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Executive control, ERP and pro-inflammatory activity in emotionally exhausted middle-aged employees. Comparison between subclinical burnout and mild to moderate depression

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ABSTRACT

Burnout is a syndrome occurring mainly in individuals with long-term stressful work. The main complaints are emotional exhaustion and reduced performance. Burnout also largely overlaps with depression. Both are characterized by increased incidence of infections due to dysregulation of the immune system, overexpression of pro-inflammatory cytokines and cognitive deficits, particularly related to executive functions. To distinguish between burnout and depression already at the pre-clinical stage, the present double-blinded study compared immunological and cognitive parameters in seventy-six employees from emotionally demanding occupations who were post-hoc subdivided into two groups scoring low (EE−) and high (EE+) in emotional exhaustion and low (DE−) and high (DE+) in depression. Immunological parameters were measured from blood samples. Executive functions were studied by analyzing event-related brain potentials (ERPs) and performance during a task switching paradigm. Psychosocial job parameters were measured with standardized questionnaires.

Burnout and mild to moderate depression largely overlapped. However, several subjects showed burnout without depressive symptoms. Higher levels of the pro-inflammatory cytokines IL-6 and IL-12 were correlated with burnout severity and depressive symptoms in male individuals. In the switch task a trend for lower performance in the EE+ vs. EE− group and no difference between DE+ and DE− groups were found. In the ERPs, however, differences were observed which distinguished between subclinical burnout and depression: the terminal contingent negative variation (CNV), indicating preparatory activity and the P3b, related to allocation of cognitive resources were generally reduced in EE+ vs. EE−, whereas no differences were found in the DE+ vs. DE− groups. The frontal P3a was selectively reduced in switch trials in the EE+ vs. EE− group and showed only a trend in DE+ vs. DE−, indicating impairment of executive control in subclinical burnout. Taken together, the results unveil specific immunological changes and declines in brain functions in employees with subclinical burnout that are not apparent in persons with moderate depression. Hence, the combination of immunological, behavioral and ERP methods renders a promising method for distinguishing both syndromes and for improving an early diagnosis of burnout before a clinical stage is reached.

1. Introduction

The term “burnout” was first introduced over four decades ago (Freudenberger, 1974), but it still remains an issue of much conceptual controversy (Bianchi et al., 2017; Epstein and Privitera, 2017). Burnout is assumed to be a possible outcome of chronic, usually work-related stress (Ahola et al., 2008; Kristensen et al., 2005). The symptoms of burnout are emotional exhaustion, depersonalization, and reduced personal accomplishment (Maslach et al., 2001). These symptoms overlap considerably with those of depression and therefore burnout was usually not considered as a distinct clinical entity (Bianchi et al., 2015, 2017). However, there is also evidence that burnout and

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depression are not identical concepts (Ahola et al., 2014; Epstein and Privitera, 2017; Gajewski et al., in press; Maslach and Leiter, 2017; Schaufeli et al., 2001; Toker et al., 2005). Apart from studies showing moderate correlations between emotional exhaustion and depression (Schaufeli et al., 2001; Toker et al., 2005), only few studies have explicitly aimed at comparing burnout and depression in the same sample of subjects to extract specific symptoms related to the one or to the other syndrome (van Dam, 2017).

Two stages of burnout should be distinguished: a mild form of work stress related problems that do not prevent an employee from working, and a serious clinically relevant pattern of personal distress and diminished performance which is the end stage of the burnout process. These two stages of burnout are mostly referred to subclinical and clinical burnout (Schaufeli et al., 2001; Edelwich and Brodsky, 1980; Oosterholt et al., 2014). The subclinical burnout group comprises relatively healthy employees, who report burnout symptoms but who do not seek help. The clinical burnout is characterized by symptom severity and inability to work and is usually diagnosed by professional experts (Oosterholt et al., 2014; van Dam, 2016).

Burnout seems to be accompanied by changes of cardiovascular, endocrine, and immunological parameters (Mommersteeg et al., 2006). However, the data are equivocal. For example, the raise of the cortisol awakening response was increased in burnout in one study (De Vente et al., 2003), while it was decreased in other studies (Juster et al., 2011; Mommersteeg et al., 2006). A meta-analysis could not find evidence for stable cardiovascular and humoral biomarkers of burnout (Danhof-Pont et al., 2011). In contrast to findings in major depression (Müller, 2014), only very few studies investigated changes in immunological parameters in burnout (Nakata, 2012). Changes in Natural Killer cell activity (Nakamura et al., 1999) or T lymphocyte numbers (Bargellini et al., 2000) were reported in single studies, while several studies found changes in pro-inflammatory cytokines associated with burnout (Toker et al., 2005; Mommersteeg et al., 2006).

Since one of the symptoms of burnout is a decrease of work performance, cognitive changes in people suffering from burnout were also investigated (Taris, 2006). Whereas cognitive impairments in major depression are well documented (Marazziti et al., 2010), the results of cognitive changes in burnout are inconsistent. Some studies did not find effects on the executive functions like working memory updating, inhibition, and switching in subclinical and clinical burnout (Oosterholt et al., 2014; Sokka et al., 2016), while other studies found memory and attentional deficits (Österberg et al., 2009) as well as declines of executive functions (Öhman et al., 2007). The precise mechanisms underlying this impairment of cognitive functions in burnout are currently unknown. A candidate mechanism is a chronic release of cortisol that affects the architecture, density and metabolism of cells of neuronal networks in vulnerable brain areas like hippocampus, involved in memory consolidation (Lupien and Lepage, 2001), and prefrontal cortex, associated with executive functions like switching, inhibition and working memory (Arnsten, 2009). Alternatively, pro-inflammatory activity enhanced in major depression may also play an important role in burnout. Recent research has shown that inflammatory mediators, particularly serum interleukin 6 (IL-6) is associated with major depression and cognitive dysfunction in elderly (Baune et al., 2008; Zadka et al., 2017).

In contrast to behavioral measures, ERPs yield information about timing and strength of different cognitive processes, which are not directly reflected in behavior. For example, the effortful preparation for an upcoming task is reflected in a slow negativity, the contingent negative variation (CNV; Falkenstein et al., 2003). Further prominent ERPs are the frontally distributed P3a associated with novelty processing, switching of task context, and orientation towards a new relevant stimulus, and the parietally distributed P3b that was associated with working memory and allocation of cognitive resources to the task (Polich, 2007). A reduced P3b was associated with lower performance (Gajewski et al., 2010). ERP studies in burnout are scarce and show mainly reduction of the P3b (Sokka et al., 2016, 2017; Van Luijtelaar et al., 2010). In this regard, a reduced status of norepinephrine (NE) might play a role. NE is the main neurotransmitter contributing to the generation of the P3b (Nieuwenhuis et al., 2005; Polich, 2007) and at the same time is one of the basic neurotransmitters responsible for the pathogenesis of depression which presumably led to P3b reduction in depressive patients (Bruder et al., 2009). NE also induces inflammation by stimulating the synthesis of pro-inflammatory cytokines like interleukin-6 (Slota et al., 2015; Zadka et al., 2017).

2. The present study

In the present study we examined whether emotional exhaustion in employees with long lasting stressful jobs is related to alterations of executive functions, brain activity and immune parameters. To test whether these alterations are specific for burnout and not for subclinical depression (and vice versa) the whole sample of participants was divided into subgroups with respect to emotional exhaustion or existence of depressive symptoms. Executive functions were measured in a memory-based task switching task that requires switches among a memorized sequence of tasks.

We assumed that executive functions are impaired in persons scoring high in emotional exhaustion. We expected a reduced CNV in burnout given that the motivation to prepare should be attenuated due to exhaustion (Falkenstein et al., 2003). Secondly, we hypothesized reduced P3a amplitude in emotionally exhausted individuals, particularly in conditions involving executive control. The P3a is generated in frontal brain areas, reflecting task set switching, re-orienting and processing of contextual novelty (Polich, 2007). These functions should be prone to long-term stress that affects frontal brain areas involved in executive functions (Arnsten, 2009). Finally, we expected an attenuated P3b, reflecting decreased allocation of cognitive resources to the task in burnout. If subclinical burnout and depression are largely overlapping syndromes, we expect similar findings in both groups.

Finally, we expected to find specific differences in pro-inflammatory cytokines between individuals scoring high in burnout and depression. This may directly affect brain functioning and production of neurotransmitters and synaptic transmission leading to impaired performance and electric brain activity.

3. Methods

3.1. Participants

Seventy-six healthy employees from emotionally demanding jobs participated as subjects. Their age ranged from 30 to 60 years with a mean of 43.9 years. They were mainly care nurses (n = 32), policemen (n = 20), teachers (n = 20), physicians (n = 3) and a fire fighter. Twenty-five of the participants worked in three-shift duty, 14 in two-shift duty, while 37 had no shift work. 47 of the participants were female (61.8%). 67% of the participants worked in a full-time job. They were recruited via a newspaper article and announcements in various hospitals, rest homes, nursing services, schools and police departments. One prerequisite for inclusion was the absence of any sensory, neurological and psychiatric diseases like clinically diagnosed major depression or burnout. Thus, only persons with subclinical burnout participated in the study. Subclinical burnout comprises relatively healthy employees, who report burnout symptoms but are currently not seeking help. One third of the participants reported common medication use for hypertension, intake of thyroid hormones, and cholesterol lowering