

Work-related Stress, over-nutrition and cognitive disability

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Abstract

Work-related stress may exert a negative impact on a variety of physical and psychological attributes relating to the health of employees and work organizations. Several studies conducted in Italy have shown that workers and employees who express less satisfaction show increased symptoms of obesity and cognitive disability. The latest evidence underlines the pathogenic relationship between stress and neurological disease through inflammatory neuro-immune activation. The aim of this review was to describe the relationship between workplace stress and adverse changes in lifestyle that develop into obesity, neuroinflammation and cognitive dysfunction. The molecular mechanisms involved and guidelines for the prevention of these trends are discussed briefly. *Clin Ter 2016; 168(1):e42-47. doi: 10.7417/CT.2017.1981*

Key words: stress, metabolic alterations, lifestyle changes, over-nutrition, neuroinflammation

Background

Studies conducted in Italian Hospitals and in the Local Health Authority have shown that workers and employees expressing less satisfaction show increased symptoms of stress and an elevated percentage of stress and percentage of stress-related chronic diseases (1) Since 2010 the necessity of assessing work-related stress (as amended by Article 18 of the Legislative Decree. N. 106 of 2009) has achieved judicial status. This type of psychological distress initiates a negative spiral culminating in affective disorder conditions and depression, thereby promoting the lack of motivation and apathy leading to a sedentary lifestyle and unhealthy behavior that accompanies the abuse of high-calorie foods, alcohol and smoking (2). The most vulnerable fragile or aggression-repressed workers, due to their individual experiences, express greater sensitivity, intolerance/vulnerability, and responsiveness to adverse conditions that arise in workplace; as a consequence of these predispositions, they suffer from ill-health/ill-being to a greater extent. Cultural factors also influence the development of psychological inadequacy

which concerns experiences of weakness, helplessness and dependency (3).

Among European workers, 25% suffer from stress and half of all sick-leave is attributable to stress-related factors. With the implementation of new legislation on occupational safety (prevention of work-related stress), corporations are expected to effectuate both economic benefits and sounder management. Each corporation is required to formulate a protocol for risk prevention of work-related stress and bullying incidents, in order to obtain higher levels of self-esteem and psychological well-being of the workers; it is also required to take steps to prevent burnout, irritability, excitement, hyperactivity, absenteeism to get employees benefits and in order to increase their productivity.

Italian INAL (The National Institute for Insurance against Accidents at Work) introduced a current research on health and safety at work that was performed on 8000 Italian workers: it shows that they perceive much more exposure to work-related stress compared to other psychosocial risks. Thus, the work situation has been recognized widely as an emerging risk for workers health & safety. These risks are linked to workplace problems, including work-related stress, harassment or mobbing, and workplace violence (2). Psychological stress-at-work is regarded as the major cause of Metabolic Syndrome (MetS) which involves medical conditions: high serum triglycerides and low content of high density lipoprotein; abdominal obesity, elevated blood pressure and fasting plasma glucose (4). MetS has been found to be 4 times increased in individuals that are chronically distressed compared to colleagues with lower stress levels, this study was carried out on Italian radiologists and radiotherapists.(1,3).

Magnavita and Fileni in 2014 investigated the correlation between work-related stress and symptoms of psychological uneasiness such as anxiety and depression (1). MetS is also associated with the risk of breast cancer in women (4) and with cognitive decline in younger people (5). For the reasons expressed above, it is necessary to examine the close relationship between stress, unhealthy diet and metabolic disorders that cause cognitive disability.

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Objective

The aim of this narrative review was to describe the relationship between workplace stress and adverse changes in lifestyle that develop into obesity, neuroinflammation and cognitive dysfunction.

Description of study

This article is a narrative review obtained respecting the parameters indicated in the literature (6). The articles selected in 2016 by three independent reviewer using traditional database (Medline and PsycINFO) and keywords as “stress”, “work-related”, “metabolic alterations”, “lifestyle changes”, “over-nutrition”, “neuroinflammation” and “cognitive disability”.

Then the resulting articles were selected using as exclusion criteria letter to editor or case reports, without restriction of time of publication or language. This allowed also to analyze the evolution time of the concept of association between stress and other variables (such as *metabolic alterations, lifestyle changes, over-nutrition, etc.*).

The selected articles submitted to an interactive process of discussion by other authors excluding items with minor interest and originality.

Results and discussion

Currently, stress remains a serious health hazard since it may accelerate the progression of multiple illnesses with dire consequences that result in a surge in medical-healthcare spending (3), as well as for the real risk of reduced employee work-time and higher absenteeism rates in the corporate world (7). McEwen defined the term “allostatic load” which is the maladaptive ability of the body to resist stress, both exogenous and endogenous (8); thus, “allostasis”, literally meaning “maintaining stability through change” or maintaining a ‘state of dynamic balance’ describes the individual’s capacity to adapt or to continually shift by adjusting to the varying environment by changing physiological data.

Behavioral physiological responses begin when the brain perceives stressful experiences leading to allostasis and adjustment under favorable conditions but under adverse conditions maladaptive reactions may occur. The final aim is to maintain balanced self-organization and autonomy under stressors with the ultimate goal of survival. When the allostatic load increases continually and progressively, the overexposure to neuroendocrine system mediators activates the immune system leading to pathologic reactions until chronic disease in which inflammation plays a major role (3). All these signals, caused by metabolic and immune dysregulation, amplified and maintained by stress, have been found to induce conditions of cognitive disability (9). Autoimmunity, aging and even cancer are considered stress related immune mediated diseases (3,8). Consequently, stress may exert certain positive outcomes, but stress-distress affects immunological, cardiovascular and neurodegenerative diseases and mental disorders and these adverse outcomes

may lead to a cascade of negative developments depending upon a multitude of intrinsic and extrinsic factors (3).

When an individual is coerced to labor without the sufficient gratification or the personal satisfaction, this lack of adequacy-benefit often initiates the onset of symptoms known as “vague and non-specific” (or MUS, Medically Unexplained Symptoms), which presents the original reason for the patient to seek health care. Following clinical assessment, MUS does not seem to be explained by a clearly defined cause or diagnosis of a defined medical disease. MUS may be related to a number of stressful events pertaining particularly to social relationships (10). The most commonly-occurring MUS reported by workers is sleep alteration due to loss of circadian rhythms. In human this synchrony is regulated in the suprachiasmatic nucleus of hypothalamus (11).

Under conditions of chronic circadian disruption, brain and behavior physiology begins to be dysregulated and as this indisposition continues individuals gain body weight and may even develop obesity, in addition to metabolic hormones alterations. This situation may be illustrated through recourse to a laboratory model of mice exposed to circadian rhythm disruptions. Experimental data on the mouse’s brain showed a loss of neuronal complexity and dendritic length in the limbic prefrontal cortex involved in perceiving emotional stress (12).

Excitatory amino acids and glucocorticoids (GC) play a role in these processes that include the involvement of brain-derived neurotrophic factor (BDNF) and endocannabinoids (12). Stress-related disorders affecting energy regulation between the immune system, the nervous system and adipose tissue (AT) are among those environmental factors inducing obesity (13,14). During psychosocial stress the brain requires extra energy (“brain pull”) (15) and this plight involves a multiplicity of changes in energy flow dynamics associated with appetite, ingestion of food, and energy conservation and expenditure (3,10,14,15). The obesogenic environment of highly palatable food with ‘hidden’ fats and sugars that may be ingested in response to prolonged unresolved stress, can promote obesity and MetS (3,7,16). Insulin and leptin resistance are first alterations that occur and they play an important role not only in vascular complication (17,18) but also in cognitive disability (9). Increased adipose tissue promotes macrophage infiltration which enhances inflammation. A chronic inflammatory state is actually a “redirection of energy-rich fuel” from storage organs (adipocytes) to an activated immune system, thereby promoting inflammation (19).

Not only MetS, but also schizophrenia, major depression, chronic mental stress, and other brain diseases are characterized by insulin resistance (20). The reaction to a continuous necessity for energy under prolonged stress (alarm stage and energy mobilization) (15) may alter the physiological regulatory signals of the stress response in favor of an adipokine release from adipocytes that sends signals to the brain leading to neurogenic inflammation (3,10).

When psychosocial stress is prolonged over an extended period and the body senses it has an unsuitable capacity to oppose this situation, the stress response engages HPA axis activation which triggers an excess release of glucocorticoids (GCs) (21). In the presence of this chronic stress, GCs

activate overeating and eventually obesity despite elevated leptin concentrations: GCs and insulin interact in the up-regulation of serum leptin concentrations (22).

In humans, insulin and cortisol increase is dependent on “comfort food” preference (high fat and sugar content). Within the stress equation, this diet leads to an excessive amount of visceral fat (VF) and dyslipidemia, hypertension, impaired glucose tolerance, insulin resistance, with all the early signs of “impaired food intake” (23). Insulin resistance induces lipolysis and this creates toxic lipids such as ceramides which further change mitochondrial function, insulin signaling and cell viability.

The preceding lipids and ceramides cross the blood brain barrier resulting in oxidative stress, insulin resistance, neuro-inflammation and cell death (24).

“Brain diabetes” (24,25,26), related to notion of “Diabetes III” (27), initially leads to cognitive impairments which progressively involves into dementia through the accumulation of free fatty acids (28).

The psychological well-being is strongly affected by obesity which is a major problem for public health. For this reason, reliable data suggests an association between cognitive dysfunction and obesity, although this phenomenon has received limited attention among primary care physicians and occupational physicians. In obese humans neuroimaging studies showed a smaller size than normal in the brain regions involved in cognition (29).

Microglial morphologic changes were found in the pre-frontal cortex of rats with diet-induced obesity and cognitive decline was associated with dendritic spine loss (29). The brain areas above described seem to be most affected by early symptoms of obesity

As previously noted, palatable, “comfort food” promotes dependence and over-eating by activating the brain reward system, similar to opioid, dopamine and endocannabinoid use (30).

Recently, Richardson et al. in 2015 (31) highlighted the notion that disinhibition and binge-eating increased when stressed individuals partake of a worse diet quality and greater intake of snack foods combined with a lower intake of fruit.

According to these authors psychological questionnaire may assess 3 eating behaviors: *restraint*, *disinhibition*, *hunger* when people are in the presence of a rich table of many foods.

Restraint is the conscious limitation of food intake; disinhibition is looking for tasty food in response to emotional stimulus and hunger is compulsive eating in response to psychological stress (need for food) (31). Findings confirm that stress-induced GCs exposure may modify the normal moderate food intake. Psychological distress and excessive food intake activates the release of leptin and the activation of mTOR (mammalian Target Of Rapamycin) that determine adverse effects on stress-related diseases.

The alteration of autophagy in the liver (lipophagy) conduces to lipid accumulation in VF and steatosis (3,32). Also CNS cell-regeneration is limited by long-term unbalanced nutrition (33).

The accumulation of metabolites is largely prevented by an effective mitochondrial autophagy that must be regarded as the main process in the protection of brain integrity (34).

It should be noted that VF has a higher density of receptors for GC compared to subcutaneous fat (SF) and stimulates lipolysis in the entire body with release of toxic FFA (35, 36). These molecules work as antigens activating the immune system and therefore this latter subtract energy to the brain and via cytokines induces inflammation (3).

In addition to its action on the hypothalamus, leptin may also act on the cortex and limbic areas, involved in cognitive and emotional regulation of feeding behaviour.

Insulin and leptin resistance depends on increased GC concentration and adiposity signals plays a role not only in energy regulation but also on the brain reward circuitry (3,15,37). In this context, individuals presenting eating disorders also seem more vulnerable to stress that determines the largest increase in VF and their intrinsic psychological vulnerability may reflect difficulty to cope with problems and provide appropriate responses to them (3,24,38). Thus, following exposure to stress, not only GCs but also pro-inflammatory cytokines (39) are released. In fact, catecholamines released during the initial phase of stress promote the release of pro-inflammatory cytokines. After trauma or a degenerative disease neurogenesis occurs by cytokines, chemokines produced by macrophages, microglia and by the same dying neurons. Sometimes, however, this process becomes abnormal due to an excess of stress-induced inflammatory cytokines: the neural plasticity of the hippocampus, cortex and hypothalamus is impaired by TNF- α , IL-1 and reactive oxygen/nitrogen species (ROS) (38,39,40).

Clinical depression presents a classical condition of sympathetic nervous system and HPA axis activation. Moreover, it is universally recognized that depressive symptoms are associated with high levels of pro-inflammatory cytokines that characterize disorder as chronic inflammation (41).

Obese individuals have psychological characteristics and emotional distress that promote inflammatory status (41,42,43,44). A chronic dysregulation of certain adipokines may exert deleterious effects upon insulin and leptin signaling. The dietary habits of the Western Society characterized by excessive consumption of sugar and saturated fats contribute to a serious level of obesity and related diseases because they favor the appearance of an inflammatory response in the brain and in other organs (45).

In other works we have emphasized the important role played by leptin in stress-immune system cross-talk (46). In any case other mediators are involved in the relationship between food intake in the presence of psychological stress in human (NPY, CRH, opioids etc.). “Leptin resistant” obesity induced by GC may contribute to the impairment of cognitive skills observed in obese patients (3,45). Taken together, the results from our study confirm the concept that there is a link between diet-induced obesity and cognitive loss (10,38,47).

Latest pan-European opinion poll on Occupational Safety and Health (OSH) conducted by the European Agency for Safety and Health at Work reported that 51% of workers consider work-related stress common to their workplace.

The inclusion in the specific OSH legislation in Italy, (Legislative Decree 81/08 and amendments) of the World Health Organization definition of health as a “state of complete physical, mental, and social well-being and not merely

the absence of disease or infirmity” served as the basis for protection against psychosocial risks at work, particularly those related to work-related stress (1).

In the presence of a chronic immune activation correlated to stress, it has become clear that the brain’s vulnerability and plasticity are altered.

Due to WHO legislature, it is necessary to understand what procedures may be undertaken to decrease work related anxiety and depression or cognitive decline (48).

The current state-of -the-art may facilitate an explanation of relationships among chronic psychological stress, over-nutrition, energy dysregulation and work disability leading to occupationally-related diseases or accidents (49). The first prevention must be the reduction of VF, which favors IR, through feeding and lifestyle suited to each individual (3,38,47,50).

We have described the use of modern technologies for analysis of body composition for the individual assessment of fat mass, fat free mass, total body water, intra/extracellular water etc, metabolism, and inflammatory status (BIA-ACC device). This method allows us to easily evaluate the relationships between body composition characteristics and cognitive functions (10,51,52,53).

We have recently described that overproduction of oxidants in presence of chronic inflammation causes many neurodegenerative diseases (38). For this reason antioxidant compounds are potential agents to treat cognitive dysfunctions. It is recommended that individuals ought to consume vegetables and fruit more frequently as suggested by Mediterranean Diet since these agents contain many antioxidant phytochemicals (50,54).

The complexity of stress, especially work-related, recognizes multiple aetiological variables, also environmental factors (55), so the main limitation of the study are the many stress comorbidities of which were taken into consideration only the major ones for deepening the reasons of the associations.

Conclusion

Work-related stress-distress generally exerts a negative impact upon a number of related and interwoven variables detrimental to the health of workers/employees and occupational organizations and associated logistics (56-57). Increments in the widespread nature of work-related stress-distress diseases and deteriorations in diet quality of the workers exerts an impact not only on their physical and mental health but also on several levels of job security (11, 58).

Stressful job and sedentary life, as well, may induce a higher Body Mass Index thereby resulting in MetS due to high-calorie diet and low physical activity. Obesity reduces the mobility and agility of individuals in their workplace and represents an increased risk for injury and accidents. An INAIL survey (2005) showed that the majority of injuries occurs in the postprandial hours most likely due to poor eating habits. The current legislation in Italy is shifting towards the promotion of health in the workplace and necessitates preventive interventions aimed at acting upon the environmental and organizational situation and to provide support

to employees. Health promotion in nutrition incorporates a change lifestyles and maladaptive behaviors that carrying out a joint action in the etio-pathogenesis of occupational diseases.

The role of the occupational physician is central in collaboration with the employer for risk- assessment and in the design and implementation of improvement measures that may become essential. Physician involvement is essential for employer information and training to which can transfer knowledge about the causes of workplace stress. He/she must define the possible consequences on the health and safety of workers in order to provide input to the assessment risk, its management and prevention. The occupational physician may also identify programs of nutritional intervention in companies in order to educate the workers to a correct lifestyle and maintaining a healthy weight by encouraging physical exercise in sedentary individuals. Among the strategies chosen to improve the well-being of the worker, one must remember the measures relating to management, communication and collaboration between colleagues. These arrangements will create the suitable and secure environment needed for workers’ health assurance.

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