Psychological underpinnings of metabolic syndrome

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Metabolic syndrome (MS) is more common among socio-economically disadvantaged individuals and is associated with certain risky lifestyle practices. MS also appears to be triggered by adverse social circumstances and chronic stress. The present paper reviews accumulating evidence to imply that individuals who have certain personality and behaviour traits are particularly predisposed to develop MS, and brings together theories that relate to possible psychological mechanisms underlying MS. It considers how such factors might interact causally to encourage the development of MS. As part of the EU-funded LIPGENE Integrated Project, multi-level modelling will be undertaken to explore potential pathways to MS, taking into consideration the interplay between a range of psycho-social, demographic, cultural and lifestyle factors thought to contribute to the development of MS. Data will be gathered for this purpose from a representative sample of >50-year-olds living in Britain (n=1000) and Portugal (n=500). It is anticipated that this information will assist in the development and targeting of future intervention to prevent and treat MS in the normal population.

Abbreviation: MS, metabolic syndrome.

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Could metabolic syndrome be triggered and/or exacerbated by psycho-social factors?

The role of negative emotions in the development of CHD is well established. The term ‘type A’ was originally coined by Friedman & Rosenman (1959) to refer to what they postulated to be a ‘coronary-prone’ behaviour pattern. The type A pattern is characterised by competitiveness, time urgency, impatience and hostility. Individuals with a type A pattern have been described as aggressive, dominant, quick-witted, self-confident, autonomous and extraverted. The trait is measured using the Minnesota Multiphasic Personality Inventory-derived Scale (Cook & Medley, 1954). Hostility, which is part of what comprises the type A pattern, has been defined as a mixture of anger and disgust often accompanied by indignation, contempt and resentment (Plutchik, 1980). Hostility appears to be stable over a period of time (Woodall & Matthews, 1993), suggesting that it could in itself be considered a trait. Anger, on the other hand, is a state of arousal that comprises behavioural, subjective, visceral and somatic components, and has been defined as the ‘urge to attack’ and as ‘the opposite of fear’ (Danesh, 1977). Anger is commonly assessed using the Trait Anger Questionnaire and the Anger Expression Scale (Spielberger, 1983). Both hostility and anger are commonly observed among those with high blood pressure and are associated with increased risk of heart disease (Haynes et al. 1980; Niaura, 2002).

Clinical features of MS are commonly observed among those individuals with a type A coronary-prone behaviour pattern (Ravaja et al. 1996). MS and CHD may, however, have different psychological precursors. Several studies have considered hostility and anger in relation to various anthropometric and biochemical markers for MS. Obesity and insulin resistance appear to be consistently related to hostility through childhood (Raikkonen et al. 2003). Associations between hostility and clinical features of MS, however, become less tenuous in adulthood. Earlier research by the same group (Raikkonen et al. 1996) has considered anger, hostility and type A behaviour as well as tiredness in Finnish middle-aged males (n 90) in relation to anthropometric, demographic and lifestyle practices, and has found no associations between type A behaviour or hostility and any of the metabolic factors associated with MS. Waist:hip ratio was, however, found to be related to high exhaustion and anger expression. A more recent study, which includes both male and female middle-aged civil servants and is part of the Whitehall II study (Feldman & Steptoe, 2003), has also found no relationship between markers of impaired glucose metabolism and hostility. Only one study (Niaura et al. 2000) appears to have found evidence of hostility in males with MS. Together the evidence suggests that there may be gender differences in the way psychological and metabolic factors interact in MS. A longitudinal cohort study of middle-aged women has indicated increased risk of MS among those who experience high levels of anger (Raikkonen et al. 2002). Further evidence that negative emotions could be particularly detrimental to women’s health comes from a study that used computed tomography scanning (Raikkonen et al. 1999a,b). This study indicates that hostility and anger contribute to visceral adipose tissue to a similar extent to smoking alcohol or lack of physical activity in post-menopausal women. Current knowledge therefore implies that hostility may be particularly detrimental to women’s health.

Chronic stress (Bjorntorp & Rosmond, 1999; Waldstein et al. 1999; Bjorntorp, 2000; Brunner et al. 2002; Vitaliano et al. 2002; Steptoe & Marmot, 2003) and stressful life events (Ravaja et al. 1996) have been linked to the development of abdominal obesity. Abdominal obesity is also commonly observed among sufferers of clinical depression (Weber-Hamann et al. 2002; McElroy et al. 2004), as well as in depressed (McCaffery et al. 2003; Kinder et al. 2004) and anxious (Landen et al. 2004) non-clinical populations. Depression may be more deleterious to women’s health than to men’s health. A large population study (n 3186; Kinder et al. 2004) has found a higher incidence of MS among young women (but not men) with a history of depression when other factors associated with MS are controlled. Features of MS also appear more common among women experiencing social anxiety (Landen et al. 2004). Again, this finding suggests gender differences in how MS develops and underlines the importance of including both genders in research exploring obesity in chronic disease pathways. Existing research, therefore, implies the possibility of different gender-specific causal pathways to MS.

Socio-economic deprivation has been shown to increase with age and to be associated with greater ill health in later years (Frost et al. 2001). Clinical features of MS are more commonly observed among more socio-economically disadvantaged individuals (Bjorntorp, 2000), in individuals who have spent less time in education (Wamala et al. 1999; Kerenyi et al. 2000; Hidvegi et al. 2001; Lidfeldt et al. 2003) and in those doing more menial jobs (Brunner et al. 1997). Coronary-prone behaviours such as hostility may to some extent explain social-class differences in health. Large population studies have observed the highest levels of hostility among individuals in the lower social classes, especially in older subjects (Barefoot et al. 1991; Niaura et al. 2000). Meanwhile, these findings may reflect a greater extent of social stress being experienced by individuals who are socio-economically disadvantaged.
The ticking time bomb: the metabolic syndrome

How does psycho-social stress lead to the development of metabolic syndrome?

The specific nature and scope of different relevant psychological and physiological mechanisms and how they bring about MS is currently unknown (Muldoon et al. 2004). Those individuals with a type A behaviour pattern typically respond to laboratory-generated challenges with exaggerated sympathetic nervous system reactivity (Diamond, 1982; Puttonen et al. 2003), implying that such individuals may be particularly prone to suffer stress. Chronic stress has been shown to be associated with visceral obesity and MS (Bjorntorp, 1999; Bjorntorp & Rosmond, 2000; Brunner et al. 2002; Vitaliano et al. 2002; Steptoe & Marmot, 2003). To explain how this association could occur, it is suggested that MS may be the result of a stress-induced cortisol-mediated acute inflammatory immune response (Kiecolt-Glaser et al. 2002; Black, 2003; Seematter et al. 2004). Chronic inflammation is associated with CVD and type 2 diabetes (and also periodontal disease and arthritis). The finding that depression and anxiety both appear to have the ability to trigger the release of pro-inflammatory cytokines (proteins that are normally released and signal to other cells in response to infection or injury) provides some support for this argument (Kiecolt-Glaser et al. 2002).

The cortisol hypothesis

Cushing’s disease, which is the result of increased adrenal secretion of corticosteroids, is often referred to in evidence for the involvement of cortisol in the development of MS. Similar to MS, Cushing’s disease is characterised by visceral fat deposition, hypertension, hyperlipidaemia, depression and hypercortisolaemia (Bjorntorp, 2000; Brown et al. 2004). There is further evidence to support the involvement of cortisol in the development of MS. Individuals treated with steroids tend to put on weight (Bjorntorp, 2000). Also, there are associations between high salivary cortisol and anthropometric (Wallnerius et al. 2003; Ward et al. 2004) and other measures of MS, such as blood pressure and lipid profile (Rosmond et al. 2000), which are consistently observed in older men. Metabolic response to stress is, however, likely to be dependent on both the sympathetic nervous system (flight and fight response) and the hypothalamic–pituitary–adrenal axis (defeat response) (Bjorntorp, 2000). According to this view, stress that is induced by adverse social conditions may trigger neuroendocrine change in two possible ways: first, through the release of the catecholamine neurotransmitters adrenaline and noradrenaline, both of which can bring about an increase in blood pressure in response to sympathetic nervous system activity. Whereas both adrenaline and noradrenaline bring about peripheral vasodilation to enable anxiety and flight, noradrenaline alone brings about peripheral vasoconstriction to enable anger and fight (Diamond, 1982); second, stress-induced hypothalamic arousal is specifically thought to activate adrenocortisol secretion, thereby bringing about increased fat deposit and MS (Brindley, 1995; Bjorntorp & Rosmond, 2000; Drapeau et al. 2003). Hypothalamic–pituitary–adrenal axis activity is controlled through negative feedback from glucocorticoid receptors in the hippocampus area of the brain, which are believed to homeostatically control blood pressure and insulin and glucose levels, in response to stressors. Chronic activation of the hypothalamic–pituitary–adrenal axis may eventually impair this negative feedback system (Bjorntorp, 2000). This mechanism may be reciprocal, given that sympathetic nervous system activity is increased by eating and decreased by fasting (Bjorntorp, 2000). Visceral fat, in turn, may release cytokines, which stimulate hypothalamic activity to further increase stress (Drapeau et al. 2003). In keeping with this idea, high levels of noradrenaline have been associated with the release of leptin (Eikelis et al. 2004). Leptin is an adipocyte hormone that appears to be released in greater quantities in obese individuals (Oppert et al. 1997). Leptin is released from fat and is believed to signal other neurochemicals, including the catecholamines, to become active in the central nervous system (Halford, 2001). Thus, it is possible that leptin stimulates sympathetic nervous system activity (Esler et al. 2001) to mediate glucose and fat metabolism (Nonogaki, 2000).

The serotonin hypothesis

Links between abdominal obesity and depression suggest dysregulation of serotonin activity that could potentially predispose certain individuals to MS. Further evidence for a role for serotonin in the development of MS comes from studies that have observed response to serotonin agonists. Despite some evidence to suggest that serotonin agonists

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(including the commonly-prescribed selective serotonin re-uptake inhibitors) can curb hunger and reduce body weight in the short term (Sargent et al. 1997), prolonged use of such drugs seems to induce MS (Baptista, 1999; Zimmermann et al. 2003; Almeras et al. 2004; Basu et al. 2004; Vieta, 2004). Both animal (Roy et al. 2004) and human research (Eikelis et al. 2004) has implied that enhanced serotonin turnover could be linked to the development of obesity. Amphetamine-like anorexic drugs such as fenfluramine and dexfenfluramine are thought to act by inhibiting re-uptake of serotonin at the central nervous system synapse, thereby enhancing and prolonging its action (Wellman et al. 2003). In speculating how enhanced serotonin activity might bring about obesity, it has been suggested that serotonin interacts with leptin and cortisol in producing stress-induced body-weight gain. Intravenous administration of a selective serotonin re-uptake inhibitor has been shown to increase plasma leptin levels and cortisol response to a greater extent in obese women than normal-weight women (Oppert et al. 1997). Serotonin activity has not only been implicated in the development of visceral fat but also in the development of other metabolic factors associated with MS. Elevated triacylglycerols, hypertension and insulin resistance have been found to be associated with lowered fenfluramine-released prolactin response (a proxy for serotonergic activity), providing further evidence for enhanced serotonin activity in the development of MS (Muldoon et al. 2004). There is, therefore, good reason for presuming that serotonin has a role in the psychology of obesity and MS. The notion that metabolic change could be serotonin mediated implies the usefulness of undertaking further research to explore the importance of psychological factors assumed to be linked to enhanced serotonin activity in relation to visceral obesity and MS.

Can risk for metabolic syndrome be predicted from anthropometric measures alone?

Large population research as part of the EU-funded LIPGENE Integrated Project will explore a novel range of potential psychological triggers of MS. A quick easily-assessed non-invasive marker of MS will be required for this purpose. Clinical characteristics of MS such as midsection obesity, high blood pressure, cholesterol, and insulin resistance appear to be both collectively and individually predictive of cardiovascular risk (Lawlor et al. 2004). Clinical features indicative of MS appear to vary in how well they predict each other and consequent risk for MS. Anthropometric assessment may provide a more stable indicator of MS over a period of time than biochemical measures (Katzmarzyk et al. 2001). Body fat composition, independently of other factors, has been shown to provide a reliable marker of MS through the life course (Yarbrough et al. 1998; Vanhala et al. 1999; Chen et al. 2000) and across cultures (Okosun et al. 1998; Onat et al. 2004). As there is a lack of studies that have assessed the value of sagittal diameter in women and because sagittal diameter is difficult and time-consuming to assess, the method remains unsuitable for use in a large group of individuals. The extent to which BMI and waist:hip ratio predict clinical features that comprise MS appears to be gender dependent (Ho et al. 2001; Siani et al. 2002; Benetou et al. 2004; Onat et al. 2004). When all anthropometric measures are considered, waist circumference appears to provide the most convenient and reliable anthropometric marker of clustering of clinical features of MS across gender (Okosun et al. 1998, 2000; Siani et al. 2002; Snijder et al. 2004). There may also be regional differences in terms of which anthropometric measures most accurately reflect metabolic change. A recent study carried out in Portugal has found waist:hip ratio to be a better predictor of MS than waist measures alone (Martins & Marinho, 2003). Both waist:hip ratio and waist circumference will together provide viable and consistent proxy indication of visceral obesity and MS for the purpose of the LIPGENE study.

Conclusions

The LIPGENE study will consider, in a large sample of >50-year-old Europeans (n = 1500), a novel range of psychological and behavioural traits reflecting activity of various neurochemicals, certain lifestyle, social and demographic factors, and cultural differences therein against anthropometric markers of MS. It will attempt to unravel the relative contribution of each of these factors to the aetiology of MS using multivariate and predictive techniques. The analysis will not only seek to determine causative relationships between variables, but also to identify different constellations of traits and behaviours that underpin MS and may represent separate pathways to CHD and/or type 2 diabetes. The research will also be unique in exploring cross-cultural differences in how psychological factors may bring about obesity and MS. The research also meets a need for a more holistic approach to understanding the psychological and behavioural underpinning and outcomes of MS.

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