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Review Article

Limbic brain structures and burnout—A systematic review

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ABSTRACT

More profound understanding of the relationship between the burnout and the limbic system function can provide better insight into brain structures associated with the burnout syndrome. The objective of this review is to explore all evidence of limbic brain structures associated with the burnout syndrome. In total, 13 studies were selected. Four of them applied the neuroimaging technology to investigate the sizes/volumes of the limbic brain structures of burnout patients. Six other studies were to investigate the hypothalamus-pituitary-adrenal (HPA) axis of burnout patients. Based on the results of the studies on the HPA-axis and neuroimaging of the limbic brain structures, one can see great impact of the chronic occupational stress on the limbic structures in terms of HPA dysregulation, a decrease of BDNF, impaired neurogenesis and limbic structures atrophy. It can be concluded that chronic stress inhibits the feedback control pathway in the HPA axis, causes the decrease of brain-derived neurotrophic factor (BDNF), then impaired neurogenesis and eventually neuron atrophy.

Contents

1. Introduction

The term ‘limbic system’ was introduced by Paul Broca. The cortical areas to form a ring around the brain stem, called later the ‘limbic lobe’, consisted primarily of the cingulate cortex, the temporal lobe cortex and the hippocampus [1]. Further studies discovered that our emotions, including our consciousness, are

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largely connected with these particular brain areas. The 'Papez circuit' included the hippocampus, fornix, mammillary bodies, anterior nucleus of the thalamus, anterior cingulate gyrus but not the amygdala [2]. Today, the limbic system structures include the hypothalamus, hippocampus, amygdala, and the nuclei septal. These structures are largely interconnected and have their own individual overlapping functions. These structures are responsible for our memory, emotions, emotional learning, and behavior, as well as motivation and reward [3].

Burnout is defined as an excessive stress reaction to the occupational or professional environment, composed of three major dimensions; emotional exhaustion, depersonalization and low personal accomplishment [4]. Burnout patients also reported having typical symptoms such as memory and concentration problems, insomnia, diffuse aches, physical fatigue, irritability, anxiety and a feeling of being emotionally drained. These symptoms are often known as subjective health complaints as up until now, no objective signs of illness have been found for these complaints. The burnout symptoms are symptom clusters comparable with characteristics of chronic fatigue syndrome (CFS) and post-traumatic stress disorder (PTSD) [5–7]. However, the burnout is preceded by a prolonged work-related stress. Work-related stress is defined as an occupational stress wherein emotional factors predominate. This is an important difference as work-related stress and burnout are usually assessed using different tools.

The attention should be paid to the key issues reflecting correlations between the burnout, work-related stress and biological parameters:

- the link between the burnout and work-related stress,
- the biological aspects of burnout, more specifically, the role of limbic system and HPA-axis in the development of burnout,
- the link between the burnout and CFS and PTSD.

Concerning stress, there are two major systems mediating most components of the stress response [8,9]. The first is the limbic-hypothalamic-pituitary-adrenal (LHPA) system which stimulates the adrenal cortex to release glucocorticoids such as cortisol into the blood. The second is the sympathico-adrenomedullary (SAM) system whose activation increases our heart rate and blood pressure by releasing catecholamines such as epinephrine and norepinephrine into the bloodstream.

Ten years ago, Langelaan et al. reported findings from a study on the burnout syndrome and level the salivary cortisol to determine the cortisol awakening response (CAR) and it kept many scientists thinking and talking about not because the authors provided a spectacular evidence but because they did not find any differences between the burnout patients and the healthy control [10]. Since then many studies have been carried out focusing on the aspect of the limbic system, especially regarding the hypothalamus-pituitary-adrenal (HPA) axis and the burnout in order to discover the relation link between them. Yet scientists are still facing many inconsistent and nonsignificant findings – the results from different studies were mixed but researchers were not able to provide any significant evidence to prove a relationship between the limbic system and the burnout syndrome. Soon after the Langelaan's [10] publication, Sonnentag [11] wrote an article to address this problem in discussion –why scientists could not find significant differences in the HPA axis and the burnout for several reasons: firstly, the complexity of the processes of the HPA axis and the associated problems of measuring its functioning. Secondly, due to the issues associated with the samples included in the analyses (the problem of defining cut off scores for differentiating between the burnt-out and healthy persons, and the small sample sizes of subjects). The third reason is related to the participants' work and life situation, and the last reason may come from the processes associated with hypocortisolism. Besides pointing out the reasons why scientists failed to find differences between the burnout and the healthy persons, the authors also provided some suggestions how to improve the methodology of burnout research.

In the past 10 years, more studies were carried out in the same area with the same focus. Despite the aforementioned attempts, it seems we have not been able to overcome those obstacles and find any significant differences in the relationship of the burnout and the limbic system structures.

The objective of this review is to explore the evidence of limbic brain structures associated with the burnout and work-related stress. This enables more profound understanding of the interrelationship between the burnout, work-related stress, brain structures, and their activation.

2. Methods

This systematic review is based on the published peer-reviewed articles. For the purpose of this systematic review, the literature search was made in two major databases (PubMed and Medline Complete) with the following keywords: 'limbic system'; 'hypothalamus'; 'hippocampus'; 'amygdala'; 'HPA'; 'burnout' and 'work-related stress'. Focus on only the studies observing burnout and limbic structures would be limited. The search period covered from 2006 to 2016 and was limited to the English language. The authors used the following inclusion and exclusion criteria:

- the inclusion criteria: the original papers published in journals and conference proceedings, peer-reviewed, the language of publication: English,
- the exclusion criteria: reviews, case studies, editorials, letters, book chapters, etc., non peer-reviewed, the language of publication: other.

The studies were evaluated by using the own quality assessment tool providing an added value and improving the quality of the review. The evaluation system:

- study design (including sampling): 0–3 pts.,
- research tools (including the use of standardized tools): 0–3 pts.,
- analysis (including used statistical and/or computational methods): 0–3 pts.

The total score: 0–9 points. The studies with higher scores were estimated to be more valuable.

3. Results

The preliminary electronic literature search resulted in the identification of total 40 studies: 34 from PubMed and 6 from Medline. All the selected studies applied Maslach Burnout Inventory (MBI) as the burnout measures, and after satisfying the inclusion criteria for this review, only total 10 studies were selected. From among of those studies, four (3 using functional magnetic resonance imaging (fMRI) and 1 using positron emission tomography (PET)) employed neuroimaging technology to investigate the differences of sizes/volumes of the limbic brain structures in the burnout patients and healthy control. Six other studies were to investigate the HPA-axis of burnout patients (Fig. 1). The detailed information of the studies (including their score) is presented in Table 1. The studies included in the analyses are heterogeneous and grouped in Table 1: firstly, some studies focus on the burnout and the others on the work-related stress.

Three of our studies [12–14] covered the cortisol studies described earlier by Danhof-Pont et al. Danhof-Pont et al. found no