were advised not to drink alcohol for 1 week nor take any anti-inflammatory analgesics for 2 weeks prior to blood donation. Also, in the case of any acute respiratory infection, blood samples were not taken until at least 1 week after the symptoms had disappeared.

Fibrinogen levels were determined from citrated plasma by the thrombin time method (Clauss, 1957) using the reagents of Baxter Dade (Miami, USA). Lipoproteins were fractionated from fresh serum samples by ultracentrifugation and selective precipitation (Carlson, 1973; Penttilä *et al.*, 1981). Cholesterol concentrations in serum and lipoprotein fractions were measured enzymatically using a commercial CHOD-PAP method (Boehringer Mannheim GmbH, Germany). Serum triglycerides were determined enzymatically (GPO-PAP method, Boehringer Mannheim GmbH). The coefficients of variation were 3·5% for fibrinogen, 1·8% for serum cholesterol, 3·1% for LDL-cholesterol, 6·7% for HDL cholesterol and 2·3% for triglycerides.

Physical activity was assessed using the Stanford Seven Day Recall Interview by adding cross-country skiing and long-distance skating to the activity list (Rauramaa *et al.*, 1995b). To assess cardiorespiratory fitness, maximal oxygen uptake (VO_2max) was measured in a symptom limited test using an electrically braked bicycle ergometer increasing the work load by 20 W/min up to a subjective or objective maximum. Respiratory gas analyses were done breath-by-breath and averaged for 15 seconds; VO_2max was determined as levelling off in spite of increased work load (Rauramaa *et al.*, 1995a).

Smoking habits were determined by an interview and used as a binary variable (current versus non-smokers) in the statistical analyses. Twenty-one per cent of the subjects were smokers.

Body mass index (BMI) was calculated as the weight in kilograms divided by the square of the height in metres. A BMI value of 25 or more was defined as first grade (mild) obesity, 30 or more as second grade (moderate) obesity, and 40 or more as third grade (severe) obesity (Garrow, 1988).

Waist circumference was measured midway between the lower rib margin and the iliac crest, and hip circumference at the level of the greater trochanter.

Education level was determined by a questionnaire. The men were classified into 6 years of education or less (79%), 7–9 years of education (14%) and 12 years or more (7%). Living conditions were analysed separately by dividing marital status into two groups, those living alone (15%) and those cohabiting (82%).

Depressive symptoms were assessed using the Center of Epidemiologic Studies Depression Scale (CES-D) for population studies. The 20 CES-D items were scored on a standard four-point scale (0–3) with a cut-off point of >16 used to 'distinguish those

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Table 1. Descriptive statistics of the 212 subjects (% of subjects in each group)

Variables	%
Basic education level	
Elementary school	79
Middle school	14
High school	7
Cardiovascular disease: yes/no	39/61
Overall social network: weak/strong	26/74
Overall social support: weak/strong	21/79
Social anchorage: weak/strong	49/51
Contact frequency: weak/strong	24/76
Social participation: weak/strong	60/40
Adequacy of participation: weak/strong	7/93
Emotional support: weak/strong	30/70
Adequacy of emotional support: weak/strong	22/78
Material and informational support: weak/strong	32/68

with a sufficient amount of depressive symptomatology so that they closely resemble depressed patients in treatment' (Weissman *et al.*, 1977).

Statistical methods

Chi-square analysis was used to analyse differences in smoking, education, and age, between the weak and strong categories of the seven social network and support variables. Student's t-test and the analysis of covariance were performed to compare serum fibrinogen levels between the study groups. The analysis of covariance was done in two steps. First, possible confounding factors (age, cardiovascular health status) and potential modifying factors (education, living conditions, smoking, depressive symptoms, BMI, weight, waist–hip ratio, cardiorespiratory fitness, triglycerides and high and low density cholesterol) were each taken into account separately. In the second step the covariates showing significant association with fibrinogen in the first analyses were simultaneously taken into the covariance model. Subjects who did not fully complete all the items of the social network and support indices, were excluded from the analyses. The association was deemed significant if the coefficient differed significantly from zero at the 0·05 level. Statistical analyses were performed using SPSS/PC + (Norusis, 1990).

Results

Descriptive characteristics of the subjects are presented in Table 1. Mean (95% CI) age of the subjects was 55·1 years (54·7; 55·5), plasma fibrinogen concentration 3·29 g/l (3·21; 3·36), maximal oxygen uptake 29·4 ml/kg/min (28·6; 30·2), BMI 27·0 kg/m^2 (26·5; 27·6) and serum cholesterol 5·5 mmol/l (5·4; 5·6). Men with a higher education level

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Table 2. Mean (g/l) plasma fibrinogen levels among 212 men in the two groups (weak, strong) of the different social network and support indices

	n	g/l	SD	CI (95%)	*p*-value
Network					
Weak	49	3·36	0·49	3·23; 3·49	0·237
Strong	144	3·26	0·57	3·16; 3·35	
Anchorage					
Weak	96	3·29	0·49	3·19; 3·39	0·813
Strong	102	3·29	0·58	3·15; 3·39	
Frequency					
Weak	49	3·26	0·68	3·06; 3·47	0·764
Strong	159	3·29	0·53	3·21; 3·38	
Participation					
Weak	121	3·34	0·56	3·24; 3·44	0·119
Strong	81	3·21	0·57	3·09; 3·44	
Adequacy of participation					
Weak	14	3·68	0·55	3·35; 3·99	0·008*
Strong	187	3·26	0·55	3·18; 3·34	
Support					
Weak	41	3·12	0·43	2·98; 3·26	0·033†
Strong	152	3·33	0·58	3·23; 3·42	
Emotional					
Weak	60	3·19	0·47	3·06; 3·31	0·110
Strong	139	3·32	0·59	3·22; 3·31	
Adequacy of emotional support					
Weak	44	3·16	0·40	3·03; 3·28	0·066
Strong	154	3·33	0·59	3·23; 3·42	
Information					
Weak	63	3·27	0·55	3·13; 3·41	0·722
Strong	137	3·30	0·56	3·21; 3·37	

*Adjusted for age ($p=0·010$), education ($p=0·012$), living conditions ($p=0·009$), depression ($p=0·002$), smoking ($p=0·011$), BMI ($p=0·025$), weight ($p=0·021$), waist–hip ratio ($p=0·027$), cardiovascular status ($p=0·009$), VO_2max ($p=0·059$), HDL ($p=0·021$), LDL ($p=0·010$), total cholesterol ($p=0·009$), triglycerides ($p=0·014$).

†Adjusted for age ($p=0·032$), education ($p=0·028$), living conditions ($p=0·036$), depression ($p=0·100$), smoking ($p=0·101$), BMI ($p=0·043$), weight ($p=0·042$), waist–hip ratio ($p=0·025$), cardiovascular status ($p=0·033$), VO_2max ($p=0·052$), HDL ($p=0·024$), LDL ($p=0·037$), total cholesterol ($p=0·035$), triglycerides ($p=0·030$).

Numbers of analysed cases vary due to missing data.

were more integrated in their neighbourhood ($p<0·001$) and participated more actively ($p<0·001$) than men with a lower education level. Older men scored higher on overall social network compared to younger ones ($p=0·009$). There were no differences between cardiovascular health status and the weak and strong groups for

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Table 3. Mean levels of LDL-cholesterol, HDL-cholesterol, triglycerides, body mass index, waist–hip ratio and maximal oxygen uptake in the two groups (weak, strong) of social support and adequacy of social participation indices*

	Social support						Adequacy of social participation					
	Weak			Strong			Weak			Strong		
	n	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD
LDL	41	3·6	0·9060	152	3·7	0·8817	14	3·8	1·133	187	3·7	0·8689
HDL	41	1·2	0·2774	152	1·2	0·2693	14	1·1	0·1970	187	1·2	0·2673
TG	41	0·7	0·2082	152	0·7	0·2023	14	0·1	0·1764	187	0·6	0·2012
BMI	41	27	3·7	148	27	3·6	14	29	4·7715	183	26	3·5666†
VO_2max	37	30	6·4	141	30	5·8	12	26	3·6587	173	30	5·8958‡
Waist–hip	41	0·97	0·0516	152	0·97	0·0511	14	0·99	0·0521	187	0·97	0·0509

*Subjects in whom serum fibrinogen levels have been measured.
†*p*-value = 0·023.
‡*p*-value = 0·032.

social network and support. Current smokers participated less in social activities ($p = 0{\cdot}001$) and had weaker overall social network scores ($p = 0{\cdot}003$) but had stronger overall social support than non-smokers.

Men who scored low in the adequacy of social participation variable had higher plasma fibrinogen [3·68 g/l (3·35; 3·99)] level than those with high scores for social participation [3·26 g/l (3·18; 3·34)] (Table 2). The difference remained significant after adjustment for age and cardiovascular health status and when several possible modifying factors were taken into account, each separately. The difference also persisted ($p = 0{\cdot}050$) when cardiovascular health status, smoking, educational level, HDL-cholesterol and waist-to-hip ratio were simultaneously entered into the covariance analysis. However, the difference did not remain significant after cardiorespiratory fitness was taken into account, either separately or together. Maximal oxygen uptake level was higher among men with high scores on the adequacy of social participation variable compared to men with low scores (Table 3).

Men with high scores on overall support had 0·20 g/l (0·15; 0·25) higher plasma fibrinogen level compared to the men with low scores (Table 2). The difference persisted after age, cardiovascular health status, education level, waist-to-hip ratio, HDL-cholesterol and cardiorespiratory fitness were taken into account. However, the difference between the groups was explained by a smaller ($p = 0{\cdot}043$) number of smokers (10%) among men with low overall support compared to those with high support (24%).

Discussion

The main finding of the study was that adequacy of social participation, one of the social network indices, was associated with plasma fibrinogen concentration. Men who were not satisfied with their social participation had higher concentrations of plasma fibrinogen than those who were satisfied. However, the difference was explained by the better cardiorespiratory fitness of the latter group. In addition, men having strong overall support had higher fibrinogen levels due to the greater number of smokers. Thus, cardiorespiratory fitness and smoking should be considered as parts of a causal chain between social network ties and disease.

There are several studies of the effect of social network and support on biological cardiovascular risk factors (Eriksen, 1994) but only one study on social network and plasma fibrinogen compares with the present results. Rosengren and his co-workers (1990) show that socially active, non-smoking, 50-year-old men have lower plasma fibrinogen levels than the less socially active. In their study the level of all social activities was measured by activities at home, activities outside the home and social activities. In the present study, no association of contact frequency or social participation subindices with plasma fibrinogen concentration was found. These subindices were comparable to Rosengren *et al.*'s outside the home and social activities variables.

In the present study a plasma fibrinogen level above 3·5 g/l, an independent risk factor for myocardial infarction (Ernst, 1993a), was exceeded among the men with weak adequacy of participation. Subjects' age and present disease status, possible determinants for fibrinogen (Stefanick *et al.*, 1995) did not explain the difference between the study groups.

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In the present study the adequacy of social participation variable describes subjects' perceived satisfaction with their possibilities of particpation in society. While most of the subjects scored weakly in social participation, measured as numbers and frequencies of social activities, only fourteen subjects were dissatisfied with their possibilities for social participation. It is possible that satisfaction is related to social class. Some studies have found that people of lower socioeconomic status have greater plasma fibrinogen concentrations than those of higher status (Wilson *et al.*, 1993; Markowe *et al.*, 1985). However, in the present study, participants' education level, one indicator of social status, did not explain the difference between the men with weak and strong adequacy of social participation. These findings support the study (Kannel, D'Agostino & Belenger, 1987a) reporting no differences in plasma fibrinogen concentration between occupational grades, another indicator of social class.

However, because subjects' satisfaction with their social participation and the way they responded to the questionnaires, may be determined by mood, adjustment was made for depressive symptoms and living conditions (living alone/cohabiting). These variables did not appear to explain the difference, either. Furthermore, the difference could not be explained by cardiovascular health status, anthropometric measures, serum lipids (Stefanick *et al.*, 1995) or smoking, a strong determinant of fibrinogen level (Kannel *et al.*, 1987a; Meade *et al.*, 1993).

It has been indicated that social support reduces cardiovascular responsivity to stress and protects for silent ischaemic episodes (Hedblad *et al.*, 1992). In the present study, the difference in fibrinogen levels between the men with weak and strong adequacy of social participation was clearly explained by cardiorespiratory fitness, a strong correlate of fibrinogen level (Rankinen *et al.*, 1994; Vanninen, Laitinen & Uusitupa, 1994; Lakka & Salonen, 1993). The men who were satisfied with their social participation had a higher maximal oxygen uptake than those not satisfied. Although the difference in energy expenditure between these groups did not reach statistical significance ($p = 0{\cdot}052$), the higher VO_2max indicates that people in the former group are also physically more active (Osler, 1995).

Fibrinogen is a relatively large protein (340,000 daltons) synthesised in the liver with a half-life of 3–6 days (Ernst & Resch, 1995). Due to rapid turnover, plasma levels of fibrinogen are subject to a quite large variation, and estimates of within-person variation have ranged from 28% (Thompson, Martin & Meade, 1987; Chambless, McMahon & Wu, 1992) to 67% (Marckmann, Sandström & Jespersson, 1992) of the total variation. These values are considerably higher than those reported for serum cholesterol (12%) but much lower than within-person variation of serum triglycerides (Thompson *et al.*, 1987; Marckmann *et al.*, 1992) or several other haemostatic factors, e.g. antithrombin III, fibrinopeptide A, β-thromboglobulin (Nguyen *et al.*, 1995). Somewhat high within-person variation could be partly explained by the fact that fibrinogen is an acute-phase protein and especially during acute and chronic bacterial infections plasma levels of fibrinogen are elevated (Ernst, 1993b). In the present study, special attention was given to minimising the confounding effects of acute-phase reactions. In the case of any acute respiratory infections, blood samples were not taken until at least 1 week after the symptoms had disappeared. Therefore, it is unlikely that the difference in plasma fibrinogen concentration between men with weak and strong adequacy of social participation is due to infection. In fact, there were no differences

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between the two groups in serum albumin, prealbumin or ferritin, other known acute-phase proteins (data not shown). Also serum γ-glutamyl transferase activities were similar in both groups indicating that the difference was not due to hepatic abnormalities.

The difference in fibrinogen levels between the men having strong overall support and those with less supportive relationships was explained by smoking. Here, the men with high scores on overall social support were more often smokers. This is in contrast to two studies suggesting that men who experience little social support are more often smokers than men with strong social network and support (Osler, 1995; Hanson & Isacksson, 1992).

The subjects here represent a random sample of men aged 50–60 years, drawn from the comprehensive national population registry. In spite of this, the results need to be considered with caution because of the relatively small number of subjects. Cardiovascular health status, biological tests and social network and support level were assessed within 3 weeks. The social network index used proved valid and reliable. There were a few men who did not want to complete all items of the social network and support questionnaire. Hence, their social network and support levels remained unknown. No attempt was made to estimate missing values by calculating means. Misclassification existed in cases where the social network and support questions were not honestly answered.

The results here provide evidence about the association of social network ties with plasma fibrinogen. Because fibrinogen is a major biological risk factor for atherosclerotic cardiovascular diseases (Qizilbash *et al.*, 1991; Di Minno & Mancini, 1990) which develops slowly to be manifested late in adult years, the results are of practical importance in health promotion. The observations additionally suggest that smoking and cardiorespiratory fitness act as mediating or modifying factors between social relationships and plasma fibrinogen.

Acknowledgments

This study was supported by a grant from the Finnish Ministry of Education (108/722/91; 131/722/91; 133/722/91; 135/722/91; 138/722/91; 190/722/92).

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https://doi.org/10.1017/S0021932097001296 Published online by Cambridge University Press