Published in final edited form as:

Aging Ment Health. 2010 September ; 14(7): 801–806. doi:10.1080/13607861003713299.

Psychosocial factors and metabolic parameters: is there any association in elderly people? The Massa Lombarda Project:

Aging & Mental Health

Marilisa Bove^a, Lucio Carnevali^a, Arrigo FG Cicero^a, Elisa Grandi^a, Morena Gaddoni^b, Giorgio Noera^b, and Antonio V Gaddi^a

^a"GC Descovich" Atherosclerosis & Metabolic Diseases Research Unit - Internal Medicine, Aging & Kidney diseases Dept. Sant'Orsola-Malpighi Hospital - University of Bologna (Italy)

^bDepartment of Cardiac Surgery, Villa Maria Cecilia, Cotignola (Ra), Italy

Abstract

Objective—Several Studies claim that psychophysical stress and depression contribute significantly to cardiovascular disease (CVD) development. The aim of our research is to discover and analyse a possible relationship between two psychosocial disorders (Depression and Perceived Mental Stress) and traditional cardiovascular risk markers.

Methods—We selected 106 subjects (M:58, F:48), mean age $79,5 \pm 3,8$ years old, from The Massa Lombarda Project, an epidemiological study including 7000 north Italian adult subjects. We carried out anamnesis, clinical and blood tests. Then we administered the Perceived Stress Questionnaire (PSQ range-score 0-1) and the Self Rating Depression Scale (SRDS range score 50-70 Z), as validated instruments for depression and stress evaluation, which focus on the individual's subjective perception and emotional response. Statistical descriptive and inferential analysis of data collected were performed.

Results—The Multiple linear regression analysis showed a negative correlation between PSQ Index score and Uric Acid, LDL-C, BMI, Systolic and Diastolic Blood Pressure values, a positive and statistically significant correlation between PSQ Index score and Triglycerides ($P < 0.05$). We found an inverse relationship between Zung SRDS score and LDL-C, Uric Acid, Glucose, Waist Circumference values, this correlation was significant only for Uric Acid ($P < 0.01$); besides a positive and significant correlation between Zung SRDS and Triglycerides ($P < 0.05$) was observed.

Conclusion—We suppose that psycho-emotional stress and depression disorder, often diagnosed in elderly people, may influence different metabolic parameters (triglycerides, Uric Acid, BMI) that are involved in the complex process of Metabolic Syndrome.

Keywords

depression; mental stress; metabolic syndrome; uric acid; triglycerides

Introduction

Recent epidemiological studies suggest that psychosocial factors contribute significantly to the pathogenesis of Cardiovascular Disease (CVD) [Rozanski, Blumenthal & Kaplan, 1999;

Corresponding author: Marilisa Bove, MD, "GC Descovich" Atherosclerosis & Metabolic Diseases Research Unit, Internal Medicine, Aging & Kidney diseases Dept., Sant'Orsola-Malpighi Hospital - University of Bologna, Via Massarenti, 9 - 40138 Bologna (Italy), Tel/Fax: ++39 0516363262, marilisa.bove@aosp.bo.it.

Strodl, Kenardy & Aroney, 2003; Rosengren et al., 2004]. Psychosocial factors which promote atherosclerosis and adverse cardiac events can be divided into two general categories: emotional factors and chronic stressors. Emotional factors include affective disorders such as Major Depressive Disorder (MDD) and anxiety as well as hostility and anger. Chronic stressors include low social support, low socioeconomic status, stress and caregiver strain [Rozanski, Blumenthal, Davidson, Saab & Kubzansky, 2005]. Research in this area has evaluated the effects of depression in both initially healthy individuals and in patients with known CVD. Depression plays a role in promoting cardiovascular events in both cohorts with various pathophysiological mechanisms. First of all, depression can mediate its effects on cardiovascular risk through lifestyle. Behavioural changes, like worse adherence to prescribed medication and other life style modifications, can result in a higher risk of cardiovascular events in aging population [Van der Kooy et al., 2007; Keyes, 2004]. However, there is a rich literature on psychosocial factors as independent predictors of CVD and it has been proved that these effects could be mediated by Metabolic Syndrome (MS) as a function of stress-related consequences [Frisman & Kristenson, 2009]. MS is a common disorder, characterised by visceral obesity, impaired glucose metabolism, raised blood pressure, atherogenic dyslipidemia, and the existence of a proinflammatory and prothrombotic state. MS is associated with a significantly increased risk of cardiovascular events and Type 2 Diabetes Mellitus (T2DM) onset. MS is defined in various ways, but the latest diagnostic criteria proposed by the International Diabetes Federation are: central obesity (defined as a waist circumference >94 cm in men and >80 cm in women), plus at least two of the followings: fasting glucose serum level higher than 100 mg/dL, blood pressure values higher than 130/85 mmHg, fasting triglycerides serum level higher than 150 mg/dL, and HDL-c level lower than 40 mg/dL in men and 50 mg/dL in women [Alberti, Zimmet, Shaw & IDF Epidemiology Task Force Consensus Group, 2005].

Hypercortisolemia, which characterises depressive syndrome, in association with blunted Growth and Sex Hormones, promotes central obesity and an increase of peripheral and portal fatty acids; these metabolic changes also contribute to more insulin resistance and T2DM onset [Weber-Hamann, Hentschel & Kniest, 2002]. Moreover, recent findings indicate an increase oxidative activity in women affected from MDD [Kodydková et al., 2009], and patients with MDD seems to have a reduced total antioxidant capacity, compared to a control group [Sarandol et al, 2007]. Overproduction of reactive oxygen species is also associated to MS and it represents a well established cardiovascular risk factor. Serum Uric Acid (SUA), a molecule which plays an important and complex role in oxidative and anti-oxidative processes, is more elevated in MS, and a positive correlation exists between SUA and CVD, especially in high risk patients [Tsouli, Liberopoulos, Mikhailidis, Athyros & Elisaf, 2006]. In fact, certain pathophysiologic and metabolic features seem to co-exist in MS and MDD [McIntyre et al., 2009]. Also chronic stress appears to exert direct pathophysiological effects on CVD, including elevation of arterial blood pressure and neurohumoral arousal [Dimsdale, 2008]. The risk associated with psychosocial factors may actually be greater than statistical evidence suggests for two reasons. First, behavioural and metabolic risk factors tend to aggregate disproportionately among individuals, especially in the elderly, with psychosocial stress. However, this potentially powerful effect is reduced because of the statistical convention to adjust psychosocial risk ratios for behavioural and metabolic risk factors. Second, because measures of psychosocial stress may be imprecise and the relationship between psychosocial stress and CVD outcomes may be underestimated [Rozanski et al., 1999; Rosengren et al., 2004].

Several studies have explored an association between lipoproteins and depression, but findings are contradictory in general population and young people [van Reedt Dortland et al., 2009]. On the other hand, among elderly people, a significant correlation was found between TC, LDL-c and MDD [Brown et al., 1994].

In consideration of the fact that affective disorder are very common among elderly people [Lebowitz et al., 1997] and the incidence of metabolic impairment increases with aging [Reynolds & He, 2005], we undertook a study on a group of elderly people to clarify the findings of literature and to investigate the relation between two very common psychosocial factors and the most important metabolic parameters. We selected 106 elderly healthy subjects from The Massa Lombarda Project (MLP). We explored the relationship between depression and Perceived Mental Stress with a number of blood and clinical features related to lipidic and glycaemic metabolism, in order to find possible correlations which could be referable to the pathophysiologic mechanisms of metabolic impairment observed in subjects with psychosocial disorders. We included the diagnostic criteria of MS (blood pressure, waist circumference, glycaemia, HDL-c, triglycerides), besides a few parameters to evaluate body mass (BMI), renal function (creatinine), complete lipid profile (TC and LDL-c) and parameters correlated to a pro-inflammatory state and oxidative stress (fibrinogen, SUA), which are often involved into atherosclerosis development. .

Materials and methods

We carried out a psychosocial investigation in a cohort of elderly subjects from MLP to discover a probable correlation between some behavior-psychological aspects and different metabolic markers. MLP is a longitudinal observational epidemiological study including 7000 subjects over 20 years old residents in Massa Lombarda, a North-Italian rural town. The elderly people of this population (N.1000 over 75 years) were submitted to a more complex analysis, as part of the study on health status in European aging populations, aimed to reveal the determinants influencing healthy aging and to identify their impact on mortality, cardiovascular and respiratory morbidity, disability and quality of life [Nascetti et al., 2004]. We selected 106 elderly subjects (M:58, F:48), mean age $79,5 \pm 3,8$ years old, who did not suffer from chronic and severe disabling diseases and had a complete self-sufficiency. No subject had a history of depression or anxiety disorder, nor was taking antidepressant medication when the study was performed. We administered to this group the Perceived Stress Questionnaire (PSQ) and the Self Rating Depression Scale (SRDS) to evaluate the degree and distribution of perceived stress and depression. Levenstein et al. have published the PSQ ten years ago, to overcome some difficulties concerning the definition and measurement of stress focusing on the individual's subjective perception and emotional response [Fliege et al., 2005]. This questionnaire is based on a range-score from 0 (lowest level of perceived stress) to 1 (highest level of perceived stress). The Zung SRDS is a short self-administered survey to quantify the depressed status of a patient, based on range-score from 25 to 80 Z, which define four levels of depression for each subject [Zung, 1965]. We considered the mean value for each metabolic parameter (Total Cholesterol, LDL-c, HDL-c, Triglycerides, Glucose, Fibrinogen, SUA levels), blood pressure and anthropometric index (Body Mass Index and Waist Circumference) of six consecutive measurements, collected into the database of MLP in the recent past (five years). All laboratory measurements were carried out using standardized immunoenzymatic methods; only HDL-c serum levels were determined after precipitation of 1,006 g/ml bottom infranatant with dextran sulphate/magnesium chloride [Warnick, Benderson & Albers, 1982], whereas LDL-c was estimated through the Friedewald Formula. Data were statistically processed with SPSS software, version 16.0 for Windows. We performed a complete descriptive analysis of all studied parameters, followed by a multiple regression (adjusted for age and gender) aimed to discover a relationship between two psychosocial factors and several metabolic risk markers.

Results

The biochemical and anthropometric characteristics of the sample concerning metabolic profile and cardiovascular risk are reported in Table 1. Most of the elderly subjects (53.4%) had Total Cholesterol (TC) levels lower than 200 mg/dL, while 29.1% had levels ranging between 200 and 239 mg/dL and 17.5 % had TC levels higher than 240 mg/dL; 25.5% of the subjects reported LDL-c levels lower than 100 mg/dL, 25.5 % reported LDL-c levels between 100 mg/dL and 130 mg/dL, 24.5% had borderline-high concentrations of LDL-c levels between 130 mg/dL and 160 mg/dL, while the remaining 24.5% had high LDL-c values beyond 160 mg/dL. Most of the subjects (76.5 %) had HDL-c values higher than 40 mg/dL and fibrinogen blood levels below 400 mg/dL; while 74.4% of the subjects reported glucose blood levels lower than 100 mg/dL, 16.1% reported glucose blood levels between 100 and 126 mg/dL and just 9.2% of the subjects suffered from diabetes. Most of the subjects (81.6%) had triglycerides serum levels below 150 mg/dL, 9.7% had borderline-high levels (between 150 mg/dL and 199 mg/dL, and 18.7% had high levels higher than 200 mg/dL. Moreover we found that 23% of our sample had a normal BMI (lower than 25 kg/m²), while 45% were overweight and 27% were obese (BMI between 25 and 30 kg/m² and higher than 30 kg/m² respectively). Psychometric evaluations with PSQ and Zung SRDS (Table 2) showed that no critical depression and stress scores were registered. We found a PSQ Index lower than 0.10 in 46.7% of elderly group, a PSQ Index between 0.10 and 0.35 in 37.8 % and values between 0.35 and 0.70 in the remaining subjects. Most of elderly people were not depressed (65%), whereas 18% of the subjects suffered from moderate depression and 17% from mild depression. The multiple linear regression analysis (adjusted for age and gender) showed a negative correlation between PSQ Index score and SUA, LDL-c, BMI, Systolic and Diastolic Blood Pressure values, a positive and statistically significant correlation between PSQ Index score and Triglycerides ($P<0.05$). We found an inverse relationship between Zung SRDS score and LDL-c, SUA, Glucose, Waist Circumference values. This correlation was significant only for SUA ($P<0.01$). Besides a positive and significant correlation between Zung SRDS and Triglycerides ($P<0.05$) was observed (Table 3, Table 4).

Discussion

Psychosocial factors contribute significantly to pathogenesis and expression of CVD, this evidence is composed largely of data relating CVD risk to five specific psychosocial domains: depression, anxiety, personality factors, character traits, social isolation and chronic life stress [Rozanski et al., 1999; Rozanski et al., 2005]. Pathophysiological process, underlying the relationship between these entities and CVD, can be divided into behavioural mechanisms, whereby psychosocial conditions contribute to an adverse health conduct (poor diet, smoking habit, worse adherence to prescribed medication), and direct pathophysiological mechanisms such as neuroendocrine and platelet activation [Black & Garbutt, 2002]. Several authors suggested the effects of psychosocial factors as independent predictors of CVD and proved that these effects could be mediated by MS, as a complex function of stress-related biological mechanisms [Frisman & Kristenson, 2009]. We found in our group of elderly subjects a positive correlation between Triglycerides values and both PSQ index ($P<0.05$) and Zung SRDS ($P<0.05$) which confirms data reported in literature [Dimsdale & Herd, 1982]. Indeed these associations underline a tendency to develop MS or lipid profile alterations in stressed or depressed elderly patients [Weber-Hamann et al., 2002; Keyes, 2004]. Moreover we found a negative relation between SUA levels and both PSQ Index ($P=0.08$) and Zung SRDS ($P=0.005$) (Figure 1) (Figure 2). The SUA level is affected by age and by genetic and environmental factors [Kasl, Cobb & Brooks, 1968; Kuzuya et al., 2008]. There are in literature different controversial opinions concerning the anti-oxidant effect of SUA and its well-known role as an independent risk factor for

cardiovascular diseases and cardiovascular mortality [Lippi, Montagnana, Franchini, Favaloro & Targher, 2008; Niskanen et al., 2004, Halliwell, 1996; Menotti et al., 2005]. The question is further motivated by the apparently dual effect of SUA *per se* as an oxidant/antioxidant agent. It has been hypothesized that antioxidant properties should be protective against aging, oxidative stress, and oxidative injury of cardiac, vascular, and neural cells [Glantzounis et al, 2005; Stocker & Keaney, 2004]. However, as the findings of recent studies have unfolded, a new paradigm shift in the relationship between SUA and health is emerging. Antioxidant compounds may become pro-oxidant compounds in certain situations [Bagnati et al, 1999], particularly when they are present in blood at very high levels. Therefore, according to this opinion, SUA is a protective agent against oxidative stress and all its possible consequences such as a rapid atherosclerosis development. Moreover oxidative stress may also be involved primarily or secondarily in the pathogenesis of depression, since the brain is much more vulnerable to oxidative stress as it uses 20% of the oxygen consumed by the body. The negative correlation between SUA and Zung test provides additional support to the hypothesis that this metabolic parameter is a strategic and important component of the antioxidant defence system. Further well designed clinical studies are needed to clarify a potential therapeutic use of uric acid (or uric acid precursors) in diseases associated with oxidative stress.

Conclusion

Our results confirm data reported in literature concerning a possible relationship between psychosocial markers and cardiovascular risk factors. The positive correlation between Triglycerides values and both PSQ index and Zung SRDS seems to underline the frequent metabolic changes that could even reveal a MS rising in stressed or depressed elderly subjects. The issue concerning the role of SUA is still confounded and made difficult by the powerful interrelations between this metabolic parameter and all CVD risk factors, that were clustered in the MS diagnosis. The negative correlation between SUA and Zung test support the already cited hypothesis that this metabolic element is a non-enzymatic antioxidant molecule with a potential therapeutic role.

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Fig 1.
Negative correlation of Uric Acid Serum levels (mg/dL) and Zung SRDS score (P<0.01)

Fig 2.
Negative correlation of Uric Acid Serum levels (mg/dL) and PSQ Index score ($P=0.08$)

Table 1

Biochemical and anthropometric characteristics of the elderly group.

Laboratory Values (mg/dL)	Minimum	Maximum	Mean	SD [^]
Total cholesterol	116.0	308.0	202.7	41.7
LDL-c [*]	57.0	226.0	131.60	37.7
HDL-c ^{**}	10	93	49.0	12.7
Triglycerides	38.0	482.0	112.6	63.3
Glycemia	52.0	214.0	95.3	24.6
Fibrinogen	155.0	428.0	269.6	64.8
Creatinine	0.40	2.10	1.06	0.27
BMI (Kg/m ²) ^{***}	20.02	44.43	27.8	4.2
Waist Circumference (cm)	63	131	98.2	11.9
Systolic Blood Pressure (mmHg)	110	190	145	14.9
Diastolic Blood Pressure (mmHg)	60	112	80	9.2

[^] Standard Deviation

^{*} Low Density Lipoprotein cholesterol

^{**} High Density Lipoprotein cholesterol

^{***} Body Mass Index

Table 2

Psychometric Test values in the elderly sample

	Maximum	Minimum	Mean	SD [^]
PSQ [*] Index	0.61	0.02	0.24	0.14
Zung SRDS ^{**}	63	29	42.8	8.37

[^] Standard Deviation

^{*} Perceived Stress Questionnaire

^{**} Self Rating Depression Scale

Table 3

Multiple Regression between Metabolic parameters and PSQ Index

Independent Variables	t	P
TC [^]	,619	,542
Triglycerides	2,462	,022
HDL-c ^{^^}	,585	,564
LDL-c ^{^^^}	-,164	,871
Uric Acid	-1,820	,082
Glycemia	,949	,352
Fibrinogeno	1,298	,207
BMI ^{^^^^}	-1.054	,301
Waist Circumference	,442	,663
Systolic Blood Pressure	-,682	,500
Diastolic Blood Pressure	-,299	,766

* Dependent Variable: PSQ Index

** Weighted Least Squares Regression -Weighted by Sex (M-F)

[^] Total Cholesterol

^{^^} High Density Lipoprotein cholesterol

^{^^^} Low Density Lipoprotein cholesterol

^{^^^^} Body Mass Index

Table 4

Multiple Regression between Metabolic parameters and ZUNG SRDS

Independent Variables	t	P
TC [^]	1,817	,081
Triglycerides	2,115	,045
HDL-c ^{^^}	1,424	,167
LDL-c ^{^^^}	-,251	,804
Uric Acid	-3,071	,005
Glycemia	-1,324	,198
Fibrinogeno	1,623	,117
BMI ^{^^^^}	2,268	,032
Waist Circumference	-1,147	,259
Systolic Blood Pressure	,813	,423
Diastolic Blood Pressure	,510	,614
Age	-1,499	,146

[^] Total Cholesterol^{^^} High Density Lipoprotein cholesterol^{^^^} Low Density Lipoprotein cholesterol^{^^^^} Body Mass Index

* Dependent Variable: Zung SRDS

** Weighted Least Squares Regression - Weighted by Sex (M-F)