

Burnout phenomenon: neurophysiological factors, clinical features, and aspects of management

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Abstract

Burnout syndrome is a distinct “occupational phenomenon” rather than a medical condition, comprising emotional exhaustion, physical fatigue, and cognitive weariness. Both exogenous work-related and endogenous personal factors determine the extent and the severity of symptoms in burnout syndrome. Persistent burnout is a cause of reduced quality of life and is associated with increased risk of sleep impairment and with several medical disorders including mild cognitive impairment, diabetes, and cardiovascular disease.

Active coping strategies promoting mental resilience and adaptive behavior, stress-reducing activities, improving work conditions, and reducing exposure to work stressors together may alleviate the distress of burnout and should be introduced early in the clinical course of burnout syndrome. The purpose of this review was to explain this complex and puzzling phenomenon and to describe burnout management.

Keywords

Burnout, emotional exhaustion, cognitive weariness, mental resilience, mindfulness, cognitive behavioral therapy

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Introduction

Burnout syndrome (hereinafter termed burnout) is a state of emotional exhaustion, physical fatigue and cognitive weariness caused by long-term uncontrolled and unresolved work stressors¹⁻⁵ and possibly by other long-term personal and environmental stressors such as major illness, family difficulties, or other persistent adversity.⁶⁻⁸ The impetus for burnout comprises interactions between endogenous person-specific and exogenous work-related factors.^{3,4} Although burnout itself is a distinct phenomenon, there is an overlap between burnout and depressive symptoms,⁹⁻¹¹ and individuals with severe clinical burnout may have transient manifestations of depression or subclinical depression.⁹ Anyone with burnout may be susceptible to frank clinical depression.¹⁰

The 11th Revision of the International Classification of Diseases (ICD-11) of the World Health Organization (WHO) states the following:

Burnout is a syndrome conceptualized as resulting from chronic workplace stress that has not been successfully managed. It is characterized by three dimensions:

- *feelings of energy depletion or exhaustion,*
- *increased mental distance from one's job, or feelings of negativism or cynicism related to one's job; and*
- *reduced professional efficacy.*¹²

Thus, according to the WHO, burnout is not considered a medical condition but is entirely an occupational phenomenon.

Initially, the signs and symptoms of burnout are subtle, with gradual progression.^{4,5} Although aware of negative changes in their mental (emotional, cognitive) and physical functioning, at first, many affected individuals neither recognize nor understand the connection between these changes and the depletion of their

resources of mental and physical energy and well-being.⁶

Although according to the WHO definition, burnout is not a medical condition, it is imperative to rule out unrelated exhausting disorders, adjustment disorder, depression, or anxiety^{8,13} and to recognize reported evidence of a link between persistently significant clinical burnout and insomnia, cardiovascular disease, and features of some metabolic disorders such as increased levels of triglycerides, low density lipoprotein, total cholesterol, and fasting glucose.^{5,14,15}

A distinction should be made between burnout with mild symptoms that do not interfere with work and do not prompt the seeking of professional help and incapacitating burnout with severe symptoms, termed clinical burnout, which both prevents the affected person from working and prompts them to seek professional help.^{8,16}

A source of concern to public health and occupational medicine professionals is evidence of the increasing numbers of workers taking extended sick leave and early retirement owing to unresolved burnout.^{1,8,17,18} Because the WHO does not recognize burnout as a medical condition and does not include it in its classification of diseases, documentation and accumulation of epidemiological information about what the WHO regards as a "phenomenon" is hindered, creating an obstacle in terms of planning preventive and interventional policies to address this highly prevalent and potentially disabling condition. The objectives of this narrative review were to discuss the clinical manifestations and causes of burnout and to outline the principles of its management.

Ethical considerations

This is a review of previously published articles. No humans or animals were

involved; therefore, no ethical approval or informed consent was needed.

Clinical and epidemiological features

It is nearly impossible to accurately determine the incidence and prevalence of burnout for several reasons, including 1) the diagnostic criteria of burnout are equivocal, vague, and open to interpretation; 2) different and sometimes conflicting diagnostic criteria have been applied in different studies; and 3) there is an overlap between symptoms of severe clinical burnout and depression.^{9,19–21} Nevertheless, it is evident that burnout most frequently affects middle-aged individuals with type A personality behavior who are ambitious, committed, motivated, highly competitive, who have an intense sense of urgency and control, and who are overly concerned with time management. Individuals with the personal trait of neuroticism, which includes anxiety, hostility, self-consciousness, and emotional vulnerability are also commonly affected by burnout.^{21–23} Although cognitive and emotional responses to stressful life experiences vary among different ethnic and social groups, the basic features of burnout are similar regardless of type of occupation and culture or ethnicity, with no significant sex difference.^{19,21}

Some 7% to 9% of working Europeans have purportedly experienced symptoms of clinical burnout, but the prevalence is much higher in some professions.^{15,24–27} One study from Austria reported symptoms of clinical burnout in approximately 50% of physicians.²⁰

Persistent clinical burnout is associated with exaggerated somatic arousal including tension, irritability, sleep impairment, and above-normal blood levels of cortisol.^{14,27} Ongoing burnout also involves impaired executive functioning with poor memory,

concentration, and attention and with difficulties in cognitive functioning and sleeping.^{8,15,27,28} Individuals with burnout experience feelings of helplessness, hopelessness, powerlessness,¹⁸ low self-esteem, cynicism, dissatisfaction with personal accomplishments,²¹ distress, ineffective coping, and difficulties with work-related demands.^{14,27}

Burnout and sleep impairment are not infrequent among individuals exposed to chronic psychosocial or work stressors, probably because depletion of energy resources and dysregulation of both the hypothalamus–pituitary–adrenal (HPA) axis and sympathetic nervous system are common pathophysiological processes underlying both conditions.^{17,29} Moreover, burnout and sleep impairment are interrelated such that burnout-associated emotional dysregulation promotes sleep impairment, and conversely, sleep impairment-associated fatigue and depletion of energy resources promote burnout. In this way, burnout and sleep impairment sustain each other.²⁹ In this context, difficulty in falling asleep, insufficient good-quality sleep, and consequent tiredness on waking, further deplete resources of cognitive and emotional energy, causing a reduction in psychological coping capacity. This results in the exacerbation of burnout.^{8,29}

Surface acting, work engagement, and performance in relation to burnout

Work engagement refers to the extent to which a worker expands their sense of self in work-related activities. Engagement includes the vigor, dedication, commitment, and absorption invested in one's work and requires the integrated application of emotional, cognitive, and physical energies.³⁰

Workers in a wide range of occupations must commonly either suppress negative

emotions or feign positive emotions.^{30,31} This kind of emotional regulation, termed surface acting, requires considerable mental effort in itself, consuming substantial resources of emotional energy and leading to their depletion and to emotional exhaustion. Then, with only limited remaining resources of mental energy, the worker has less to invest in work activities,³⁰ resulting in diminished work performance.³²

Genesis of the burnout syndrome

Burnout is a psychological response to continuous intensive occupational demands and stressors, although not necessarily a response to the experience of a monotonous or boring occupation;³³ in other words, burnout can develop irrespective of the nature of the occupation.³⁴ In essence, burnout is an insufficient coping response to chronic stressors in the workplace,¹⁴ characterized by a state of profound mental exhaustion and physical fatigue as a consequence of depleted emotional and physical energy resources.^{21,35} Cynicism, manifesting as doubt in the purpose of the occupation or in the ethical values of an employer, and disengagement from some aspects of the work with reduced occupational efficacy, are likely secondary psychological mechanisms that help to preserve remaining energy resources and to cope with persistent unresolved work-related chronic stress.²

Every person's mental and physical energy resources are finite.³⁵⁻³⁸ Mental energy is the inner psychological resource that controls emotion, cognition, executive functioning (i.e., attention, working memory), and behavior. Mental energy regulates motivational orientation, the self-reward of gratification, appropriate judgment and decision-making, mental and physical endurance, inhibition of inappropriate responses, tolerance, and will power.³⁶ This regulation of self-control

consumes much of one's finite mental energy resource.³⁸ Mental energy itself is dynamic and adaptive, determined by complex interactions between endogenous factors such as genetics, epigenetics, personality, general health, sleep, and psychological elements and exogenous factors such as social support, exposure to environmental stressors, and lifestyle (e.g., diet, physical exercise).³⁷

The conservation of existing energy resources, or their "recharging" if depleted, can be achieved through social support via enhancing one's sense of mastery and competence by whatever means and whenever possible, such as by avoiding exposure to psychosocial or work stressors and through the pursuit of meaningful cognitive, emotional, or spiritual activities.^{4,38,39} Adequate resources of mental energy ensure physical and mental vigor, motivation, enthusiasm, cognitive resilience, effective coping with stress, and willpower.³⁷

The symptoms of burnout are maladaptive responses to chronic unresolved stressors. These symptoms are brought about by many factors including dysfunctional regulation of the neuroendocrine stress network, particularly the HPA axis with cortisol as its central agent.^{24,40} Glucocorticoid receptors are abundant in the cerebral prefrontal cortex and in the limbic system where they mediate normal stress responses, promoting or opposing mental resilience.⁴¹

The amygdala plays an essential role in regulating the function of the HPA axis. In response to chronic psychosocial stress, there is an increase in glutaminergic signaling in the amygdala, with consequent upregulation of its functional activity. This results in increased activity of the HPA axis, with consequent maladaptive stress responses. Additionally, chronic stress-induced release of noradrenaline triggers excitatory transmission of neural impulses in the amygdala, further dysregulating stress responses.⁴²

The HPA axis is interconnected with other neuroendocrine networks, and together, these regulate cognition, emotion, mood, sleep, and mental energy resources.^{24,40} Furthermore, it has been reported that clinical burnout is associated with functional dysregulation of inflammatory responses and with elevated levels of proinflammatory cytokines and markers of inflammation.^{5,13,43}

Normal activity of the prefrontal cortex is essential for executive functioning and executive control of adaptive behavior and for effective coping with psychosocial stressors. Executive functions refer to a set of mental processes, including self-control, working memory, attention control, and cognitive flexibility, which together consciously and unconsciously, voluntarily or involuntarily, regulate higher-order executive functioning such as abstract thinking, reasoning, problem-solving, judgment, planning, and decision-making. All these together mediate social interaction and execution of goal-directed behavior in an adaptive, flexible way.^{16,44}

Chronic exposure to psychosocial stressors may cause actual structural and functional alterations with consequent aberrant neural activity in the prefrontal cortex, leading to maladaptive responses. However, the genetic, developmental, cellular, or molecular factors that determine either resilience or susceptibility to psychosocial stressors, with an adaptive or maladaptive behavioral phenotype, are poorly understood.^{45,46}

Persistent clinical burnout is associated with a reduction in the volume of gray matter of the anterior cingulate cortex and dorsolateral prefrontal cortex as well as in the volume of the caudate and putamen structures, with reduced dendritic arborization and number of dendritic spines and reduced synaptic density.^{8,41,47,48} Persistent burnout is also related to an increase in the structural volume of the amygdala;⁴⁷ a reduction in 5-HT_{1A} receptor binding in

the limbic structures, hippocampus, and anterior cingulate cortex; and with interconnective dysfunctional regulatory activity between the amygdala, anterior cingulate cortex, and medial prefrontal cortex.⁴⁹

Physiologically, when stimulated by glutamatergic neural pathways, the medial prefrontal cortex and anterior cingulate cortex, via GABAergic neural pathways to the amygdala, send inhibitory signals that regulate the interpretation of psychosocial or work-related stressors in the amygdala. However, under circumstances of persistent chronic stress as in clinical burnout, the chronic stress-induced excessive release of glutamate, and possibly of glucocorticoids in the prefrontal cortex, mediate excitotoxic changes and neurotoxic damage in the prefrontal cortex. This disturbs the inhibitory effect of the prefrontal cortex on the amygdala, rendering it hyperactive, resulting in maladaptive responses to psychosocial or work stressors.^{8,47,48} As mentioned earlier, the volume of the amygdala is increased, and its enlargement is associated with an increase in dendritic arborization and spine density and with higher measurable levels of perceived stress.⁴⁷

All the cerebral functional activities mentioned above are also involved in integration of cognitive, emotional, and autonomic activities.⁵⁰ The neurotoxic effects of persistent stress-induced morphological changes and of functional dysregulation of neural pathways may explain the symptoms of clinical burnout. These include impaired executive functioning, attention control, and working memory; emotional exhaustion and dysregulation; and irritability, anxiousness, and physical fatigue.^{8,16,44,47,48} Individuals with clinical burnout must invest more mental energy in solving cognitive problems, resulting in mental exhaustion, and they need more time to recover mentally after the termination of cognitive effort.^{13,16} However, it is unclear whether or to what extent the deficits in executive

functioning, and the alterations in structural and functional activity of the brain, affect higher cognitive functions such as judgment and decision-making.¹⁶

Mental resilience

Personal mental resilience is the ability to remain functionally proficient or to rapidly recover following exposure to significant emotional, cognitive, or physical stressors. Resources of mental resilience (personal skills, competencies, attitudes, insight, patience, self-reliance) are not finite but rather have the capacity to either develop, accumulate, and become more effective or to become depleted or insufficient.^{25,51} Thus, mental resilience should be viewed as a dynamic process enabling successful cognitive and emotional adaptation to chronic stressors.⁵² The interactions between endogenous factors (molecular, genetic, general health, personality, brain function) and exogenous factors (social support, family support, nature of work-related stressors) determine an individual's response to psychosocial or occupational stressors, whether via adaptive coping or via dysfunction in cognitive, emotional, or physical domains. The roles played by complex epigenetics and genetics in dictating risk or resilience in the face of chronic psychosocial or occupational stressors cannot be overemphasized.^{41,51,52}

Mental resilience is associated with a functionally intact neuroendocrine system with no abnormalities in key molecular determinants of the neural pathways of stress responses. It is also associated with inherent molecular and cellular factors or with acquisition of molecular alterations and cellular adaptations that impart the successful coping responses underlying active dynamic resilience.⁴¹ There is some evidence that certain genetic and epigenetic elements related to the HPA axis and serotonergic, dopaminergic, and neuropeptide

Y neural pathways in the brain are associated with a resilience phenotype.⁴¹ Other factors include a competently functioning neuroendocrine stress system, adequate communication skills, and effective control of emotional and cognitive processes, which are all associated with successful adaptation to persistent stress. However, the molecular, genetic, and developmental aspects of mental resilience are poorly understood.⁵³ Resilience should not be viewed as either a specific genetic profile or a specific hard-wired neural brain network but rather as a dynamic adaptation process associated with acquiring goal-directed and problem-solving behaviors and with seeking social support.²⁵

Growing up in a healthy, loving family and in a protective and supportive environment is associated with well-developed resilient mental resources whereas growing up in a hostile, disapproving environment and experiencing adversity and emotional distress is associated with depleted mental resources of resiliency. Having a strong sense of control over self and one's environment as well as a sense of purpose, commitment, meaningfulness, optimism, tolerance, flexibility, motivation, self-efficacy, and a goal-directed attitude all impart resilience in mental resources.⁵¹

The interplay between social, psychological, and biological factors generates a person-specific phenotype of resilience. This may change over time with changes in these factors and with exposure to novel, non-occupational stressors.⁵² Individuals who may previously have coped successfully with psychosocial stressors appear to have enhanced coping abilities, probably because they have acquired new preventive skills and have undergone meaningful changes in their perspective on life, or because they have undergone epigenetic and genetic alterations associated with effective resilience.⁵²

Exposure to moderate levels of psychosocial stressors, particularly during childhood and adolescence, imbues a sense of self-control, promoting the development of active adaptive coping mechanisms and future mental resilience. However, exposure to either low or high levels of psychosocial stressors during childhood and adolescence impairs the development of adaptive coping mechanisms. However, few individuals exposed to substantial psychosocial stressors develop significant mental dysfunction.⁴¹

Cognitive behavioral therapy (CBT) in the context of burnout

CBT is an interactive psychological technique aimed at supporting mental health by promoting the identification of one's personal negative thinking and emotional processes related to psychological or work stressors, and the mental and physical maladaptive responses to these. CBT also focuses on current situations and self-awareness regarding objectives in life. This is intended to normalize emotional status and to promote focused thinking, mental coping, task adaptation, and the ability to defuse potentially problematic situations and to correct maladaptive behaviour.^{54,55} In the context of burnout, CBT has been found to be relatively beneficial in improving work-directed behavior, overall work performance, and in reducing mental strain.⁵⁵ Together with work-related intervention, CBT is clinically beneficial and can promote a speedy return to work.⁵⁶ However, to further improve the efficacy of CBT, the specific factors associated with the genesis of burnout should be targeted more directly.

After approximately 10 weeks of CBT, individuals with clinical burnout may become aware of a general improvement in their symptoms, including in their cognitive difficulties; however, these individuals

still underperform on cognitive tests in comparison with controls. It may be that people who develop burnout may have previously experienced a diminution in their executive functions, predisposing them to burnout. In such cases, burnout becomes an additional burden superimposed on already deficient executive functioning, further reducing cognitive resilience, coping ability, and self-control. Although improbable, persistent cognitive difficulties owing to burnout may become permanent, or more time may be required for the cognitive difficulties to resolve.¹⁶

Mindfulness in the context of burnout

Mindfulness is a mental process to bring about a state of conscious attentional awareness through non-judgmental engagement with, and deliberate, free observation of one's own emotions, feelings, thoughts and actions as they unfold.^{57,58} Those who practice mindfulness show expanded psychological flexibility and can effectively control negative internal experiences to therefore positively engage with the immediate environment.⁵⁵ This can pave the way for a shift in cognitive perception, with reappraisal of negative emotions and life events, allowing finding of some sense of meaning, compassion, and self-identity in relation to adverse experiences and to consequently modify maladaptive behaviours.^{57,58}

Improvement in emotional, attentional, and behavioral regulation induced by mindfulness is associated with increased levels of personal mental energy, self-control, satisfaction, conscientiousness, empathy, and competence as well as with positive structural and functional changes in regions of the brain (prefrontal cortex, amygdala, hippocampus) that regulate executive functioning, learning, and responses to stress.^{57,59}

In the context of burnout, mindfulness-mediated positive reappraisal of work stressors and of the cognitive-affective responses to these stressors (emotional exhaustion and cognitive weariness), through mentally assigning them a more benign connotation, may promote self-understanding of the burnout experience, thus enhancing mental resilience and restoring a sense of meaning despite the adversarial circumstances that caused burnout.^{57,60}

Management

An increase in personal psychological capacity to cope with occupational stressors on the one hand, and implementation of positive changes in the workplace on the other hand, are both necessary to control the burnout phenomenon.^{4,21,61} Through coping strategies such as CBT, mindfulness, stress-management activities, and striving to improve communication, time management, and professional skills, individuals experiencing burnout can change some aspects of behavior at work, strengthen internal energy resources and sense of self-control, and improve stress-coping skills and overall mental resilience.^{21,25,27,61}

Conscious avoidance of and disengagement from some work-related stressors is a passive coping strategy also worth considering.

Clinical burnout is usually an affliction of idealistic individuals who no longer find meaning in their occupation, so they should be encouraged to find existential meaning outside of the workplace.^{62,63} Finding some sense of purpose in any aspect of life leads to increased work satisfaction and reduces the symptoms of burnout.²⁶

Anyone susceptible to burnout must use adaptive and compensatory strategies to combat occupational stress-induced mental energy depletion that negatively affects work-related performance. Such strategies include activation of the sympathetic nervous system, leading to an increase in

work-related efforts. However, this carries the risk of further depletion of already compromised energy resources, thus exaggerating overall emotional exhaustion, physical fatigue, and cognitive weariness. Additionally, reframing work goals, lowering expectations regarding the end product of one's efforts, or reducing the degree of energy used for low-priority goal-directed activities or even neglecting them altogether, may help to conserve mental energy for high-priority goals.³²

Engagement in multiple occupational roles may result in substantial depletion of mental energy resources, inter-role conflict, psychological stress, and in impaired cognitive, emotional, and physical functioning, which may ultimately lead to burnout.⁶⁴ In this situation, the affected person should try to prioritize tasks and to focus mainly on the most important occupational targets while reducing attention to or delegating less important, time-consuming activities.³²

Thoughtful management in the workplace should include the introduction of measures aimed at reducing the incidence of occupational burnout among leaders as well as subordinates. For example, regular staff meetings should be held for team building, briefing, debriefing, and reflections on organizational matters, for voicing of concerns regarding responsibility, accountability, and equity and consideration of flexible work options, when possible. Other important matters include stress-reduction programs and the promotion of career development and opportunities for advancement.^{25,61,65}

It is important that the workplace be friendly and comfortable, with places set aside for relaxing and socializing but that still allow for privacy when necessary.⁶⁵ Whether in a larger organization or a small private enterprise, managers should make every effort to reduce work-related stress and to foster a non-toxic, supportive

environment that is focused on fairness and equity.^{4,21}

Symptoms of burnout usually diminish markedly during a break from work, such as a vacation. However, the relief is only temporary, and unless work-related stress is reduced, burnout tends to reappear not long after returning to work.⁴ Therefore, employees should be encouraged to take periodic short vacations to minimize the buildup of emotional and cognitive fatigue.

Severe burnout is sometimes associated with both structural and functional dysregulation of central neural pathways, and possibly with frank psychological disorders. Individuals with clinical burnout should therefore undergo thorough neurological and psychological investigations and receive treatment when necessary. Occasionally, however, medical practitioners either do not recognize burnout as a medical condition or mistake it for depression.^{19,48}

Because studies investigating the efficacy of burnout interventions are heterogeneous with regard to diagnostic criteria, study design, sample size, type of intervention, methods of measuring outcomes, and duration of follow-up, and because most study samples are small, with low statistical significance and insufficiently documented comorbidities and associated treatments, it is not possible to draw meaningful conclusions about the efficacy of specific interventions. Moreover, adequate information about the natural course of burnout and the nature of its recovery does not exist.^{56,63}

Discussion

A limitation of this study is that we conducted neither a meta-analytical nor a systematic review but rather a narrative review addressing important neurophysiological factors, clinical features, and management aspects of burnout. At present, there are no standardized and internationally accepted diagnostic criteria for burnout, and the

incidence and prevalence of burnout vary from country to country; therefore, it is not possible to determine the global epidemiological features of burnout.²⁷ Nevertheless, it is clear that burnout occurs more frequently among health care professionals, policemen, firefighters, and other workers in the service or helping professions who are chronically exposed to work overload and intense work-related stress.^{66–69} In this context, during the ongoing COVID-19 pandemic, all health care workers in contact with patients who have COVID-19 infection are at especially high risk of burnout. There are many factors exacerbating this risk such as understaffing, work overload, lack of sleep, physical fatigue, psychological stress, and ethical dilemmas associated with treatment, among others.^{70,71}

Implementing organizational and structural changes in the workplace cannot reduce the severity of burnout among professionals like nurses and physicians without strengthening of personal intrinsic factors such as stress management, psychological coping, and resilience capacities, as well as communication and teamwork competencies. However, addressing these intrinsic personal factors may only lead to a small improvement in the mental well-being of such professionals. The best clinical outcomes are achieved when both personal and organizational interventions are used concurrently.⁶¹

Conclusion

Burnout is a work-related, stress-induced, psychological syndrome. Coping strategies by which the characteristics and perceptions of work-related stressors are assessed and reframed, together with engagement in meaningful collateral activities, can enhance psychological resilience and consequent behavioral adaptability, which may reduce the distress of burnout.

Further studies are needed to determine the efficacy of mindfulness, CBT, and other stress-coping interventions in reducing the extent and severity of burnout; whether burnout may occur outside the workplace; what percentage of individuals with burnout develop frank depression; the central neural circuits that mediate either resilience or susceptibility to occupational stress; and the complex epigenetic and genetic combinations involved in the genesis of burnout.

Author contributions

LF designed and conceptualized the article. LF and RAGK wrote the first draft. LF, JL, and RAGK wrote the second and final draft. GF and SN performed the literature search and literature review. All authors edited the final version of the article. RAGK, SN, GF, JL, and LF read and approved the final version of the article. RAGK and GL managed the project.

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