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## Public Health Burden of Chronic Stress in a Transforming Society

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### Abstract

In this paper chronic stress is proposed as an integrating model that can be applied to the explanation of the suddenly changing patterns of premature mortality rates in transforming societies of Central-Eastern-Europe, especially in Hungary. The temporal factor in existing stress models is often neglected. Chronic stress has been shown to lead to typical pathogenetic results in animal experiments. Literature and the different models in the field of psychology, behavioural sciences, and epidemiology are reviewed in terms of the chronic stress theory. There are several conceptual bridges between psychological alterations and the risks, onset and prognosis of chronic disorders of great epidemiological significance. Depending on the field of research there are several parallel concepts, which analyse practically the same phenomena. These are the stress theories in physiology, learned helplessness and control theory in psychology, depression research in psychiatry, the concept of vital exhaustion and the psychosocial risk research in sociology. Because chronic stress results in adverse health effects through biological, social and behavioural pathways, this theory might also have the best explanatory power to understand the premature male morbidity and mortality crisis in Central and Eastern Europe in the last decades. The special features of premature mortality and morbidity crisis in Hungary might be regarded as an experimental model to understand better the human consequences of chronic stress and those processes where psychology meets physiology.

**Keywords:** chronic stress, depression, learned helplessness, gender differences, transforming societies

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### **The special importance of chronic stress models**

Stress models in physiology are mostly based on acute or relatively short term experiments. The temporal factor in existing stress models is often neglected. Laboratory investigations frequently focus on the short term physiological effects of acute stressors, while chronic stress shows different patterns (Kubzansky & Kawachi, 2000). If we return to the original concept of the General Adaptation Theory of Hans Selye (1936, 1976), the three phases of stress are alarm reaction, resistance phase and, the third, physiologically most harmful phase, exhaustion. Among all of the existing hypotheses chronic stress theory could be the most fruitful explanation, which incorporates the learned helplessness model, the psychosocial and psychiatric models of depression, the control theory of stress and health, and the concept of vital exhaustion as a cardiovascular risk factor (Hyland, 1987; Steptoe, 1990, 2000; Wortmaan & Brehm, 1975; Appels, 1997; Appels & Mulder, 1988; Falgers & Schouten, 1992; Kopp, Falger, Appels & Szedmák, 1998a). Such a unified stress model could best explain the morbidity and mortality crisis in the middle aged male population in Central and Eastern Europe in the last decades (Cornia & Panicia, 2000; Knox, Viigma, Uden, Elofson & Johansson, 2002; Kopp, Szedmák & Skrabski, 1998b, 2000, 2002, 2007; Kopp, 2000, 2007; Kopp & Skrabski, 1989; Marmot et al., 1987, 1991; Marmot & Wilkinson, 1999).

Although the enduring negative emotional evaluation of a life situation depends primarily on the given situation, however, the vulnerability of the person is similarly important. The subjective appraisal, interpretation of the situation depends to a great extent on the early environmental influences on development, both in respect to the development of the brain structures and psychological coping abilities. One type of the animal "social stress model" of depression can be characterised with an early life chronic stress situation. It is the result of the disruption of mother-infant or peer bonding, which seems to resemble human depression or vulnerability to depression. Initially, the infant displays so-called "protest" behaviour (acute and resistance phases of stress). This is generally followed by a second phase, which is characterised by locomotor inactivity and a disinterest in motivationally salient external stimuli. This state is characterised by "despair". The third phase is called "detachment". This process seems to be "hardwired" in the brain of many social mammals and results in high vulnerability (Matthews, 2000). In the last decades attachment theory has become the organising framework of studies related to physiological, psychological and developmental importance of the early childhood, affective mother-child bond and the negative consequences of the disruption of this relationship (Bowlby, 1969). According to follow up studies, insecure attachment predicts later emotional instability and health deterioration. Maltreatment at an early age can have enduring negative effects on a child's brain development and function, and on his or her vulnerability to stress.

Learned helplessness means a condition of loss of control created by subjecting animals or humans to an unavoidable, emotionally negative life situation (such as unavoidable shocks, relative deprivation, role conflict, etc). Being unable to avoid or escape (flight or fight) an aversive situation for a long period of time produces a feeling of helplessness that generalises to subsequent situations (Seligman, 1975; Seligman & Isaacowitz, 2000). Learned helplessness is a typical chronic stress situation, when a persistent deadlock, feeling of total lack of control makes the avoidance of an emotionally negative situation impossible. An animal exposed to inescapable, uncontrollable stress shows subsequent deficits in learning how to terminate the noxious stimulus, even when it is escapable or controllable. In such a state, the hippocampus appears to become primarily affected by the long-lasting elevations of circulating corticosteroids resulting from uncontrollable stress. Severe stress for a prolonged period causes damage in hippocampal pyramidal neurons, especially in the CA3 and CA4 region and reductions in the length and arborization of their dendrites (Huether, 1996). In connection with the physiological consequences of chronic stress the feeling of lack of control has central importance.

Stephens (1990, 2000) has summarised the adverse effects of uncontrollable stress in comparison with matched controllable aversive stimulation. These effects are: decreased food, water consumption, greater weight loss, higher plasma corticosteron, increased gastric lesions, reduced production of specific antibodies, reduced lymphocyte reactivity, decreased cytotoxic activity of natural killer cells, decreased tumour rejection, increased susceptibility to malignancy.

Sense of control is an individual belief pattern that also has developmental and social determinants. Animal studies indicate that monkeys, provided with experiences of controllable (contingent) events early in life, are subsequently less reactive to stressful events in adulthood. The experience of a major uncontrollable event in childhood, such as the death of one's mother, is associated with increased likelihood of depression following negative life events in adult life.

The unique conceptual review of Gerald Huether (1996) makes an attempt to combine data from biological and psychosocial stress literature. According to his evolutionary model stress responses act as triggers for the adaptive modification of the structure and the function of the brain. Stress responses serve to adjust in the physical, emotional and personality development in a self-optimising manner, in accordance with the ever-changing requirements of the external world. The repertoire of emotional, cognitive and behavioural coping strategies might partly be due to hereditary factors governing the expression of certain genes for specific hormones, receptors or enzymes. The magnitude and duration of aversive experiences, the critical timing of the events, the actual genetic vulnerability of an individual determine the possibility for adaptive modifications of the functions and structure of the neuronal circuits and associative networks involved in the regulation of the behavioural and endocrine responses of an individual to aversive stressful experiences.

According to animal studies, males appear to be more vulnerable to long-lasting, stress-induced hippocampal damage than females (Uno, Tarara, Else, Suleman & Sapolsky, 1989), as the decline of circulating testosterone levels resulting from uncontrollable stress seem to play an additional role. It is an interesting parallel finding that depression seems to influence cardiovascular risk more among men than among women according to follow up studies (Musselman, Evans & Nemeroff, 1998). Despite similar free cortisol responses of men and women (studied in the luteal phase) to psychosocial stress, gender may exert differential effects on the immune system by modulating glucocorticoid sensitivity of proinflammatory cytokine production (Rohleider, Schommer, Hellhammer, Engel & Kirschbaum, 2001).

Recent data suggest that chronic stress results in slowly developing neurochemical changes, possibly via changes in gene expression. Haller, Bakos, Rodriguiz, Caron, Wetsel and Liposits (2002) examined the interaction between chronic social stress and the resulting depressive behaviours in noradrenaline transporter knockout (NET-KO) mice. In these animals the situation specific behavioural depression was similar to NET mice, but this reaction was not generalised to subsequent situations, which might mean relative protection against learned helplessness in the NET-KO animals.

Learned helplessness might be called a behavioural depression resulting from exposure to inescapable stress. Learned helplessness might be conceptualised as a limbic system dysregulation, with different brain regions involved as medial prefrontal cortex, hippocampus, septum, hypothalamus, amygdala and nucleus accumbens.

Seligman asserted that learned helplessness appears very much like human depression. Seligman hypothesised that both learned helplessness and reactive depression result from the expectancy that responses and outcomes are uncontrollable and might result in only emotionally negative consequences. In humans, learned helplessness also refers to the motivational, cognitive and emotional components of the interpretation of the environmental stimuli. In humans, defensive mechanisms also operate at mental level through putative ego defences, the psychological function of which is to preserve self-esteem by hindering the access of disturbing emotional material into awareness. (Seligman, 1975; Seligman & Isaacowitz, 2000).

Human psychological stress reactions depend on the subject's interpretation of the changes perceived from their outside world and on the optimisation principles of the person. The ability to deal successfully with stressors strengthens the self-esteem, self-efficacy and the problem solving, coping skills of the person. The experience of the controllability of stress situations is the driving force of the so-called learned resourcefulness, which is the opposite of learned helplessness.

A special feature of human stress is when an imaginary scenario is constructed. The scenario may never occur, but it is still regarded as a real and constant risk by

the person. Therefore the cognitive, mental interpretation of the situations has a central importance in human stress research.

### **The public health importance of chronic stress in modern societies**

While in modern societies our living conditions have improved in many respects, other aspects have been fundamentally damaged. Important factors of personality development, for instance mother child relationship, social models of the extended family, and in what order values are passed on are challenged. The accelerated pace of life, unpredictable environmental changes are added to the above factors, for this reasons it is understandable that in all developed countries the number of adults and children suffering from mental disorders, especially from anxiety and depression has increased (WHO, 2001). Compared to other countries, in this respect more dramatic changes could be experienced in the suddenly changing Central-Eastern-European and Eastern-European countries. For example in Hungary the prevalence of severe depressive symptomatology increased between 1988 and 1995 from 2.9% to 7.1%. (Kopp et al., 1999, 2000).

From an evolutionary perspective the development of modern medical practice depreciated natural selection by its achievements to reduce prenatal and infant mortality leading to a rise of phenotypically silent mutations from generation to generation. As a consequence we carry more and more chaperone-buffered, silent mutations. These phenotypically exposed mutations contribute to a more abundant manifestation of multigene diseases, such as atherosclerosis, cancer, diabetes, hypertension and several psychiatric illnesses (Csermely, 2001).

Over the last two centuries, although technology and civilization have achieved unbelievable successes, little attention has been given to what effect these absolutely new historical "experiments" have had on people.

In humans uncontrollable stress is experienced particularly by individuals who failed to develop a broad spectrum of behavioural strategies for the control of psychosocial conflicts. This might explain, why depressive symptomatology shows a strong socioeconomic gradient, especially in suddenly changing societies (Kopp et al., 1995, 1996, 2000; Kristensen & Kucinskiene, 2002; Kristenson, Kucinskiene, Bergdahl, Calkauskas, Urmonas & Orth-Gomer, 1998; Réthelyi, Berghammer & Kopp, 2001).

One social stress model observable in hierarchy systems of primates is very relevant in connection with this type of stress. After falling in rank, monkeys can exhibit prolonged withdrawal from social interactions and produce depression like symptoms and increased cardiovascular risk (Sapolsky, 1989, 1990; Sapolsky, Romero & Munck, 2000).

In the last decade possibly the most important observation in "new public health" is that relative socio-economic disadvantage constitutes a basic health risk

in society. If morbidity and mortality data are corrected with the traditional risk factors, such as smoking, obesity, lack of exercise, then relative social disadvantage has a far greater effect than the other factors (Wilkinson, 1996a, 1996b). In practice this means that an English unskilled worker dies several years earlier than a person with higher education, even if he does not drink or smoke more. The surveys of Marmot (1996), Marmot and Wilkinson (1999), and Marmot et al. (1991) conducted among English civil servants showed that their level of employment is in close and inverse relation with their mortality rates, just as with the occurrence of cardiovascular diseases and chronic, nonspecific respiratory disorders. Adverse social circumstances in childhood are strongly and independently associated with increased risk of insulin resistance and other metabolic risk factors. Since modern Western European societies grant adequate nutrition conditions, housing and medical care for the whole society, the question arises: why is a relatively disadvantageous socio-economic situation the most significant risk factor?

While health status in developing countries improves proportionally with national income, in developed (OECD) countries the greater income and social differences in the country itself bring about higher mortality rates (Wilkinson, 1996b).

### **Central-Eastern European health paradox**

Up to the end of the 1970s mortality rates in Hungary had been actually lower than in Britain or Austria. Subsequently, mortality rates continued to decline in Western Europe, whereas in Hungary and in other Central East European (CEE) countries this tendency reversed, especially among middle-aged men (Black, 1992; Bobak & Marmot, 1996; Bobak, Pikhart & Rose, 2000; Marmot & Wilkinson, 1999). In the late 1980s, the mortality rates among 45-64 year old men in Hungary rose to higher levels than they were in the 1930s, while the mortality rates in the older age groups were comparable to the worst in Western-Europe (Cornia & Panicia, 2000; Kopp et al., 1998a, 1998 b, 2000, 2002, 2007).

What is the explanation for the vulnerability of middle aged men during this period of rapid economic change? This deterioration cannot be ascribed to deficiencies in health care, because during these years there was a significant decrease in infant and old age mortality and improvements in other dimensions of health care. Furthermore, between 1960 and 1989 there was a constant increase in the gross domestic product in Hungary. Thus the worsening health status of the Hungarian male population cannot be explained by a worsening material situation.

A growing polarisation of the socio-economic situation occurred in the CEE countries, especially in Hungary between 1960 and 1990. The vast majority of the population lived at similarly low level in 1960, with practically no income inequality, and there were no mortality differences between socio-economic strata.

Since that time increasing disparities in socio-economic conditions have been accompanied by a widening socio-economic gradient in mortality, especially among men (Kawachi & Kennedy, 1997).

One of the most interesting features of the so-called “Central-Eastern-European health paradox” is the gender difference in worsening mortality, in spite of the fact that men and women share the same socio-economic and political circumstances. In Hungary the male/female differences in life expectancy in 2001 was 8.3 years, which is considerably higher than the average difference found in countries of Western Europe, for example 5.8 years in the neighboring Austria, 4.8 years in Denmark and Great Britain. The mortality ratio comparing the lowest to highest educational stratum is 1.8 for Hungarian males, while 1.2 for females (MacKenbach et al., 1999). There are also marked morbidity and mortality differences according to the Hungarian counties and sub-regions.

Based on the data of our national representative surveys conducted in the Hungarian population (Hungarostudy 1983, 1988, 1995, 2002, 2006)(Kopp et al., 1995, 1996, 1998b, 1999, 2000, 2007), we found that a worse socioeconomic situation is linked to higher morbidity and mortality rates in Hungary as well. According to multi-variate analyses, however, higher morbidity rates are connected to relatively poor socioeconomic situations mainly through the mediation of depressive symptoms. Consequently, not only the difficult social situation in itself, but the subjective experience of relative disadvantage, the prolonged negative emotional state, that is chronic stress proves to be the most important health risk factor.

Presumably a self-destructive circle develops from the enduring relatively disadvantageous socioeconomic situation and depressive symptoms. This circle resulting in chronic stress, plays a significant role in the increase of morbidity and mortality rates in the lower socioeconomic groups of the population. Until the 1970s with the uniformly low living standards, Hungarian health statistics showed more favourable data, than in several Western countries, such as in Great Britain or in Austria. During rapid socioeconomic changes the disadvantaged continuously blame themselves or their environment, consider their future hopeless, experience permanent loss of control and helplessness, because they cannot afford a car, better living conditions, higher income, while others around them are able to achieve these. They constantly rate their own situation negatively, feel helplessness, and a loss of control. This experience becomes widespread when society becomes rapidly polarised and social cohesion, trust, reciprocity and social support decrease dramatically (Skrabski, Kopp & Kawachi, 2003, 2004).

Men were found to be more susceptible to the effects of relative income inequality and material deprivation, but the pathway of this relationship is yet to be explained. Two possible explanations can be hypothesised. One is that the income inequality is much higher among men. The other possible explanation might be that men are more susceptible to loss of status than women. Animal experiments have

shown males to be more sensitive than females to loss of dominance position, that is loss of position in hierarchy (Sapolsky, 1990, 2000). Most animal studies on social rank examine males, where social rank is the best predictor of quality of life and health. The relationship between social inequality and health applies to women as well as to men in several respects according to several studies, although the income and occupation of women are not as powerful predictors of mortality as they are for men. Especially in a suddenly changing society, such as Hungary, the social inequalities in mortality rates are much more pronounced among men. In such a situation, in a more traditional society, the relative income deprivation might be a more important risk factor for men than for women. There are significant gender differences in ways of coping during the sudden changes of the political-economic system, male morbidity seems to be more affected by the socio-economic changes. During the modernisation process of society the female patterns of inequity, risk factors and health might approach male patterns as it could also be experienced in several Western countries.

In comparison to women among men socio-economic factors are nearly four times more important predictors of middle-aged mortality differences among regions. Social distrust and the rival attitude are important predictors of middle aged mortality differences among men (Kawachi et al., 1998; Kennedy & Kawachi, 1998; Skrabski et al., 2003, 2004). This indicates that in a suddenly changing socio-economic situation relative economic deprivation, rival attitude and social distrust are all more important risk factors for men while the strong collective efficacy could be a protective factor, even in the case of men. Rival attitude was in highly significant negative association with participation in civic organisations, consequently the protective effect of participation in civic associations might influence health through a lower rival, competitive attitude in members of civic networks among men.

The existing and broad socio-economic differences among the Hungarian regions are less important regarding the middle aged female mortality differences. Neighbourhood cohesion, religious involvement, trust and reciprocity were not so much influenced by sudden socio-economic changes in the last decades, therefore the protective network of women remained relatively unchanged.

The results of a Swedish and Lithuanian research, the so-called LiViCordia study are very similar to our results (Kristenson et al., 1998, 2002). In the seventies the cardiovascular mortality rate of Lithuanian men was not worse than that of Swedish men, but in 1994 the incidence of CHD mortality for middle aged men was fourfold higher in Lithuania compared to Sweden. In this study a thorough medical and psychological examination was conducted among a representative sample of the male population of Linköping and Vilnius. They found that the traditional risk factors of cardiovascular diseases were not worse in Vilnius than in Linköping, the Lithuanians did not smoke more, the serum-cholesterol level of Swedish men was even higher. However, they found significant differences in



psychological features, more men from Vilnius suffered from depression, more of them felt that in difficult situations they could not depend on the help of others, and the occurrence of chronic stress or the so-called vital exhaustion was far more frequent among them. Their physiological reaction patterns differed as well, the patterns of Vilnius men showed the signs typical of chronic stress. The men from Vilnius had an attenuated cortisone response to stress. Several studies showed an attenuated cortisone response to stress among groups exposed to chronic stress.

A stress situation in itself does not affect health harmfully when it is accompanied by the feeling that one is able to overcome difficulties successfully, which is actually the basis of physical and mental development. Challenges, new situations lead to deterioration if one does not know the solutions, if one is faced with too long lasting, too many and seemingly unsolvable situations, if society seems unpredictable, chaotic and uncontrollable.

The dramatic features of premature male mortality and morbidity in Hungary might be regarded as a special experimental model to understand better the human consequences of chronic stress and those processes where psychology meets physiology. Given the magnitude of the problem, it is surprising that this deterioration in the health of the Hungarian male population has not received more attention. In 2007, on the centenary anniversary of the birth of Hungarian born scientist, Hans Selye it is high time to recognise chronic stress as the invisible hand behind Hungarian middle aged men's tragic early death rates.

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