PERGAMON

Personality and Individual Differences 26 (1999) 285–304

PERSONALITY AND INDIVIDUAL DIFFERENCES

Biological and psychosocial risk factors in ischaemic heart disease: Empirical findings and a biopsychosocial model

Andrej Marušič[a,*], Gisli H. Gudjonsson[a], Hans J. Eysenck[a,✠], Radovan Starc[b]

[a]*Department of Psychology, Institute of Psychiatry, University of London, De Crespigny Park, Denmark Hill, London SE5 8AF, U.K.*

[b]*Clinical Department of Cardiology, Clinical Centre, Ljubljana, Slovenia*

Received 20 January 1998

Abstract

The objective of this research was to investigate simultaneously biological and psychosocial risk factors in groups of 187 male ischaemic heart disease (IHD) patients and 187 controls. Initially, a multivariate logistic regression was used to compare the two groups on 11 standard biological and 7 suggested psychosocial risk factors. The multivariate regression model supported altogether 9 risk factors for IHD: 5 individual ones with sensitisation amongst them and 4 interactions of risk factors including a synergistic one between neuroticism and smoking. Next, the principal component analysis of all 18 (11 biological and 7 psychosocial) was used to extract 4 biopsychosocial and 2 biological correlates of IHD risk factors. It was concluded that psychosocial coronary proneness plays an important role in predicting IHD, even after taking into account the main, most notably atherogenic, biological risk factors. Two potential mechanisms of psychosocial pathogenicity have been suggested, notably alterations in health related behaviours and behaviourally evoked perturbations of neuroendocrine responses. Moreover, the presence of synergistic psychobiological interaction between neuroticism and smoking suggests the involvement of the former risk factor in sudden deteriorations in the coronary flow due to vasoconstriction. The results and related implications are consistent with the present knowledge about the risk of developing IHD.

Keywords: Coronary artery disease; Coronary-prone personality; Neuroticism; Sensitisation of emotions; Biological coronary risk factors; Synergistic interactions

* To whom all correspondence should be addressed. E-mail: spjtanm@bpmf.iop.ac.uk

✠ Deceased.

0191-8869/98/$ - see front matter
PII: S0191-8869(98)00132-9

1. Introduction

The Framingham Heart Study and the majority of other medically orientated investigations have identified *abnormalities of lipid metabolism*, *hypertension* and *smoking* (Bierman, 1991; Lakier, 1992; Farmer and Gotto, 1997) as the three major modifiable risk factors for ischaemic heart disease (IHD). Although studies have demonstrated that individuals with all three risk factors have about six times the chance of developing clinical IHD relative to those with no risk factor, only about 10% of such individuals will show clinical manifestations of IHD over a 10-year period of observation (Marmot and Winkelstein, 1975; Syme, 1984; Dembroski and Czajkowski, 1989). Other important **biological risk factors** include *clotting factors* (Hultin, 1991), *disturbances of glucose metabolism* (Stolar, 1988; Williams et al., 1997), *central obesity* type (Fontbonne et al., 1992) and the three unmodifiable risk factors, namely *age* (Lakatta et al., 1997), *male gender* (Farmer and Gotto, 1992) and *family history of IHD* (Grech et al., 1992).

On the other hand, epidemiological evidence over the last two decades is controversial regarding the predictive significance of globally defined *type A behaviour*. More consistent associations with IHD morbidity, mortality and angiographically defined severity emerge when considering only the type A pattern's hostility component, or related aspects of anger (Barefoot et al., 1983; Shekelle et al., 1983; Matthews and Haynes, 1986; Dembroski et al., 1989; Smith, 1992). However, type A behaviour or trait of hostility do not exhaust the range of **psychosocial risk factors** for IHD. By interpreting almost everything in terms of type A behaviour or hostility, one may lose appreciation for the multidimensional nature of the coronary-proneness, which should also include other personality traits, different aspects of the coronary-prone behaviour and stress-related issues, such as maladaptive coping styles. The personality traits, most commonly investigated in previous IHD studies are *depression*, *emotional instability*, *anxiety*, *somatic complaints* (Blumenthal et al., 1979; Weiss and Richter-Heinrich, 1985; Costa, 1987; Cramer, 1991; Fielding, 1991; Shekelle et al., 1991; Barefoot et al., 1992; Bolger and Schilling, 1992), *hostility* (Barefoot et al., 1983; Williams et al., 1984; Dembroski et al., 1985; Hearn et al., 1989), *impulsivity* (Innes, 1980; Chesney et al., 1981) and *cynicism* (Williams et al., 1984; Almada et al., 1991). In terms of other aspects of the coronary-prone behaviour, prospective studies done by Grossarth-Maticek and Eysenck (1990) suggested specific reactions to interpersonal stress as being important. Their so called psychosocial type II as opposed to personally autonomous psychosocial type IV is described as an overaroused person due to the failure to disengage from significant others. Schmitz (1992) replicated Grossarth-Maticek and Eysenck (1990) findings that coronary-prone subjects are high on *overarousal* and have *low personal autonomy*. In terms of coping with stress, only *emotional coping* was found to predict deteriorated health (Friedman and Booth-Kewley, 1987; Roger, 1995).

Most recently, an investigation of mechanisms that may mediate **psychosocial influences on IHD** has taken place. Apart from well known *alterations in health-related behaviours* (Ornish et al., 1990; Wright et al., 1994), some other mechanisms have been suggested. These are: *increased myocardial oxygen demand* (Goldstein et al., 1988; Meredith et al., 1990), *decreased coronary blood supply* by precipitating vasoconstriction of atherosclerotic coronary arteries (Yeung et al., 1993), *haemoconcentration* (Fujii and Imataka, 1993), *enhanced blood clotting* (Cannon, 1929; Patterson and Krantz, 1993) and *increase in plasma lipoproteins* (McCann et

al., 1995). Each of the suggested mechanisms implies possible relationships between psychosocial and biological risk factors. Of particular importance to us should be the synergistic interactions that may contribute substantially to the prediction of IHD risk over and above the sum of the independent risks due to those factors, like in cases of dyslipidaemia and hypertension (Kannel, 1978; Perkins, 1989) and smoking and neuroticism (Friedman et al., 1983; Eysenck et al., 1991).

Indeed, **neuroticism** should be of particular importance as it has been suggested to be at least to a certain extent related to individual differences in excitability and emotional responsiveness, which are reflected in autonomic activation (Eysenck and Eysenck, 1985; Gramer and Huber, 1994). It represents a personality trait of increased reactivity to stressors and this reactivity in a stressful situations may adversely affect bodily homeostasis and, thus, promote progression of IHD (Friedman and Booth-Kewley, 1987). Moreover, neuroticism and chronically disturbing emotions have repeatedly been found to be associated with the presence of different forms of IHD (Jenkins and Zyzanski, 1980; Weiss and Richter-Heinrich, 1985; Cramer, 1991; Fielding, 1991). However, the interpretation of the results has been complicated by the fact that neuroticism is also positively associated with worry about health and with a relatively benign, non-atherosclerotic condition, namely atypical chest pain (Ahnve et al., 1979; Bass and Wade, 1982; Shekelle et al., 1991; Naidoo and Patel, 1993). Persons that score high on neuroticism are more likely than others to visit physicians (Blumenthal et al., 1979), which may result in earlier diagnosis of possible IHD. The notion that neuroticism or emotional instability precede IHD has been criticised by Costa (1987), who claimed that neuroticism was related to increased somatic complaints but was not causally related to objective signs or pathophysiological evidence of disease, especially coronary artery disease. Furthermore, Stone and Costa (1990) proposed that a disease-prone personality is in fact a distress-prone personality.

The best way to deal with the above dilemma would be to investigate neuroticism together with a variable of over-reporting of emotional reactions as determined by physiological measures of emotional reactivity, referred to as **sensitisation**. Gudjonsson (1981) directly investigated the discordance between physiological and self-reported measures and formed a hypothesis about personality and defensiveness traits. In his study the subjects were divided into three groups according to their accuracy of self perception: repressors who reported low subjective disturbance but reacted relatively strongly electrodermally, sensitisers who amplified their disturbance and others. The hypotheses that repressors would have a high defensiveness score or L score and low trait anxiety or N score and that sensitisers would have the opposite results, notably high N and low L scores, were confirmed (Gudjonsson, 1981). It was also suggested by Weinberger et al. (1979) that both sensitisers and repressors coped ineffectively with stress relative to truly low-anxious people. In fact, a study of Kneier and Temoshok (1984) showed sensitisation to be important in cardiovascular disease subjects.

The hypotheses tested in the study are as follows:

(1) All tested psychosocial variables (neuroticism, psychoticism, low score on lie scale, sensitisation of emotions, coronary-prone behaviour, low personal autonomy and emotional coping) are significant predictors of the presence of IHD.

(2) All standard biological risk factors are significant predictors of the presence of IHD.

(3) The following pairs of risk factors interact synergistically in the prediction of presence of IHD: low-density and high-density lipoprotein ratio (LDL/HDL), hypertension and LDL,

fibrinogen and LDL, smoking and LDL, fibrinogen and hypertension and the biopsychosocial one of smoking and neuroticism.

(4) The psychosocial variables are correlates of the following biological risk factors: fibrinogen, smoking history and hypertension.

2. Methodology

2.1. Participants

A total of 374 subjects took part in the study. The **IHD sample** constituted 187 consecutive patients (56.8 year old; S.D. 9.5) who underwent coronary angiography at the Clinical Centre in Ljubljana. They had at least 50% narrowing of at least one coronary artery and/or had been diagnosed for myocardial infarction. The **control sample** constituted 144 inpatients from other departments in the same institution and 43 outpatients invited to a preventive medical examination elsewhere. There were no important differences found when comparing the outpatients and inpatients subgroups of controls on all the testing variables. In 187 controls the diagnosis of IHD was ruled out by a close examination of medical records and history data and, when necessary, by clinical examination and specialised diagnostic procedures. They were well matched for age (mean 56.5; S.D. 10.2) as well as for place of data acquisition and testing. In addition, any exclusions or restrictions made in the identification of the IHD cases applied equally to the controls and vice versa. Due to the lower percentage of women with IHD only men were included in the study. Among the exclusion criteria was a history of terminal illness, head injury and mental illness.

2.2. Variables

The **outcome variable** of the case-control study was *presence or absence of evidence of IHD*.

The 18 **exploratory variables** constituted of 11 biological and 7 suggested psychosocial risk factors. In the former group, the majority of standard IHD risk factors were included:

(1) *Family history of IHD (Fam IHD)* as the percentage of relatives with IHD.

(2)–(6) *Total cholesterol (Chol)*, *high-density lipoprotein (HDL)*, *low-density lipoprotein (LDL)*, *triglyceride (Tg)* and *lipoprotein(a), Lp(a)*, as 5 measurements of lipid profile.

(7) *The presence or absence of hypertension (Hyp)*.

(8) *Plasma fibrinogen (Fib)* measurement as a blood clotting factor.

(9) *The presence or absence of smoking history (Smok)*.

(10) *The presence or absence of disturbances of glucose metabolism (Disgl)* (diabetes mellitus or hyperinsulinaemia).

(11) *Waist–hip ratio (W–h)* as a measurement of the obesity type (waist or umbilical circumference divided by gluteal or hip circumference).

As far as suggested psychosocial risk factors were concerned, three important topics in the field of the health psychology were included, namely personality traits, behavioural types and coping styles:

(1)–(3) *Neuroticism (N)*, *psychoticism (P)* and *lie scale (L)*. The Eysenck Personality Questionnaire (EPQ) (Eysenck and Eysenck, 1975) was used to measure these personality traits. The alpha coefficients for N, P and L in the present study ($N = 393$) were 0.87, 0.32 and 0.81, respectively;

(4) *The presence or absence of sensitisation of emotion (Sen)*, another variable that originated from EPQ scores; according to Gudjonsson (1981) criteria, sensitisation is present when the subject has the N score above and the L (EPQ-lie scale) score below the median.

(5)–(6) *Psychosocial type II or overarousal and type IV or personal autonomy* as measured by the Short Interpersonal Reactions Inventory (SIRI) (Grossarth-Maticek and Eysenck, 1990). The alpha coefficients for types II and IV in the present study ($N = 393$) were 0.67 and 0.66, respectively.

(7) *Emotional coping style (Emcop)*, measured by the Coping Styles Questionnaire (CSQ) (Roger et al., 1993). The alpha coefficient for Emcop in the present study ($N = 393$) was 0.69.

The information for the outcome variable and the biological risk factors were obtained from a structured interview, medical history, medical records, clinical examination and specialised diagnostic procedures, including analyses of fasting blood samples and coronary angiography. For all the psychosocial variables, the Slovene versions of the three psychological questionnaires were used. One of them, namely the EPQ has been standardised and widely used in Slovenia since the late 1970s (Lojk, 1979). The other two, SIRI and CSQ were adapted for the Slovene population just prior to the beginning of the present study. Psychometric and statistical techniques were used to establish the equivalence of the source and target language versions of the instrument. These are presented in the original study report (Marušič, 1997), where information on the evaluation of their validity is also provided.

3. Results

3.1. Psychosocial multivariate logistic regression model

The present study contrasted the ischaemic heart disease (IHD) patients' group with the comparison group of controls. To start with, all suggested psychosocial exploratory variables were investigated as possible predictor variables by fitting the univariate logistic regression models in which the dependent variable is dichotomous, notably presence or absence of IHD. All suggested psychosocial risk factors were found to be statistically significant predictors of the presence of IHD. However, based on the univariate logistic regression models, we began to analyse the multivariate model using the forward stepwise method with all the variables that could be selected as suggested psychosocial IHD risk factors:

- EPQ: high N and P and low L; presence of sensitisation.
- SIRI: high type II and low type IV.
- CSQ: high Emcop.

As shown on Table 1, only N and sensitisation were included in the final model, concluded when no variable in the equation was eligible for removal and no variable not in the equation

Table 1
Final mutivariate logistic regression model for suggested psychosocial IHD risk factors

Variable	*B*	S.E.	Wald	*df*	Sig	*R*	Exp(*B*)
Neuroticism	0.08	0.02	9.85	1	0.0017	0.12	1.08
Sensitisation	0.62	0.28	4.84	1	0.0278	−0.07	1.86
Constant	−1.09	0.28	15.48	1	0.0001		

Model Chi-square = 32.8; $df = 2$; $p < 0.0001$; $N = 374$.

was eligible for entry. The final Chi-square was 32.8 (*df* 2; $p < 0.0001$) with an improvement of 4.9 (*df* 1; $p = 0.0270$) after the addition of sensitisation as the second variable. The classification table (Table 2) shows predictions and observed outcomes for the multivariate model.

3.2. Biological multivariate logistic regression model

The standard biological factors were also investigated as testing variables by fitting the logistic regression models. In the first place, univariate logistic regression models were fitted. Based on the univariate logistic regression models, we began to analyse the multivariate logistic regression model using the forward stepwise method with all 11 biological risk factors, although the univariate logistic model predictions of cholesterol and triglyceride levels were significant only in the borderline area ($0.05 < p < 0.10$). This was, however, not enough for their exclusion from the further analysis bearing in mind other recent studies with positive findings. The final model, concluded when no variable in the equation was eligible for removal and no variable not in the equation was eligible for entry, included in order HDL, familial aggregation of IHD, hypertension, LDL, plasma fibrinogen, Lp(a), smoking and disturbances of glucose metabolism. Abdominal obesity type or high waist–hip ratio, serum total cholesterol and triglyceride levels did not enter the model. For a more detailed report on biological risk factors, see Marušič (1997).

3.3. Biopsychosocial multivariate logistic regression model

Based on the first two multivariate logistic regression models of psychosocial and biological risk factors for IHD, we began to analyse the multivariate logistic regression model using the

Table 2
Classification table for IHD using the final multivariate model with neuroticism (*N*) and sensitisation (Table 1)

		Predicted IHD		
		Absent	Present	Percent
Observed IHD	Absent	126	61	67%
	Present	79	108	58%
				overall: 63%

Table 3
Final multivariate logistic regression model using the forward stepwise method with all the variables and hypothesised interactions

Variable	*B*	S.E.	Wald	*df*	Sig	*R*	Exp(*B*)
LDL/HDL	1.01	0.17	36.96	1	< 0.0001	0.27	2.76
Hyp*LDL	−0.17	0.04	17.44	1	< 0.0001	−0.18	0.85
Fam IHD	5.38	1.33	16.43	1	0.0001	0.18	217.83
N*Smok	−0.03	0.01	5.64	1	0.0175	−0.09	0.97
Fib	1.19	0.31	15.14	1	0.0001	0.17	3.28
Disgl	−0.42	0.17	6.41	1	0.0114	−0.10	0.66
Sen	−0.42	0.16	6.51	1	0.0107	−0.10	0.66
LDL*Fib	−0.17	0.07	6.48	1	0.0109	−0.10	0.85
Lp(a)	0.11	0.04	6.02	1	0.01	0.09	1.11
Constant	−6.22	0.91	46.25	1	< 0.0001		

Model Chi-square = 188.2; $df = 9$; $p < 0.0001$; $N = 340$. *: interaction between two variables.

forward stepwise method with all the important variables considered to be independently associated with IHD:

- Psychosocial risk factor: N and sensitisation.
- Biological risk factors: serum HDL, hypertension, familial aggregation of IHD, serum LDL, plasma fibrinogen, Lp(a), smoking and disturbances of glucose metabolism.

All variables but N entered the final model. The final Chi-square was 171.0 (df 9; $p < 0.0001$) with an improvement of 4.8 (df 1; $p = 0.0284$) after the addition of smoking as the last independent risk factor.

The next planned step was to repeat the multivariate logistic regression analysis including this time all the variables considered to be associated with IHD according to the last biopsychosocial multivariate model together with all the hypothesised interactions:

- Single biological and psychosocial risk factor: HDL, hypertension, familial aggregation of IHD, LDL, plasma fibrinogen, Lp(a), smoking, disturbances of glucose metabolism and sensitisation.
- Combined risk factors as six interactions of pairs of risk factors: LDL/HDL ratio, LDL and hypertension, LDL and fibrinogen, LDL and smoking, hypertension and fibrinogen, and smoking and N.

Table 3 gives the final results of stepwise logistic regression. All variables were included; some as single variables [family history of IHD, sensitisation, disturbances of glucose metabolism and Lp(a)], some as combined ones (LDL/HDL ratio, LDL with hypertension, LDL with fibrinogen and N with smoking) and fibrinogen as a single variable and in interaction with LDL. The final Chi-square is much higher than the previous one (Chi-square 188.2; df 9; $p < 0.0001$). Moreover, it provides more information about the nature of the obtained biopsychosocial set of IHD risk factors. Note that category variables, such as presence of hypertension, history of smoking and disturbances of glucose metabolism have been recorded so that parameter estimates for logistic regression (1, −1) are not the same as for indicator variables (0, 1).

Above, once again the classification table (Table 4) shows predictions and observed outcomes for this model.

Table 4
Classification table for IHD using the biopsychosocial multivariate model including two interactions (Table 3)

		Predicted IHD		
		Absent	Present	Percent
Observed IHD	Absent	140	32	81%
	Present	34	134	80%
				overall: 81%

3.4. Biopsychosocial correlates of IHD risk factors

Investigation of correlations between the suggested psychosocial and the standard biological risk factors provides a possible way of understanding the underlying psychosocial pathogenicity mechanisms. Below, the correlation table is presented (Table 5). It displays correlation coefficients between single psychosocial risk factors and biological ones. Here, once again all the 18 variables that were statistically significant predictors of presence of IHD in the univariate context are studied. Note that only highly significant ($p < 0.01$ or $p < 0.001$) coefficients are marked.

Already displayed correlations between biological and psychosocial risk factors indicated the existence of biopsychosocial correlates of IHD risk factors. We decided to use principal component analysis to show such correlates and to suggest distinguishing features of different types of biopsychosocial risk patterns. The principal component analysis provided 6 principal components with eigenvalues greater than 1.00: 3.57, 1.98, 1.71, 1.52, 1.18 and 1.10. Table 6 displays the six-factor solution. The first and the fourth components are predominantly psychosocial correlates. All the others are predominantly biological correlates.

Two mainly biological principal components tend to be associated with some psychosocial risk factors and mainly psychosocial principal components also correlate with biological risk factors. The first principal component, for example, is characterised by high loadings on N and other emotionally characterised variables. On top of these, it also correlates with Lp(a), the waist–hip ratio, hypertension and fibrinogen, the last three of them being related to stress. It

Table 5
Correlations between standard biological and suggested psychosocial risk factors for IHD

r	Fam	Chol	LDL	HDL	Lp(a)	Tg	Hyp	Smok	Fib	Disgl	W–h
P	0.06	0.04	0.03	−0.06	0.00	0.06	0.02	0.12	0.11	0.04	0.03
N	0.11	0.04	0.00	−0.12	0.12	0.12	***0.19***	**0.15**	***0.19***	0.09	0.13
L	−0.11	−0.07	−0.05	0.06	0.04	−0.05	0.00	−0.13	−0.08	−0.02	0.03
Sen	**0.15**	0.08	0.07	−0.11	0.03	0.08	0.06	0.13	0.08	0.00	0.00
II	0.02	0.05	−0.02	−0.05	0.12	**0.16**	0.12	0.08	0.13	0.10	0.09
IV	0.02	−0.04	−0.02	0.07	−0.14	−0.08	−0.08	−0.12	−0.13	−0.10	−0.11
EC	0.10	0.10	0.06	−0.08	**0.15**	0.12	**0.14**	0.08	**0.15**	0.08	***0.20***

$p < 0.01$ (bold); $p < 0.001$ (italic); $N \leq 374$ (minimum 356). EC: emotional coping.

could be named *emotionality with stress-related biological factors*. The second one seems not to be related to any of the suggested psychosocial risk factors and could be simply named *pure hyperlipidaemia* with high loadings of cholesterol and LDL and low loadings of Lp(a) and triglyceride. The third one is again a biopsychosocial one as it is characterised by high loadings of HDL, smoking, fibrinogen and some other biological risk factors, but it also yields high correlations with psychosocial risk factors such as N and P: *dyslipidaemic and haemostatic complex with behavioural components*. The fourth factor is a set of psychosocial risk factors with high loadings of P and sensitisation and low loadings of smoking: *tough mindedness and sensitisation*. The set of IHD risk factors that are included in the fifth principal component (dyslipidaemia, disturbances of glucose metabolism, hypertension and central obesity type) is medically also known as the *metabolic syndrome X* (Reaven, 1993). The last factor is the association between family history of IHD and presence of two major diseases as risk factors for IHD, namely hypertension and diabetes (disturbances of glucose metabolism). It also correlates with psychosocial factors of emotionality and sensitisation and could be, therefore,

Table 6
Structure matrix and factor correlation matrix of the principal component analysis of the standard biological and suggested psychosocial risk factors for IHD ($N = 337$)

	PC1	PC2	PC3	PC4	PC5	PC6
N	**0.79**		0.25	−0.33		0.22
Type II	**0.78**					
Emcop	**0.77**					
Type IV	**−0.68**					
Chol		**0.96**			−0.20	
LDL		**0.93**				
Fib	0.19		**0.68**			
HDL			**−0.63**		0.41	
Smoking			**0.52**	−0.19		
Lp(a)	0.27	0.28	**0.37**	0.28		
L				**0.83**		
Sen	0.46			**−0.72**		0.20
P	0.24		0.20	**−0.56**		
Tg		0.25	0.22		**−0.70**	−0.22
Disgl					**−0.69**	0.26
Waist–hip	0.21			0.19	**−0.53**	0.24
Fam IHD						**0.75**
Hyp	0.20		0.19		−0.22	**0.62**
IHD	0.20	0.19	0.60	(0.10)	−0.25	**0.62**
	PC1	0.14	0.20	−0.11	−0.11	0.11
		PC2	0.13	0.04	−0.06	0.01
			PC3	−0.07	−0.12	0.15
				PC4	0.01	−0.03
					PC5	−0.14
						PC6

PC: principal component.
Bold: variables as key correlates of a given principal component.

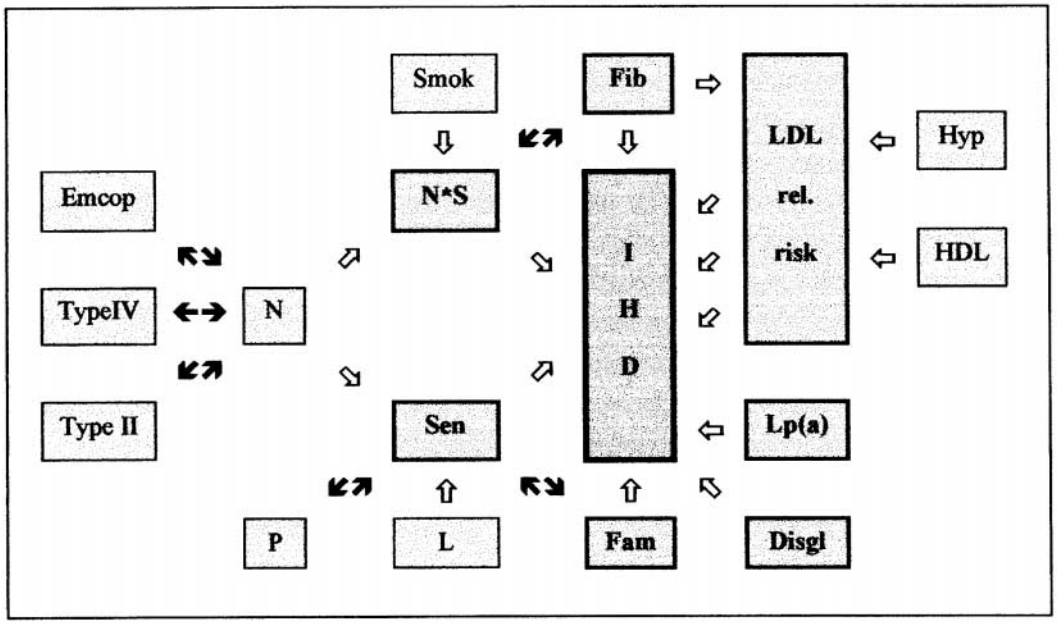

Fig. 1. Biopsychosocial model of IHD risk factors: possible directions (⇗) for biological, psychosocial and biopsychosocial risk factors' influence in IHD and some other correlations (⇙⇗) between risk factors. Legend: N*S: interaction between neuroticism and smoking; LDL rel. risk: LDL-related risk factors' interactions.

named *positive family and medical history with sensitisation*. Similar six principal components were obtained when the analysis was repeated without the outcome variable concerning presence or absence of IHD.

To conclude with our results, the last figure should be presented, which summarises previously displayed results (Tables 3, 5 and 6). Fig. 1 shows altogether 9 possible independent risk factors' influences in IHD as obtained by the means of the final multivariate logistic regression model (Table 3). These were named "directions" as they may also show origins of synergistic interactions (N and smoking for example) or other types of combined effects (LDL and HDL ratio and sensitisation as a combination of N and the lie scale-L). Fig. 1 also shows some other correlations between biological and psychosocial risk factors and psychosocial factors themselves as obtained by means of the correlation matrix (Table 5) and the principal component analysis (Table 6). In other words, Fig. 1 represents the suggested model of possible relationships between different biological and psychosocial risk factors and IHD and between risk factors themselves.

4. Discussion

4.1. Predicting IHD

On the basis of the multivariate analysis of all suggested **psychosocial risk factors**, only neuroticism (N) as a personality trait and sensitisation as a combination of the same trait with

low defensiveness (L) appeared to be independent predictors of IHD, there being no advantage in measuring other suggested psychosocial risk factors. This result should be understood in terms of a hierarchical arrangement of personality types, traits and behavioural variables. Traits are relatively enduring descriptive characteristics of a personality type, predisposing the person to similar behaviour in a variety of situations (Eysenck, 1994).

The strong relationship found between *neuroticism* and IHD supports previous findings by Jenkins and Zyzanski (1980), Weiss and Richter-Heinrich (1985) and Fielding (1991). Moreover, the result is based on the angiographically confirmed diagnosis of IHD and it therefore also represents a challenge to Costa (1987), who claimed that neuroticism is related to increased somatic complaints but is not related to organic illness in cases of IHD. On the other hand, *sensitisation* as an exaggerated part of N would be more consistent with Costa (1987) findings and conclusions about neuroticism. Sensitisers are characterised by the over-reporting kind of inconsistency between emotional reactions and physiological reactivity. Such persons are more likely than others to report their angina pectoris episodes, which may result in earlier diagnosis of possible IHD (Freeman and Nixon, 1987).

All tested **biological risk factors** were either more frequent or showed more dangerous values in IHD patients when compared to their control matches. However, only eight out of eleven variables entered the final multivariate biological model whereas no improvement in the overall prediction of IHD was noted by adding the remaining three risk factors, namely total cholesterol, triglyceride levels and central obesity type. The same order of biological risk factors contributing to the overall IHD risk would be expected according to a recent overview by Farmer and Gotto (1997). Similarly, the obtained interrelations between the studied biological risk factors are consistent with a recent medical hypothesis (Farmer and Gotto, 1997).

In order to understand the relevance of psychosocial risk factors for IHD when assessed in a more plausible biological risk context, biological and psychosocial variables were tested simultaneously. In the multivariate model, the possibility of risk factors' interactions was expected, given the unexplained variance in IHD risk after accounting for the effects of all relevant biological and suggested psychosocial IHD risk factors taken individually. In fact, the biopsychosocial model improved considerably after including all the significant interactions.

The first risk factor that entered the final biopsychosocial multivariate interactional model was the *LDL/HDL ratio*, both lipoproteins reflecting the two-way traffic of cholesterol entering and leaving the tissues. Similar results about the outstanding importance of the given ratio have been obtained by other researchers (Simons, 1986; Kannel and Wilson, 1992).

The second risk factor was another interaction. The synergistic effects between the two most important risk factors, namely *hypertension and LDL*. Similar synergistic impact was reported in the Framingham study (Kannel, 1978) and by Perkins (1989). Hypertension probably increases the filtration of lipid from plasma to the intimal cells by virtue of increased arterial pressure and injury of the intima, especially in the presence of elevated plasma lipids.

The notion that *family history of IHD* remains more frequent in IHD patients than others after stratification by all known risk factors (ten Kate et al., 1982; Shea et al., 1984; Jorde and Williams, 1988) was to a certain extent confirmed in the present study with the family history of IHD entering the multivariate logistic regression model as the third salient variable.

After the individual risk factor of family history, another synergistic interaction entered the model, notably the biopsychosocial one between *N and smoking*. The given interaction is synergistic in the sense that their universal effect does not add but multiply the individual effects. The major consequences would be that we should concentrate efforts for prevention on those groups combining both risk factors. As an example, it seems more dangerous for high N people to smoke than for their low N counterparts. Similarly, Friedman et al. (1983) and Eysenck et al. (1991) reported that the risk of smokers having IHD, as compared to non-smokers, was related to actual coronary-proneness and stress.

Surprisingly, almost all possible mechanisms by which cigarette smoking may accelerate the process of atherosclerosis, such as raised blood pressure during smoking (Trap-Jensen, 1988) or after smoking cessation (Gerace et al., 1991), the detrimental effect on the lipid profile (Tiwari et al., 1989; Kreitler et al., 1991; McCall et al., 1994) and markedly increased uptake of fibrinogen by the arterial wall (Kannel et al., 1987; Allen et al., 1989), could be explained by the variables that entered the model independently of smoking and, interestingly enough, the apparent prediction of IHD by smoking did not vanish completely. Obviously, the mechanism that can explain the synergistic interaction between smoking and N should be also important. Most importantly, Winniford et al. (1987) reported that the blockade of alpha 1 receptors in patients with IHD attenuates the coronary vasoconstrictor response to cigarette smoking. Hence, the possible effects of smoking may be mediated by the stimulation of alpha 1 receptors, which is presumably the case with subjects who score high on emotionality. In fact, Yeung et al. (1991) reported that mental stress caused dilation of the arteries with normal endothelium but constriction of vessels with evidence of endothelial dysfunction. A similar pattern of response has been observed with other stimuli that are also accompanied by activation of the sympathetic nervous system (Ganz and Braunwald, 1997).

Apart from the other four individual risk factors that entered the model (*fibrinogen*, *glucose disturbances*, *Lp(a)* and *sensitisation*), another interaction was capable of improving the overall prediction of IHD, namely the synergistic interaction between *fibrinogen and LDL*. This proved the real interrelation between haemostatic factors and dyslipidaemia in the process of atherosclerosis. Fibrin is together with cholesterol deposited within an atherosclerotic plaque (Farmer and Gotto, 1997). While LDL is a carrier of cholesterol to the cells, fibrin is formed from fibrinogen.

4.2. Biopsychosocial correlates of IHD risk factors

In this research a large number of biological and psychosocial risk factors have been collected. It was a natural objective to try to reduce the number of variables whilst preserving as much of the original information as possible. Indeed, the correlation matrix of biological and psychosocial risk factors has shown that certain biological risk factors, especially hypertension and fibrinogen level, tend to correlate significantly with psychosocial variables, mainly with neuroticism and emotional coping. The principal component analysis provides one way of tackling the above objective.

Primarily, a principal component with emotionally saturated risk factors such as N, coronary-proneness, low personal autonomy and emotional coping was extracted. The interrelation of similar variables has been reported by other researches. For example, Watson

and Clark (1992) and Feldman (1993) reported negative affectivity as a disposition to experiencing negative affect in non-psychiatric population. All these psychosocial variables can be explained by emotional instability with maladaptive coping and, as a consequence, chronic stress with stimulation of sympathetic-adrenomedullary and hypothalamic–pituitary–adrenocortical activity (Schneiderman and McCabe, 1985). It therefore does not come as a surprise that the same principal component is also characterised by high loadings of stress-related biological risk factors such as fibrinogen and hypertension. As far as the former is concerned, Cannon (1929) was the first to suggest that more rapid clotting during emotional arousal was adaptive to survival because it reduced blood loss during injury. Interestingly, platelets have been later on found to possess adrenoceptors (Patterson and Krantz, 1993). Accordingly, systemic platelet activation in the absence of apparent vascular injury can be enhanced by increases in circulatory adrenaline. Moreover, there is evidence that chronic adrenergic stimulation or stress may increase levels of fibrinogen (Hultin, 1991), which in turn binds specifically to activated platelets, resulting in platelet aggregation. On the other hand, mental stress (Goldstein et al., 1988) and stressful events (Herd, 1991) have long been known to invoke increases in blood pressure and both relevant systems, sympathetic-adrenomedullary (Meredith et al., 1990) and hypothalamic–pituitary–adrenocortical activity (Yeung et al., 1993) have been implicated. However, this response rarely endures following termination of the aversive stimuli (Pickering and Gerin, 1990). Moreover, Rosenman (1996) extensively reviewed the possible role of emotions and behaviours in essential hypertension and failed to find valid and consistent evidence. Nevertheless, due to the loadings of fibrinogen and hypertension, the first principal component could be named *emotionality with stress-related biological factors*.

The second extracted factor yields characteristics of *pure hyperlipidaemia*. Apparently, no association exists between this lipid factor and psychosocial risk factors for IHD, although considerable correlations were obtained between triglyceride level on one side and emotionally saturated variables on the other. Two hypotheses could explain these correlations. According to the stress-induced lipolysis model, the increased circulating plasma levels of cholesterol or triglyceride during stress is a result of enhanced lipolysis (McCann et al., 1995). On the other hand, the haemoconcentration hypothesis states that the rapid increases in a given lipid concentration seen after brief laboratory challenge are due to stress-induced haemoconcentration (Muldoon et al., 1992; Patterson et al., 1993).

Apart from the biopsychosocial associations discussed so far, fibrinogen and smoking also tend to correlate with psychoticism, which explain loadings of certain psychosocial factors in the third principal component, namely *dyslipidaemic and haemostatic complex with behavioural components*. This principal component was so named as it is characterised by high loadings of smoking and both risk factors that may explain, at least in part, pathogenicity of smoking behaviour. In an animal model, inhalation of nicotine has been shown to markedly increase uptake of fibrinogen by the arterial wall (Allen et al., 1989), which is affecting one of the critical determinants of the atherosclerotic process, notably the maintaining of the integrity of the endothelium. Among the other determinants (Bierman, 1991), prevention of cholesterol accumulation is affected by decreased HDL that participate in the reverse transport of free cholesterol (Oram et al., 1983). Accordingly, heavy smokers have lower levels of HDL (McCall et al., 1994). Another risk factor is included in this pattern, namely Lp(a), which because of its structural similarities with plasminogen (Loscalzo et al., 1990), may inhibit the thrombolytic

activity of naturally occurring tissue plasminogen. Plasminogen normally binds to fibrin during fibrinolysis. A structurally similar Lp(a) may compete with plasminogen for access to fibrin (Braunwald, 1991). It may, therefore, provide a link between lipids, the clotting system and atherosclerosis. Behavioural components were added to the name of this mainly biological risk factors' pattern as there are two psychosocial links that may help us to understand the whole pattern. First, emotional instability produces more stress, which in turn leads to increased fibrinogen levels (Hultin, 1991) and, possibly, more pronounced dyslipidaemia (Muldoon et al., 1992; Patterson et al., 1993; McCann et al., 1995). Secondly, smoking behaviour tends to correlate with many psychosocial factors. Among these, the obtained correlation between smoking and P confirmed previous findings (Eysenck, 1980; Spielberger and Jacobs, 1982; Wakefield, 1989).

The fourth factor is another pattern of psychosocial risk factors with high loadings of psychoticism and sensitisation and low loadings of smoking and family history of IHD: *tough mindedness and sensitisation*. This pattern could be explained by borrowing Gossop and Eysenck (1980) insight on a relatively different topic. Sensitisers are those persons who tend to exaggerate their emotional reactions. On the other hand, people who score high on P tend to have manipulative, attention seeking personalities. It is, therefore, possible that exaggerated emotional reactions of these patients get rewarded by their receiving more attention when bringing up difficulties experienced in relation to the illness.

The set of IHD risk factors that are included in the fifth principal component (dyslipidaemia, disturbances of glucose metabolism, hypertension and central obesity type) is also known as *the metabolic syndrome X* (Reaven, 1993). It also does not show any associations with psychosocial risk factors. However, abdominal obesity itself tends to correlate with emotional variables, especially with emotional coping style. This particular link could be explained by some previous research that found emotional coping style to lead to emotional responses that are damaging to health (Friedman and Booth-Kewley, 1987), such as changes in eating patterns (Canter et al., 1982) and cigarette smoking (Chereck, 1982).

The last extracted factor is the association between family history of IHD and presence of two major diseases as risk factors for IHD, namely hypertension and diabetes (disturbances of glucose metabolism), which as a result does not come as a surprise. They have in common the mechanism by which risk factors enhance the likelihood of atherosclerosis. They may cause the injury of the intimal areas of the artery by the means of genetic disposition (family history of IHD), increased susceptibility from shear forces, torsion and lateral wall pressure changes (hypertension), produced abnormalities of major coronary arteries (diabetes mellitus) (Sokolow et al., 1990) and by cell proliferation stimulation (insulin as a growth hormone) (Dzau, 1990). The factor was named *positive family and medical history with sensitisation* as it tends to correlate with psychosocial factors, especially with sensitisation. Undoubtedly, family history is one of the more important factors to be weighed in the assessment of IHD risk.

Finally, all the above stated associations between biological and psychosocial risk factors could be summarised by suggesting potential intervening mechanisms that mediate psychosocial influences on IHD. These could be explained as stress-related alteration in health-related behaviour (smoking and obesity) and behaviourally evoked perturbations of the body's principal axes of neuroendocrine responses, such as increased myocardial oxygen demand (hypertension), enhanced blood clotting (fibrinogen) and lipolysis or haemoconcentration

(triglyceride). It seems possible that psychosocial variables and neuroticism (N) in particular, may be important because of their relevance for sensitivity to biological risk factors.

As far as the psychological measures are concerned, it was only the N and L scores from the EPQ which proved important. Interestingly, these were the only two measures which had acceptable alpha coefficients (i.e. >0.80). The other measures, including the EPQ P score, had poor internal consistency which undoubtedly undermines their validity due to excessive error variance. The reasons for the low internal consistency of some of the psychological measures are unknown, but these may relate to the nature of the samples studied (i.e. patients).

4.3. Biopsychosocial model of IHD risk factors

So far, the discussion has covered the two main parts of our research. In the first, the development of an interactional multivariate biopsychosocial model for the prediction of IHD has been suggested. In the second, all significant biological and psychological variables have formed the biopsychosocial correlates of risk factors for IHD. Altogether, the relationships between risk factors and IHD and correlations between some biological and psychosocial risk factors hereby presented fit well into the present knowledge about the risk of developing IHD and suggests a biopsychosocial model of IHD risk factors. Standard biological risk factors and their interactions do coincide with the generally accepted response-to-injury hypothesis about atherosclerosis, which as a result increases validity and plausibility of the other, more original findings.

Fig. 1 showed altogether 9 supported independent risk factors in a multivariate biopsychosocial context. Two of them came from the psychosocial context on the left, notably sensitisation and synergistic interaction between N and smoking. Other emotionally saturated risk factors, like coronary-prone behaviour, low personal autonomy and emotional coping are probably representing more specific and, therefore, hierarchically lower psychosocial characteristics than the personality trait of emotionality (N). Both psychosocial risk factors represent two different forms of the same personality dimension, neuroticism (N). The first one, N as such can be defined as general emotional lability, whereas the second one, namely sensitisation, means emotional exaggerations as it represents the same emotional lability only when defensiveness is relatively low. Correlations between N and stress-related biological risk factors do speak in favour of a possible causal relation between the emotional lability trait, emotional distress, evoked perturbations of neuroendocrine responses and, finally, deterioration of a biological risk factors profile. Moreover, synergistic interaction between N and smoking suggests its involvement in sudden deterioration in the coronary flow due to the vasoconstriction. On the other hand, sensitisation as an exaggerated part of neuroticism goes along with Costa (1987) suggestions. He claimed that neuroticism was related to somatic complaints but was not causally related to objective evidence of disease. Initially a surprising correlation between sensitisation and family history of IHD does support this conclusion as it can be explained with the tendencies of sensitisers to amplify their disturbances, including perhaps the overvalued history of similar problems in the family.

The next two independent effects come from fibrinogen and family history of IHD, both of them being in strong relationship with the previous psychosocially saturated risk factors, fibrinogen with N and family history with sensitisation. The most atherogenic factor, LDL, is

involved in three interactions, each of these being with one of the three most relevant risk factors according to the response-to-injury hypothesis about atherosclerosis (Ross, 1997): HDL, hypertension and fibrinogen. Two additional independent predictors were confirmed, namely Lp(a) and glucose disturbances (Fig. 1).

5. Conclusion

The majority of studies of ischaemic heart disease (IHD) conducted to date have failed to consider simultaneously both the biological and the psychosocial aspects of the issue. Here, the majority of recognised biological risk factors were investigated, as well as several relevant psychosocial parameters. Generally, the choice of risk factors is predetermined by the researcher's speciality. The studies involving an accurate laboratory and angiographic evaluation of IHD patients tend to restrict their psychometrics to the use of only one psychological tool, most probably the type A behaviour scales or structured interview. Conversely, investigations of IHD conducted by health psychologists use a much wider range of psychological tests, yet tend to consider only a few biological risk factors, such as total cholesterol levels, high blood pressure and cigarette smoking.

By conducting the present study with biological and psychosocial risk factors simultaneously, it was possible to investigate the extent to which psychosocial factors independently contribute in IHD. It was also possible to explore in which way they tend to correlate or even interact with more biologically plausible ones such as dyslipidaemia, hypertension, fibrinogen, age and family history of the same disease. Demonstrated through this research were independent associations between synergistic interaction smoking-neuroticism and sensitisation of emotion on one side and the presence of IHD on the other, after taking into account the main atherogenic factors such as dyslipidaemia, hypertension and fibrinogen levels.

Moreover, the relationship between risk factors and IHD and correlations between some biological and psychosocial risk factors hereby presented are highly suggestive of the existence of biopsychosocial patterns of IHD risk factors. Surprisingly, no studies to date have reported factor analytic results among biological and psychosocial IHD risk factors. However, given the nature of IHD risk, it would be more realistic to expect that a specific profile, i.e. a specific combination of biological and psychosocial characteristics, rather than individual features, operates as a risk factor correlated with IHD. On the other hand, only changing of a whole combination or behaviour pattern, rather than individual risk factor correction, results in successful primary or secondary IHD prevention.

The generalisability of these findings may be somewhat limited, as the study sample only included male patients. Moreover, the behaviour and morbidity of individuals residing outside the Republic of Slovenia may be different. However, the study findings tightly replicate the study findings from other parts of the world. One may also argue that these findings could only be a suggestion obtained by a retrospective approach, as it is difficult to disentangle what factors preceded and what factors were consequences of the IHD. However, the majority of studied risk factors are characterised by at least a certain degree of stability throughout the adult life. As an example, people are likely to display their usual way of coping with stress (Temoshok, 1990) and reflect enduring personality traits (Cassileth et al., 1984) when

confronted by life-threatening diseases such as IHD. Similarly and accordingly, already diagnosed patients do not necessarily modify their life style towards smoking cessation, diet, physical exercise and avoiding unnecessary stress. Moreover, some of them may not even keep taking prescribed medications for lipid profile correction or blood pressure adjustment once they are discharged from the in-patient treatment. The best explanation would therefore be that results of the present study are based on the current status of IHD with its underlying atherosclerosis on one side and presence or most probable lifelong values of main IHD risk factors on the other side.

Further research of the relationships between biological and psychosocial risk factors and their relationships with IHD is warranted to improve our understanding of the biological mechanisms of the psychosocial IHD pathogenicity. Just as the Framingham Study was necessary to prove that hypertension, hypercholesterolaemia and smoking are risk factors for IHD and a similarly designed Western Collaborative Group Study was undertaken to test the hypothesis about type A behaviour, so a similar prospective study should be designed including simultaneously broad coverage of biological and psychosocial risk factors. A good start in terms of a pilot study could be the periodic assessment of IHD morbidity in the present control sample and the same type of assessment of IHD mortality in the present IHD group.

References

Ahnve, S., de Faire, U., Orth-Gomes, K., & Theorell, T. (1979). Type A behaviour in patients with non-coronary chest pain admitted to a coronary care unit. *J. Psychosom. Res., 23,* 219–223.

Allen, D. R., Browse, N. L., & Rutt, D. L. (1989). Effects of cigarette smoke, carbon monoxide and nicotine on the uptake of fibrinogen by the canine arterial wall. *Atherosclerosis, 77,* 83–88.

Almada, S. J., Zonderman, A. B., & Shekelle, R. B. et al (1991). Neuroticism and cynicism and risk of death in middle-aged men: The western electric study. *Psychosom. Med., 53,* 165–175.

Barefoot, J. C., Dahlstrom, W. G., & Williams, R. B., Jr. (1983). Hostility, CHD incidence and total mortality: A 25-year follow-up study of 255 physicians. *Psychosom. Med., 45,* 59–63.

Barefoot, J. C., Beckham, J. T., Peterson, B. L., Haney, T. L., & Williams, R. B., Jr. (1992). Measures of neuroticism and disease status in coronary angiography patients. *J. Consult Clin. Psychol., 60,* 127–132.

Bass, C., & Wade, C. (1982). Type A behaviour: Not specifically pathogenic? *Lancet, 2,* 1147–1150.

Bierman, E. L. (1991). Atherosclerosis and other forms of arteriosclerosis. In J. D. Wilson, E. Braunwald, K. J. Isselbacher *et al.* (Eds.), *Harrison's principles of internal medicine* (12th ed., pp. 992–995). New York: McGraw-Hill.

Blumenthal, J. A., Thompson, L. W., Williams, R. S., & Kong, Y. (1979). Anxiety-proneness and coronary heart disease. *J. Psychosom. Res., 23,* 17–21.

Bolger, N., & Schilling, E. (1992). Personality and the problems of everyday life: The role of neuroticism in exposure and reactivity to daily stress. *J. Pers., 59,* 355–380.

Braunwald, E. (1991). Cellular and molecular biology of cardiovascular disease. In J. D. Wilson, E. Braunwald, K. J. Isselbacher *et al.* (Eds.), *Harrison's principles of internal medicine* (12th ed., pp. 838–841). New York: McGraw-Hill.

Cannon, W. B. (1929). *Bodily changes in pain, hunger, fear and rage*. Boston: Branford.

Canter, M. B., Smith, S. E., & Bryan, B. R. (1982). Feeding the face: Adjunctive eating, drinking and grooming in human subjects. *Appetite, 3,* 1–12.

Cassileth, B. R., Lusk, E. J., & Strouse, T. B. et al (1984). Psychosocial status in chronic illness: A comparative analysis of six diagnostic groups. *N. Engl. J. Med., 311,* 506–511.

Chereck, D. R. (1982). Schedule-induced cigarette self-administration. *Pharmacol. Behav., 17,* 523–527.

Chesney, M., Black, G. W., Chadwick, J. H., & Rosenman, R. H. (1981). Psychological correlates of the type A behaviour patterns. *J. Behav. Med., 4,* 217–229.

Costa, P. T. (1987). Influence on the normal personality dimension of neuroticism on chest pain symptoms and coronary artery disease. *Am. J. Cardiol., 60,* 20J–26J.

Cramer, D. (1991). Type A behaviour pattern, extraversion, neuroticism and psychological distress. *Br. J. Med. Psychol., 64,* 73–83.

Dembroski, T. M. & Czajkowski, S. M. (1989). Historical and current developments in coronary-prone behavior. In A. W. Siegman & T. M. Dembroski (Eds.), *In search of coronary-prone behavior: Beyond Type A* (pp. 21–39). Hillsdale, New Jersey: Lawrence Erlbaum Associates, Publishers.

Dembroski, T. M., MacDougall, J. M., Williams, R. B., Haney, T. L., & Blumenthal, J. A. (1985). Components of type A, hostility and anger-in: Relationship to angiographic findings. *Psychosom. Med., 47,* 219–233.

Dembroski, T. M., MacDougall, J. M., Costa, P. T., Jr., & Grandits, G. A. (1989). Components of hostility as predictors of sudden death and myocardial infarction in the Multiple Risk Factor Intervention Trial. *Psychosom. Med., 51,* 514–522.

Dzau, V. J. (1990). Atherosclerosis and hypertension: Mechanisms and interrelationships. *J. Cardiovasc. Pharmacol., 15 (Suppl. 5),* S59.

Eysenck, H. J. (1980). *The causes and effects of smoking*. London: Temple-Smith.

Eysenck, H. J. (1994). Trait theories of personality. 7.3. In A. M. Colman (Ed.), *Companion encyclopaedia of psychology* (Vol. 1., pp. 622–640). London: Routledge.

Eysenck, H. J. & Eysenck, S. B. G. (1975). *The Eysenck Personality Questionnaire*. London: Hodder & Stoughton. San Diego: Educational and Industrial Testing Service.

Eysenck, H. J. & Eysenck, M. W. (1985). *Personality and individual differences*. New York: Plenum Press.

Eysenck, H. J., Grossarth-Maticek, R., & Everitt, B. (1991). Personality, stress, smoking and genetic predisposition as synergistic risk factors for cancer and coronary heart disease. *Integr. Physiol. Behav. Sci., 26,* 309–322.

Farmer, J. A. & Gotto, A. M. (1992). Risk factors for coronary artery disease. In E. Braunwald (Ed.), *Heart disease. A textbook of cardiovascular medicine* (pp. 1125–1160). Philadelphia: WB Saunders.

Farmer, J. A. & Gotto, A. M., Jr. (1997). Dyslipidemia and other risk factors for coronary artery disease. In E. Braunwald (Ed.), *Heart disease. A textbook of cardiovascular medicine* (5th ed., pp. 1126–1160). Philadelphia: WB Saunders.

Feldman, L. A. (1993). Distinguishing depression and anxiety in self-report: Evidence from confirmatory factor analysis on nonclinical and clinical samples. *J. Consult Clin. Psychol., 61,* 631–638.

Fielding, R. (1991). Depression and acute myocardial infarction: A review and reinterpretation. *Soc. Sci. Med., 32,* 1017–1027.

Fontbonne, A., Thibult, N., Eschwege, E., & Ducimetiere, P. (1992). Body fat distribution and coronary heart disease mortality in subjects with impaired glucose tolerance or diabetes mellitus: The Paris Prospective Study, 15-year follow-up. *Diabetologia, 35,* 464–468.

Freeman, L. J., & Nixon, P. G. F. (1987). The effect of the type A behaviour pattern on myocardial ischaemia during daily life. *Int. J. Cardiol., 17,* 145–154.

Friedman, G. D., Fireman, B. H., & Petitti, D. B. et al (1983). Psychological questionnaire score, cigarette smoking and myocardial infarction: A continuing enigma. *Prev. Med., 12,* 533–540.

Friedman, H. S., & Booth-Kewley, S. (1987). The "disease-prone personality": A meta-analytic view of the construct. *Am. Psychol., 42,* 539–555.

Fujii, J., & Imataka, K. (1993). Elevation of blood pressure and hemoconcentration induced by mental stress. *Homeostasis, 34,* 280–288.

Ganz, P. & Braunwald, E. (1997). Coronary blood flow and myocardial ischemia. In E. Braunwald (Ed.), *Heart disease. A textbook of cardiovascular medicine* (5th ed., pp. 1161–1183). Philadelphia: WB Saunders.

Gerace, T. A., Hollis, J., Ockene, J. K., & Svendsen, K. (1991). Smoking cessation and change in diastolic blood pressure, body weight and plasma lipids. MRFIT Research Group. *Prev. Med., 20,* 602–620.

Goldstein, H. S., Edelberg, R., & Meier, C. F. et al (1988). Relationship of resting blood pressure and heart rate to experienced anger and expressed anger. *Psychosom. Med., 50,* 321–329.

Gossop, M. R., & Eysenck, S. B. G. (1980). A further investigation into the personality of drug addicts in treatment. *Br. J. Addict., 75,* 305–311.

Gramer, M., & Huber, H. P. (1994). Individual variability in task-specific cardiovascular response patterns during psychological challenge. *Ger. J. Psychol., 18,* 1–17.

Grech, E. D., Ramsdale, D. R., Bray, C. L., & Faragher, E. B. (1992). Family history as an independent risk factor of coronary artery disease. *Eur. Heart J., 13,* 1311–1315.

Grossarth-Maticek, R., & Eysenck, H. J. (1990). Personality, stress and disease: Description and validation of a new inventory. *Psychol. Rep., 66,* 355–373.

Gudjonsson, G. (1981). Self-reported emotional disturbance and its relation to electrodermal reactivity, defensiveness and trait anxiety. *Person. Individ. Diff., 2,* 47–55.

Hearn, M. D., Murray, D. M., & Luepker, R. V. (1989). Hostility, coronary heart disease and total mortality: A 33-year follow-up of university students. *J. Behav. Med., 12,* 105–121.

Herd, J. A. (1991). Cardiovascular response to stress. *Psychol. Rev., 71,* 305–329.

Hultin, M. B. (1991). Fibrinogen and factor VII as risk factors in vascular disease. *Prog. Hemost. Thromb., 10,* 215–241.

Innes, J. M. (1980). Impulsivity and the coronary-prone behaviour pattern. *Psychol. Rep., 47,* 976–978.

Jenkins, C. D., & Zyzanski, S. J. (1980). Behavioral risk and coronary heart disease. *Psychother. Psychosom., 34,* 149–177.

Jorde, L. B., & Williams, R. R. (1988). Relation between family history of coronary artery disease and coronary risk variables. *Am. J. Cardiol., 62,* 708–713.

Kannel, W. B. (1978). Hypertension, blood lipids and cigarette smoking as co-risk factors for coronary heart disease. *Ann. N. Y. Acad. Sci., 304,* 128–139.

Kannel, W. B., & Wilson, P. W. (1992). Efficacy of lipid profiles in prediction of coronary disease. *Am. Heart J., 124,* 768–774.

Kannel, W. B., D'Agostino, R. B., & Belanger, A. J. (1987). Fibrinogen, cigarette smoking and the risk of cardiovascular disease: Insights from the Framingham study. *Am. Heart J., 113,* 1006–1010.

Kneier, A. W., & Temoshok, L. (1984). Repressive coping reactions in patients with malignant melanoma as compared to cardiovascular disease patients. *J. Psychosom. Res., 28,* 145–155.

Kreitler, S., Weissler, K., Kreitler, H., & Brunner, D. (1991). The relation of smoking to psychological and physiological risk factors for coronary heart disease. *Person. Individ. Diff., 12,* 487–495.

Lakatta, E. G., Gerstenblith, G. & Weisfeldt, M. L. (1997). The aging heart: Structure, function and disease. In E. Braunwald (Ed.), *Heart disease. A textbook of cardiovascular medicine* (5th ed., pp. 1687–1703). Philadelphia: WB Saunders.

Lakier, J. B. (1992). Smoking and cardiovascular disease. *Am. J. Med., 93 (Suppl. 1A),* 8S–12S.

Lojk, L. (1979). *EPQ: Eysenckov osebnostni vprašalnik: Priročnik [EPQ: The Eysenck Personality Questionnaire: Handbook].* Ljubljana: Zavod SR Slovenije za produktivnost dela, Center za psihodiagnostična sredstva.

Loscalzo, J., Weinfeld, M., Fless, G. M., & Scanu, A. M. (1990). Lipoprotein(a), fibrin binding and plasminogen activation. *Arteriosclerosis, 10,* 240–245.

Marmot, M., & Winkelstein, W., Jr. (1975). Epidemiologic observations on intervention trials for prevention of coronary heart disease. *Am. J. Epidemiol., 101,* 177–181.

Marušič, A. (1997). *Some relationships between standard biological and suggested psychosocial risk factors and ischaemic heart disease.* Ph.D. thesis, University of London, London.

Matthews, K. A., & Haynes, S. G. (1986). Type A behavior pattern and coronary disease risk: Update and critical evaluation. *Am. J. Epidemiol., 123,* 923–960.

McCall, M. R., van der Berg, J. J., & Kuypers, F. A. et al (1994). Modification of LCAT activity and HDL structure: New links between cigarette smoke and coronary heart disease risk. *Arterioscler. Thromb., 14,* 248–253.

McCann, B. S., Magee, M. S., & Broyles, F. C. et al (1995). Acute psychological stress and epinephrine infusion in normolipidemic and hyperlipidemic men: Effects on plasma lipid and apoprotein concentrations. *Psychosom. Med., 57,* 165–176.

Meredith, I. T., Esler, M. D., Eisenhofer, G. & Jennings, G. L. (1990). The effects of simple daily life stresses on cardiac sympathetic activity, myocardial oxygen consumption and hemodynamics. *Circulation*, *82*, III–516.

Muldoon, M. F., Bachen, E. A., & Manuck, S. B. et al (1992). Acute cholesterol responses to mental stress and change in posture. *Arch. Int. Med., 152,* 775–780.

Naidoo, P., & Patel, C. J. (1993). Stress, depression and left-side psychogenic chest pain. *Acta Psychiatr. Scand., 88,* 12–15.

Oram, J. F., Brinton, E. A., & Bierman, E. L. (1983). Regulation of high-density lipoprotein receptor activity in cultured human skin fibroblasts and human arterial smooth muscle cells. *J. Clin. Invest., 72,* 1611–1621.

Ornish, D., Brown, S. E., & Scherwitz, L. W. et al (1990). Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial. *Lancet, 336,* 129–133.

Patterson, S. M., & Krantz, D. S. (1993). Effects of psychological and physical stress on platelet function. *Homeostasis, 34,* 271–279.

Patterson, S. M., Gottdiener, J. S., & Hecht, G. M. et al (1993). Effects of acute mental stress on serum lipids: Mediating effects of plasma volume. *Psychosom. Med., 55,* 525–532.

Perkins, K. A. (1989). Interactions among coronary heart disease risk factors. *Ann. Behav. Med., 11,* 3.

Pickering, T., & Gerin, W. (1990). Cardiovascular reactivity in the laboratory and the role of behavioral factors in hypertension: A critical review. *Ann. Behav. Med., 12,* 3–16.

Reaven, G. M. (1993). Role of insulin resistance in human disease (syndrome X): An expanded definition. *Annu. Rev. Med., 44,* 121–131.

Roger, D. (1995). Emotion control, coping strategies and adaptive behavior. In C. D. Spielberger, I. G. Sarason, J. M. T. Brebner *et al.* (Eds.), *Stress and emotion: Anxiety, anger and curiosity* (Vol. 15, pp. 255–264). Washington, D.C.: Taylor and Francis.

Roger, D., Jarvis, G., & Najarian, B. (1993). Detachment and coping: The construction and validation of a new scale for measuring coping strategies. *Person. Individ. Diff., 15,* 619–626.

Rosenman, R. H. (1996). Personality, behavior patterns and heart disease. In C. L. Cooper (Ed.), *Handbook of stress, medicine and health* (pp. 217–231). Boca Raton, New York, London, Tokyo: CRC Press.

Ross, R. (1997). The pathogenesis of atherosclerosis. In E. Braunwald (Ed.), *Heart disease. A textbook of cardiovascular medicine* (5th ed., pp. 1105–1125). Philadelphia: WB Saunders.

Schmitz, P. G. (1992). Personality, stress-reaction and disease. *Person. Individ. Diff., 13,* 683–691.

Schneiderman, N. & McCabe, P. (1985). Biobehavioral responses to stressors. In T. M. Field, P. M. McCabe, & N. Schneiderman (Eds.), *Stress and coping* (pp. 13–61). Hillsdale: Lawrence Erlbaum Associates.

Shea, S., Ottman, R., Gabrieli, C., Stein, Z., & Nichols, A. (1984). Family history as an independent risk factor for coronary artery disease. *J. Am. Coll. Cardiol., 4,* 793–801.

Shekelle, R. B., Gale, M., & Ostfeld, A. et al (1983). Hostility, risk of coronary heart disease and mortality. *Psychosom. Med., 45,* 109–114.

Shekelle, R. B., Vernon, S. W., & Ostfeld, A. M. (1991). Personality and coronary heart disease. *Psychosom. Med., 53,* 176–184.

Simons, L. A. (1986). Interrelations of lipids and lipoproteins with coronary artery disease mortality in 19 countries. *Am. J. Cardiol., 57,* 5G–10G.

Smith, T. W. (1992). Hostility and health: Current status of a psychosomatic hypothesis. *Health Psychol., 11,* 139–150.

Sokolow, M., McIlroy, M. B. & Cheitlin, M. D. (1990). *Clinical cardiology* (5th ed.). Connecticut: Appleton & Lange.

Spielberger, C. D., & Jacobs, G. A. (1982). Personality and smoking behavior. *J. Person. Assess., 46,* 396–403.

Stolar, M. W. (1988). Atherosclerosis in diabetes. The role of hyperinsulinemia. *Metabolism, 37 (Suppl. 1)*(2), 1–9.

Stone, S. V. & Costa, P. T., Jr. (1990). Disease-prone personality or distress-prone personality? The role of neuroticism in coronary heart disease. In H. S. Friedman (Ed.), *Personality and disease*, Wiley series on health psychology/behavioral medicine (pp. 38–64). New York: John Wiley & Sons.

Syme, S. L. (1984). Sociocultural factors and disease etiology. In W. D. Gentry (Ed.), *Handbook of behavioral medicine*. New York: Guilford Press.

Temoshok, L. (1990). On attempting to articulate the biopsychosocial model: Psychological–psychophysiological homeostasis. In H. S. Friedman (Ed.), *Personality and disease* (pp. 203–225). New York: Wiley.

ten Kate, L. P., Boman, H., Daiger, S. P., & Motulsky, A. G. (1982). Familial aggregation of coronary heart disease and its relation to known genetic risk factors. *Am. J. Cardiol., 50,* 945–953.

Tiwari, A. K., Gode, J. D., & Dubey, G. P. (1989). Effect of cigarette smoking on serum total cholesterol and HDL in normal subjects and coronary heart disease patients. *Indian Heart J., 41,* 92–94.

Trap-Jensen, J. (1988). Effects of smoking on the heart and peripheral circulation. *Am. Heart J., 115,* 263–267.

Wakefield, J. A., Jr. (1989). Personality, health and cigarette smoking. *Person. Individ. Diff., 10,* 541–546.

Watson, D., & Clark, L. A. (1992). Affects separable and inseparable: On the hierarchical arrangement of the negative affects. *J. Pers. Soc. Psychol., 62,* 489–505.

Weinberger, D. A., Schwartz, G. E., & Davidson, R. J. (1979). Low-anxious, high-anxious and repressive coping styles: Psychometric patterns and behavioural and physiological responses to stress. *J. Abnorm. Psychol., 88,* 369–380.

Weiss, M., & Richter-Heinrich, E. (1985). Type A behaviour in a population of Berlin, GDR: Its relation to personality and sociological variables and association to coronary heart disease. *Acta Nerv. Super., 27,* 7–9.

Williams, G. H., Lilly, L. S. & Seely, E. W. (1997). The heart in endocrine and nutritional disorders. In E. Braunwald (Ed.), *Heart disease. A textbook of cardiovascular medicine* (5th ed., pp. 1887–1913). Philadelphia: WB Saunders.

Williams, R. B., Barefoot, J. C. & Shekelle, R. B. (1984). The health consequences of hostility. In M. A. Chesney, S. E. Goldstone & R. H. Rosenman (Eds.), *Anger, hostility and behavioural medicine*. Washington, D.C.: Hemisphere, McGraw-Hill.

Winniford, M. D., Jansen, D. E., & Reynolds, G. A. et al (1987). Cigarette smoking-induced coronary vasoconstriction in atherosclerotic coronary artery disease and its prevention by calcium antagonists and nitroglycerin. *Am. J. Cardiol., 59,* 203–207.

Wright, L., Murcer, S., Adams, K., Welch, S., & Paris, D. (1994). The factor analytic structure of seven physical CHD risk factors: A replication study. *J. Clin. Psychol., 50,* 216–219.

Yeung, A. C., Vekshtein, V., & Krantz, D. S. et al (1991). The effect of atherosclerosis on the vasomotor response of coronary arteries to mental stress. *N. Engl. J. Med., 325,* 1551–1556.

Yeung, A. C., Ganz, P., & Selwyn, A. P. (1993). Interactions between mental stress and coronary endothelial dysfunction. *Homeostasis, 34,* 244–251.