SOCIAL ENCOUNTERS IN DAILY LIFE AND TWO-YEAR CHANGES IN METABOLIC RISK FACTORS IN YOUNG WOMEN

by

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Abstract

Research shows that poor social ties increase risks of morbidity and mortality from cardiovascular disease (CVD). However, little is known about the nature of everyday social encounters that give rise to this association, or when in the course of development they begin to shape disease-relevant biological processes. In this study, 122 adolescent females recorded the qualities of their everyday social interactions using electronic diaries. At the same time we measured components of the metabolic syndrome, a precursor to CVD that includes central adiposity, high blood pressure, insulin resistance, and lipid dysregulation. Metabolic symptoms were reassessed 12 and 24 months later. Hierarchical linear modeling revealed an association between negative social interactions and metabolic symptom trajectories. To the extent that participants had more intense negative social encounters in daily life, they showed increasing scores on a composite indicator of metabolic risk over two years. This association was independent of a variety of potential confounders, and persisted when symptoms of depression and broader personality traits were controlled. There was no association between positive social encounters and metabolic risk trajectories. These findings suggest that even in otherwise healthy adolescents, abrasive social encounters may accelerate the progression of CVD's early stages.

Preface

All data used in these analyses were collected as a part of a larger research project, the Depression and Atherosclerosis Study. Dr. Gregory Miller was the primary investigator of the Depression and Atherosclerosis Study and is my supervisor, so provided feedback at all stages of analysis and write up. Tara Martin was the Depression and Atherosclerosis Study project manager and provided access to data files and answered questions on methods. Dr. Edith Chen provided feedback on and edited the original manuscript that was submitted for publication. All other work, including responsibility for data analyses, abstract, manuscript and thesis preparation and research, was done by me, Kharah Ross. All procedures and methods were approved by the University of British Columbia Research Ethics Board (UBC BREB # H04-80567). These analyses were presented as a citation poster at the March 2010 annual meeting of the American Psychosomatic Society, and an initial, abbreviated version of this thesis has been published:

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Table of contents

Abstract ii

Preface iii

Table of contents iv

List of tables vii

List of figures viii

List of abbreviations ix

Acknowledgements x

Introduction 1

- Cardiovascular disease 3
- Social relationships and cardiovascular disease 7
- Biological consequences of social relationships 12
  - Neuroendocrine system. 12
  - Cardiovascular system. 15
  - Immune system. 18
  - Summary 19
- Perceived quality of social encounters 20
- Personality and mood 24
- Social relationships and development 24
- Specific aims and hypotheses 26
  - Hypothesis 1. 26
  - Hypothesis 2. 27
  - Hypothesis 3. 27

Hypothesis 4 27
Methods 28
Participants 28
Procedure 28
Measures 29
Perception of social encounters. 29
Metabolic risk. 30
Alternative explanations. 32
Depressed mood. 32
Neuroticism, agreeableness, and extraversion. 33
Physical activity. 33
Results 34
Statistical approach 37
Preliminary results 37
Positive and negative social encounters 39
Alternative explanations 45
Discussion 50
Negative social encounters and the metabolic syndrome 51
Positive social encounters: do they matter at all? 52
Mechanisms 55
Developmental context 56
Potential for interventions 57
Limitations and future directions 58

Conclusions 60

References 61

List of tables

Table 1. Characteristics of the Sample (N = 122) 35

Table 2. Descriptive statistics for metabolic parameters over the course of study. 36

Table 3. Results of HLM model predicting metabolic profiles over time from control variables. 38

Table 4. Results of HLM model predicting metabolic profiles over time from control variables and negative social interactions..... 42

Table 5. Results of HLM model predicting metabolic profiles over time from control variables and positive social interactions. 43

Table 6. Results of HLM model predicting metabolic profiles over time from control variables and the interaction between positive and negative encounters. 44

Table 7. Results of HLM model predicting metabolic profiles over time from control variables, negative social encounters, and depressed mood (level 1)..... 46

Table 8. Results of HLM model predicting metabolic profiles over time from control variables, negative social encounters, and extraversion. 47

Table 9. Results of HLM model predicting metabolic profiles over time from control variables, negative social interactions, and neuroticism..... 48

Table 10. Results of HLM model predicting metabolic profiles over time from control variables, negative social interactions, and agreeableness. 49

List of figures

Figure 1. Negative social encounters and metabolic composite scores over two years. Participants who had more negative social encounters in day-to-day life showed increasing scores on the metabolic composite over follow-up, $b = 3.79\text{x}10^{-3}$, $SE = 1.91\text{x}10^{-3}$, $p = 0.049$. Conversely, participants with fewer negative social encounters showed a decline in metabolic composite scores over the same timeframe. 40

List of abbreviations

ABP	ambulatory blood pressure	BDI	Beck Depression Inventory
BFI	Big Five Inventory	BP	blood pressure
CHD	coronary heart disease	CV	cardiovascular
CVD	cardiovascular disease	CVS	cardiovascular system
DBP	diastolic blood pressure	GC	glucocorticoid
HDL	high-density lipoprotein	HPA	hypothalamic-pituitary-adrenal
HR	heart rate	LDL	low-density lipoprotein
LVMI	left-ventricular mass index	MI	myocardial infarction
OC	oral contraceptive	SAM	sympathetic adrenomedullary
SD	standard deviation	SES	socioeconomic status
SBP	systolic blood pressure	SNS	sympathetic nervous system
TOD	target organ damage		

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Introduction

Over 35 years of research draws a profound link between our social environment and a diverse range of health indicators and outcomes (Cohen, & Janicki-Deverts, 2009). The social environment is an immensely broad concept, which themes such as socioeconomic status (SES), material considerations like access to social resources (e.g., schools or health care), neighbourhood or work environment quality, and social relationships. For the purposes of this thesis, social environment will be confined to the area of social relationships. Social relationships alone is a broad subject area, and has been defined and conceptualized many different ways, ranging from more "quantity" approaches (e.g., social network diversity) through to "quality" (e.g., perceptions of social encounters) measures of social relationships. Regardless of how it is conceptualized, social relationships are consistently reported to be strong predictors and shapers of both our physical and mental well-being.

Social integration is defined as "the degree to which a person is linked to or involved with his/her social environment at different levels, including community, individual network of social ties, and intimate relationships" (Graham, Christian, & Kiecolt-Glaser, 2007, p. 782). Conversely, lack of social integration is social isolation, or "lack of regular contact with friends, neighbours, co-workers, family members, and social groups" (Graham et al., 2007, p. 782). A common brute force measure of degree of social integration and isolation is social network size or diversity, often measured by assessing the number of individuals, types of relationships, and frequency of contact within a social network. Many social network indices exist, but many assess common aspects of social relationships, including marital status, community or church involvement, and number of close friends and family. In general, more socially integrated individuals, less socially isolated individuals, or those with larger or more diverse social

networks are healthier and have better health outcomes. For example, greater social network diversity has been associated with better overall quality of life (Achat et al., 1998), less susceptibility to the common cold (Cohen, Doyle, Skoner, Rabin, & Gwaltney, 1997), reduced incidence of dementia (Fratiglioni, Wang, Ericsson, Maytan, & Winblad, 2000), and improved survival after a diagnosis of breast cancer (Kroenke, Kubzansky, Schernhammer, Holmes, & Kawachi, 2006). Social isolation has also been found to be a potent predictor of poor health and mental well-being (House et al., 1988), and mortality (Berkman, 1995). In some studies, the mortality risk associated with social isolation was on par with that due to cigarette smoking, high blood pressure (BP), and obesity (House, Landis, & Umberson, 1988).

What is it about being socially integrated or having diverse social networks that is beneficial? One well-supported view is that social integration increases an individual's access to a range of resources that can protect or buffer them from negative events and life situations, such as information, material goods, tangible assistance, or emotional support. These resources are often considered under the rubric of social support, itself a broad and variously defined construct. Indeed, social support has been defined as the individual belief that one is "cared for and loved, esteemed, and a member of a network of mutual obligations" (Cobb, 1976, p. 300), through to "the perception that assistance would be available if and when it is needed, as well as receipt of assistance during such times" (Graham et al., 2007, p. 781). Regardless, access to social support has been associated with decreased all-cause mortality (Barth, Schneider, & von Kanel, 2010), reduced negative impact of stressors (Cohen, & Wills, 1985; Cohen et al., 2009), decreased risk of depression (Brown, Andrews, Harris, Adler, & Bridge, 1986), a more healthful lifestyle (Muhlencamp, & Sayles, 1986), and reduced cardiovascular (CV) and hormonal responses to laboratory stressors (Thorsteinsson, & James, 1999).

Social support can be viewed as one particular aspect of how individuals can perceive or apply value to social exchanges. The overall quality of social encounters, for example, whether they are viewed as beneficial and positive or detrimental and negative, also affects well-being and physical health (e.g. Edwards, & Hershberger, 2001; Melchior, Berkman, Niedhammer, Chea, & Goldberg, 2003). Perceived social competence, or "perceptions of one's own ability to engage in effective social interactions" (Lee, Hankin, & Mermelstein, 2010, p. 604), has, for example, been reported to predict depressive symptoms in a study of adolescents (Lee et al., 2010). There are also aspects of social relationships that are acute events or do not fit well into either "quantity" or "quality" measurements of social relationships, such as social losses (e.g. Stroebe, Schut, & Stroebe, 2007), loneliness (e.g. Cacioppo, Hawkley, & Berntson, 2003), and marriage (e.g. Kiecolt-Glaser, & Newton, 2001), that have also been associated with health and well-being.

Essentially, no matter how social relationships are conceptualized or measured, they are linked to a variety of physical health and well-being indicators, including depression, diabetes, healthy lifestyles, and cancer. However, social relationships have particularly and consistently been predictive of cardiovascular disease (CVD) and related processes. Indeed, social relationships have been implicated in overall cardiovascular (CV) health, presence of CV risk factors, and CVD morbidity and mortality (Barth et al., 2010). An overall purpose of this thesis is to further understanding of how social relationships relates to CVD.

Cardiovascular disease

Cardiovascular disease is of particular interest to researchers for two important reasons: first, it was the second leading cause of death in Canada as of 2007 (Leading Causes of Death in Canada, 2007), and so understanding the factors that contribute to CVD progression is important

to prevent new cases and improve prognosis of current cases. Second, CVD is both a lifestyle and life-course disease, meaning that it begins early in life and is at least partially a product of lifestyle and environment. Therefore, understanding how our environment and lifestyle relates to CVD development may allow us to intervene in a manner that prevents, or forestalls, the appearance of clinical disease.

The most prevalent clinical manifestations of CVD, such as angina, myocardial infarctions (MIs), strokes and aneurisms, are often atherosclerotic in origin. Atherosclerosis is a hardening of the arteries due to build-up of fatty material along the arterial walls (Duff, & McMillan, 1951). The atherosclerotic process begins in the early decades of life, in childhood and adolescence (McGill et al., 2000), and overt CVD is often the end-product of decades of atherosclerotic progression.

Atherosclerosis does not occur in a linear fashion, and it may proceed at different rates and at multiple sites within one individual. There may also be genetic or biological factors that can delay or speed the process up, and there are many aspects of atherosclerosis that are not yet understood. As such, the following can only be considered a rough outline of how atherosclerosis progresses into overt CVD: The first stage of atherosclerosis is characterized by the build up of fatty material, or fatty streaks, along the arterial wall, often in areas where damage or tears have occurred. Fatty streaks consist mostly of lipid-filled macrophages, or foam cells. Macrophages posses cell receptors that recognize and stimulate phagocytosis of low-density lipoproteins (LDL), "bad" cholesterol, as part of their more general role as tissue "garbage collectors." Macrophages patrol arterial tissue and may aggregate in response to damage or tears in the arterial wall. Under specific conditions like the presence of large concentrations of LDL, low LDL oxidation rates, or cytokine stimulation, macrophages will increase their rate of LDL

uptake. If the foam cells are unable to match LDL metabolism to uptake they may lyse and form a pool of extracellular lipids on the arterial wall. Fatty streaks that contain dead or dying macrophage are known as transitional lesions. All the while, macrophages are also stimulating adjacent smooth muscle tissue in the arterial wall to increase lipid uptake and to release cytokines that attract more macrophages to the area. This spawns and perpetuates a chronic inflammatory cycle, and leads to further deterioration of the arterial wall.

As the inflammatory cycle continues, extracellular lipids and cholesterol ester crystals build up at the site and a necrotic core, the product of coagulation necrosis and cellular apoptosis, develops within the transitional lesion. In response to increasing cell death, a collagenous fibromuscular cap develops over the transitional lesion to produce a fibrous plaque. The fibrous plaque continues to grow, but this is believed to be the product of further cell death rather than the result of cell migration into the plaque or further fibrous tissue growth (Frink, 2002).

Beginning as early as the second decade of life, these enlarged fibrous plaques begin to undergo calcification, during which the fibrous plaques become impregnated with calcium. Calcification is an active, not passive, process and similar in nature to bone formation (Wexler et al., 1996): through a mechanism not completely understood, hydroxyapatite, the predominant crystalline form in calcium deposits, is produced by the arterial wall cells to form bone-like deposits along the artery. It is believed that this is an adaptive process that occurs in response to weakening of the arterial wall as a result of tissue death within the fibrous plaque, and is meant to maintain wall integrity and prevent further cell necrosis (Frink, 2002). At this stage, if a plaque has grown large enough or become calcified enough to partially occlude blood flow, some overt forms of CVD may begin to appear, such as angina and ischemic strokes.

At some point during this process, a plaque may become disrupted due to tears or cracks that develop in the fibromuscular cap. If the plaque's cap tears or cracks, circulating blood, clotting elements and immune factors can enter the plaque and come into contact with the necrotic core. Clotting elements are activated and produce a plaque hemorrhage or an intraplaque thrombus (Davies, 1996). If the fibromuscular cap is badly damaged and is sheared off plaque ulceration may occur: the necrotic and tissue core of the plaque is exposed to circulating blood, and the plaque is like an open sore on the arterial wall. Due to mechanisms not completely understood, plaques may remain in an ulcerated state for a long period of time before clots develop (Frink, 2002).

Eventually, as a result of plaque damage, hemorrhaging and/or ulceration, a clot will develop over the plaque site. If the clot is large enough and/or tears free, a thrombotic occlusion will occur. Clinical disease precipitates depending on which tissue is affected by the occlusion: MIs if coronary arteries are blocked, strokes if brain arteries are blocked, and gangrene if arteries in the periphery are blocked (McGill et al., 2000). Alternatively, if the plaque has developed at a point in the arterial wall that experiences greater blood flow-related stress, and the plaque has fatally compromised the integrity of the arterial wall, the artery may fail and an aneurism can result.

Atherosclerosis is a life-long process, and many factors are involved in its progression and retardation. For example, a high fat diet, obesity, low physical activity, genetic predispositions, and hypertension can all contribute to plaque development and progression. Recently, researchers began to realize that a number of these CVD risk factors co-occur at greater-than-chance levels. This collection of abnormalities that predisposes to CVD is known as Metabolic X or the metabolic syndrome. The most commonly used criteria for the metabolic

syndrome comes from the National Cholesterol Education Program Adult Treatment Panel III (ATP III), which requires the presence of three of the following five criteria for a diagnosis (Grundy et al., 2005): Central adiposity, defined as having a waist circumference of greater than 102 cm in men or 88 cm in women. Dyslipidaemia, which consists of two criteria: 1) having fasting blood levels of high-density lipoprotein (HDL), "good cholesterol," of less than 40 mg/dL in men and 50 mg/dL in women, and 2) having fasting blood levels of triglycerides of 150 mg/dL or more. Hypertension is characterized as having systolic BP (SBP) greater than 130 mmHg and/or diastolic BP (DBP) of 35 mmHg or more. And finally, insulin resistance, which is defined as having a fasting blood glucose level of 110 mg/dL or higher, or having been diagnosed with diabetes (Grundy et al., 2005). It is believed that these risk factors are due to some common underlying cause (Grundy et al., 2005). The purpose of these diagnostic criteria is to identify individuals who are at increased long-term risk for developing atherosclerotic CVD, and who may benefit from clinical and lifestyle interventions.

The metabolic syndrome is of particular interest to researchers as it is fairly easy to assess and diagnose, and has a clear role in atherosclerotic progression. Furthermore, individuals with the metabolic syndrome have not yet reached that clinical threshold where more aggressive treatments, such as surgery, are necessary. As such, the symptoms of the metabolic syndrome are potentially a key intervention target, and understanding what can influence and reduce these symptoms may help prevent later development of CVD.

Social relationships and cardiovascular disease

As stated above, there is compelling evidence that social relationships are predictive of CV health. Social relationships have been strongly and consistently related to CVD morbidity and mortality (e.g. Barth et al., 2010). In particular, an astonishing number of prospective and

epidemiological studies have reported associations between social network diversity and CVD. A classic study by Berkman and Syme (1979) of Alameda County residents reported that participants who lacked social and community ties were at greater risk for death over the 9 years of follow up, independent of baseline health status, SES, year of death, and health practices. Another study of HMO members followed over a 15-year period revealed that social network indices at baseline were associated with 15-year mortality hazards, independent of age, sex, smoking, SES, and baseline health status. Social network diversity was also an independent predictor of ischemic heart disease, as well as cause-specific and all-cause mortality in participants diagnosed with ischemic heart disease, cancer or strokes over the study (Vogt, Mullooly, Ernst, Pope, & Hollis, 1992). An etiological study of 4653 Japanese-ancestry Hawaiian men reported an inverse relationship between social network indices at baseline and prevalence of MI, angina, and coronary heart disease (CHD), controlling for age, BP, physical activity, smoking status, alcohol consumption, SES, diet and blood metabolic indicators (Reed, McGee, Yano, & Feinleib, 1983). Yet another prospective study followed over 25,000 middle aged, male health professionals over 10 years and, even after controlling for age, occupation, health behaviours, physical health, coronary risk factors and diet, found that men who were not socially integrated had higher relative risk for total mortality and fatal CHD compared to socially integrated men, and were more likely to die from accidents, suicide and non-cancer, non-CVD causes. In fact, a one categorical unit increase in social integration was related to a 29% decrease in death risk over the follow-up (Eng, Rimm, Fitzmaurice, & Kawachi, 2002). Another study of over 32,000 American men followed over a 4-year period noted that men who were socially isolated at baseline were at greater risk for CVD mortality, death by accident or suicide, and stroke incidence (Kawachi et al., 1996). However, the literature is not unanimous, and opposing

reports do exist. For example, increased social integration has been associated with increased fibrinogen concentration, a potential risk factor for CVD, in a sample of older men (Loucks, Berkman, Gruenewald, & Seeman, 2005). It is also noteworthy that most of these studies have been done exclusively in men. Although a few have included both men and women and reported an association between CVD and social network diversity (e.g., Berkman et al., 1979; Vogt et al., 1992), it is still not clear if social integration or social isolation affects men and women in the same way or to the same extent.

Social network diversity most likely does not have a direct influence on health but instead affects health through five mechanisms (Berkman, Glass, Brisette, & Seeman, 2000): social influence (e.g., social comparison, peer pressure, health norms), social engagement, (e.g., social roles, and bonding), person-to-person contact, access to material resources and goods (e.g., housing and healthcare), and social support. The last mechanism has garnered a great deal of research attention: individuals who are socially isolated are likely at greater risk for CVD morbidity and mortality because they do not have access to social resources that can buffer the consequences of stressors or negative life events (Berkman, 1995; Knox, & Uvnas-Moberg, 1998; Rozanski, Blumenthal, & Kaplan, 1999). For example, aspects of social support (network instrumental support and feelings of being loved) were more predictive of coronary artery atherosclerosis than social network size, independent of a variety of CVD risk factors, in a sample of middle-aged men and women undergoing coronary angiography (Seeman, & Syme, 1987).

Indeed, the assertion that it is quality and not necessarily quantity of social relationships that drives the social relationships-CVD relationship is widely supported by the literature. One review article reported that low social support was associated with a risk 1.5 to 2.0 of CHD in

healthy populations, and a risk of 1.5 to 2.0 of further disease progression in samples with established CHD (Lett et al., 2005). The authors did acknowledge that not all the studies they reviewed supported an association between social support and CHD morbidity and progression, but they noted that this is not surprising given the range of ways used to define and assess social support. Regardless, social support seems to be a good predictor of CHD: another systematic review of prospective, epidemiological cohort studies also reported that there is consistent evidence that social support is associated with CHD etiology and prognosis (Kuper, Marmot, & Hemingway, 2002). Research also suggests that social support is an important predictor of CVD mortality. A prospective, community-based cohort study of elderly men and women hospitalized for acute MI observed that lack of emotional support was associated with 6 month mortality, controlling for disease severity, co-morbidities, risk factors and demographic characteristics (Berkman, Leo-Summers, & Horwitz, 1992). Another study of MI patients who were not taking medication also reported that lack of social support predicted mortality over a two year period, independent of disease severity, such that a 1 point decrease in perceived social support was equal to an adjusted Hazards ratio of 1.46 (Gorkin et al., 1993). In summary, social support, one component of the quality of a person's social relationships, is independently predictive of CVD morbidity and mortality.

In addition to overt CVD, social relationships have also been associated with CVD precursors and intermediaries, such as atherosclerosis (e.g., Knox et al., 1998). In a sample of 783 middle-aged men and women who underwent coronary artery calcification imaging, social isolation was independently associated with increased presence of coronary artery calcification, controlling for age, sex, SBP, blood glucose, and LDL (Kop et al., 2005). Day-to-day social encounters have also been related to indicators of atherosclerosis: men that reported frequent

interactions with their spouses showed less progression of atherosclerosis in the carotid artery over 3 years, provided they also had high marital quality. However, this was not observed in the women sampled (Janicki, Kamarck, Shiffman, Sutton-Tyrell, & Gwaltney, 2005).

Social relationships have also been associated with development of the metabolic syndrome or its symptoms. For example, some studies have reported that indicators of social integration, such as childhood social isolation (Caspi, Harrington, Moffitt, Milne, & Poulton, 2006) and loss of a spouse through death or divorce (Troxel, Matthews, Gallo, & Kuller, 2005) are risk factors for developing the symptoms of the metabolic syndrome. A study of Swedish women reported that socially isolated participants were more likely to have the metabolic syndrome, controlling for age, menopausal status, educational level, smoking status, physical activity and alcohol consumption. In fact, women in the most socially isolated quartile had a relative risk ratio for the metabolic syndrome of 3.5 compared to women in the least socially isolated quartile (Horsten, Mittleman, Wamala, Schenck-Gustafsson, & Orth-Gomer, 1999). More qualitative aspects of social relationships, including marital quality (Troxel et al., 2005), have also been associated with the metabolic syndrome and its symptoms. For example, a study of Polish adults reported that both men and women with low social support level were more likely to be diagnosed with the metabolic syndrome compared to those with high levels of support (Pakalska-Korcala et al., 2008). However, research in this area is not yet as extensive, and opposing reports do exist (Ikedo, Kawachi, Inoue, & Tsugane, 2010).

In sum, social relationships have a strong and pervasive impact on CV health, CVD precursors, and CVD morbidity and mortality. In general, social network diversity and access to social support may provide protection from CVD; conversely, social isolation may increase risk for CVD.

Biological consequences of social relationships

All in all, there is robust and fairly consistent research suggesting that social relationships may have causal influences on both health and well-being (House et al., 1988). This influence may be exerted through a variety of mechanisms, including but not restricted to: social (e.g., stress buffering, social control and social support), psychological and affective (e.g., through effects on emotion regulation, self-esteem, locus of control, and purpose in life), and behavioural (e.g., by altering performance of health–related behaviours like smoking and exercise). One last set of mechanisms that are of particular interest are direct physiological or biological consequences of social relationships (e.g., Cohen et al., 2009; Uchino, Cacioppo, & Kiecolt-Glaser, 1996). In other words, not only do social relationships effect health indirectly through access to resources and health behaviours, but they may "get under the skin" directly and alter physiological systems in such a way to promote disease processes.

Social interactions have had a documented influence on a range of physiological systems, including the CV, neuroendocrine, and immune systems (Uchino, 2006). Due to the complexity of these systems and the nature of social interactions, most research examines associations between one aspect of interactions and a handful of physiological indicators. However, it should be noted that no one aspect of social relationships exists in isolation or exerts an influence on just one physiological system (see Kiecolt-Glaser et al., 2001 for a detailed example), and no physiological system exists in isolation. As such, the research presented below represents only a very small and overly simplistic overview of how social interactions may directly affect physiology.

Neuroendocrine system. The neuroendocrine system is comprised of the nervous system, the endocrine system, and the interaction between the two. Homeostasis through physiological regulation is a key purpose of this system, so it is of no surprise that it is complex, feeds into all

other physiological systems, and has effects that are not homogenous but rather depend on time since activation and endpoint targets (Sapolsky, Romero, & Munck, 2000). There are two major components: the sympathetic nervous system (SNS) and the hypothalamic-pituitary-adrenal (HPA) axis. Together, these systems play a key role in regulating physiological responses to stressors. Both are activated by internal and external stimuli and are regulated by negative feedback loops. This allows rapid, adaptive responses to acute stressors while minimizing long-term exposure to glucocorticoids (GCs; discussed below), which can have deleterious physiological consequences (DeVries, Glasper, & Detillion, 2003).

The SNS is the first-activated component of the sympathetic-adrenomedullary (SAM) axis, and is responsible for the acute stress response, which occurs seconds after challenge. The sympathetic nervous system (SNS), in addition to having direct innervation to most organs, activates the adrenal gland medulla, which secretes catecholamines, and the hypothalamus. The hypothalamus, as part of the HPA axis, responds by secreting hormones that act on the pituitary gland, which secretes hormones that cause the adrenal gland cortices to secrete GC hormones (e.g. cortisol) and that cause the pancreas to produce hormones that mobilize glucose and fat energy reserves. During acute stressors, GCs at first enhance activation of physiological systems important to survival, but over time become suppressive in order to prevent over-activation of stress-induced defenses. The GCs are also responsible for adapting physiology in preparation for future stressors, and then activating those preparations when exposed to subsequent stressors (Sapolsky et al., 2000). The end-product acute stressor activation, for which this system is well-designed, is the classic "fight-or-flight" response: the body's resources are mobilized, the threat is dealt with and a return to baseline follows. However, at the same time that fight-or-flight is initiated a second, slower GC response begins that can progress into the chronic stress response

(Sapolsky et al., 2000). The body is not capable of sustaining fight-or-flight levels of activation indefinitely. Indeed, consistent over-activation or over-stimulation of these stress-responses is called "allostatic load," and persistent exposure to allostatic load has been linked to physiological damage or increased wear-and-tear of physiological systems (McEwen, 1998). Over time, this damage may accumulate and predispose to or cause a diverse range of disease-related outcomes (McEwen, 1998). As such, this slower second wave response is designed to adapt the body to long-term exposure to stress, which often has negative consequences for health and well-being.

In particular, glucocorticoids produce a variety of effects that directly influence the CV system (CVS), for example by changing heart rate (HR), BP, cardiac output and fluid retention; acting as a general suppressant of the immune system in order to prevent over-activation of the inflammatory response; and affecting metabolism by mobilizing glucose stores (Sapolsky et al., 2000). A plethora of review articles have been written on how social relationships (e.g., marital interactions, social isolation, social support) can alter cortisol secretion in both real-world and experimental settings, animal and human models (e.g., DeVries et al., 2003; DeVries, Craft, Glasper, Neigh, & Alexander, 2007; Kiecolt-Glaser et al., 2001; Seeman, & McEwen, 1996; Uchino et al., 1996). One meta-analysis that looked only at experimental studies of social support and reactivity to laboratory stresses reported an average effect size of 0.83 for cortisol, meaning that, across studies, the presence of social support reduces stress-induced cortisol secretion by almost a full standard deviation (SD) compared to no support conditions (Thorsteinson et al., 1999).

Social interactions may also directly modify and activate components of the neuroendocrine system, which then has a trickle-down effect on other CVD-relevant physiological systems (Knox et al., 1998). Several hormones produced as a result of SAM and

HPA axis activation have a direct effect on the CVS. For example, rat research provides evidence that circulating pituitary-derived hormones are necessary for stimulating arterial smooth muscle proliferation following injury to the arterial wall (Fingerle et al., 1992). What this suggests is that stressful aspects of social interactions, such as marital conflict, can directly influence pituitary hormone secretion and thus arterial lesion development and CVD progression (Knox et al., 1998). The catecholamines have also been observed to directly regulate CVS health: beta-blocker monkey studies report that untreated monkeys exposed to social stress had greater lesion formation at points in the artery that experience high sheer forces, suggesting that sympathetic activation may be involved in atherosclerotic progression that stems from social environment stressors (Knox et al., 1998). Indeed, elevations in epinephrine have been observed following stressful social encounters, such as marital conflicts (e.g., Kiecolt-Glaser et al., 1996; Kiecolt-Glaser et al., 2001).

In summary, abrasive social interactions, like marital conflict, may increase CVD risk by increasing HPA and SAM activation. In particular, chronic activation of the neuroendocrine system may also exacerbate the symptoms of the metabolic syndrome, resulting in increased BP and metabolic changes that increase circulating glucose and tryglyerides, and thus affect central adiposity and insulin resistance (Bjorntrop, & Rosmond, 1999; Bjorntorp, & Rosmond, 2000). Conversely, more positive social encounters, such as social support, may buffer any negative consequences of HPA and SAM activation by attenuating hormonal responses (Devries, 2002).

Cardiovascular system. The CVS is perhaps most intuitively related to CVD. Research in this domain has focused on how both supportive and conflictual interactions influence CVD pathogenesis, and much of this work has been done in laboratory settings. In general, CVS function is assessed through two measurement methods: indicators of increased CVS load (e.g.,

CV reactivity and high BP), and indicators of excess CV wear-and-tear (e.g., signs of target organ damage).

Cardiovascular reactivity is defined as "the magnitude or pattern of an individual's hemodynamic responses to behavioural stressors" (Treiber et al., 2003, p. 46). The reactivity hypothesis posits that someone who exhibits increased CV reactivity to stressors, defined as the difference between baseline and peak CV function during a stressor, will have greater overall load on their CVS compared to those who react less. Over time, consistently greater load will increase the "wear" on the CVS, may progress into hypertension (a metabolic syndrome symptom), and speed up degenerative processes like atherosclerosis, eventually accumulating in overt CVD (Treiber et al., 2003). The CV reactivity hypothesis is well supported by the literature, and has been shown to be an independent risk factor for CVD in both healthy and clinical populations (e.g., Alderman, Ooi, Madhavan, & Cohen, 1990; Keys et al., 1971; Krantz et al., 1999; Manuck, Olsson, Hjemdahl, & Rehnqvist, 1992; Sheps et al., 2002; see review by Treiber et al., 2003). The stress-buffering model of social support suggests that social support may be associated with decreased risk for CVD because it buffers or decreases CV reactivity to stressors (Uchino, Carlisle, Birmingham, & Vaughn, 2010). Several studies support this theory: A study of female university students randomly assigned to complete mental arithmetic and concept formation tasks with or without the presence of a friend reported that the presence of a friend reduced HR reactivity during the stress tasks (Kamarck, Manuck, & Jennings, 1990). Another study randomly assigned college students to give a speech either alone, in the presence of a supportive confederate, or in the presence of a non-supportive confederate. Participants who delivered their speech in the presence of supportive confederates had significantly less SBP and DBP reactivity compared to the non-supportive confederate group, and less SBP reactivity

compared to the speech alone group (Lepore, Mata Allen, & Evans, 1993). In fact, merely knowing that social support is available even if someone is not actually present can produce decreased SBP and DBP reactivity during a public speaking stress task (Uchino, & Garvey, 1997). Most of the reactivity research has focused on undergraduate student samples, but there are also studies that suggest these trends also generalize to other populations: compared to a non-aversive collaborative problem solving interaction, a marital conflict discussion produced greater BP reactivity, which persisted well past the end of the discussion, in a sample of middle-aged and older couples (Smith et al., 2009). Marital discord may be associated with greater risk of CVD through heightened CV reactivity (Smith et al., 2009); this association has been replicated elsewhere (e.g., Heffner, Kiecolt-Glaser, Loving, Glaser, & Malarkey, 2004).

One limitation of the CV reactivity research is that it is restricted to experimental settings, an artificiality that could compromise day-to-day generalizability. To solve this problem, researchers use ambulatory BP (ABP) monitoring to assess reactivity in vivo through real-time monitoring of participants. Results from ABP research mirror the CV reactivity research conclusions: one study asked participants to rate marital adjustment and marital quality and undergo ABP assessment at baseline and three years later. An interaction was reported such that men with higher marital satisfaction and high spousal contact had lower ABP values, and men with low marital satisfaction and high spousal contact had higher ABP values, suggesting that quality of spousal interactions affects ABP levels and day-to-day CVS load (Baker et al., 2000). A 3 day daily-diary ABP study of older adults noted a similar trend: episodes of social conflict were associated with greater SBP and DBP activity, above and beyond potential confounds such as posture and activity at the time of measurement (Kamarck et al., 2002). Similar patterns have been observed in adolescents: anxious- and avoidant-attachment boys had

augmented ambulatory HR and BP during electronic diary-recorded social interactions compared to other boys (Gallo, & Matthews, 2006), and adolescents who had a tendency to read threat into ambiguous situations exhibited higher ABP during social interactions than when they were alone; the reverse was observed in adolescents who tend not to read threat into ambiguous situations (Chen, Matthews, & Zhou, 2007). In sum, regardless of whether it occurs in a lab or in day-to-day life, qualitative aspects of social relationships are known to either increase (e.g., social conflict) or attenuate (e.g., social support) CV reactivity to stressors.

Cardiovascular reactivity, although a CVD risk factor, only suggests that CVS load may be unusually high, but not necessarily that CVS harm has occurred. Target organ damage (TOD), on the other hand, is an indicator of actual damage that results from persistent high BP. There are several indicators of TOD, but most studies use left-ventricular mass index (LVMI) and carotid intima media thickness, both of which suggests over-exertion of the heart muscle and greater systemic BP. Not surprisingly, qualitative aspects of social relationships are also predictive of TOD: low marital adjustment at study entry was predictive of greater increases in LVMI three years later in a sample of essential hypertensive patients, controlling for LVMI at baseline, smoking and alcohol consumption (Baker et al., 2000). In sum, qualitative components of our social relationships may affect CVD risk by directly affecting CVS health, and in particular by producing heightened BP, a component of the metabolic syndrome.

Immune system. The immune system is generally deemed to include the tissue, cells and molecules responsible for the body's defense against infection and injury. An immune response can be divided into innate responses, which occur immediately after challenge, are non-specific and involve cells such as macrophages and neutrophils, and adaptive responses, which take a few days to develop, are specific, and involve B and T cells. Immune cells activated at the site of

injury or infection communicate with other immune cells and tissues, and orchestrates an immune and inflammatory response, via cytokine signaling.

The immune system does not exist in isolation, and receives and gives feedback to other physiological systems. The GCs released by the neuroendocrine system regulate immune responses by preventing inflammatory response overshooting, and the immune system influences the neuroendocrine system by secreting molecules that mimic HPA hormones and act on the adrenal gland (Sapolsky et al., 2000). The immune system also plays a key role in the atherosclerotic process: macrophages responding to tissue damage in arterial walls form the basis of fatty streaks, and cytokines secreted by those macrophages propagate an inflammatory cycle that continues the atherosclerotic process and eventually culminates in thrombosis formation.

Over 20 years of research evidences an association between social relationships and immune system responses associated with CVD (Graham et al., 2007; Kiecolt-Glaser, 1999). Small social networks, lack of social integration, bereavement, divorce and loneliness are all associated with maladaptive immune alterations. For example, one study assessed wound healing in married couples both following a marital disagreement and after completion of a structured social support task. Wound healing following the marital disagreement task was slower, and there was less cytokine production at the site of injury compared to the social support condition, which suggests that marital discord may down-regulate immune response to injury (Kiecolt-Glaser et al., 2005). Conversely, positive social encounters, such as social support, have been associated with beneficial immune responses, possibly due to the ability of social support to buffer the effect of negative or stressful life events (Graham et al., 2007).

Summary. Both laboratory and ambulatory studies have evaluated the biological sequelae of social interactions. These studies indicate that conflictual interactions raise BP and HR, trigger

activation of the SAM and HPA axis, and increase immune and inflammatory responses. Supportive interactions have been shown to buffer the negative consequences of stressors on those same systems (e.g., Baker et al., 2000; Graham et al., 2007; Heffner et al., 2004; Kiecolt-Glaser et al., 1993; Kiecolt-Glaser et al., 1996; Kiecolt-Glaser et al., 1997; Kiecolt-Glaser et al., 2005; Smith et al., 2009). As reviewed, these affected neuroendorcine, CV and immune-related processes have been implicated in CVD development and progression (Kop, 1999). Collectively, these findings suggest that the social interactions have direct biological consequences that relate to CVD pathogenesis.

Perceived quality of social encounters

During the review of the social relationship literature thus far, we have focused on quantity of social contacts and encounters (network diversity, social isolation, and social integration), and some specific types of interactions (social support and marital conflict). However, clearly these aspects do not completely represent or encompass the entire domain of social relationships, which may explain why research does not always consistently associate the above aspects of social relationships with CVD. For example, although the research reviewed above reports beneficial effects of social support, other research suggests social support can be harmful if it is unwanted or offered from the wrong source (Uchino et al., 1996). And although greater social diversity tends to be linked to improved health it is also recognized that individuals with larger social networks have a greater chance of encountering detrimental aspects of social relationships, such as negative social encounters and social losses (Cohen et al., 2009). The presence of social ties and the exchange of resources along those ties does not fully account for the association between social relationships and health: researchers are beginning to realize that

the perceived quality of those interactions is also important (Kamarck et al., 2002; Uchino et al., 2010).

Social encounters are typically assessed as being positive or negative. Initially researchers believed that positive and negative perceptions of social encounters represented opposite extremes on a single spectrum, but this has not been shown to be the case: Rook and colleagues (1984) reported that positive and negative social outcomes are correlated but not inversely related, suggesting that these two traits are not polar opposites but independent domains of experience. This has since been confirmed by factor analysis in a sample of older adults, such that positive and negative social encounters were related but essentially independent: negative encounters predicted psychological well-being and distress, whereas positive encounters predicted only psychological well-being (Finch, Okun, Barrera, Zautra, & Reich, 1989). As such, negative and positive qualities of social encounters should be separately assessed, and it is theoretically possible to have social encounters that are both highly positive and highly negative at the same time.

Perceiving social encounters as negative has been more robustly associated with poorer outcomes overall, including increased risk for depression, anxiety, and distress; reduced self-reported quality of life, personal mastery, self-esteem and self-efficacy; and hindered goal-directed activities and use of resource (Ruehlman, & Karoly, 1991). A link between positive social encounters and well-being and/or health has proven to be either much more inconsistent or elusive. For example, one study assessed the association between well-being and both positive social outcomes (relationships characterized by sources of social support) and negative social outcomes (relationships characterized by invaded privacy, being taken advantage of, broken promises, and causing anger and conflicts) in a sample of elderly widowed women. Negative

encounters consistently and strongly predicted well-being in comparison to positive ones, even after controlling for age, SES and health. In fact, positive social encounters predicted well-being only after positive affect and sociability were considered, which suggests that any relationship between positive encounters and health is not as straightforward as that between negative encounters and health (Rook, 1984). Another study of adults explored the relationship between quality (supportive and negative) of social encounters with spouses, friends and family, and depressed mood. Results revealed that negative social encounters were as important, if not more important, than positive social encounters in predicting depressed mood (Schuster, Kessler, & Aseltinel, 1990). The authors noted that, traditionally, most social interaction research focuses on the benefits of positive encounters, which they found surprising given that the evidence suggests that the negative psychological consequences of poor social interactions outweigh any benefit of positive ones (Schuster et al., 1990). Be that as it may, there are some studies that indicate that psychological distress can be attenuated by positive encounters, such as the presence of positive social support (Lepore, 1992). Another study of older adults reported that, although negative social encounters were associated with psychological distress and that increases in negative encounters also increased the risk of depression, positive exchanges appeared to attenuate any consequences of negative exchanges on affect (Rook, 2001).

It is also recognized that social encounters may also affect physiology directly. Negative encounters have been associated with poorer physical health: negative social exchanges in a sample of university students accounted for more variance in reported physical symptoms than life-event stress, daily hassles and social support, after controlling for psychological well-being (Edwards et al., 2001). Similarly, dissatisfaction with social relationships was predictive of poorer self-reported health status in the Gazel French cohort (Melchior et al., 2003). Negatively

perceived social encounters are also directly associated with physiological changes, such as increased cortisol secretion (Dikcerson, Mycek, & Zaldivar, 2008), changes in immune function and CV reactivity (Kiecolt-Glaser et al, 1993). One study evaluated salivary cortisol secretion in undergraduate students randomly assigned to deliver speeches in front of either no one, an evaluative audience or an indifferent audience. Compared to the other conditions, those in the social evaluative condition who were self-conscious (or perceived the evaluation as negative or a threat) produced more cortisol, suggesting that the presence of negative evaluation, and not just an audience, is necessary to increase cortisol secretion (Dickerson et al., 2008). Another study reported that marital conflict characterized by more negative or hostile behaviour was associated with greater 24-hour decrements in functional immunological assays, increased circulating T lymphocytes, and increased BP. However, positive or supportive behaviours during marital interactions were not associated with changes in immune function or BP (Kiecolt-Glaser et al., 1993). There may be some evidence that positive encounters can buffer deleterious physiological changes that arise due to stressors, but this work has mostly been done in animal models and it is unclear how this translates into human social exchanges (Devries et al., 2007). Overall, the literature suggests that "bad is stronger than good," and evidence for beneficial effects of positive social encounters, whether on physiology or affect, are not as consistent as that for negative encounters (Baumeister, Bratslavsky, Finkenauer, & Vohs, 2001).

A number of important questions in this literature have not yet been answered. The first has to do with the nature of the association between social interactions and disease processes. Although preliminary research suggests that perceptions of social encounters produce physiological changes that are associated with increased risk for CVD, such as increased cortisol output and increased BP, there appears to be no research that directly explores a relationship

between perceived quality of social encounters and CVD-related outcomes. Additionally, there is relatively little research on both the separate and combined effect of positive and negative day-to-day social encounters on CVD. To what extent do positive and negative encounters interact to influence disease process? And can positive interactions serve as a buffer, offsetting any effects of negative encounters? The primary purpose of this thesis is to begin to address this gap in the literature.

Personality and mood

Another unanswered question in the literature has to do with the role that broader personality and affective characteristics play in driving any association between quality of social encounters and CVD. Indeed, personality traits like extraversion, neuroticism/emotional stability, and agreeableness have robust influences on the quantity and quality of a person's social encounters (Doeven-Eggens, De Fruyt, Hendriks, Bosker, & van der Werf, 2008; Scarr, & McCartney, 1983; Swickert, Hittner, & Foster, 2010). These traits are also been associated with risk for CVD morbidity and mortality (e.g, Shipley, Weiss, Der, Taylor, & Deary, 2007; Smith & MacKenzie, 2006; Terracciano, Lockenhoff, Zonderman, Ferrucci, & Costa, 2008). Depression and depressed mood have been similarly associated with poorer social relationships, and increased risk for the metabolic syndrome and CVD (Kinder et al., 2004; Rugulies, 2002). Thus, it remains unclear whether the observed associations are causal effects of social encounters per se, or attributable to other more distal (personality) and proximal (emotion) factors.

Social relationships and development

It is also unclear where during the course of development the effects of social relationships on CV health appear. Most of the research reviewed here was done in samples of university students or older; and so little is known about the role of social interactions and

disease processes in a developmental context (Matthews, 2005). Researchers are increasingly emphasizing the importance of viewing disease development from a life-course perspective. Cardiovascular disease is a particularly good candidate for a developmental perspective given that atherosclerosis begins and is evident in youth (Kavey et al., 2003; McGill et al., 2000; Strong et al., 1999), and that CVD risk factors are generally stable across time (Morrison, Friedman, & Gray-McGuire, 2007). As such, CV risk factors observed in adolescence are likely to still be present in adulthood.

Adolescence is also of special interest psychologically, given that major socio-emotional changes occur during this period. Indeed, adolescence is a time when many youth struggle for independence from their parents, have their first romances, assemble their own friendship networks, and navigate the interpersonal complexities of their school and social environments. These considerations make adolescence a rich time of life to observe everyday social interactions and their biological consequences. Although most research has focused on young adults or older, there has been some research on children and adolescents that suggests social relationships in youth are linked to adult health outcomes, and that aspects of social relationships are fairly stable from childhood to adulthood. For example, Caspi and colleagues (2006) followed participants from birth through to their late twenties. They reported that social isolation in childhood was prospectively associated with poorer metabolic and CV health in adulthood, and social isolation in childhood and adolescence increased the risk of being socially isolated as an adult (Caspi et al., 2006).

Several studies have explored the metabolic syndrome in childhood and adolescence, but as of yet no one has determined whether social interactions are predictive of the metabolic syndrome in such a young age group. Given the stability of CV risk factors, the early evidence of

atherosclerosis, and that adolescence is a period during which social relationships begin to solidify and stabilize, adolescence is a potent developmental period in which to assess whether quality of social encounters is predictive of the metabolic syndrome. Thus, a third purpose of this thesis is to explore how these linkages play out in adolescence.

Specific aims and hypotheses

Based on a thorough review of the literature, a number of gaps were identified in the social relationship-CVD literature. First, relatively little is known about how quality of social interactions, both positive and negative, affect physiological processes, and whether positive encounters may buffer any consequences of negative ones. Second, the role that personality traits and general affect plays in the association between social encounters and metabolic syndrome is also not well understood: do social encounters act independently of these constructs? And third, it is unclear how social encounters may influence disease course from a developmental perspective. Given that adolescence is a time period during which social relationships are explored and social habits begin to take shape, this is a developmental period that is of particular interest. Healthy adolescents generally do not have overt CVD, but components of the metabolic syndrome can emerge at this phase of life, and tend to be fairly stable across time (Goodman, Daniels, Meigs, & Dolan, 2007; Morrison et al., 2007). As such, we were interested in whether quality of social encounters is predictive of the metabolic syndrome components in a sample of adolescents, and whether this relationship is independent of by personality and affect. The following is hypothesized:

Hypothesis 1. A relationship between quality of social encounters and the trajectory of metabolic syndrome symptoms over follow up will be observed in adolescents.

Hypothesis 2. Negative social encounters would be predictive of increasing metabolic syndrome symptoms over the follow up.

Hypothesis 3. Positive social encounters would not be independently predictive of metabolic syndrome symptoms, but will interact with negative encounters such that positive encounters attenuate any increase in metabolic syndrome symptoms.

Hypothesis 4. Positive and negative social encounters will be independently predictive of metabolic syndrome symptoms over follow up, such that controlling for personality traits (neuroticism, agreeableness, and extraversion) and negative affect will not affect the relationship.

Methods

Participants

Data were collected as part of a larger project on depression and atherosclerosis in young women at risk for affective disorders. The participants were recruited from the Vancouver, BC community through advertisements. Eligibility criteria included being (1) female, 15-19 years old, and fluent in English, (2) free of acute illness in the past 2 weeks, and (3) without a history of chronic medical or psychiatric disorders. A total of 157 young women were enrolled in the study; our analyses included only the 147 participants who were recruited to be at high risk for developing an initial episode of depression. High-risk was defined as having a first-degree relative with a history of affective disorder, and/or scoring in the top quartile of the population on cognitive vulnerability to depression. (The other 10 participants, who were excluded from these analyses, were enrolled as low-risk controls.) Over the course of the 2 year follow-up, 25 of the 147 admissible participants were lost to attrition (17.0%): 6 of them moved away, we lost contact with 4, and 15 withdrew. Thus, the final sample consisted of 122 young, healthy female participants. All procedures and methods were approved by the University of British Columbia Research Ethics Board. Written consent was obtained from all participants prior to participation. For participants younger than 18 years of age, a parent or guardian consent was also obtained.

Procedure

Participants visited the research centre on six occasions over a 2.5 year period. The analyses in this manuscript focus on the data gathered at study entry, 12 and 24 months later (referred to hereafter as Visits 1, 2, and 3, respectively.) These were the only study visits in which daily social interactions and metabolic symptoms were assessed. At each visit, participants

arrived between 8 and 11 AM, following an overnight fasting period. After obtaining informed consent, participants completed a battery of interviews and questionnaires, described in more detail below, which were used to evaluate alternative explanations such as mood, personality characteristics, and health practices. Blood pressure values, waist circumference and a blood sample for assessment of high density lipoproteins (HDL), triglycerides, and glucose were obtained (see below for details). Following the testing sessions at Visits 1 and 2, participants were given a Palm Pilot which prompted them to rate the quality of social encounters in daily life. The diary was completed twice daily over a two-day period using a format similar to the Rochester Interaction Record (see below). In addition, participants were also asked questions about daily physical activity practices.

Measures

Perception of social encounters. On each day of monitoring, participants were queried twice about their social interactions (4 and 14 hours after waking). The first item asked if they had interacted with their closest friend, romantic partner, parent/guardian, and other friends since the last diary entry. For each category of interaction answered 'yes,' the Palm Pilot prompted them to rate the encounter(s) on 8 negative (conflict, criticism, disappointment, exclusion, sense of inferiority, anger, shame or embarrassment, prying) and 7 positive (pleasantness, intimacy, helpful advice, helpful assistance, care, sense of confidence, value or respect) dimensions. These items were drawn from the Rochester Interaction Record (Reis, & Wheeler, 1991) and the Diary of Ambulatory Behavioral States (Kamarck et al., 1998). Ratings were made on a 0 (not at all) to 4 (very much/a lot) scale. For each encounter, composite positive and negative scales were calculated by averaging ratings across the appropriate dimensions. Both of the scales were internally consistent, with Cronbach's $\alpha = 0.75$ for negative perception of social encounters and

$\alpha = 0.82$ for positive. Scores on the negative scale could range from 0 to 32, whereas those on the positive scale could range from 0 to 28. Scores on the two scales were inversely correlated in a modest fashion, $r = -0.17$, $p = 0.05$. Participants' ratings of their interactions were fairly stable over time: over the year that elapsed between diary ratings at Visits 1 and 2, the stability of scores on the negative scale was $r = 0.36$ ($p < 0.001$) and on the positive scale was $r = 0.60$ ($p < 0.001$). Thus, ratings were collapsed across these periods to form more trait-like indicators of positive and negative interaction tendencies. Each of these indicators was comprised of 8 separate diary entries (2 entries per day, for 2 days, at both Visits 1 and 2), which could have included ratings of up to 4 separate social encounters each.

Metabolic risk. Following recommendations as issued in a joint statement by the American Heart Association and National Heart, Lung and Blood Institute, metabolic risk was assessed by considering levels of HDL and triglycerides, as well as fasting glucose, SBP and DBP, and waist circumference (Grundy et al., 2005). To measure resting SBP and DBP, participants were seated in a chair with an occluding cuff on one arm. Following a 5-minute rest period, 4 BP readings, spaced 2 minutes apart, were collected using an automatic, calibrated, oscillometric BP monitor (BPM-100, VSM MedTech, Coquitlam, BC). Appropriately sized BP cuffs were selected according to the diameter of the participant's arm. Average SBP and DBP were calculated by averaging the last 3 measures (the first reading is excluded as it tends to be elevated due to the novelty of the procedure). This device and protocol has been validated in pediatric populations and yield BP readings that meet the standards of the British Hypertension Society for accuracy and reliability (Mattu, Heran, & Wright, 2004).

Waist circumference was measured from the side at the midpoint between the upper iliac crest and lower costal margin at the mid-axillary line using a standard measuring tape. Measurements were taken at least twice, and repeated until a consistent reading was obtained.

Overnight fasting blood samples were collected at each visit to quantify other metabolic parameters. A 10 mL sample of blood was collected into a serum separator Vacutainer tube (Becton-Dickinson, Oakville ON) through antecubital venipuncture. The sample was spun for 12 minutes at 1200 x g. After the serum had been aspirated, it was frozen at -30 C until assayed in batch. The analyses were performed in the Clinical Chemistry laboratory of St Paul's Hospital in Vancouver. Triglycerides were determined enzymatically on a Hitachi 747 (Kyowa Medex, Japan) after hydrolysis to glycerol. This method has an inter-assay coefficient of variation of 1.1%. High-density lipoprotein was measured using standard enzymatic techniques with cholesterol esterase and cholesterol oxidase, after low-density, intermediate density, and very-low density lipoproteins had been precipitated through centrifugation, on a Hitachi 911 instrument (Kyowa Medex, Japan). This method has an inter-assay coefficient of variation of 5.1%. Glucose was measured with an enzymatics technique that uses hexokinase and glucose-6-phosphate dehydrogenase enzymes on an ADVIA 1650 Chemistry System (Bayer Diagnostics, Tarrytown, NY) with an inter-assay coefficient of variation of 1.2%.

Because our sample was recruited to be young and healthy, none of the participants met criteria for diagnosis with the metabolic syndrome either at study entry or during the follow-up period. Therefore, in order to model the evolution of metabolic risk during follow-up, and based on previous research that has focused on these processes in healthy youth (e.g., Eisenmann, 2008; Ekelund et al., 2005), we computed a composite score comprised of values on the six components of the metabolic syndrome: HDL, triglycerides, fasting blood glucose, waist

circumference, SBP and DBP. Scores on each component were converted to a *z*-score; HDL was reverse coded to match risk direction of the others. Composite metabolic risk was then calculated for each visit by averaging the *z* scores across components. Scores were fairly stable across time, with correlations of 0.47 ($p < 0.001$) and 0.44 ($p < 0.001$) across one and two years of follow-up, respectively.

Alternative explanations. Several other variables were assessed as potential alternative explanations for any association observed between social interaction tendencies and metabolic risk trajectories. These included demographic characteristics (age, ethnicity, SES), oral contraceptive (OC) use, depressed mood (as measured by the Beck Depression Inventory (BDI), see below), daily physical activity, and neuroticism, agreeableness and extraversion (as measured by the Big Five Inventory (BFI), see below). Socioeconomic status was indexed by the highest years of education completed by either the participant's mother or father.

Depressed mood. Depression has profound influences on the quantity and quality of people's social interactions, and is also independently associated with increased risk for the metabolic syndrome and CVD more generally (Kinder et al., 2004; Rugulies, 2002). Coupled with the fact that this sample was recruited specifically to be at risk for affective disorders, these considerations led us to consider whether depression was underlying any observed associations between social interactions and metabolic outcomes. Thus, we had participants complete the BDI (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) at Visits 1, 2 and 3. The BDI is a widely used measure of the intensity of depressive symptoms. It consists of 21 items assessing symptoms and attitudes of depression experienced during the past week, with possible scores for each question ranging from 0 to 3. The BDI was internally consistent in our sample, with an average Cronbach's α of 0.93 across visits.

Neuroticism, agreeableness, and extraversion. Personality was assessed at Visit 1 using the BFI (1991), a 44-item inventory that provides assessment of the Big Five dimensions of personality. Participants are asked to rate the degree to which they agree with a characteristic presented in a statement, with responses ranging from 1 (strongly disagree) to 5 (strongly agree). For the purposes of this article, we considered 3 dimensions closely linked to social interactions and health outcomes in past research: neuroticism, which is characterized by traits like tenseness, moodiness, and anxiety (8 items) (Cronbach's $\alpha = 0.76$); extraversion, which encompasses traits like talkative, energetic, and assertive (8 items) (Cronbach's $\alpha = 0.84$); and agreeableness, which includes traits like sympathetic, kind and affectionate (9 items) (Cronbach's $\alpha = 0.75$).

Physical activity. Low levels of physical activity have been associated general negative mood (e.g., Dunn, Trivedi, & O'Neal, 2001; Janisse, Nedd, Escamilla, & Nies, 2004; Penedo, & Dahn, 2005; Scully, Kremer, Meade, Graham, & Dudgeon, 1998) and increased risk of the metabolic syndrome (e.g., Ekelund et al., 2005; Laaksonen et al., 2002; Lakka et al., 2003). To rule out physical activity as a possible confound, we chose to include it as a control variable in analyses. At the end of each day of monitoring participants were asked about physical activity using an item from the Paffenbarger Activity Scale (Paffenbarger, Blair, Lee, & Hyde, 1993). They were asked "Did you engage in any activity today akin to brisk walking, jogging, bicycling, etc., long enough to work up a sweat?" If they responded affirmatively, they were asked for how long. The average per-day minutes of exercise was then averaged over the monitoring periods following Visits 1 and 2. This approach to assessing physical fitness has been validated in previous research, which shows that self-reported brisk activity is related to VO2 max scores during treadmill tests (Paffenbarger et al., 1993).

Results

The sample consisted of healthy adolescent females, as can be seen from the information presented in Table 1. Participants were primarily of Asian and European descent, and whose parents had, on average, a university education. Table 2 contains descriptive statistics for individual components of the metabolic index. Over the two-year follow-up period the sample as a whole displayed increases in HDL, $F(1.8, 169) = 8.384$, $p = 0.001$, and glucose, $F(2, 184) = 4.951$, $p = 0.008$. There was also a trend towards increasing SBP over follow-up, $F(2, 184) = 2.452$, $p = 0.081$. The sample as a whole did not show changes in triglycerides, $F(1.5, 134) = 1.19$, $p = 0.296$, DBP, $F(2, 184) = 0.346$, $p = 0.708$ or waist circumference, $F(1.8, 167) = 0.682$, $p = 0.494$, over time. The sample as a whole did not show changes in the metabolic composite over the follow-up period, p = .75. However, further analyses revealed that there was marked within- and between-person variability in metabolic trajectories. The intra-class correlation for the metabolic composite was 0.54, indicating that about half of the total variance in this construct over time was between participants. The other half was due to within-person changes and person by time interactions. These figures suggest that there is sufficient variability in metabolic trajectories in the sample to justify exploring the potential influence of participants' social encounters.

Table 1. Characteristics of the Sample (N = 122)

Variable	Mn +/- SD or Number (%)
Ethnicity	
European descent	67 (48.6)
Non-European descent	71 (51.4)
Age (years)	17.0 +/- 1.34
SES (highest parental years of education)	16.1 +/- 2.96
Using oral contraceptives	27 (19.9)
Intensity of social encounters	
Average negative encounter (0-32)	3.13 +/- 2.45
Average positive encounter (0-28)	11.6 +/- 3.57
Average daily brisk physical activity (minutes)	23.4 +/- 27.1
Agreeableness	33.6 +/- 5.19
Neuroticism	24.6 +/- 5.52
Extraversion	26.5 +/- 5.80
Depressed mood from BDI	
Visit 1	7.18 +/- 5.91
Visit 2	6.77 +/- 5.69
Visit 3	6.00 +/- 5.18

Table 2. Descriptive statistics for metabolic parameters over the course of study.

Variable	Mn +/- SD or Number (%)
HDL (mmol/L)	
Visit 1	1.48 +/- 0.282
Visit 2	1.52 +/- 0.297
Visit 3	1.58 +/- 0.306
Triglycerides (mmol/L)	
Visit 1	0.865 +/- 0.342
Visit 2	0.964 +/- 0.747
Visit 3	0.961 +/- 0.417
Fasting blood glucose (mmol/L)	
Visit 1	4.52 +/- 0.356
Visit 2	4.53 +/- 0.483
Visit 3	4.65 +/- 0.385
Systolic BP (mmHg)	
Visit 1	105 +/- 8.43
Visit 2	103 +/- 8.61
Visit 3	103 +/- 9.91
Diastolic BP (mmHg)	
Visit 1	66.7 +/- 7.77
Visit 2	66.6 +/- 8.28
Visit 3	67.4 +/- 8.81

Table 2 continued. Descriptive statistics for metabolic parameters over the course of study.

Variable	Mn +/- SD or Number (%)
Waist circumference (cm)	
Visit 1	72.0 +/- 7.33
Visit 2	71.3 +/- 6.37
Visit 3	71.8 +/- 7.91

Statistical approach

To determine whether perceived quality of social encounters predicted changes in metabolic risk over time, we estimated a series of multi-level models with HLM 6.08 (Raudenbush, Bryk, & Congdon, 2006). The within-person (level 1) models included a variable reflecting time since study entry (in months). The between-person (level 2) models included the relevant indices reflecting social interactions, as well as 5 standard control variables: age, ethnicity (European descent vs. non-European descent), OC use, parental education, and average minutes of physical activity. In later models we added depressive symptoms and personality characteristics as covariates, to evaluate their role in shaping the observed associations. In all cases we estimated random slope models, in which Level 2 error terms were allowed to vary freely. Models were estimated with robust standard errors.

Preliminary results

To estimate how much the control variables explained metabolic change over time, we ran an initial model that included time from study entry at level-1, and age, ethnicity, oral contraceptive use, and parental education at level-2. The results are presented in Table 3. Age

was associated with change in metabolic composite over time, b = $3.85x10^{-3}$, SE = $1.68x10^{-3}$, p = 0.024, such that participants who were older at study had larger increases in metabolic composite scores over the follow-up. None of the other standard control variables was associated with the metabolic composite, either at study entry or over time.

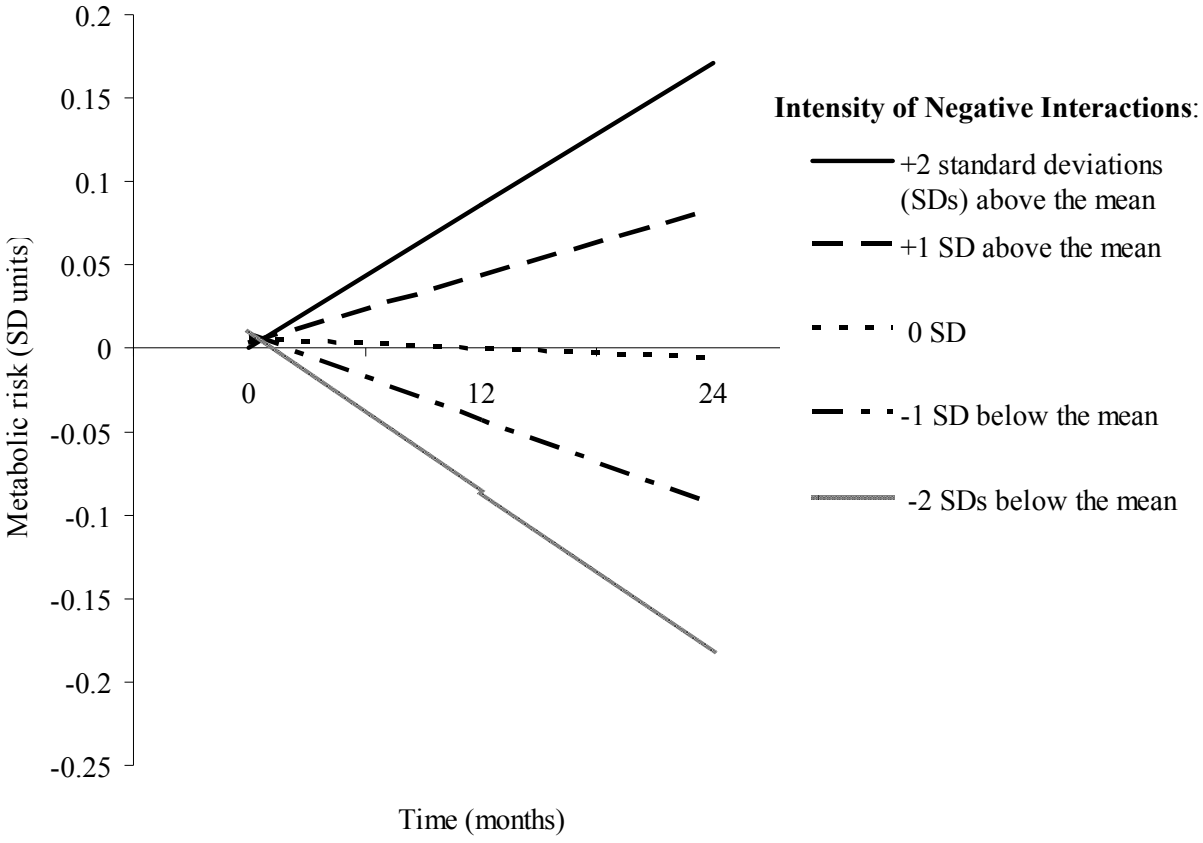
Table 3. Results of HLM model predicting metabolic profiles over time from control variables.

Variable	b	SE	p
Intercept (Baseline)			
Ethnicity	-0.105	0.080	0.193
Age	-0.033	0.030	0.281
SES	-0.015	0.014	0.309
Physical Activity	$1.73x10^{-4}$	$1.61x10^{-3}$	0.915
OC	0.046	0.097	0.632
Slope (Trajectory)			
Ethnicity	$-1.66x10^{-3}$	$3.91x10^{-3}$	0.672
Age	$3.85x10^{-3}$	$1.68x10^{-3}$	0.024
SES	$5.49x10^{-4}$	$7.78x10^{-4}$	0.482
Physical Activity	$7.40x10^{-5}$	$8.10x10^{-5}$	0.363
OC	$-2.22x10^{-3}$	$5.17x10^{-3}$	0.668

Positive and negative social encounters

Next we evaluated our principal hypotheses by including variables reflecting the quality of social interactions in the level-2 models. As Table 4 shows, older subjects, $b = 4.15\text{x}10^{-3}$, $SE = 1.67\text{x}10^{-3}$, $p = 0.015$, continued to show larger increases in metabolic symptoms over the follow-up. Over and above the contribution of the control variables, negative social interactions were associated with metabolic composite trajectories. As Figure 1 shows this was a positive association, such that participants who had more intense negative social encounters in day-to-day life showed increasing scores on the metabolic composite over the 2-year follow-up, $b = 3.79\text{x}10^{-3}$, $SE = 1.91\text{x}10^{-3}$, $p = 0.049$. Conversely, participants with less intense negative encounters showed a decline in metabolic composite scores over time.

Figure 1. Negative social encounters and metabolic composite scores over two years. Participants who had more negative social encounters in day-to-day life showed increasing scores on the metabolic composite over follow-up, $b = 3.79\text{x}10^{-3}$, $SE = 1.91\text{x}10^{-3}$, $p = 0.049$. Conversely, participants with fewer negative social encounters showed a decline in metabolic composite scores over the same timeframe.



Further analyses revealed that there was no association between the intensity of positive encounters and the metabolic composite at baseline, $b = -0.10$, $SE = 6.2\text{x}10^{-2}$, $p = 0.10$, or over follow-up, $b = 3.34\text{x}10^{-3}$, $SE = 1.9\text{x}10^{-3}$, $p = 0.083$ (Table 5). There also was no evidence of a statistical interaction between the two dimensions of social encounters, $b = 3.5\text{x}10^{-4}$, $SE =$

$2.0x10^{-3}$, $p = 0.86$ (Table 6). Thus, positive encounters did not offset the apparent metabolic consequences of negative ones.

Table 4. Results of HLM model predicting metabolic profiles over time from control variables and negative social interactions.

Variable	b	SE	p
Intercept (Baseline)			
Ethnicity	-0.103	0.082	0.211
Age	-0.034	0.030	0.265
SES	-0.015	0.015	0.322
Physical Activity	1.67×10^{-4}	1.61×10^{-4}	0.918
OC	0.045	0.098	0.644
Negative Encounters	-2.52×10^{-3}	0.048	0.959
Slope (Trajectory)			
Ethnicity	-2.60×10^{-3}	3.79×10^{-3}	0.495
Age	4.15×10^{-3}	1.67×10^{-3}	0.015
SES	3.85×10^{-4}	7.49×10^{-4}	0.607
Physical Activity	7.00×10^{-5}	7.80×10^{-5}	0.369
OC	-3.61×10^{-3}	5.13×10^{-3}	0.483
Negative Encounters	3.79×10^{-3}	1.91×10^{-3}	0.049

Table 5. Results of HLM model predicting metabolic profiles over time from control variables and positive social interactions.

Variable	b	SE	p
Intercept (Baseline)			
Ethnicity	-0.104	0.079	0.193
Age	-0.023	0.031	0.465
SES	-9.86×10^{-3}	0.015	0.518
Physical Activity	2.09×10^{-4}	1.59×10^{-4}	0.896
OC	0.052	0.097	0.589
Positive Encounters	-0.103	0.062	0.100
Slope (Trajectory)			
Ethnicity	-1.18×10^{-3}	3.96×10^{-3}	0.766
Age	3.52×10^{-3}	1.70×10^{-3}	0.040
SES	4.47×10^{-4}	7.88×10^{-4}	0.766
Physical Activity	7.40×10^{-5}	8.50×10^{-5}	0.392
OC	-2.57×10^{-3}	5.21×10^{-3}	0.622
Positive Encounters	3.34×10^{-3}	1.91×10^{-3}	0.083

Table 6. Results of HLM model predicting metabolic profiles over time from control variables and the interaction between positive and negative encounters.

Variable	b	SE	p
Intercept (Baseline)			
Ethnicity	-0.088	0.083	0.288
Age	-0.020	0.032	0.524
SES	9.24×10^{-3}	0.015	0.537
Physical Activity	1.09×10^{-3}	1.69×10^{-4}	0.520
OC	0.130	0.107	0.226
Negative Encounters	-0.038	0.054	0.489
Positive Encounters	-0.080	0.050	0.113
Interaction Term	0.156	0.081	0.055
Slope (Trajectory)			
Ethnicity	-1.96×10^{-3}	3.78×10^{-3}	0.604
Age	3.85×10^{-3}	1.68×10^{-3}	0.024
SES	2.76×10^{-4}	7.51×10^{-4}	0.714
Physical Activity	6.60×10^{-5}	8.30×10^{-5}	0.428
OC	-4.39×10^{-3}	5.29×10^{-3}	0.408
Negative Encounters	4.44×10^{-3}	2.05×10^{-3}	0.032
Positive Encounters	3.99×10^{-3}	1.92×10^{-3}	0.039
Interaction Term	-3.49×10^{-4}	1.99×10^{-3}	0.861

Alternative explanations

The final models evaluated alternative explanations. We began by testing whether symptoms of depression might be driving the observed associations. Beck Depression Inventory scores from Visits 1, 2 and 3 were added to the level-1 models. However, the intensity of negative social encounters continued to predicted changes in the metabolic composite under these conditions, $b = 5.4\text{x}10^{-3}$, $SE = 2.1\text{x}10^{-3}$, $p = 0.013$, suggesting this association was not being driven by underlying depressive symptoms (Table 7).

We next evaluated the contribution of the personality traits extraversion, neuroticism, and agreeableness. Variables reflecting these traits were added to the level-2 equations in separate models. None of the variables were associated with scores on the metabolic composite at study entry. Only extraversion was associated with changes in the metabolic composite, $b = 5.8\text{x}10^{-4}$, $SE = 2.9\text{x}10^{-4}$, $p = 0.05$. Moreover, the intensity of negative encounters continued to predict larger increases in metabolic composite scores over time when extraversion, $b = 4.0\text{x}10^{-3}$, $SE = 1.9\text{x}10^{-3}$, $p = 0.037$ (Table 8), neuroticism, $b = 3.9\text{x}10^{-3}$, $SE = 1.9\text{x}10^{-3}$, $p = 0.045$ (Table 9), and agreeableness, $b = 4.3\text{x}10^{-3}$, $SE = 1.9\text{x}10^{-3}$, $p = 0.027$ (Table 10) were in the model, suggesting these traits were not driving the observed associations.

Table 7. Results of HLM model predicting metabolic profiles over time from control variables, negative social encounters, and depressed mood (level 1).

Variable	b	SE	p
Intercept (Baseline)			
Ethnicity	-7.85×10^{-3}	0.131	0.953
Age	-0.050	0.053	0.348
SES	-3.45×10^{-3}	0.021	0.868
Physical Activity	1.37×10^{-3}	2.38×10^{-3}	0.565
OC	0.288	0.160	0.073
Negative Encounters	-0.088	0.070	0.210
Slope (Trajectory)			
Ethnicity	-5.42×10^{-3}	4.69×10^{-3}	0.251
Age	4.90×10^{-3}	1.83×10^{-3}	0.009
SES	2.81×10^{-4}	7.51×10^{-4}	0.709
Physical Activity	6.60×10^{-5}	9.00×10^{-5}	0.464
OC	-7.53×10^{-3}	5.64×10^{-3}	0.185
Negative Encounters	5.41×10^{-3}	2.40×10^{-3}	0.026

Table 8. Results of HLM model predicting metabolic profiles over time from control variables, negative social encounters, and extraversion.

Variable	b	SE	p
Intercept (Baseline)			
Ethnicity	-0.120	0.079	0.133
Age	-0.037	0.030	0.215
SES	-0.012	0.015	0.399
Physical Activity	3.01×10^{-4}	1.57×10^{-4}	0.849
OC	0.057	0.101	0.575
Extraversion	-0.012	7.60×10^{-3}	0.113
Negative Encounters	-7.88×10^{-3}	0.050	0.874
Slope (Trajectory)			
Ethnicity	-1.86×10^{-3}	3.91×10^{-3}	0.634
Age	4.31×10^{-3}	1.67×10^{-3}	0.011
SES	2.84×10^{-4}	7.30×10^{-4}	0.698
Physical Activity	5.90×10^{-5}	7.90×10^{-5}	0.458
OC	-4.06×10^{-3}	5.13×10^{-3}	0.430
Extraversion	5.79×10^{-4}	2.93×10^{-4}	0.050
Negative Encounters	4.05×10^{-3}	1.92×10^{-3}	0.037

Table 9. Results of HLM model predicting metabolic profiles over time from control variables, negative social interactions, and neuroticism.

Variable	b	SE	p
Intercept (Baseline)			
Ethnicity	-0.132	0.080	0.103
Age	-0.023	0.032	0.469
SES	-0.013	0.015	0.387
Physical Activity	6.32×10^{-4}	1.60×10^{-3}	0.694
OC	0.040	0.101	0.693
Neuroticism	-0.014	9.57×10^{-3}	0.158
Negative Encounters	-9.21×10^{-3}	0.049	0.853
Slope (Trajectory)			
Ethnicity	-3.10×10^{-3}	4.40×10^{-3}	0.482
Age	4.17×10^{-3}	1.73×10^{-3}	0.017
SES	3.31×10^{-4}	7.57×10^{-4}	0.663
Physical Activity	7.30×10^{-5}	8.00×10^{-5}	0.363
OC	-4.08×10^{-3}	5.21×10^{-3}	0.436
Neuroticism	-5.50×10^{-5}	4.03×10^{-5}	0.893
Negative Encounters	3.87×10^{-3}	1.91×10^{-3}	0.045

Table 10. Results of HLM model predicting metabolic profiles over time from control variables, negative social interactions, and agreeableness.

Variable	b	SE	p
Intercept (Baseline)			
Ethnicity	-0.112	0.079	0.163
Age	-0.022	0.033	0.492
SES	-0.011	0.015	0.442
Physical Activity	7.07×10^{-4}	1.60×10^{-3}	0.658
OC	0.025	0.102	0.804
Agreeableness	-0.020	0.011	0.063
Negative Encounters	-0.035	0.053	0.508
Slope (Trajectory)			
Ethnicity	-2.54×10^{-3}	3.84×10^{-3}	0.509
Age	3.95×10^{-3}	1.72×10^{-3}	0.024
SES	3.31×10^{-4}	7.49×10^{-4}	0.659
Physical Activity	6.00×10^{-5}	8.00×10^{-5}	0.453
OC	-3.47×10^{-3}	5.16×10^{-3}	0.503
Agreeableness	2.93×10^{-4}	3.50×10^{-4}	0.404
Negative Encounters	4.27×10^{-3}	1.90×10^{-3}	0.027

Discussion

With mounting evidence that poor social relationships increase the risk of morbidity and mortality from CVD, greater focus has been placed on exploring and understanding the biological consequences of social relationships. However, relatively little research attention has been paid to social relationships in a developmental context, how quality of social encounters may relate to CVD and CVD outcomes, and whether personality traits and affect may influence any association between social encounters and CVD outcomes. The goal of this thesis was to address several gaps in the literature by determining whether the quality of day-to-day social interactions presaged changes in symptoms of the metabolic syndrome in a sample of healthy young women at risk for depression. Our first and second hypotheses were confirmed: we found evidence that the intensity of negative social encounters was associated with trajectories of metabolic risk over a two-year period. To the extent that our participants had more intense negative encounters in day-to-day life, participants showed increasing scores on the metabolic composite over follow-up. Conversely, participants with less intense negative social interactions showed a decline in metabolic composite scores over the same timeframe. This observation persisted after adjustment for age, ethnicity, SES, OC use, and daily physical activity. Our third hypothesis was not supported by the data: positive encounters were not associated with metabolic trajectories, and did not offset the apparent influence of negative ones. And finally, the data also supported our fourth hypothesis: the relationship between negative social encounters and metabolic syndrome trajectories was not accounted for by depressed mood or personality traits (agreeableness, neuroticism, and extraversion).

These results further our understanding of how everyday social interactions affect the development of metabolic processes involved in CVD. In doing so they may help to explain why

broader social relationship constructs, like perceived social support or social network diversity, relate to CVD outcomes in such a robust fashion. These results also suggest that the effect of social encounters on metabolic health is observable relatively early in development, and in otherwise healthy participants.

Negative social encounters and the metabolic syndrome

As stated above, we predicted that negative social interactions would be associated with worsening metabolic trajectories. The results were consistent with this hypothesis. To the degree that they experienced more intense negative encounters, participants showed increasing scores on the metabolic composite over time. In complement, those who experienced less intense negative encounters had decreasing scores in metabolic composite over time.

This association was fairly small in its magnitude, with each SD increment in negative interactions associated with a 0.0038 SD greater increase in metabolic composite trajectories. Differences of this size are unlikely to have any immediate clinical significance, especially in this sample of healthy adolescents. However, if this dynamic was sustained through adolescence and adulthood it could presumably contribute to the development of frank metabolic syndrome, either directly or by interacting with other factors to increase risk.

Apart from the potential clinical implications, these findings are noteworthy in two more theoretical respects: First, they suggest the presence of a graded association between social interactions and metabolic risk, whereby even small variations in people's tendencies to have negative exchanges seem to have biological repercussions. In short, there is no level at which negative social encounters suddenly become detrimental: any variation in negative social encounters presages variation in metabolic risk trajectories. Second, they suggest that this dynamic begins early in life, when people are still in good overall metabolic health. The

implication is that aversive social encounters, often viewed as a normative development experience for adolescents, may set off biological trajectories that, if sustained, ultimately contribute to the development of CVD.

When considered alongside the roughly linear effects that emerged for negative encounters, these results suggest that young women are likely to accrue more metabolic benefits by reducing the intensity of negative social interactions than increasing the intensity of positive ones. In this context, interventions that target particularly noxious social interactions, such as bullying and abusive romantic or parental relationships, and/or improving social skills that may help reduce negative encounters may not only improve current quality of life, but may offset future CVD development.

Positive social encounters: do they matter at all?

We also expected that positive social interactions would relate to better metabolic outcomes, or at least offset the consequences of negative encounters. However, neither of these hypotheses was borne out. These findings indicate that, at least in our sample, there are no metabolic benefits associated with having regular positive social interactions. In general, this pattern of findings is consistent with the literature on well-being, which suggests that negative events tend to be more impactful than positive ones (Baumeister et al., 2001; Finch et al., 1989; Finch at al., 1999; Newsom, Rook, Nishishiba, Sorkin, & Mahan, 2005; Rook, 2001; Schuster et al., 1990). It is also consistent with a study of BP responses to marital conflict, which concluded that "not being nasty matters more than being nice" (Ewart, Taylor, Kraemer, & Agras, 1991, p. 155).

Even so, there remains a strong body of research that suggests that there are numerous physiological, cognitive and affective benefits to having access to social support, which is

considered a form of positive social interaction, in the face of negative or stressful events. There is also an intuitive appeal to believing that positive social encounters are beneficial, if only for the positive feelings that accompany and follow them. So what is going here? Why does social support buffer the negative consequences of life stressors, including negative encounters, and yet so little research has reported any benefit of positive encounters in general? Why does something that most people would consider and report as beneficial have no actual, apparent benefit?

It is always possible that the null findings herein stem from problems with the study's research design. For example, our social encounters sampling method assumed that social interactions are positive and negative, but it is also possible that other (e.g. neutral) or sub-categories (e.g. exchange of support) of social encounters exist that we did not assess here. In short, how participants rated their social encounters may have been somewhat restricted or limited by the items we used to assess social encounters. Negative interactions are easier to identify: they involve conflict, criticism, disappointment, a sense of not being wanted and inferiority, and induce anger and shame. They are stressors, produce stress-associated physiological responses, and are easily identifiable as uncomfortable, undesirable or just plain 'bad.'

On the other hand, positive encounters may be more nebulous and/or complex. An encounter that is not negative is also not necessarily positive, and a neutral encounter is more likely to be lumped into the positive encounter than the negative encounter category. Furthermore, not all positive encounters may take the same shape or form. For example, our positive encounter items could be split roughly into "supportive" (expressed care or concern, expressed confidence, provided oral support, provided instrumental support) and "just pleasant" (pleasant, intimate, respectful) categories, although a factor analysis would be needed to confirm

this. It is possible that positive interactions may be beneficial, but only if they are of a particular kind and occur at a particular time. For example, positive encounters that occur during a stressor (particular time) and are supportive (particular kind) may be able to buffer the effects of that stressor. On the other hand, positive encounters that are supportive in the absence of a stressor would not confer protection because there is nothing from which to protect. In the same vein, positive encounters that are merely pleasant when support is needed would also not be expected to be helpful or protective.

As such, we may not have observed any association between positive encounters and metabolic syndrome symptoms here for two reasons: First, because our measure of positive interactions did not differentiate between type of positive encounter. Instead, our measure consisted of both "pleasant" and "supportive" items and it is possible that any benefit of predominately "supportive" encounters may have been masked by ones that were merely "pleasant." It is equally possible that our positive encounter questions did not adequately tap into those dimensions of social encounters (for example, support) that may be beneficial to health, or that positive encounters would've emerged as more influential had we considered them in the context of stressful events or other times when people needed support. In future, it would be interesting to determine which aspects of positive encounters (supportive or pleasant) may be linked to health.

The second reason we may not have observed any association between positive encounters and metabolic syndrome symptoms may have to with the timing of our assessments. One potential methodological weakness is the brevity of our daily diary sampling period, which occurred only twice over a year period, and for only two days at each assessment. It is possible that this window may have been too narrow to capture the full extent of our participants' positive

encounters, especially if they occur infrequently, and/or it may have been too short to capture the rare but intense negative encounters that could be attenuated by positive interactions. However, our participants tended to rate their social encounters as more positive than negative, suggesting that either only extremely positive social encounters can counter the effect of negative encounters, or that some threshold exists such that positive social encounters can only counter the deleterious effects of highly but not moderately negative social exchanges. Although this is possible, it is more likely that our two-day sampling period was too short to capture any after-stressor (or negative encounter) positive social exchanges that may have been beneficial. As such, it would be interesting in future to lengthen the social encounter assessment period, in order to see if there is a temporal relationship between stressors, positive social encounters and changes in metabolic risk, and if intensity of negative and positive encounters influences any effect of positive social exchanges.

Mechanisms

Though these data suggest that negative interactions worsen metabolic symptoms over time, the underlying mechanism through which this process occurs is not yet understood. Our analyses help to eliminate some of the more plausible explanations, such as confounding by age, ethnicity, SES, and physical activity. In short, this relationship does not appear to be the result of demographics or health behaviours. The observed patterns also do not seem to be a result of negative affect or personality characteristics like neuroticism, agreeableness, and extraversion, which shape the quality of people's social encounters and also have been related to CVD outcomes. It is possible that other confounds exist that we did not consider, measure or include in our analyses. For example, it is possible that the more narrow facets of personality not captured by the Big 5's major dimensions could play a role in the relationship between negative social

encounters and metabolic composite scores, and future research should explore this possibility. But it is also possible that metabolic health may be somehow directly affected by negative encounters. In short, that negative encounters may get 'under the skin' to directly influence metabolic processes.

Assuming that the association between negative social encounters and changes in metabolic profiles reflect a process that is causal in nature, changes in metabolic composite scores could be driven by the direct biological consequences of the negative social encounters themselves. As we noted earlier, negative encounters have been associated with changes in the CV, neuroendocrine and immune systems that may increase the risk of developing CVD. For example, acute episodes of social conflict have been observed to raise BP (Gallo et al., 2006; Kamarck et al., 2002), which is a component of the metabolic syndrome. Conflictual interactions also trigger activity of the SNS and the HPA axis (Graham et al., 2007; Heffner et al., 2004; Kiecolt-Glaser et al., 1996; Kiecolt-Glaser et al., 1997; Kiecolt-Glaser et al., 2005), whose hormonal products are thought to increase fat accumulation and impair glucose control, among other things (Bjorntorp et al., 1999; Brunner et al., 2002). And in young women, more chronic exposure to negative social encounters has been prospectively linked to upregulation of inflammatory processes (Miller, Rohleder, & Cole, 2009), which are known to play a key role in the pathogenesis of most components of the metabolic syndrome (Hotamisligil, 2006). It will be important for the next wave of studies in this area to evaluate the role these proposed mechanisms may play in the link between social encounters and metabolic trajectories.

Developmental context

Future research is also needed to explain the temporal dimension of our findings, both across the two years of follow up here and beyond adolescence. In particular, the metabolic

disparities associated with abrasive encounters were not apparent at baseline, but seemed to gradually accumulate as the study's follow-up period progressed. The reasons for this pattern are unclear. During adolescence there are profound changes in body size and shape, as well as BP, insulin resistance, and other metabolic processes related to CVD (e.g., see Moran et al., 2008). There are also considerable within-person symptom fluctuations. For example, although the underlying metabolic syndrome factor is consistent throughout adolescence, there is enough fluctuation in the symptoms themselves to result in 50% of youth who have been classified as having metabolic syndrome to lose their diagnosis within 3 years (Goodman et al., 2007). It may be that our observations occurred during a particularly important developmental phase during late adolescence, when fluctuations in metabolic syndrome symptoms begin to subside and stable, adult trajectories begin to take shape.

We also do not yet know how stable this relationship is over time, beyond our two years of observation. It is possible that the relationship between negative social encounters and the metabolic syndrome symptoms will persist into adulthood, and it is possible that these results are generalizable to older and younger samples, but as of yet there is no research to support these assertions. Further research is necessary to assess whether this relationship holds during childhood and early adolescence, and whether metabolic syndrome composite trajectories are stable across adulthood.

Potential for interventions

Meanwhile, as suggested above, there could be value in targeting social processes as a way to intervene and slow early disease processes. If our findings do indeed reflect a causal process, interventions that reduce the frequency and/or severity of negative interactions could have consequences for metabolic trajectories. Targeting social encounters may also be a

particularly effective intervention target due to social relationships' wide influence on overall health and well-being. Indeed, there is evidence that family systems therapy, which aims to improve parent-child relationships, can improve blood glucose control in teenagers with diabetes (Wysocki et al., 2007).

Another potential intervention target is bullying, a particularly noxious negative social interaction. Although no research has yet directly assessed any relationship between bullying and CVD in adolescence and childhood, research in adults suggests that victims of work-place bullying are at increased risk for CVD (e.g., Kivimaki et al., 2001; Tuckey, Dollard, Saebel, & Berry, 2009). Bullying in adolescence and childhood has been associated with increased risk for emotional problems (e.g., Bond, Carlin, Thomas, Rubin, & Patton, 2001) and poorer health-related quality of life (e.g., Frisen, & Bjarnelind, 2010), and being the victim of bullying as a child or adolescence is associated with poorer self-reported health as an adult (Allison, Roeger, & Reinfeld-Kirkman, 2009). Although research is required to establish if this is the case, it is conceivable that being the victim of bullying, a specific type of negative encounters, could also affect metabolic health and risk for CVD. If so, then targeting bullying may be another way to both improve immediate quality of life in children and adolescents, and reduce future risk of metabolic and CVD.

Limitations and future directions

This study has several limitations that should be considered. First, because it focused on young women who were at risk for affective disorders, it is unclear how well the results can be generalized to other populations. The women studied herein may be especially sensitive to negative social encounters, and some may have attributional tendencies that would exaggerate responsibility for and consequences of abrasive interactions that occurred with friends, family, or

even strangers. It is also possible that the social relationships and social networks of young men are somehow different from those of young women, in terms of their structure and influence on the individual. In addition, we also do not know how differences in social network maturity, from childhood to adulthood, may influence this relationship. Thus, replication of these findings in other populations is necessary before they can be safely generalized.

Related to the above limitation, and as stated above, we do not yet know if the relationship between negative social encounters and the metabolic syndrome symptoms is stable over time and across developmental periods. As such, in addition to replication in other populations, longitudinal research across developmental periods is needed in order to determine long-term stability.

Second, our daily diary sampling was limited to two 48-hour periods. Although this duration was adequate to capture the individual differences in negative interactions that associated with metabolic trajectories, it may have been too short to tap positive encounters that may have been impactful or too short to assess any temporal relationship between negative events and positive encounters. In future, more extended periods of sampling would help to alleviate this concern, and allow for a more robust test of the hypotheses we considered.

Third, as is the case with any study that has an observational design, there are potential alternative explanations for our findings that involve as yet unthought-of of or unmeasured confounds. Particularly worrisome in this regard are genetic liabilities that predispose individuals to both abrasive social encounters and symptoms of metabolic syndrome. One especially rigorous way to evaluate whether our findings are causal in nature would be to assess metabolic endpoints in people who received (or did not receive) an intervention to improve the quality of their social interactions (e.g., couples therapy). Related to this limitation is the fact that we did

not assess potential underlying physiological mechanisms, such as CV, neuroendocrine, and immune system function. If negative social encounters do have a direct, causal influence on metabolic risk, then the underlying mechanisms should be identified in future research.

And finally, our measures of encounters were fairly crude, in that we did not determine how more minute or intricate aspects of social encounters could affect metabolic composite trajectories, or whether facets of personality traits or mood could influence this relationship. For example, does this relationship persist across all types of negative social encounters, such as bullying and abrasive marital encounters? Again, future research should examine these possibilities in order to improve generalizability of these observations.

Conclusions

In summary, this study's findings suggest that, in adolescent females, there is a graded association between the negativity of social encounters and trajectories of metabolic symptoms over time. Positive interactions do not seem to have an influence on metabolic profiles, and also do not appear to function as a buffer against the metabolic consequences of negative interactions. Furthermore, the relationship between negative social encounters and metabolic profiles was independent of relevant demographic, health, personality and mood variables. Collectively, these findings shed light on some of the mechanisms that might underlie the broader epidemiologic linkage between social relationships and CVD morbidity and mortality (e.g., Barth et al., 2010; Berkman et al., 1992; Eng et al., 2002; Frasure-Smith et al., 2000; Gorkin et al., 1993; Kawachi et al., 1996; Knox et al., 1998; Kuper et al., 2002; Lett et al., 2005; Seeman et al., 1987; Vogt et al., 1992). They also highlight the important role that adolescence experiences may play in early stages of the disease process.

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