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Burnout in the brain at work

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Contents

Abstract

Long-term exposure to a stressful working environment where demands of the job exceed the resources of the worker may develop into job burnout. It is a major concern in working life, and in Finland, approximately one fourth of working aged people experience symptoms of burnout. Burnout is a psychological syndrome typically characterized by exhaustion, cynicism, and reduced professional efficacy. Individuals who experience symptoms of burnout often report decreased sense of efficacy in performing their daily work, as well as difficulties in concentration and memory. To date, however, little is known about the relationship between burnout and cognitive processes in the brain. The present thesis explores how pre-attentive auditory processing, and attentional and cognitive control processes are associated with burnout. As a method, we used scalp recordings of event-related potentials (ERPs) extracted from continuous electroencephalogram (EEG). The participants were 41 volunteers reporting a wide range of burnout symptoms, and 26 control participants. The results showed that burnout is associated with alterations in ERP responses reflecting involuntary attention shift and voluntary task-related processes. More specifically, momentary involuntary capture of attention to emotionally valenced speech sounds is faster for negative, and slower for positive utterances in burnout than in the control group as reflected by divergent P3a latencies even when the burnout symptoms are relatively mild. Burnout is also associated with dysfunctions in cognitive control needed to monitor and update information in working-memory as reflected by a decrease in task-related P3b responses over posterior scalp and increase over frontal areas. Perhaps, in burnout, sustaining a similar performance level as that of the control group might require additional recruitment of anterior regions to compensate the decrement in posterior activity. In addition, orienting of attention towards potentially significant unexpected sounds is ineffective in burnout during working-memory processing as indicated by reduced P3a responses elicited by the distractor sounds. Finally, severe burnout is associated with less accurate performance and inadequate processing when rapid shifting of attention between tasks is required as reflected by smaller P3 responses compared to the mild burnout and control groups. The findings of the present thesis provide new information about dysfunctions in electrophysiological processes related to cognitive control in burnout.

Tiivistelmä

Kun työtilanne ylittää yksilön voimavarat ja työstressi pitkittyy, seurauksena voi olla työuupumus. Työuupumus on merkittävä ammatillinen huolenaihe työelämässä, ja Suomessa noin joka neljäs työikäisistä kokee eriasteisia työuupumuksen oireita. Työuupumukseen liittyy uupumusasteista väsymystä, joka ei liity yksittäisiin työn kuormitushuippuihin. Muita ominaispiirteitä ovat oman työn merkityksen kyseenalaistaminen sekä ammatillisen itsetunnon heikkeneminen. On tavallista, että henkilöt, joilla on työuupumusoireita, kokevat muistin ja keskittymisen vaikeuksia. Vielä ei kuitenkaan tiedetä, miten työuupumus liittyy tiedonkäsittelyn toimintoihin aivoissa. Tässä väitöskirjassa tutkittiin työuupumuksen yhteyttä esitietoiseen kuuloinformaation käsittelyyn sekä tarkkaavaisuuden ja kognitiivisen kontrollin prosesseihin. Tutkimusmenetelmänä käytimme aivosähkökäyrässä (EEG) esiintyviä tapahtumasidonnaisia jännitevasteita (*event-related potential,* ERP). Tutkimukseen osallistui 41 työssäkäyvää henkilöä, jotka kokivat eriasteisia työuupumusoireita sekä 26 verrokkihenkilöä. Tulokset osoittivat, että työuupumus on yhteydessä poikkeaviin ERP-vasteisiin, jotka ilmentävät tahattoman ja tahdonalaisen tarkkaavaisuuden prosesseja. Jo verrattain lievä työuupumus on yhteydessä muutoksiin tarkkaavaisuuden kääntymisessä emotionaaliseen puheääneen. Tätä ilmentää P3a-vasteen kesto siten, että työuupuneet reagoivat sävyltään kielteiseen puheääneen tavallista nopeammin ja vastaavasti sävyltään myönteiseen puheääneen tavallista hitaammin. Työmuistiprosessoinnin aikainen aivotoiminta poikkeaa siten, että työuupuneilla tehtävätyöskentelyyn liittyvät P3b-vasteet olivat tavanomaista pienemmät päälaenlohkolla ja suuremmat otsalohkon alueella. On mahdollista, että työuupuneilla verrattain hyvä tehtäväsuoriutuminen edellyttää tavallista voimakkaampaa aivojen etuosien aktivaatiota kompensoimaan taaempien alueiden heikompaa aktivaatiota. Myös pienemmät P3a-vasteet yllättäviin häiriöääniin työskentelyn aikana osoittivat, että tarkkaavaisuuden kääntyminen tällaisiin mahdollisesti merkityksellisiin ääniin ei ole työuupuneilla yhtä tehokasta kuin verrokeilla. Lisäksi vakava työuupumus oli yhteydessä virheiden lisääntymiseen ja pienempiin P3-vasteisiin tehtävästä toiseen vaihdettaessa verrattuna lievästi uupuneisiin ja verrokkiryhmään. Tulokset tuovat uutta tietoa työuupumukseen liittyvistä kognitiivisen kontrollin poikkeavuuksista aivojen sähköisessä toiminnassa.

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Helsinki, on Valentine’s Day, 2017

Laura Sokka

List of original publications

This thesis is based on the following original publications, referred to in the text by Roman numerals (Study I-IV).

I Pakarinen, S., Sokka, L., Leinikka, M., Henelius, A., Korpela, J., & Huotilainen, M. (2014). Fast determination of MMN and P3a responses to linguistically and emotionally relevant changes in pseudoword stimuli. *Neuroscience Letters,* 577, 28-33.

II Sokka L., Huotilainen M., Leinikka M., Korpela J., Henelius A., Alain C., Müller K., & Pakarinen S. (2014). Alterations in attention capture to auditory emotional stimuli in job burnout: An event-related potential study. *International Journal of Psychophysiology*, 94, 427-436.

III Sokka L., Leinikka M., Korpela J., Henelius A., Ahonen L., Alain C., Alho K., & Huotilainen M. (2016). Job burnout is associated with dysfunctions in brain mechanisms of voluntary and involuntary attention. *Biological Psychology,* 117, 56-66.

IV Sokka, L., Leinikka, M., Korpela, J., Henelius, A., Lukander, J., Pakarinen, S., Alho, K., & Huotilainen, M. (2017). Shifting of attentional set is inadequate in severe burnout: Evidence from an event-related potential study. *International Journal of Psychophysiology*, 112, 70-79.

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Abbreviations

ANOVA	analysis of variance
BAI	Beck’s Anxiety Inventory
BBI-15	Bergen Burnout Indicator 15
BDI-II	Beck's Depression Inventory
BNSQ	Basic Nordic Sleeping Questionnaire
DSM-5	Diagnostic and Statistical Manual of Mental Disorders (5th edition)
EEG	electroencephalography
ERP	event-related potential
fMRI	functional magnetic resonance imaging
ICD-10	International Statistical Classification of Diseases and Related Health Problems (10th revision)
KSS	Karolinska Sleepiness Scale
MBI-GS	Maslach Burnout Inventory – General Survey
MMN	mismatch negativity
NASA-TLX	NASA Task Load Index questionnaire
RSI	response-stimulus-interval
RT	reaction time
SMBM	Shirom-Melamed Burnout Measure
SOA	stimulus onset asynchrony

1 Introduction

1.1 Job burnout is a stress-related syndrome

At work, it is common to encounter cognitively demanding tasks and contexts on a daily basis. For example, for successful performance it is essential to be able to focus on a given task even in the presence of distracting events, to flexibly switch between tasks and assignments, to modify one's behavior in light of new information, to solve novel problems or to generate new strategies. In addition, performance at and commitment to work are affected by numerous psychosocial factors such as emotions or attitudes, requirements for social skills, opportunities to influence one's workplace conditions or working time, and competition-related changes in working life (Work and Health Survey in Finland 2012; Kauppinen et al., 2013). Individuals who experience long-term work-related mental strain often report decreased sense of efficacy in performing their daily work, as well as difficulties in concentration, information processing, and memory.

Long-term exposure to a stressful working environment where demands of the job are high and the resources of the worker are low may gradually develop into job burnout (Maslach, Schaufeli, & Leiter, 2001; Melamed et al., 1999; Schaufeli & Enzmann, 1998). The central characterizations of job burnout share the idea that burnout is a psychological syndrome-like condition resulting from such prolonged, unresolvable stress at work. It concerns working life not only at an individual level but also at interpersonal and organizational levels (Le Blanc, de Jonge, & Schaufeli, 2008).

According to the most consensual characterization, burnout is a three-dimensional syndrome consisting of emotional exhaustion, cynicism toward work, and lack of professional efficacy (Maslach & Jackson, 1981; Maslach et al., 2001). Exhaustion, or fatigue, as the core symptom reflects the stress dimension of burnout while cynicism is considered as a way to cope with the work overload by distancing oneself emotionally and cognitively from work. Sense of inefficacy, or reduced personal accomplishment, seems less essential to the syndrome than the two other dimensions (Cox, Tisserand, & Taris, 2005). It is thought to emerge from lack of resources while exhaustion and cynicism arise from work overload and social conflict (Maslach et al., 2001). Another widely cited conception views burnout as relating to individuals' feelings of emotional exhaustion, physical fatigue, and cognitive weariness (Melamed et al., 1999; Melamed, Kushnir, & Shirom, 1992; Melamed, Shirom, Toker, Berliner, & Shapira, 2006). This characterization thus focuses on the depletion of one's empowering coping resources as a result of long-term work-related stress.

In addition, burnout is typically associated with impaired sleep (Ekstedt et al., 2006; Ekstedt, Söderström, & Åkerstedt, 2009). This is indicated by more sleep fragmentation and wake time, shorter latencies of slow wave sleep and rapid eye movement sleep, as well as lower sleep efficiency in burnout than control participants. Consequently, individuals with burnout show greater sleepiness and mental fatigue at most times of the days than others (Ekstedt et al., 2006).

Burnout overlaps with other stress-related disorders (van Dam, 2016), such as depressive disorders (Ahola, Hakanen, Perhoniemi, & Mutanen, 2014; for a review, see Bianchi, Schonfeld, & Laurent, 2015), anxiety (Blonk, Brenninkmeijer, Lagerveld, & Houtman, 2006; Ekstedt et al., 2006, 2009), and chronic fatigue syndrome (Huibers et al., 2003). Especially the relationship with burnout and depressive disorders has been under debate since the onset of burnout research in the 1970s (Freudenberger, 1974). For example, until the 1990s, it was suggested that burnout and depression can be conceptually and empirically distinguished, not only because burnout is job-related, but also because burnout includes social and attitudinal symptoms thought to be absent in depression (Schaufeli & Enzmann, 1998). Since then, however, Ahola and colleagues (2014) have proposed a conceptual similarity between burnout and depressive symptoms in the work-context. In a similar vein, according to a recent review, the distinction between burnout and depression is thought to be conceptually rather fragile, albeit empirically the distinction is partly supported (Bianchi et al., 2015). Definite conclusions about burnout-depression overlap are difficult to draw, partly due to somewhat inconsistent definitions of burnout among studies but also insufficient consideration of the heterogeneity of the spectrum of depressive disorders, too.

In terms of medical decision-making, no diagnostic criteria are available for identifying individual burnout cases. Burnout does not appear in the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) while in the 10th revision of the International Statistical

Classification of Diseases and Related Health Problems (ICD-10; World Health Organization, 1992) it is identified as a factor influencing health status and contact with health services, and as a problem related to life management difficulty. However, in clinical practice in Finland, a substitute diagnosis such as adjustment disorder, or depression, is sometimes made for individuals especially with severe burnout symptoms, and the diagnosis is used as a starting point for further actions and interventions (Tuunainen, Akila, & Räisänen, 2011). In Sweden, in turn, burnout has been established as a legitimate justification for sick leave (Friberg, 2009). Nevertheless, whether burnout should be regarded as an illness in its own right or not, remains an issue in scientific and clinical debate (Bianchi et al., 2015; van Dam, 2016).

The prevalence of job burnout varies somewhat together with the general circumstances in working life. For example, approximately 23-25% in working populations in Finland experience mild burnout symptoms (Ahola et al., 2005; Koskinen, Lundqvist, & Ristiluoma, 2012). Severe burnout, in turn, has been found to be rather stable in nature (Shirom, 2005), and its estimated prevalence varies between 2-7% in working populations according to studies conducted in the Netherlands (Schaufeli & Enzmann, 1998), Sweden (Hallsten, 2005), and Finland (Ahola et al., 2005; Koskinen et al., 2012). Such population based estimates have been suggested to be indicative of the situation in other developed western countries as well (Shirom, 2005). Thus, burnout appears to be quite prevalent, and it represents considerable economic, social, and psychological costs to employees and employers in all kinds of vocational groups (Ahola et al., 2006, 2008; Shirom, 2005). As a comparison, occasional insomnia-related symptoms are common among Finnish employees and they continue to increase as shown by a recent population-based study (Kronholm et al., 2016). In 2002, the prevalence of occasional insomnia-related symptoms were approximately 35%, whereas in 2013 the estimation was 45% in the general adult population. In parallel with this increase, the prevalence of depressive disorders in Finland has significantly increased from 7.3% to 9.6% during a follow-up period from the year 2000 to 2011 (Markkula et al., 2015).

In the research literature, burnout symptoms are assessed with questionnaires, and the most commonly applied instrument is the Maslach Burnout Inventory – General Survey (MBI-GS; Schaufeli, Leiter, Maslach, & Jackson, 1996). It is a standardized instrument, addressing 16 items clustered in three dimensions:

exhaustion, cynicism, and lack of professional efficacy. Other tools have been designed for assessing burnout, too, such as the Shirom-Melamed Burnout Measure (SMBM) covering physical fatigue, emotional exhaustion, and cognitive weariness as the core symptoms with 14 items (Melamed, Kushnir, & Shirom, 1992; Shirom & Ezrachi, 2003; Shirom & Melamed, 2006). In clinical settings in Finland, although no definite assessment guidelines exist, occupational health professionals commonly use the Bergen Burnout Indicator 15 (BBI-15; Näätänen, Aro, Matthiesen, & Salmela-Aro, 2003) to assess the severity of burnout symptoms. In the present thesis, grouping of the participants into burnout and control groups was based on the MBI-GS.

1.1.1 Cognitive functioning in burnout

Several behavioral studies have indicated that burnout is associated with impairments in cognitive functions (for a review, see Deligkaris, Panagopoulou, Montgomery, & Masoura, 2014), especially processing speed (Eskildsen, Andersen, Pedersen, Vandborg, & Andersen, 2015; Jonsdottir et al., 2013; Österberg, Karlson, & Hansen, 2009), working-memory updating (Jonsdottir et al., 2013; Oosterholt, Van der Linden, Maes, Verbraak, & Kompier, 2012), sustained attention and response inhibition (Sandström, Rhodin, Lundberg, Olsson, & Nyberg, 2005; Van der Linden, Keijsers, Eling, & Schaijk, 2005), as well as switching between tasks (van Dam, Keijsers, Eling, & Becker, 2011). Such deficits have been observed particularly in groups consisting of burnout outpatients, many of whom being on sick leave due to their severe burnout symptoms. However, the findings have been somewhat inconsistent with some of the results giving only partial support to the hypothesis of burnout-related impairments in cognitive functioning. For example, in the studies of Oosterholt and colleagues (2014), and Österberg and colleagues (2009), severe burnout was related only to a slightly slower performance in tests assessing processing speed but not in any other cognitive functions studied such as verbal memory, working-memory updating, inhibition or task shifting.

When the burnout symptoms are relatively mild, performance can be sustained at an equally good level as that of others (Castaneda et al., 2011; Oosterholt et al., 2014). Yet, despite this relatively comparable performance on traditional behavioral cognitive tests, Österberg and colleagues (2009) observed that subjective cognitive complaints about attention and memory were considerably more common among individuals with burnout symptoms than their control participants. The authors suggested that in reporting of the subjective cognitive problems, negative self-perception, or worry about future health and career due to decreased working capacity may be important determinants. Together these could lead to disturbances or decreased performance in everyday situations, and consequently, experienced as cognitive impairment.

Evidence from brain imaging studies suggests burnout-related alterations, too, especially in the functional connectivity of the limbic networks (Golkar et al., 2014; Jovanovic, Perski, Berglund, & Savic, 2011). The limbic system contains a group of interacting cortical and subcortical brain structures essential for processing of emotion and stress, and regulating motivational behavior (e.g., Heimer & Van Hoesen, 2006; Morgane, Galler, & Mokler, 2005). For example, the regulation of stress responses during emotional conflict is thought to be processed via functional connectivity between the amygdala and anterior cingulate cortex, parts of the limbic system, and the connected prefrontal cortical areas (Egner, Etkin, Gale, & Hirsch, 2008; Ochsner & Gross, 2005; Wager, Davidson, Hughes, Lindquist, & Ochsner, 2008). Notably, in a recent functional magnetic resonance image (fMRI) study of Golkar and colleagues (2014), participants with burnout symptoms showed weaker functional connectivity in the circuitry of the amygdala, anterior cingulate cortex, dorsolateral prefrontal cortex, and motor cortex than the control participants. Burnout symptoms were also associated with higher startle responses during down-regulation of negative emotion as measured with electromyographic recordings. Consequently, the authors suggested that the ability to modulate stressful emotions is impaired in burnout. Imbalanced interaction between the prefrontal cortex, anterior cingulate cortex, and amygdala has also been shown in relation to anxiety suggesting negative biases in the interpretation of emotion eliciting stimuli and enhanced selective attention to threat (Bishop, Duncan, Brett, & Lawrence, 2004; Bishop, 2007), as well as major depression (Davidson, Pizzagalli, Nitschke, & Putnam, 2002) and chronic psychosocial stress (Liston et al., 2006; Liston, McEwen, & Casey, 2009). In addition, regional morphological changes in the brain have been reported in association with burnout, as shown by reductions in cortical thickness in the dorsolateral prefrontal cortex and anterior cingulate cortex (Blix, Perski, Berglund, &

Savic, 2013), as well as in the medial prefrontal cortex (Savic, 2013), all of which have an essential role in the cortico-limbic circuitry (e.g., Ochsner & Gross, 2005).

All in all, however, a coherent theoretical framework for cognitive functioning in burnout is to date still lacking, and the underlying brain mechanisms are largely unknown due to scarcity of the literature and a number of methodological differences between the studies (Deligkaris et al., 2014). For instance, these studies vary in terms of cognitive functions of interest and methods with which they are evaluated, the applied methods for assessing burnout symptoms, or the nature of samples of participants (clinical vs. non-clinical). Moreover, electrophysiological studies related to burnout are still almost absent. Notably however, brain research methods provide a means to study fast cognitive processes in a more objective manner than behavioral methods. Consequently, they may have the potential to contribute to our understanding of the health and performance consequences of long-term stress at work. The present thesis addresses the association of burnout with attention and task-related brain mechanisms by means of electrophysiological recordings.

1.2 Electroencephalography (EEG) and event-related potentials (ERP)

Cortical processes associated with sensory, cognitive, and motor events can be studied with electroencephalography (EEG). It is a non-invasive brain research technique in which the electrical activity of neurons is recorded with a set of electrodes placed on the surface of the scalp. The temporal resolution of the EEG is high, that is, in the range of milliseconds. From EEG, one can extract neural responses that are time-locked to specific events of interest, such as processing of a sound or allocation of visual or auditory attention, by averaging EEG signals typically across tens, hundreds or thousands of presentations of experimental stimuli (Luck, 2014). These time-locked responses are called *event-related potentials* (ERPs). ERPs consist of a series of positive and negative voltage deflections, and they can be described across three dimensions: amplitude, latency, and scalp distribution. ERP recordings have been essential in understanding the cortical basis of fast sensory and cognitive processes. They are widely applied both in basic research, and in studies with different clinical subgroups such as patients with depression (McNeely, Lau, Christensen, & Alain, 2008), insomnia and/or excessive sleepiness (Gumenyuk, Belcher, Drake, & Roth, 2015), chronic fatigue syndrome (Polich, Moore, & Wiederhold, 1995), a brain lesion (Knight, 1984; Polich & Squire, 1993), coma patients (for a meta-analysis, see Daltrozzo, Wioland, Mutschler, & Kotchoubey, 2007), schizophrenia (Alain, Hargrave, & Woods, 1998) or attention deficit hyperactivity disorder (Oja et al., 2016).

1.2.1 Central auditory processing

Occurrence of a discrete sound elicits the auditory N1 response, a negative deflection of the ERP peaking at around 100 ms from stimulus onset over the fronto-central scalp. The N1 consists of several distinct components as it has multiple active neuronal generators highly overlapping in time (for a review, see Näätänen & Picton, 1987). Its amplitude is sensitive to the acoustical properties of eliciting sound as well as the stimulus-onset asynchrony (SOA, i.e., the time between onsets of successive stimuli) within a sequence of sounds, the N1 amplitude reducing with decreasing SOAs.

A stream of repeated standard sounds is thought to induce a transient memory trace. When a deviant sound is occasionally presented within such stream, the mismatch negativity (MMN) ERP response is generated even when the participant's attention is directed away from this sound stream (Näätänen, Gaillard, & Mäntysalo, 1978; for reviews, see Näätänen, Paavilainen, Rinne, & Alho, 2007; Näätänen, Astikainen, Ruusuvirta, & Huotilainen, 2010). The MMN appears to be elicited by any distinguishable change in a predictable pattern of sounds. Thus, while the N1 is suggested to reflect some stage of stimulus or feature detection, the MMN reflects detection of occasional changes in stimulus sequences. The MMN has its (negative) amplitude maximum over fronto-central scalp areas at about 100-250 ms after deviance onset. Since the MMN can be elicited in the absence of attention it was proposed to reflect a relatively automatic change detection process where the incoming stimulus is compared to and found deviating from the internal model of the auditory environment (Näätänen et al., 1978). More recent accounts on MMN elicitation stress the role of a larger neural model used to predict the future auditory events. On these theories, the MMN is related to the comparison process of a single acoustic event against the full neural model (Näätänen & Winkler, 1999; Näätänen et al., 2010), or even to the updating of the model (Sussman & Winkler, 2001; Winkler, Denham, & Nelken, 2009).

Traditionally, the MMN has been recorded using the so-called oddball paradigm (Näätänen et al., 1978) where infrequent (probability, p = 10-20%) deviant sounds are randomly or pseudo-randomly scattered within a sequence of standard (p = 80-90%) sounds. Such recordings, however, are time-consuming. In the new multi-feature paradigms (e.g., Näätänen, Pakarinen, Rinne, & Takegata, 2004; Pakarinen, Takegata, Rinne, Huotilainen, & Näätänen, 2007) several different types of sound changes are presented within the same stimulus sequence while reducing the number of standard stimulus presentations proportionally. This allows for several MMNs to be elicited by changes in different auditory attributes in the same sequence of sounds, thereby markedly shortening the recording time. It is assumed that the deviant stimuli can strengthen the memory trace of the standard with respect to those stimulus features they have in common with (Nousak, Deacon, Ritter, & Vaughan, 1996), albeit the MMN to a change in one feature is not, however, fully independent of all other stimulus features (Huotilainen et al., 1993; Paavilainen, Valppu, & Näätänen, 2001). Multi-feature paradigms have enabled an unprecedentedly fast parametric evaluation of central auditory processing of physical changes in simple tones (Näätänen et al., 2004; Pakarinen, Huotilainen, & Näätänen, 2010; Pakarinen et al., 2007), phonetic and acoustic changes in spoken syllables (Pakarinen et al., 2009) and pseudowords (Partanen, Vainio, Kujala, & Huotilainen, 2011), changes in emotional prosody in spoken pseudowords (Thönnessen et al., 2010), as well as changes in sounds integrated in a musical context (Huotilainen, Putkinen, & Tervaniemi, 2009; Vuust et al., 2011). In the present thesis, a new variant of the multi-feature paradigm was developed in Study I, and applied in Study II with a sample of participants with burnout symptoms.

1.2.2 ERPs related to involuntary attention and target detection

Attention is directed to a certain event either voluntarily or involuntarily (for reviews, see Corbetta & Shulman, 2002; Soltani & Knight, 2000). An important function of cognitive control is to regulate the interplay of voluntary and involuntary attention in order to flexibly adapt to changes in the environment. For example, attention is easily captured by unexpected events in the acoustical environment, which thereby disrupt the ongoing activity. Such sudden changes occurring outside the current focus of attention, however, may provide significant information for further adaptive behavior, and thus demand a switch of attention (Berti, 2008; Escera, Alho, Schröger, & Winkler, 2000).

When attention is allocated to an auditory or a visual stimulus, a large positive deflection, the P3, is elicited. The P3 typically consists of more than one positive-polarity ERP components peaking between 250-600 ms from stimulus onset. Voluntary and involuntary attention allocation yield distinct ERPs differing in relation to their cortical distribution, peak latency, and cognitive function (for reviews, see Polich, 2007; Soltani & Knight, 2000).

Involuntary attention involves orienting towards an unexpected event (e.g., Alho et al., 1998; Escera, Alho, Winkler, & Näätänen, 1998; Hölig & Berti, 2010; Soltani & Knight, 2000). In the acoustic domain, task-irrelevant unexpected novel sounds elicit a P3a response, peaking approximately 250-400 ms following stimulus onset (Escera, Alho, Winkler, & Näätänen, 1998; Friedman, Cycowicz, & Gaeta, 2001; Knight, Scabini, Woods, & Clayworth, 1989; Knight, 1984), but also shorter P3a peak latencies have been reported when novel environmental sounds are used as the eliciting stimuli (Alho et al., 1998). The P3a is thought to reflect involuntary capture of attention. Emotionally strongly valenced stimuli have been shown to elicit stronger and faster P3a responses than neutral stimuli (Campanella et al., 2002; Domínguez-Borràs, Garcia-Garcia, & Escera, 2008). Especially stimuli with negative contents may enhance novelty processing under potentially threatening conditions. In the present thesis, Studies I-III address the topic of novelty processing.

Task-relevant stimuli, in turn, elicit a P3b response, peaking approximately at 300-600 ms after stimulus onset over parietal scalp sites. It is thought to reflect a range of cognitive processes, such as context updating in working-memory, or activation of relevant task set (Donchin & Coles, 1988; Hölig & Berti, 2010; Picton, 1992; Polich, 2007; Soltani & Knight, 2000). In the research literature, the terms "P3", "P300", and "P3b" are often used partially synonymously to refer mainly to volitional target stimulus processing. In the present thesis, the "P3b" is used in Study III, and "P3" in Study IV to refer to the late positive response associated with target detection.

The scalp distribution of the P3a is more anterior than that of the P3b suggesting different neural generators. Both involuntary attention capture and voluntary target detection are generated by a widespread network of cortical regions, apparently including the dorsolateral prefrontal cortex, temporo-parietal junction, and medial temporal regions (Escera et al., 1998; Friedman et al., 2001; Knight et al., 1989; Knight, 1997; Polich, 2007; Soltani & Knight, 2000).

Because responses in the P3 family are thought to reflect attention and memory processes, they have been widely studied in clinical and subclinical groups (Polich & Kok, 1995; Polich & Herbst, 2000; Polich, 2007; Soltani & Knight, 2000). For example, the P3 response has been suggested to be susceptible to stress as well as fluctuations in the participant's level of arousal. More specifically, the P3b amplitude tends to attenuate with high stress (Shackman, Maxwell, McMenamin, Greischar, & Davidson, 2011), and both P3a and P3b amplitudes have been shown to reduce with increased sleepiness following sleep deprivation (for reviews, see Colrain & Campbell, 2007; Polich & Kok, 1995). In addition, there is evidence suggesting depression-related attenuation both in P3a amplitude in response to novel auditory stimuli (Bruder et al., 2009) and in task-related P3b amplitude together with lengthened P3b latency in response to emotionally positively valenced visual stimuli (Cavanagh & Geisler, 2006). Together these findings suggest disturbed attention- and task-related electrical brain activity in these conditions.

1.3 Top-down mechanisms in goal-directed behavior

At work, goal-directed behavior and the ability to rapidly and accurately switch attention between tasks and assignments are essential prerequisites for efficient and coherent performance. For this, specific cognitive processes need to be adaptively controlled and coordinated. Such top-down control mechanisms are called executive functions. Factor analytic and meta-analytic reviews have consistently identified three core executive functions: updating and monitoring working-memory representations, attentional shifting between task sets, and inhibition of prepotent responses (Miyake et al., 2000). Working-memory is the cognitive system responsible for storing, integrating, updating, and manipulating information during complex activities (Baddeley & Hitch, 1974; Baddeley, 1992, 2000). Typically in working-memory tasks, an increase in memory load results in longer reaction times (RTs) and higher error rates (e.g., Smith & Jonides, 1997). Also attentional switching between tasks, or task rules, typically comes with a cost, that is, responses are slower and, often, more error-prone immediately after a switch in the task compared to repeating the same task, a phenomenon called switch cost (Meiran, 1996; Monsell, 2003; Rogers & Monsell, 1995). Inhibition, in turn, refers here to one's ability to intentionally suppress inappropriate responses and behaviors (Jurado & Rosselli, 2007; Miyake et al., 2000).

In summary, working-memory and attention interact in a way that enables us to focus on relevant items and maintain current goals. In the present thesis, Study III addresses the association between burnout and distractibility during working-memory performance. Study IV, in turn, addresses the association between burnout and shifting of attentional set.

1.3.1 Widespread cortical activation in working-memory updating

In order to investigate the neural underpinnings of working-memory, the n-back paradigm is commonly applied. In this paradigm, participants are asked to monitor a series of stimuli and to respond if the incoming stimulus matches to the one presented *n* trials before. Several neuroimaging studies have shown that working-memory updating brings about considerable load-dependent activation on a fronto-parietal network, including the dorsolateral prefrontal cortex, posterior and inferior regions of the frontal cortex, and the posterior parietal cortex (e.g., Alain, Shen, Yu, & Grady, 2010; Carlson et al., 1998; Cohen et al., 1997; Leung & Alain, 2011; Owen, McMillan, Laird, & Bullmore, 2005; Rämä et al., 2001; Smith & Jonides, 1997). Evidence from ERP studies suggests that demands placed on the working-memory affect the P3 in such a way that as the memory load increases, the P3 amplitude decreases over parietal regions (Wintink, Segalowitz, & Cudmore, 2001; for a review, see Kok, 2001).

Clinical studies have shown that performance on an n-back task is not necessarily affected by partial or total sleep deprivation (Lo et al., 2012), or major depression (Harvey et al., 2005). However, despite comparable working-memory task performance, Harvey and colleagues (2005) observed in their fMRI study that the depressed patients showed greater activation of the lateral prefrontal cortex and the anterior cingulate compared to healthy control participants to achieve similar performance.

1.3.2 Working-memory load affects involuntary attention

Unexpected, novel sounds delivered during performance of a visual task cause a delay in participants' responses to task-relevant stimuli, as shown by studies using auditory-distraction paradigms, that is, participants are instructed to ignore the auditory stimulation while performing a visual task (Escera et al., 1998; Escera, Yago, & Alho, 2001; Escera & Corral, 2007). Two distinct consecutive phases, early and late, of the auditory P3a response have been identified to be elicited by distractor sounds, peaking approximately 230 and 320 ms after stimulus onset, respectively (Escera et al., 1998; Winkler, Denham, & Escera, 2015; Yago, Escera, Alho, Giard, & Serra-Grabulosa, 2003). The early phase of the P3a is maximal over temporo-parietal and fronto-temporal locations, whereas the later phase has a wider distribution spreading towards prefrontal and superior parietal regions (Escera et al., 1998; Yago et al., 2003).

When the task requires working-memory, the memory load modulates the distraction caused by the task-irrelevant auditory stimuli (Berti & Schröger, 2003; SanMiguel, Corral, & Escera, 2008). The distracting effect of novel sounds over the performance on the working-memory task is reduced when the memory load is high. This is indicated both behaviorally and by attenuation of the P3a amplitude, especially the later phase of the P3a, elicited by the distractor sounds. It should be noted, however, that other studies have suggested contradictory effects, that is, distractor effects are greater in high than in low working-memory load (Lavie & de Fockert, 2005; Lavie, 2005). In such proposals, working-memory load will increase distraction only when a conflict between target stimuli and distractor stimuli needs to be resolved but not when there is no response conflict generated by the stimuli as is the case in the auditory-distraction paradigms.

1.3.3 Attentional set shifting in the brain

Goal-directed control of attention is commonly investigated using task switching paradigms (for a review, see Monsell, 2003) requiring rapid shifting between simple task sets, or specific rules of a task. Good performance requires sustained attention on the task at hand when the task rule remains the same, but also flexibility that allows rapid execution of task set shifting when necessary. This switching between task-sets typically results in performance decrement, that is, the switch cost (Meiran, 1996; Monsell, 2003; Rogers & Monsell, 1995). Furthermore, performance is decreased to a greater extent following sleep deprivation (Heuer, Kleinsorge, Klein, & Kohlisch, 2004), and in certain clinical conditions affecting frontal functions, such as severe burnout (van Dam et al., 2011; van Dam, Keijsers, Eling, & Becker, 2012), depression (Meiran, Diamond, Toder, & Nemets, 2011), and prefrontal cortical lesions (Barceló & Knight, 2002).

There are a number of versions of the task switching paradigm. A widely applied paradigm is the alternating runs paradigm introduced by Rogers and Monsell (1995) in which switching between two simple tasks is predictable as the trials are presented in succession in a clockwise manner. Another popular variant is the task-cueing paradigm in which switch and repetition trials are randomly presented in a sequence with each upcoming target stimulus indicated by a cue, that is, whether the task rule will be switched or repeated (Meiran, 1996). The time interval between the cue and the target affects the switch cost: the shorter the interval, the larger the switch cost (Logan & Bundesen, 2003, 2004; Meiran, 1996). When the cue and target are presented simultaneously, for instance, when the location of the target stimulus indicates the task to be completed on a given trial, the cue and the possible task switch it instructs need to be encoded in parallel with target stimulus processing which may be disrupted, resulting in a further increase in switch cost (Logan & Bundesen, 2003; Nicholson, Karayanidis, Poboka, Heathcote, & Michie, 2005). In addition, with short cue-target interval or simultaneous cue-target presentation, there is a substantial temporal overlap between cue-related and target-related processes as indicated by coinciding switch-related positive deflections in the ERP waveforms (Nicholson et al., 2005).

Neural processes related to task switching can indeed be studied separately, for example, in relation to the cue, the target, or the motor response. ERP responses time-locked to the onset of the cue, presented separately from the target, typically show a larger posterior positivity for switch trials than repetition trials, as indicated by enhanced cue-related centro-parietal P3-like responses (Barceló, Periáñez, & Knight, 2002; Gajewski & Falkenstein, 2011; Karayanidis et al., 2010; Kieffaber & Hetrick, 2005; Kieffaber, O'Donnell, Shekhar, & Hetrick, 2007; Kopp & Lange, 2013;

Lange, Seer, Müller, & Kopp, 2015; Nicholson, Karayanidis, Bumak, Poboka, & Michie, 2006; Nicholson et al., 2005; Tarantino, Mazzonetto, & Vallesi, 2016) and a fronto-central task-novelty P3 response (Barcelo, Escera, Corral, & Periáñez, 2006; Barceló et al., 2002; Periáñez & Barceló, 2009). Recently, Berti (2016) applied a memory updating task in which either the same or another memory items were compared with the preceding trials, resulting in switch and repetition trials. Both trial types elicited a large bi-phasic P3-like response being more pronounced for the switch than the repetition trials.

By contrast, P3-like responses time-locked to the target stimulus have been typically shown to be smaller in amplitude for switch trials compared to repetition trials (Barceló, Muñoz-Céspedes, Pozo, & Rubia, 2000; Gajewski & Falkenstein, 2011; Goffaux, Phillips, Sinai, & Pushkar, 2006; Hsieh & Liu, 2008; Kieffaber & Hetrick, 2005; Tarantino et al., 2016) suggesting potentially functionally distinct target-related and cue-related processes. Furthermore, ERPs related to the response given to the preceding trial are characterized by a parietally maximal negativity between the response and the onset of the subsequent stimulus, reaching its maximal around 400 ms post-response (Karayanidis, Coltheart, Michie, & Murphy, 2003). When the response-stimulus interval is short so that there is only little time to prepare for the upcoming stimulus, there is likely a temporal overlap between response-related and stimulus-related processes (Karayanidis et al., 2003).

In sum, several studies applying a wide variety of stimulus and task manipulations indicate that the switch-related ERP responses consist of many underlying components, and that various control processes are recruited during performance of task switching, including context monitoring and updating, rapid reconfiguration, and task set preparation and execution (for a review, see Karayanidis et al., 2010). In the present thesis, we applied a paradigm with random switches, simultaneous cue-target presentation, and short response-stimulus interval (Study IV).

2 Aims of Studies I-IV

The present thesis explores attentional and cognitive control processes associated with burnout as reflected by ERPs. *First*, in Study I, we aimed at developing a variant of the multi-feature paradigm that allows the assessment of natural speech-sound processing as well as involuntary attention switch towards speech sound stimuli containing strong emotional prosody within one short recording time. *Second*, in Study II, we used the paradigm developed in Study I to investigate whether pre-attentive auditory change-detection processing as reflected by the MMN, and attention capture towards emotionally uttered speech sounds as reflected by the P3a are affected by burnout. *Third*, the aim was to explore whether or not burnout is associated with performance in a visual task with varying memory loads, and involuntary orienting of attention to unexpected, novel sounds during task performance (Study III), and *fourth*, rapid shifting between task sets (Study IV). In Studies II and III, the group comparisons were made between two groups, that is, burnout and control groups, whereas in Study IV, the group comparisons were conducted between three groups, that is, mild burnout, severe burnout, and control groups.

3 Methods

3.1 Participants and procedure

All studies in the present thesis are part of the *"Job Burnout and Cognition"* research project carried out at the Finnish Institute of Occupational Health (FIOH) in collaboration with the Occupational Health Centre of the city of Helsinki. The number of initially volunteered participants was 67, age range being 27-62 years (Studies II-IV). However, in Study III, one participant did not complete the applied paradigm, thus resulting in data from 66 participants. In Study IV, three participants did not complete the applied paradigm, resulting in data from 64 participants.

The participants were customers of the Occupational Health Centre of the city of Helsinki, or employees of the city of Helsinki. They were recruited through advertisements informing about the present research project in which association between burnout symptoms and cognitive functions was explored by means of brain research and neuropsychological methods. The advertisements were displayed at the local occupational health care station, as well as on the intranet sites of the aforementioned organizations. Alternatively, the participants were referred by a physician, psychologist, or nurse during appointments at the local occupational health care station to participate in the study. All control participants and approximately four fifths of the burnout participants entered the study after noticing the advertisement. About one fifth of the burnout participants were referred by an occupational health practitioner. At the time of the study, the participants were working.

All participants were first interviewed by telephone by the author of the present thesis to ensure that the potentially experienced symptoms of burnout were work-related, or to find out whether they volunteered as possible control participants. The interview included questions about, for instance, the symptoms and their onset, possible diagnosed neurologic or severe psychiatric illnesses (exclusion criteria), other possible etiology for the symptoms, education, and employment status. All worked only during daytime, that is, shift workers were included but night-shift workers were excluded. Other exclusion criteria were (i) excessive use of alcohol (i.e.,

≥ 40 g of ethanol per day for men, ≥ 20 g of ethanol per day for women; Alcohol: Current Care Guidelines, 2011) or drugs, (ii) diagnosed severe psychiatric or neurological disorders, and (iii) schizophrenia in first grade family members. Also other diagnosed illnesses of organic origin resulting in fatigue, such as an organic sleep disorder or severe anemia, were considered as exclusion criteria. All participants reported having normal or corrected-to-normal vision, and no hearing deficits. After recruitment, an appointment was made for the participation in the study.

Written informed consent for voluntary participation was obtained from all participants before entering the study. The protocol followed the Declaration of Helsinki for the rights of the participants and the procedures of the study. An ethical approval of the present research protocol was obtained from The Coordinating Ethics Committee of the Hospital District of Helsinki and Uusimaa. For their participation in the study, all participants were given a book gift and a gift card.

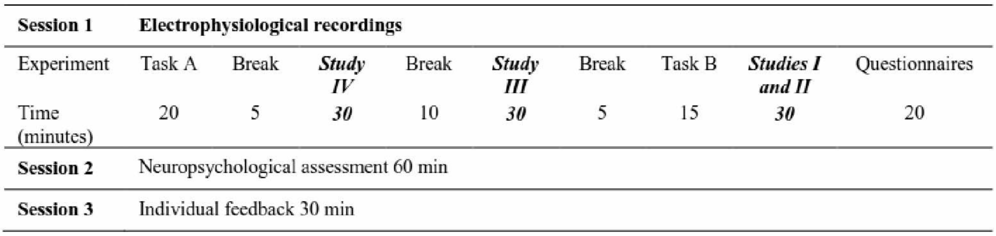
Final groupings of the participants into the burnout and control groups (Studies II and III) as well as to the mild burnout, severe burnout, and control groups (Study IV) were implemented in the following way. The Finnish version of the Maslach Burnout Inventory – General Survey (MBI-GS; Kalimo, Hakanen, & Toppinen-Tanner, 2006) was completed only after the ERP recordings, and the scores of the survey were used as a grouping criterion (Studies II and III: the total score cut-off point of 1.5, i.e., at least mild burnout, and Study IV: cut-off points of 1.5 for mild burnout, and 3.5 for severe burnout). The participants in Study I were the same as the control participants in Study II.

Based on exclusion criteria of EEG analysis (see section *"3.4 EEG data acquisition and analysis"* for details), complete datasets of 61, 49, and 57 participants were selected for further analysis in Studies II, III, and IV, respectively. In Study II, data from six participants (4 burnout and 2 control participants) were discarded due to excessive artifacts in their EEG, or technical difficulties in the EEG recordings. In Study III, data from 17 participants (10 burnout and 7 control participants), and in Study IV, data from 7 participants (3 mild burnout, 2 severe burnout, and 2 control participants) were discarded due to aforementioned reasons. The resulting groups did not differ statistically in terms of age, gender, education or working experience.

The participants were tested individually in two sessions, one consisting of measurements of ERPs in five different paradigms after which self-reports were completed, and the other of neuropsychological assessment (Table 1). The participants were given the opportunity to attend both sessions on one day or on two separate days, according to their preference. The ERP recordings were conducted in the morning: they began around 9 am, they lasted approximately 2.5 hours (including breaks). They were completed in a similar manner for all participants, starting from the cognitively most demanding experiments. Within 1-2 months after the entire study protocol, the participants were offered an opportunity to get individual feedback on the self-reports as well as the performance in the neuropsychological assessment, and to discuss their work situation with a psychologist (the author of the present thesis) and a neurologist from the Finnish Institute of Occupational Health.

In the present thesis, results from three out of five ERP paradigms are reported: the multi-feature MMN paradigm with emotional utterances of rare sounds (Studies I and II), the n-back paradigm with distractor sounds (Study III), and the task switching paradigm (Study IV). The two ERP paradigms not reported in the present thesis (Tasks A and B in Table 1) also required active engagement in cognitively demanding tasks.

Table 1. The ERP recording sessions always began in the morning around 9 am, and they lasted approximately 2.5 h (including breaks). Final grouping of the participants into study groups was completed after the ERP recordings on the basis of their responses to the burnout symptom questionnaire MBI-GS.



Session 1	**Electrophysiological recordings**								
Experiment	Task A	Break	***Study IV***	Break	***Study III***	Break	Task B	***Studies I and II***	Questionnaires
Time (minutes)	20	5	***30***	10	***30***	5	15	***30***	20
Session 2	Neuropsychological assessment 60 min								
Session 3	Individual feedback 30 min								

3.2 Collection of self-reports

In order to evaluate burnout symptoms, the Finnish version of the MBI-GS (Kalimo, Hakanen, & Toppinen-Tanner, 2006) and the Shirom-Melamed Burnout Measure (SMBM; Melamed, Kushnir, & Shirom, 1992; Shirom & Ezrachi, 2003; Shirom &

Melamed, 2006) were used. We chose to use the MBI-GS as the grouping criterion as it is widely used in research and maintains a consistent factor structure across a variety of occupations (Leiter & Schaufeli, 1996; Schutte, Toppinen, Kalimo, & Schaufeli, 2000). The MBI-GS manual provides instructions for calculating the total score (range 0-6), and separate scores for each subscale (exhaustion, cynicism, and professional inefficacy).

In addition, the following clinical measures were completed: the Finnish versions of Beck's Depression Inventory (BDI-II, scoring range 0-63; Beck, Steer, & Brown, 1996, Finnish norms, 2004) and Beck's Anxiety Inventory (BAI, scoring range 0-63; Beck & Steer, 1990), a questionnaire concerning possible prescribed medication for sleep disturbances and mood disorders, and a modified version of the Basic Nordic Sleeping Questionnaire for screening sleep disturbances (BNSQ, scoring range 0-11; Partinen & Gislason, 1995). Based on the BNSQ, sleep disturbances were evaluated with four weighted dimensions (weight coefficient in parenthesis): insufficient sleep (high), insomnia (high), sleep-apnea related symptoms (low), and excessive daytime sleepiness (very low). In addition, the participants were asked about caffeine intake within 24 hours prior to the recordings. Before the start of the ERP recording session, and between experimental paradigms, the participants were asked to rate their subjective sleepiness on the 9-point Karolinska Sleepiness Scale (KSS; Åkerstedt & Gillberg, 1990) as reported in Studies II and III. They were also asked to fill in the NASA Task Load Index questionnaire (NASA-TLX; Hart & Staveland, 1988) to evaluate subjective workload (e.g., effort put to the task) while performing the preceding task in the ERP recording session as reported in Study IV.

Table 2. Summary of the paradigms.

Paradigm	Stimuli	Task of the participant	Behavioral response	Number of stimuli
Studies I and II				
Multi-feature MMN with rare emotional utterances	Spoken pseudowords: standard /ta:ta/, nine deviants, three emotionally uttered variants	Ignore the pseudowords Concentrate on watching a muted video film	No behavioral response required	Standard and deviants: 210 each ($p \approx 0.09$) Emotionally uttered variants: 42 each ($p \approx 0.02$)
Study III				
N-back with distractor sounds	*Visual:* numbers (0-9)	Concentrate on performing the visual task:	*In all conditions:*	*In each condition:*
		0-back: Identify the current stimulus as predetermined '5' or any other stimulus	Button press for each visual stimulus (keyboard ctrl buttons covered with tape were used)	Visual: 212, 33% matches
		1-back: Determine whether the current number was the same or not as the previous one	Response to 'match' stimulus: button press with right index finger	
		2-back: Each stimulus was compared with the stimulus presented two trials before	Response to 'mismatch' stimulus: button press with left index finger	
	Sounds: environmental sounds	Ignore the auditory stimuli	No behavioral response for the auditory stimuli	Distractor sounds: 32
Study IV				
Task switching	Latin letters (A,E,I,U,G,K,M,R), and Arabic numbers (2-9) Letter-number pairs presented either above or below a solid stationary line	*Above the line:* classify the number in the letter-number pair as odd or even *Below the line:* classify the letter in the letter-number pair as consonant or vowel	Button press for each stimulus pair with right or left index finger (see text for detailed instructions)	545 stimulus pairs with 122 task switches

3.3 Experimental paradigms in Studies I-IV

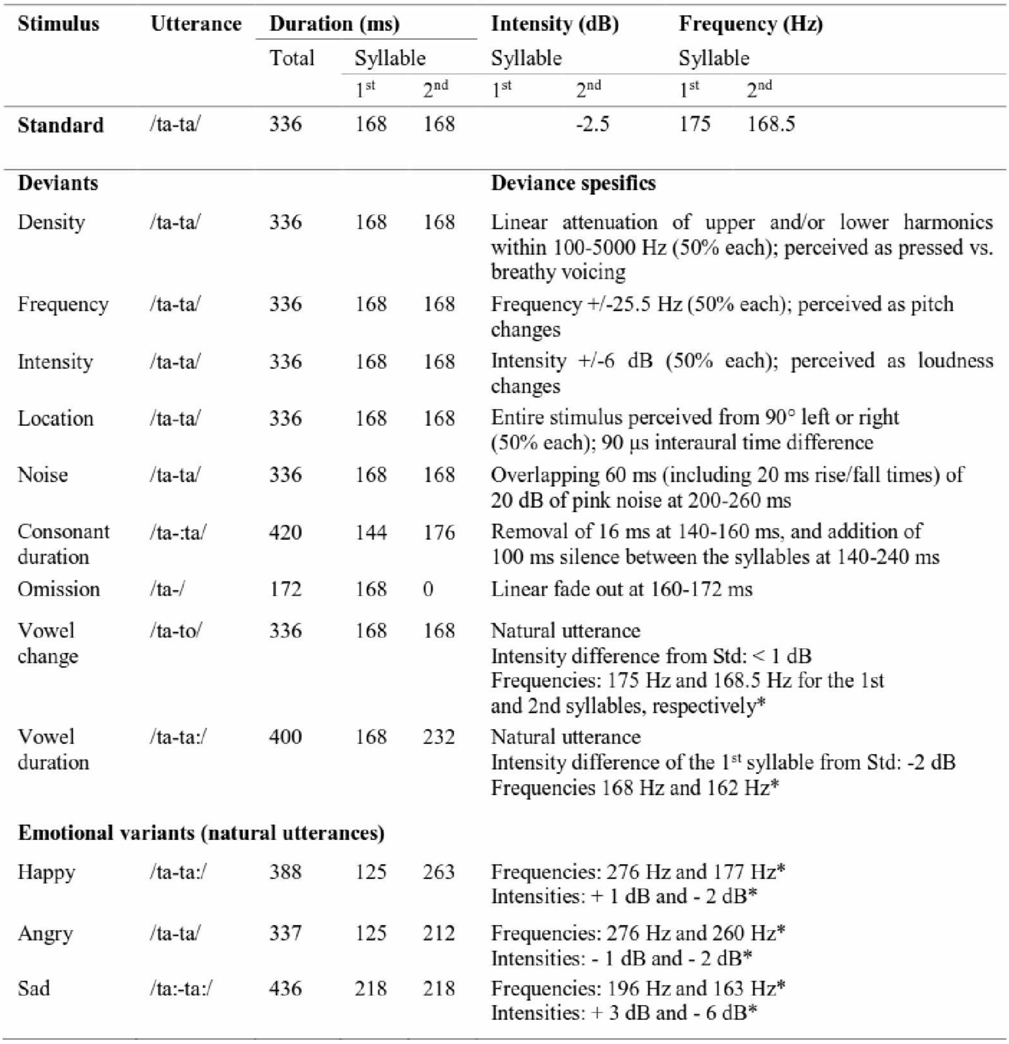
Stimulus presentation. The auditory stimuli (Studies I-III) were presented via two loudspeakers (Genelec, Iisalmi, Finland) placed on the wall of the chamber at a height of 160 cm and at a distance of 130 cm from the participant. The loudspeakers were placed at approximately 50 degrees to the left and right of the participant. Average sound intensity was 57 decibels (dB) sound pressure level (SPL), and it was measured with an SPL meter placed at the position of the participant's head.

The visual stimuli were white numbers (Study III) and letter-number pairs (Study IV) on a black background (static contrast ratio 1000:1), presented in the center of a computer screen each character subtending a visual angle of $1^{\circ} \times 1.9^{\circ}$ (Study III) and $2.4^{\circ} \times 1.6^{\circ}$ (Study IV) at a distance of 80 cm in front of the participant. In Study IV, a solid, white horizontal stationary line (height 0.3°, length 5.6°) was present at the center of the screen throughout the paradigm, and the vertical gap between the letter-number pair and the line was 0.5°. In Studies I and II, a muted nature film was used as a visual stimulus. All experiments were constructed and presented with Presentation software (version 14.9, Neurobehavioral Systems, Inc., Berkeley, California). Table 2 summarizes the experimental paradigms applied in the present thesis, and they are described in detail in the text below.

Multi-feature MMN with emotional utterances of rarely occurring sounds (Studies I and II). The stimuli in the multi-feature MMN paradigm were as follows, and described in detail in Table 3: The standard stimulus was a 336-ms natural utterance of a bisyllabic pseudoword /ta-ta/, uttered by a native Finnish female speaker. As is typical of the Finnish language, the stress was on the first syllable as indicated by slightly higher F0 and intensity compared to the second syllable. The nine deviants differed from the standard in linguistically relevant manners such as spectral density, frequency, intensity, location, consonant duration, or vowel change. The deviation always occurred in the second syllable of the pseudoword except for the location deviant. It was identical to the standard with the exception of the 90 µs interaural time difference between the stereo channels so that half of the location deviants were perceived as coming 90° from the left and half 90° from the right. The vowel-change deviant as well as the vowel-duration deviant were recordings of natural utterances, and thus the physical characteristics of these deviants slightly differed from the standard on the first syllable, too. The remaining seven deviants were created by digitally editing the standard stimulus and were hence identical to the standard except for the edited auditory attribute. In addition, three variants of the standard sound with strong emotional prosody, that is, happy, angry, and sad, were used as rarely occurring, novelty-like variants of the standard. The physical characteristics of these emotional variants differed considerably from those of the standard, for example in length, pitch, and momentary intensity.

All stimuli were presented within the same stimulus sequence. The probabilities of the standard and the nine deviant stimuli were identical. The standard stimulus and each deviant were presented 210 times each ($p \approx 0.09$ for each), and the three emotional utterances were presented 42 times each ($p \approx 0.02$ for each). The stimuli were pseudo-randomized in a way that neither the same deviant type nor the standard were ever repeated consecutively, and the emotionally uttered rare pseudowords were presented in varying intervals, once every 10 to 16 seconds. Thus, the arrangement of stimuli is similar to the no-standard multi-feature paradigm (Pakarinen et al., 2010) except that the present paradigm includes the standard and the emotionally uttered rare stimuli. The stimulus-onset asynchrony (SOA) was 750 ms, and the total recording time was 28 min.

Table 3. Stimulus characteristics for Studies I and II.



Stimulus	Utterance	Duration (ms)			Intensity (dB)		Frequency (Hz)	
		Total	Syllable		Syllable		Syllable	
			1st	2nd	1st	2nd	1st	2nd
Standard	/ta-ta/	336	168	168		-2.5	175	168.5
Deviants					**Deviance spesifics**			
Density	/ta-ta/	336	168	168	Linear attenuation of upper and/or lower harmonics within 100-5000 Hz (50% each); perceived as pressed vs. breathy voicing			
Frequency	/ta-ta/	336	168	168	Frequency +/-25.5 Hz (50% each); perceived as pitch changes			
Intensity	/ta-ta/	336	168	168	Intensity +/-6 dB (50% each); perceived as loudness changes			
Location	/ta-ta/	336	168	168	Entire stimulus perceived from 90° left or right (50% each); 90 µs interaural time difference			
Noise	/ta-ta/	336	168	168	Overlapping 60 ms (including 20 ms rise/fall times) of 20 dB of pink noise at 200-260 ms			
Consonant duration	/ta-:ta/	420	144	176	Removal of 16 ms at 140-160 ms, and addition of 100 ms silence between the syllables at 140-240 ms			
Omission	/ta-/	172	168	0	Linear fade out at 160-172 ms			
Vowel change	/ta-to/	336	168	168	Natural utterance Intensity difference from Std: < 1 dB Frequencies: 175 Hz and 168.5 Hz for the 1st and 2nd syllables, respectively*			
Vowel duration	/ta-ta:/	400	168	232	Natural utterance Intensity difference of the 1st syllable from Std: -2 dB Frequencies 168 Hz and 162 Hz*			
Emotional variants (natural utterances)								
Happy	/ta-ta:/	388	125	263	Frequencies: 276 Hz and 177 Hz* Intensities: + 1 dB and - 2 dB*			
Angry	/ta-ta/	337	125	212	Frequencies: 276 Hz and 260 Hz* Intensities: - 1 dB and - 2 dB*			
Sad	/ta:-ta:/	436	218	218	Frequencies: 196 Hz and 163 Hz* Intensities: + 3 dB and - 6 dB*			

Note: Deviation always occurred in the 2nd syllable of the pseudoword, except for the sound-source location deviant which was identical to the standard except for the 90 µs interaural time difference between the left and right ears (compared to the front location of all other stimuli). Std denotes the Standard.
* Presented values for the first and second syllables of the pseudoword, respectively.

N-back task (Study III). The participants completed a visual n-back task consisting of 0-, 1-, and 2-back conditions. The conditions were presented in the same order (0-1-2) for all participants. Table 2 summarizes the tasks the participants performed on a given condition. Response to a 'match' stimulus was given with a button press with right index finger, and response to a 'mismatch' stimulus was given with a button press with left index finger. Each condition consisted of a total of 212 stimuli delivered in a pseudorandom order so that 33% of them were matches and 67% mismatches in a given n-back task (Figure 1). Stimulus duration was 500 ms, and the SOA was 2000 ms. During the delay period, a black screen was visible.

During the visually presented n-back tasks, participants were presented with isolated complex environmental distractor sounds, such as those produced by a hammer, drill, telephone ringing, door or rain. Sound duration was 200 ms. The sounds were the same as used by Escera and colleagues (Escera et al., 1998; Escera, Yago, Corral, Corbera, & Nunez, 2003). Ninety-six most identifiable novel sounds according to the classification of Escera and colleagues (2003) were presented in varying intervals, once every 10-16 seconds. Each complex sound was presented only once during the experiment. In each condition, thirty-two distractor sounds were presented.

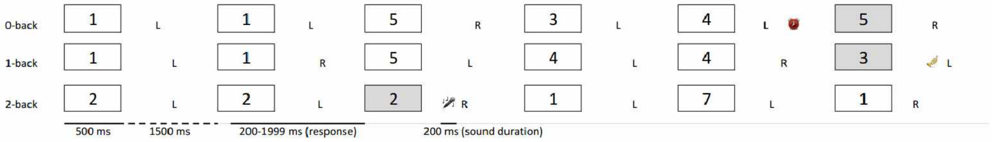


Figure 1. Schematic example of the experimental design in Study III. Each line in the figure represents one condition. Each condition comprised 212 visual stimuli, 33% of them being matches in the 0-back, 1-back, and 2-back task. During the visual tasks, ninety-six novel sounds were presented, thirty-two in each n-back condition, once every 10-16 seconds. Participants were instructed to concentrate on the visual task, respond to every visual stimulus with right or left button press, and ignore the sounds. The gray toned visual stimuli are preceded or followed by a distractor sound. ‘L’ denotes a correct response with the left button press; ‘R’ denotes a correct response with the right button press.

Task switching (Study IV). Each letter-number pair was presented in pseudorandom order with the letter presented on the left side of the pair. The position of the letter-number pair was always either above or below the horizontal line, and this served as a cue according to which the participants were required to judge the stimulus pairs: when the stimulus pair occurred above the horizontal line, the participant had to classify the number in the letter-number pair as odd or even. When it occurred below the line, the participant had to classify the letter as consonant or vowel. The decision to be made in each task was hence unknown to the participant until the letter-number pair was presented. The participants were instructed to respond to each stimulus pair with a button press: consonants and odd numbers required a response with the left index finger while vowels and even numbers required a response with the right index finger. To avoid the possibility of participants fixating their gaze on exact upcoming stimulus locations above or below the line, a horizontal jitter in the location of the stimulus was applied. The pairing of the letter-number pairs was semi-randomized so that approximately half of the letter-number pairs were unambiguously correct in the task context and half of them were ambiguously correct in the task context, that is, the task-irrelevant stimulus in the stimulus pair was mapped either to a response with same or the other hand (e.g., when the task was to classify the number as odd or even in 'E5', a correct response was given with left hand, whereas the task-irrelevant character was mapped to a correct response with right hand).

In all, the paradigm consisted of 545 stimulus pairs with 122 task switches (22%) and 423 task repetitions (78%). Task runs of one to nine stimulus pairs were presented in succession above or below the line before a switch. In the entire sequence, there were 20 task runs (16%) consisting of only one stimulus pair before a switch, 26 task runs (21%) constituting two repetitions before the switch, and on average 11 task runs (9%) of 3 to 9 repetitions, each.

Each stimulus pair was shown until response, however, not longer than 2500 ms (Figure 2). The presentation rate was tied to the participant's response in the following way: a correct response was followed by a 150 ms delay period after which the next stimulus pair was presented. An incorrect or missed response was followed by a 1500 ms delay until the next stimulus pair was presented.

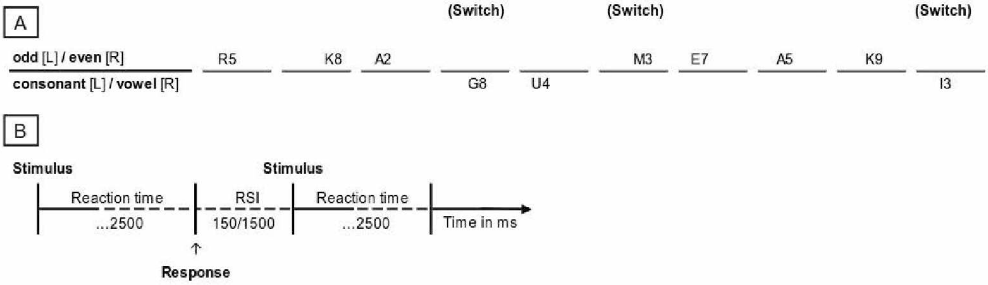


Figure 2. Study IV: Schematic example of the experimental design (A), and illustration of the presentation rate (B). The location (above or below the horizontal line) of the stimulus pair signaled the task to be completed on that trial. For illustration purposes, switch trials are marked with (Switch). [L]: response with left button press, [R]: response with the right button press. Response-stimulus interval (RSI; the temporal interval between the response given to the preceding stimulus pair and the onset of the next one) was either 150 ms or 1500 ms, depending on the response given (correct or incorrect, respectively).

Performance and feedback in behavioral tasks. In Studies III and IV, task performance, that is, accuracy and reaction times (RTs), was recorded. Speed and accuracy of response were equally emphasized in the task instructions. Responses were given with keyboard button presses (left and right ctrl buttons covered with tape). In Study III, participants did not receive feedback on their performance whereas in Study IV, the length of the delay period between the stimulus pairs served as feedback of a correct or incorrect response. Prior to the tasks in Studies III and IV, participants were presented with written instructions and they practiced the tasks in order to familiarize themselves with the experiments. In Study IV, the participants first practiced the tasks separately above and below the solid line and, thereafter, the task switching task was practiced. In Study III, the participants had a brief break between conditions. The experiment in Study IV was divided into two blocks, enabling a brief break between the blocks.

3.4 EEG data acquisition and analysis

In all studies of the present thesis, the EEG recordings were conducted in a similar manner. The recordings were carried out in a soundproofed chamber where the participants were comfortably seated at an office workstation. The participants were instructed to sit still and to blink as little as possible. The EEG was recorded using a 32-channel active electrode system (actiCAP, Brain Products GmbH, Gilching, Germany) connected to a neurOne amplifier (Mega Electronics Ltd., Kuopio, Finland). The EEG was recorded from 26 electrodes placed according to the extended international 10-20 electrode system (excluding channels O1, O2, TP9, TP10, PO9, and PO10). The common reference and ground were located at FCz and AFz, respectively. Two additional electrodes were placed at the left and right mastoids to allow re-referencing in later analyses. In addition, a bipolar horizontal electro-oculogram was recorded from two electrodes placed on the left and right canthi, and a vertical electro-oculogram was recorded from electrodes placed above and below the left eye. All biosignals were sampled at 500 Hz.

In all studies, the EEG analyses were conducted using EEGLAB (Delorme & Makeig, 2004). Filtering, epoching, and artefact rejection were conducted in the following way, after which individual waveforms were separately created for each participant, stimulus type, and task condition/trial type. In all studies, the EEG was bandpass-filtered offline (0.5-30 Hz), and re-referenced to the mean signal of the mastoid electrodes. Epochs were extracted from the continuous EEG records as follows. In Studies I and II, ERPs were obtained by averaging 600-ms EEG epochs including a 100-ms pre-stimulus period and a 500-ms post-stimulus period, baseline corrected, and separately averaged for each electrode site, and each of the 13 stimulus types (i.e., standard, nine deviants, and three emotionally uttered variants). The mean voltage of the pre-stimulus period served as a baseline for the amplitude measurements in all studies. In Study III, the signals were averaged over a time-interval of -100-800ms relative to the stimulus onset, separately for each electrode site, stimulus type (i.e., auditory and visual), and task condition (0-back, 1-back and 2-back). In Study IV, the signals were averaged over a time-interval of -100-700ms relative to the stimulus onset. The signals for the switch trials were averaged separately, whereas the repetition trials (2-9 repetitions) were averaged together to increase the signal-to-noise ratio. Furthermore, in Studies III (regarding visual trials) and IV, only trials preceding correct responses (to matched stimuli in Study III) were analyzed (see sections *"3.4.2 Study III"*, and *"3.4.3 Study IV"* for details). In all studies, the epochs contaminated by artifacts caused by eye movements, blinks or other extracerebral factors and producing voltage changes exceeding ±65 μV at any electrode were omitted from averaging.

The following fronto-parietal midline electrodes with the most pronounced amplitude were chosen for further calculation of ERPs: Fz in Studies I and II, as well as for the auditory ERPs in Study III; Pz in Study IV and for the visual ERPs in Study III.

3.4.1 Studies I and II

In Studies I and II, only data from those participants whose averaged ERP contained more than 65% of the total number of the presented stimuli (equals at least 137 standard trials, 137 of each of the deviant trials, and 28 of each of the emotional variant trials) were included in further analyses.

In order to evaluate early perceptual auditory processing, the averaged responses to the standard stimulus were used to calculate the N1 mean amplitudes and peak latencies in Study II. To delineate the MMN in Studies I and II, the averaged signal to the standard stimulus was separately subtracted from those to the deviants and emotional utterances, thus resulting in nine difference signals for the deviant stimuli and three for the emotionally uttered rare stimuli. Within the vowel-change, vowel-duration, and omission deviant trials, two consecutive MMN responses were detected for each deviant due to the nature of the deviants. Thus, a total of 12 MMN responses were detected for the deviant stimuli. The P3a amplitudes and latencies, also in Studies I and II, were measured from the ERPs to the three rare emotional utterances (happy, angry, and sad).

The N1 was determined as the largest negative deflection between 50 and 150 ms from stimulus onset in the grand average ERP. For each participant, the N1 mean amplitude was calculated as a mean voltage at the 40-ms period centered at the peak latency in the grand average signal. The MMN signals were identified as the most negative peaks within a time window of 100-220 ms from deviance onset in the grand average difference signals. Thereafter, the MMN mean amplitudes for each deviant type and each participant were calculated as a mean voltage of a 40-ms window centered at the peak latency in the grand average ERP difference signal of the deviant type. The same was done for the MMN mean amplitudes for the emotionally uttered rare pseudowords, with the exception that we used a 60-ms window. In the signals for the emotional utterances of rare sounds, the P3a responses were identified as the most positive peaks within a predetermined time windows from deviance onset (200-300 ms for happy, and 250-350 ms for angry and sad). The P3a mean amplitudes were calculated as a mean voltage at the 60-ms period centered at the peak latency in the grand average signal. In Study II, the individual peak latencies for the N1 and P3a were measured from the largest peak occurring at the 100-ms period centered at the peak latency in the grand average signal. For the peak latencies of the MMNs, the same was done but using the grand average difference signal.

3.4.2 Study III

Only data from those participants whose averaged auditory ERP contained more than 55% of the novel sound trials were included in further analyses of the auditory ERP and behavioral data. The group mean of novel sound trials per condition included in the ERP average was 23.7 (SD = 4.5) trials for the burnout group while for the control group it was 23.3 (SD = 4.3). Correspondingly, the data used in the visual ERP analysis were from the same participants as in the auditory ERPs with the exception that in addition, data from one control participant was discarded due to technical difficulties in recording the visual ERPs. Based on the 0-back condition, the group means of visual trials included in the ERP average were 42.3 (SD = 18.2) and 43.1 (SD = 15.9) trials for the burnout and control group, respectively.

For the auditory ERPs, the early and late P3a were identified as the largest positive deflections in the two measurement windows (170-270 ms for the early phase and 280-480 ms for the late phase) in the grand average signal of the 0-back condition. The mean amplitudes of the two phases of the P3a were calculated as a mean voltage at the 100-ms time windows around the peak of each phase in the grand average signal. The same was done for the visual P3b with the exception that the measurement interval was 300-500 ms from stimulus onset. The auditory N1 was computed in the same way as in Study II.

3.4.3 Study IV

The number of switch trials included in the single-participant average ERP ranged from 45 to 118 (M = 94, SD = 24) in the mild burnout group, from 43 to 115 (M = 88, SD = 22) in the severe burnout group, and from 64 to 119 (M = 97, SD = 16) in the control group. Temporal windows around the ERP responses of interest were identified by visual inspection in the grand average signal of the switch condition across all participants. The P3 was double-peaked: its earlier phase was determined as the largest positive deflection in the measurement windows of 180-280 ms, and the later phase was measured between 300-400 ms from stimulus onset. The mean amplitudes were calculated as a mean voltage over 80-ms periods centered at the peak latency of each phase of the P3 in the grand average signal. Individual peak latencies were measured from the largest peak occurring at the 100-ms period centered at the peak latency in the grand average signals in switch and repetition trials.

3.5 Statistical analysis

3.5.1 ERPs

Group differences in the demographic and symptom characteristics, and other background variables of the participants (Studies II-IV) were assessed with t-tests, chi-square tests, and univariate analysis of variance (ANOVA). Correlations between symptom variables were measured with Pearson correlation coefficient *r*.

Group differences in the ERP parameters relative to stimulus type (Studies II and III), task load (Study III), trial type (Study IV), and electrode position (Studies III and IV), as well as performance in the cognitive tasks (Studies III and IV) were assessed with repeated measures analysis of variance (ANOVA). The analyses are next described in more detail.

In Study I, one-tailed t-tests were conducted in order to test the statistical significance of the MMN and P3a mean amplitudes at midline electrodes Fz, Cz, and Pz. The MMN mean amplitudes were compared between the stimulus types (12 MMNs for deviants, and 3 for rare emotional utterances) and electrode position (Fz, Cz, Pz) with repeated-measures ANOVA. Similarly, P3a mean amplitudes were compared between the utterance types (happy, angry, and sad) and electrode sites (Fz, Cz, Pz) with repeated measures ANOVA. In Study II, group differences in the MMN and P3a mean amplitudes and peak latencies were analyzed using Group × Stimulus Type repeated-measures ANOVAs. In addition, in Study II, the N1 amplitudes and latencies were compared between the standard stimulus and study groups with one-way ANOVA.

In Studies III and IV, different subsets of electrodes were taken together to investigate the effects of burnout on the topographical distribution of the ERPs. The anterior-posterior distribution of the auditory ERP analysis in Study III comprised the following electrode sites: anterior (F3, Fz, F4), central (C3, Cz, C4), and posterior (P3, Pz, P4). The corresponding electrode sites for the analysis of the visual ERPs in Studies III and IV were anterior (F3, F7, Fz, F4, F8, Fp1, Fp2), central (C3, Cz, C4, FC1, FC2), and posterior (P3, P7, Pz, P4, P8, CP1, CP2).

In Study III, mean amplitudes of the auditory and visual ERPs were analyzed using a repeated-measures ANOVA with Group (burnout, control) as the between-participants factor, and Task Load (0-, 1-, 2-back condition), and Electrode Position (anterior, central, posterior) as the within-participant factors. In Study IV, mean amplitudes for each of the peaks in the ERP were analyzed using a repeated-measures ANOVA with Group as between-participants factor, and Trial Type (switch, repetition) and Electrode Position (anterior, central, posterior) as within-participant factors.

3.5.2 Behavioral data

We used individual median response times (RT) for correct responses (Studies III and IV), hit rates (Study III), error percentages (Study IV), and intraindividual RT variability calculated using the standard error in relation to median RTs (Study IV) as performance metrics. A correct button press within 200-1999 ms (Study III) and 200-2500 ms (Study IV) after the onset of the visual stimulus was regarded as a hit. The individual median RT was chosen as in a task with varying requirements and performance, the median gives the most stable results (Ratcliff, 1993).

In Study III, a repeated-measures ANOVA with Group as the between-participants factor, and Task Load and Auditory Distractor (present, absent) as the within-participant factors was performed for the means of the median RTs of the correct responses. Visual stimuli were defined as "distractor present" when preceded or followed by a distractor sound (i.e., occurred in a stimulus-response chain of "Picture – Sound – Response", or "Sound – Picture – Response"; Figure 1). The hit rates were compared by means of a Group × Task Load repeated-measures ANOVA.

In Study IV, all trials followed by a correct response were chosen for further analysis because the RTs were observed to be comparable for unambiguous and ambiguous trials ($t_{112} = -0.17$, $p = 0.87$). In addition, although the trial position for the repetition trials (positions 2 to 9) had an effect on the RTs ($F_{7, 392} = 20.14$, $p < 0.001$, $\varepsilon = 0.48$, $\eta^2 = 0.03$), the pairwise comparisons revealed no differences between repetition trials in the task runs (Holm-Bonferroni corrected, $p > 0.05$) except for one difference between the 2nd and the 8th position ($p = 0.03$). Therefore, for the non-switch trials, trials in positions two to nine in the runs were taken together to explore the association between burnout and task repetition as was the case in the ERP analysis. For the group means of the individual median RTs and the intraindividual variability of the RTs, repeated-measures ANOVAs with Group (mild burnout, severe burnout, control) as the between-participants factor, and Trial Type (switch, repetition) as the within-participant factor were performed. RT switch costs were calculated as the difference in RT between switch and repetition trials. In addition, for further analysis of the error rates, all trials followed by an incorrect response were used as the difference between the error rates for unambiguous and ambiguous trials was not significant ($t_{112} = 1.75$, $p = 0.08$). The group mean error rates were compared using a Group × Trial Type repeated-measures ANOVA.

The assumption of sphericity was evaluated using Mauchly's procedure and, when violated, the Greenhouse-Geisser correction was used to adjust the degrees of freedom for the ANOVA *F*-distribution. For all studies, *F*-values, original degrees of freedom, and corrected *p*-values are reported. In addition, for Studies III and IV, effect sizes using generalized eta squared (Olejnik & Algina, 2003; Picton et al., 2000) are reported together with the Greenhouse-Geisser correction factor epsilon when this correction was needed. After finding a significant main effect or interaction, post-hoc t-tests were carried out to investigate the pairwise effects. The *p*-values were adjusted using the Holm-Bonferroni (Studies II-IV) and Bonferroni (Study I) methods for multiple comparisons. We chose to use the scores derived from the following self-reported questionnaires as covariates in the analyses when comparing group differences in the ERP and behavioral results: symptoms of depression (BDI-II; Study II); sleepiness ratings during the recordings, and symptoms of anxiety (KSS, BAI; Study III); symptoms of anxiety, depression, and sleep disturbances (BAI, BDI-II, BNSQ; Study IV). All statistical analyses were carried out using the R software environment with a set of packages for statistical computing and graphics (Lawrence, 2013; R Core Team, 2014; Sarkar, 2008; Wei, 2013; Wickham, 2007, 2009, 2011, 2012).

4 Results

4.1 Participant characteristics

Figure 3 shows the correlations between the self-reported symptoms of burnout, depression, anxiety, and sleep disturbances. As shown in the matrix, the correlations were positive and statistically significant between all evaluated symptom measures except for three insignificant correlations (i.e., the correlation of sleep disturbances with anxiety, professional inefficacy as evaluated in MBI-GS, and emotional exhaustion as evaluated in SMBM). The burnout measures (MBI-GS and SMBM) with all their subscales correlated strongly with each other. Furthermore, the stronger the burnout symptoms, the higher the scores were on depression, anxiety, and sleep disturbance scales. Of the 67 initially volunteered participants, complete datasets of 61, 49, and 57 participants were included in further analysis in Studies II, III, and IV, respectively.

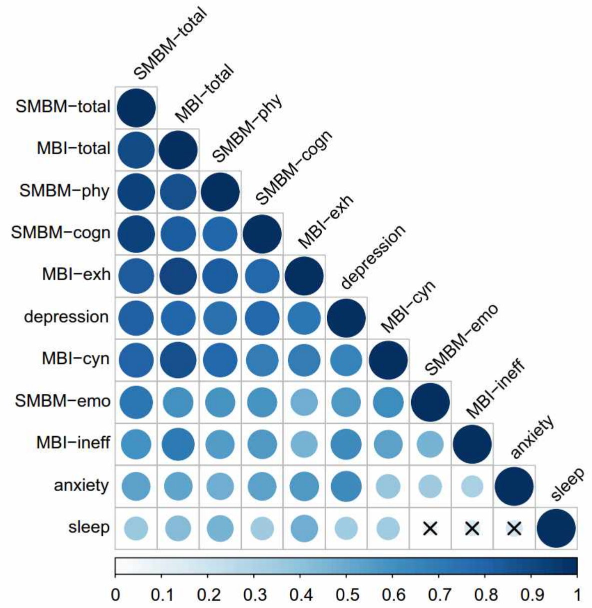


Figure 3. Correlations between self-reported symptoms of burnout (MBI-GS and SMBM; total scores and subscales), depression (BDI-II), anxiety (BAI), and sleep disturbances (BNSQ). Data are from 67 initially volunteered participants. All correlations were positive. Color intensity and the size of the circle are proportional to the correlation coefficients. Level of statistical significance was set at $p < 0.05$. All correlations were statistically significant except those marked with ×. Subcomponents of the burnout measures: MBI-exh: emotional exhaustion in the MBI-GS; MBI-cyn: cynisicm; MBI-ineff: professional inefficacy; SMBM-phy: physical fatigue in the Shirom-Melamed Burnout Measure; SMBM-emo: emotional exhaustion; SMBM-cogn: cognitive weariness.

Table 4. Demographic and symptom characteristics of the participants in Studies I-IV.

		Studies I-II			**Study III**			**Study IV**			
		Burnout (n=37)	Control (n=24)	*p* value	Burnout (n=30)	Control (n=19)	*p* value	Mild burnout (n=21)	Severe burnout (n=12)	Control (n=24)	*p* value
Demographic	Age	47.8 (8.5)	46.2 (9.2)	0.49 (t)	47.5 (8.2)	43.4 (8.7)	0.09 (t)	47.7 (8.6)	47.1 (8.4)	45.1 (8.7)	0.59 (F)
	Female/male	34/3	21/3	0.90 (χ^2)	27/3	15/4	0.51 (χ^2)	19/2	11/1	20/4	0.69 (χ^2)
	Education	15.5 (2.0)	15.2 (1.9)	0.52 (t)	15.5 (2.0)	15.2 (2.1)	0.59 (t)	15.9 (1.7)	14.9 (2.6)	15.3 (1.9)	0.40 (F)
	Work experience	22.1 (10.1)	21.5 (13.3)	0.87 (t)	22.1 (10.5)	19.1 (13.9)	0.40 (t)	20.9 (9.9)	22.1 (11.4)	21.3 (12.9)	0.95 (F)
Symptom	MBI-GS total	3.1 (0.9)	0.9 (0.4)	<0.001 (t)	3.1 (0.9)	0.9 (0.4)	<0.001 (t)	2.5 (0.5)	4.2 (0.6)	0.9 (0.4)	<0.001 (F)[a]
	Exhaustion	3.9 (1.3)	0.9 (0.7)	<0.001 (t)	3.93 (1.27)	0.84 (0.63)	<0.001 (t)	3.21 (0.90)	5.07 (1.07)	0.87 (0.63)	<0.001 (F)[a]
	Cynicism	3.3 (1.5)	1.0 (0.8)	<0.001 (t)	3.30 (1.52)	1.05 (0.84)	<0.001 (t)	2.62 (1.41)	4.58 (0.92)	1.06 (0.82)	<0.001 (F)[a]
	Inefficacy	1.9 (1.2)	0.7 (0.6)	<0.001 (t)	1.87 (1.26)	0.69 (0.53)	<0.001 (t)	1.59 (1.06)	2.75 (1.21)	0.82 (0.67)	<0.001 (F)[b]
	BDI-II	16.4 (6.1)	5.3 (5.2)	<0.001 (t)	16.0 (6.2)	4.6 (5.2)	<0.001 (t)	14.1 (5.7)	19.9 (5.1)	4.9 (5.3)	<0.001 (F)[a]
	BAI	10.2 (5.7)	4.0 (3.6)	<0.001 (t)	9.5 (5.2)	3.7 (3.7)	<0.001 (t)	9.1 (4.0)	10.2 (6.6)	3.6 (3.4)	<0.001 (F)[c]
	BNSQ	3.0 (1.9)	1.6 (1.6)	0.004 (t)	3.1 (1.9)	1.7 (1.6)	0.009 (t)	2.1 (1.5)	4.1 (2.1)	1.6 (1.6)	<0.001 (F)[d]

Age, education, and work experience are presented in years. Data are mean values (with standard deviations) except for gender. The participants in Study I are the same as the control participants in Study II. MBI-GS: Maslach Burnout Inventory – General Survey; BDI-II: Beck's Depression Inventory; BAI: Beck's Anxiety Inventory; BNSQ: Basic Nordic Sleeping Questionnaire. *p* values are derived from t-tests (t), chi-square tests (χ^2), and one-way ANOVAs (F). Pairwise comparisons in Study IV:

[a] Control < Mild < Severe, $p < 0.001$

[b] Control < Mild, $p = 0.005$; Mild < Severe, $p = 0.007$; Control < Severe, $p < 0.001$

[c] Control < Mild, $p < 0.001$; Control < Severe, $p < 0.001$; Mild vs. Severe, $p = 0.56$

[d] Control vs. Mild, $p = 0.23$; Mild < Severe, $p = 0.004$; Control < Severe, $p < 0.001$

Table 4 summarizes the demographic and symptom characteristics of the participants in Studies I-IV. Figure 4 shows the correlations between the burnout scores (MBI-GS) and the subjective sleepiness ratings (KSS) during the entire recording session. The correlations were positive and statistically significant. Group comparisons in Study II showed that the average score for the KSS before the onset of the entire ERP recording session was higher for the burnout group (M = 5.0, SD = 1.34) than for the control group (M = 4.0, SD = 1.67; $t_{58} = 2.49$, $p = 0.02$). Also the KSS score prior to the last ERP recording (Study II) was higher for the burnout group (M = 5.6, SD = 1.14) than for the control group (M = 4.5, SD = 1.19; $t_{58} = 3.30$, $p = 0.002$).

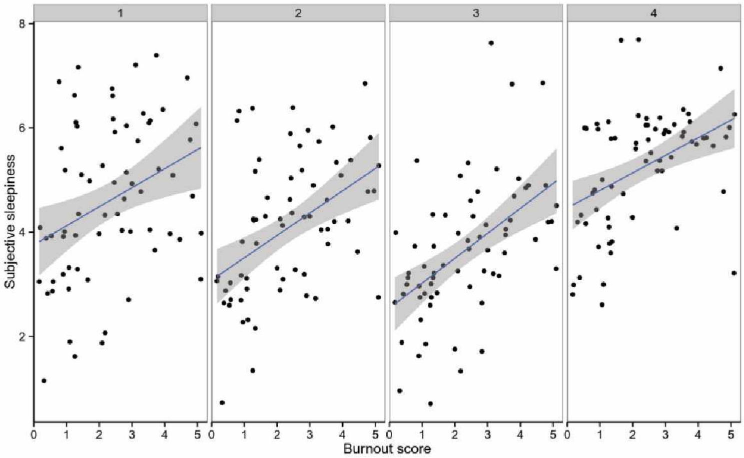


Figure 4. Scatter plot showing the distribution of subjective sleepiness ratings during the ERP recording session in relation to self-reported symptoms of burnout (MBI-GS). Linear regression lines with 95% confidence region is included. For illustration purposes, a jitter for the positioning of the data points is used. Data are from 67 initially volunteered participants except for one participant from whom the KSS ratings are missing due to technical difficulties, resulting in data from 66 participants. KSS ratings are presented in a chronological order:
1. Before the entire recording session, r = 0.34, $p = 0.005$
2. After the task switching paradigm (Study IV), r = 0.46, $p < 0.001$
3. Before the n-back paradigm (Study III), r = 0.51, $p < 0.001$
4. Before the MMN paradigm (Study II), r = 0.42, $p < 0.001$

In Studies II-IV, the self-reported prescribed medication within 24 hours prior to ERP recordings for the burnout groups were 7-8% for sleep disorders, and 24-27% for mood disorders, depending on the samples included in the analyses. The corresponding percentages for the control groups were 0% for sleep disorders, and 17% for mood disorders. Caffeine consumption 24 hours before the recordings did not differ statistically between the groups in any of the studies.

4.2 Speech sound processing and attention capture to emotional utterances in burnout (Studies I and II)

The MMN signals varied across the deviant types and emotionally uttered variants, as shown by significant main effects of Stimulus Type on MMN mean amplitude in both studies (Study I: $F_{14,322} = 16.32$, $p < 0.001$; Study II: $F_{14,826} = 39.97$, $p < 0.001$, $\eta^2 = 0.35$), and on peak latency in Study II ($F_{14,826} = 977.13$, $p < 0.001$, $\eta^2 = 0.94$). Figure 5 shows the ERP signals and voltage maps for the nine deviant stimuli and the three rare emotional utterances.

In Study II, the N1 mean amplitudes and peak latencies for the standard stimulus did not differ between the burnout and control groups ($F_{1,59} = 0.08$, $p = 0.78$, $\eta^2 < 0.001$; $F_{1,59} = 0.85$, $p = 0.36$, $\eta^2 = 0.01$, respectively). Neither did the MMN parameters for the deviants and emotionally uttered rare variants differ between the groups (Amplitude: $F_{1,59} = 0.67$, $p = 0.42$, $\eta^2 = 0.002$; Latency: $F_{1,59} = 0.08$, $p = 0.78$, $\eta^2 < 0.001$). For the MMN latencies, the interaction between Group and Stimulus Type was significant ($F_{14,826} = 2.45$, $p = 0.009$, $\eta^2 = 0.04$), resulting from two inconsistent latency differences related to duration changes when comparing the groups.

The emotional variant type had an effect on the P3a mean amplitudes (Study I: $F_{2,46} = 17.14$, $p < 0.001$; Study II: $F_{2,118} = 23.48$, $p < 0.001$, $\eta^2 = 0.17$) and peak latencies (Study II: $F_{2,118} = 176.67$, $p < 0.001$, $\eta^2 = 0.69$). For the peak latencies in Study II, a significant interaction between the group and the emotional variant type was observed ($F_{2,118} = 5.98$, $p = 0.005$, $\eta^2 = 0.07$; Figures 6 and 7). The P3a latencies for the burnout group were longer for the happy ($p = 0.02$), and shorter for the angry ($p = 0.01$) variants than those for the control group whereas the latencies for the sad variant did not differ between the groups ($p = 0.25$).

In summary, the results suggest that the multi-feature paradigm developed in Study I allows evaluation of natural speech-sound processing and involuntary attention allocation towards emotionally uttered speech within one, approximately 30-minute recording session. This is indicated by significant MMN responses for the nine deviants as well as P3a responses for the three rare emotionally uttered variants of the standard. The results of Study II suggest that momentary involuntary capture of attention to emotionally valenced speech is altered in burnout as indicated by longer P3a latencies for the happy, and shorter P3a latencies for the angry variants in the burnout group than the control group.

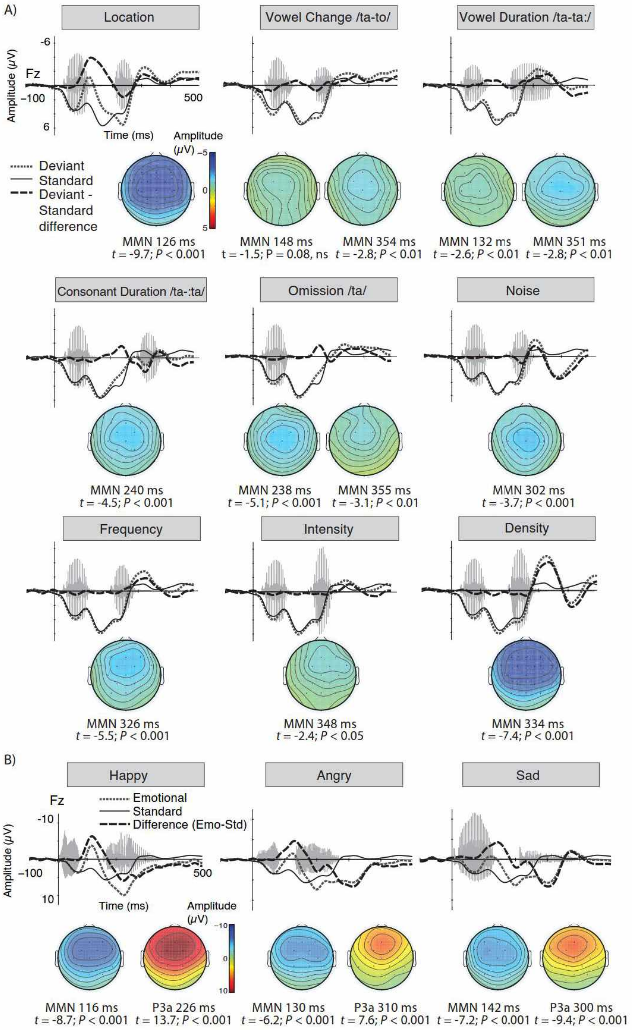


Figure 5. ERP signals and voltage maps for the nine deviant stimuli (panel A; MMN responses) and the three rare emotionally uttered variants (panel B; MMN and P3a responses) overlapped with the time amplitude illustrations of the stimuli consisting of two spoken syllables. The solid line denotes the ERP to the standard stimulus, the dotted line denotes the ERP to the deviant stimuli (panel A) or emotional uttered variants (panel B), and the dashed line the difference signal. Time-amplitude illustrations of the stimuli appear in grey. For the frequency, density, and intensity deviants, only the increasing deviant tones are illustrated. The location deviant is identical to the standard except for the 90 μs interaural time difference between the left and right ears. t-values and *p*-values are presented for the mean amplitude at Fz.

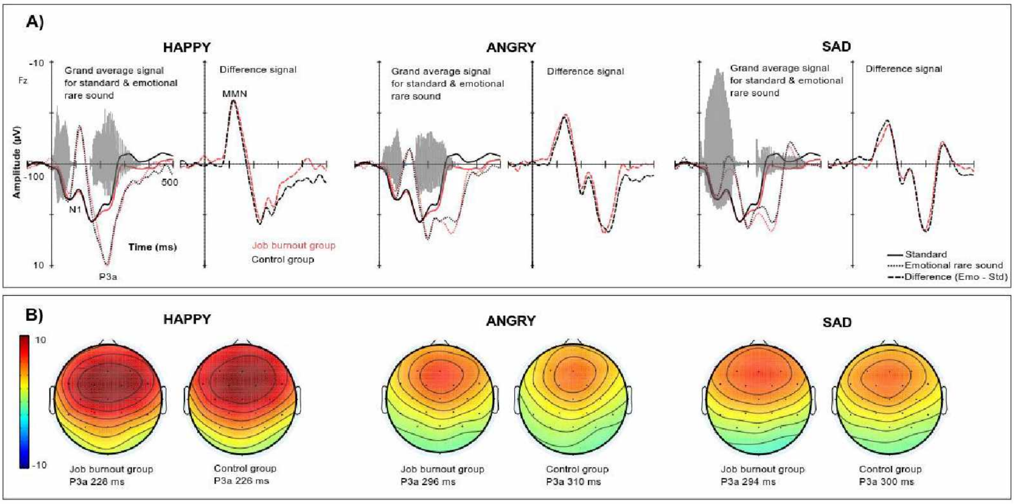


Figure 6. Grand average and difference signals to the rare emotional utterances in the burnout and control groups overlapped with time-amplitude illustrations of the stimuli (panel A). The red line denotes the burnout group, the black line the control group. Time-amplitude illustrations of the stimuli appear in grey. Panel B: Topographical voltage maps for P3a peak latencies (Fz) for the rare emotional utterances for both groups (26 electrodes were used for calculating the voltage maps).

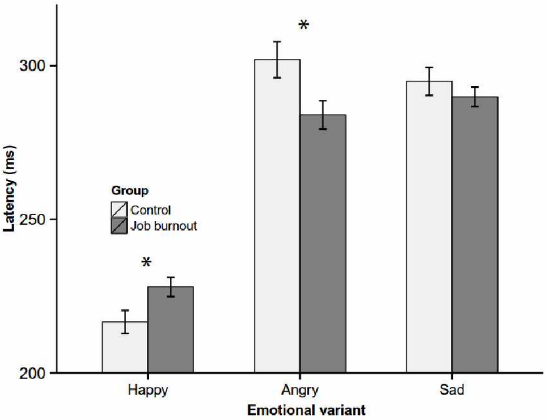


Figure 7. Barplots showing the group mean P3a peak latencies (ms) and the standard errors for the rare emotional utterances at electrode site Fz in the burnout and control groups. * denotes $p = 0.02$ for happy; $p = 0.01$ for angry variants.

4.3 Burnout-related dysfunctions in involuntary and voluntary attention (Study III)

4.3.1 Behavioral data

As expected, the task load level had an effect on the hit rate ($F_{2,94}$ = 152.39, p < 0.001, ε = 0.56, η^2 = 0.66), and the RTs ($F_{2,94}$ = 61.44, p < 0.001, ε = 0.55, η^2 = 0.35). With increasing cognitive load, the overall hit rate decreased (0-, 1-, 2-back: 93.1%, 88.7%, 72.8%, respectively; pairwise comparisons: 0-back > 1-back > 2-back, p < 0.001), and the RTs became longer (0-back < 1-back < 2-back, p < 0.001). However, the hit rates and RTs were comparable between the burnout and control groups ($F_{1,47}$ = 1.55, p = 0.22; $F_{1,47}$ = 0.05, p = 0.80, main effects of Group for hit rate, and RT, respectively).

The main effect of distraction caused by presenting novel sounds was significant ($F_{1,47}$ = 55.74, p < 0.001, η^2 = 0.01). However, RTs only tended to be longer on distracted trials than on silent trials not preceded or followed by a novel sound (p = 0.08) indicating a trend towards a distracting effect of novel sounds over the performance on the visually presented task with three load levels. The interaction between Task Load and Auditory Distractor (present vs. absent) was significant ($F_{2,94}$ = 10.1, p = 0.007, ε = 0.70, η^2 = 0.005) but pairwise comparisons revealed no significant differences in the distracting effects.

4.3.2 ERP data

In both groups, auditory novelty-related electrophysiological activity was characterized by an N1 wave, followed by a large P3a response with two phases. For the visual ERPs, a large P3b response was elicited for trials preceding correct responses. Figures 8-10 show the grand average signals and scalp potential distribution mapping of the auditory and visual responses for both groups. The auditory early P3a was maximal over the central scalp regions whereas the late phase was distributed over fronto-central regions. The visual P3b was maximal over the centro-parietal scalp regions with the lowest task load. With higher task loads, the amplitude of the P3b was decreased compared to the low-load condition, and the amplitude maximum shifted towards more posterior parietal scalp regions.

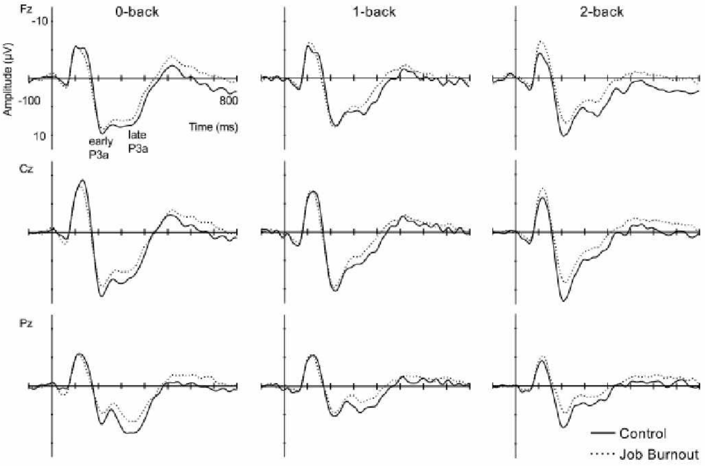


Figure 8. Grand average waveforms from the novel sounds for job burnout and control groups in 0-, 1-, and 2-back conditions at electrode sites Fz, Cz, and Pz. The dashed line denotes the job burnout group, the solid line the control group.

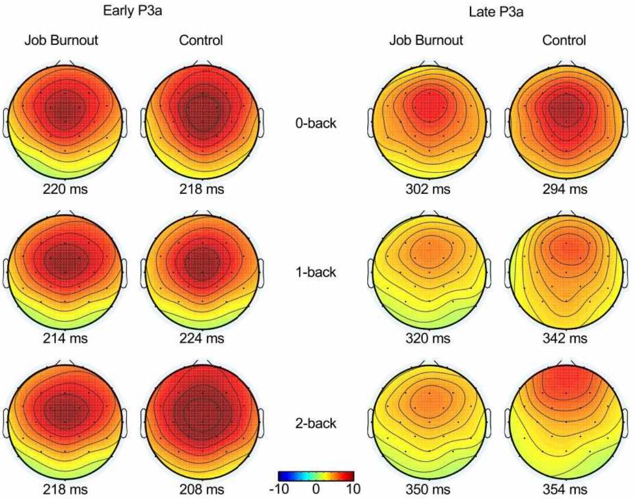


Figure 9. Voltage distribution over the scalp for the early and late P3a peak latencies (Fz) for the novel sounds for both groups (26 electrodes were used for calculating the voltage maps).

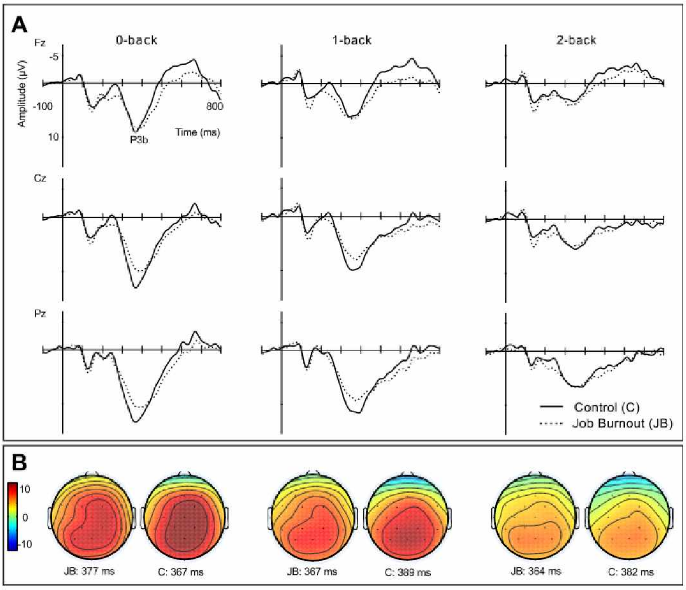


Figure 10. Grand average waveforms from the visual trials preceding correct responses to match stimuli for burnout and control groups in each condition at electrode sites Fz, Cz, and Pz. (panel A). The dashed line denotes the job burnout group, the solid line the control group. Panel B: Voltage distribution over the scalp for the P3b peak latencies (Pz) for the corresponding visual trials for both groups (data from 26 electrodes were used for calculating the maps).

For the auditory early P3a mean amplitudes, the main effect of Group was not significant ($F_{1,47} = 1.85$, $p = 0.18$) nor were the main effect of Task Load significant ($F_{2,94} = 0.31$, $p = 0.73$). However, the interaction between Group and Task Load was significant ($F_{2,94} = 3.11$, $p = 0.049$, $\varepsilon = 0.99$, $\eta^2 = 0.01$). The burnout group showed smaller early P3a amplitudes than the control group in the 2-back condition ($p < 0.001$) while in the 0- and 1-back conditions the responses did not differ between the groups ($p = 0.34$, $p = 0.95$, respectively).

As seen in Figure 11, the auditory late P3a amplitudes were affected by the groups ($F_{1,47} = 4.34$, $p = 0.04$, $\eta^2 = 0.05$) and the task loads ($F_{2,94} = 16.42$, $p < 0.001$, $\varepsilon = 0.93$, $\eta^2 = 0.09$). The late P3a amplitudes were smaller in the burnout group than in the control group. Furthermore, the late P3a was the largest (most positive) in the 0-back condition, intermediate in the 1-back, and the smallest in the 2-back condition (0-back > 1-back: $p < 0.001$; 0-back > 2-back: $p < 0.001$; 1-back > 2-back: $p = 0.049$).

For the auditory responses, the amplitude was significantly dependent of the electrode position (early P3a: $F_{2,94} = 90.42$, $p < 0.001$, $\varepsilon = 0.69$, $\eta^2 = 0.16$; late P3a:

$F_{2,94} = 31.64$, $p < 0.001$, $\varepsilon = 0.57$, $\eta^2 = 0.08$). The P3a amplitudes were the largest at anterior scalp locations, and the smallest over the posterior regions (early P3a: anterior vs. central, $p = 0.87$, anterior > posterior, and central > posterior: $p < 0.001$; late P3a: anterior > central: $p = 0.04$; anterior > posterior, and central > posterior: $p < 0.001$).

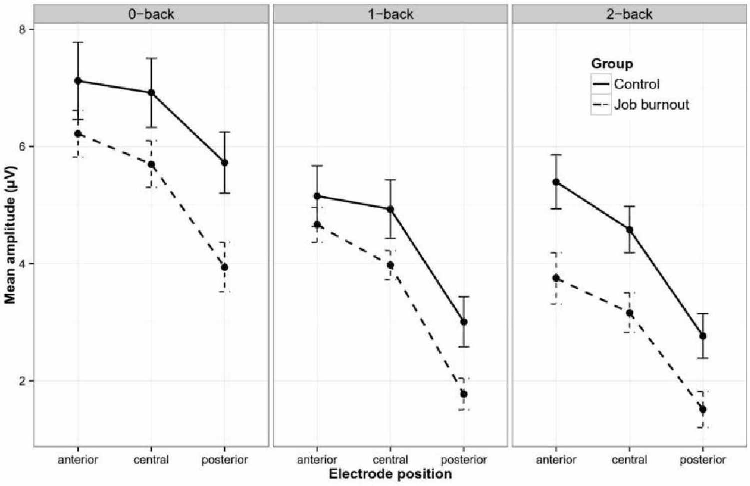


Figure 11. Line plots showing the group mean amplitudes (µV) with standard errors of the auditory late P3a for both groups at anterior, central, and posterior scalp.

For the visual P3b mean amplitudes, the main effect of Group was not significant ($F_{1,46} = 2.21$, $p = 0.14$). However, the amplitudes were affected by the task load ($F_{2,92} = 37.47$, $p < 0.001$, $\varepsilon = 0.87$, $\eta^2 = 0.12$) in such a way that the amplitudes became smaller as the task load increased (0-back > 1-back > 2-back, $p < 0.001$). As expected, there was a significant main effect of Electrode Position ($F_{2,92} = 61.14$, $p < 0.001$, $\varepsilon = 0.68$, $\eta^2 = 0.15$), with the largest amplitudes at posterior and central scalp locations, becoming smaller towards anterior regions (posterior > anterior, central > anterior, $p < 0.001$; posterior vs. central, $p = 0.056$). Notably, the interaction between Group and Electrode Position was significant ($F_{2,92} = 4.39$, $p = 0.03$, $\varepsilon = 0.68$, $\eta^2 = 0.01$). For the burnout group, the responses were smaller over the posterior ($p = 0.002$) and central ($p = 0.03$) regions, but larger over the anterior ($p = 0.003$) regions than for the control group (Figure 12). The interaction between Task Load and Electrode Position was also significant ($F_{4,184} = 7.45$, $p < 0.001$, $\varepsilon = 0.69$, $\eta^2 = 0.004$). The P3b amplitudes were the largest at central and posterior scalp locations when the task load was the lowest, decreasing as a function of increase in task load, and the smallest at anterior regions also decreasing with an increase in task load.

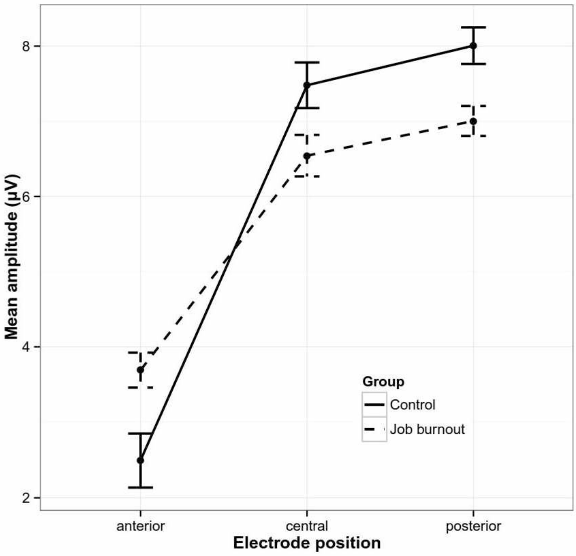


Figure 12. Line plots showing the group mean amplitudes (µV) with standard errors of the visual P3b for both groups at anterior, central, and posterior scalp.

In summary, the key findings in Study III were the following two burnout-related alterations: 1) a decrease in the auditory P3a amplitude in response to distractor sounds during task performance, and 2) smaller working-memory related visual P3b amplitudes over posterior scalp and larger P3b amplitudes over frontal areas in the burnout group compared to the control group.

4.4 Inadequate attentional set shifting in severe burnout (Study IV)

4.4.1 Behavioral data

Overall, the participants found the paradigm cognitively demanding. In terms of the self-reported effort put on the task as evaluated by the NASA-TLX, an insignificant difference between the groups was observed ($F_{2,53} = 2.45$, $p = 0.09$, $\eta^2 = 0.08$). The participants with mild burnout symptoms tended to report that they invested somewhat more effort (M = 67.4, SD = 11.8) in the task than those in the control group (M = 54.8, SD = 22.8) in order to accomplish their level of performance while the ratings in the severe burnout (M = 65.17, SD = 24.14) did not differ from the other groups.

Switch cost was indicated by a significant main effect of Trial Type ($F_{1,54} = 619.74$, $p < 0.001$, $\eta^2 = 0.65$). RTs on switch trials (M = 1210.4 ms, SD = 165.6 ms) were ~400 ms slower than on repetition trials (M = 810.4 ms, SD = 145.6 ms). However, the group means of the individual median RTs were comparable between the groups ($F_{2,54} = 0.15$, $p = 0.86$) as was the intraindividual RT variability (main effect of Group: $F_{2,54} = 0.01$, $p = 0.99$). Notably, the group had an effect on the error rates ($F_{2,54} = 3.28$, $p = 0.04$, $\eta^2 = 0.09$). Pairwise comparisons revealed that the group mean error rate was the largest for the severe burnout group, but comparable in mild burnout and control groups, (control vs. severe, $p = 0.009$, mild vs. severe, $p = 0.004$, control vs. mild, $p = 0.67$; Figure 13). The main effect of Trial Type was significant ($F_{1,54} = 28.97$, $p < 0.001$, $\eta^2 = 0.08$), with the error rate being higher for switch trials (5.2%) than for repetition trials (3.1%).

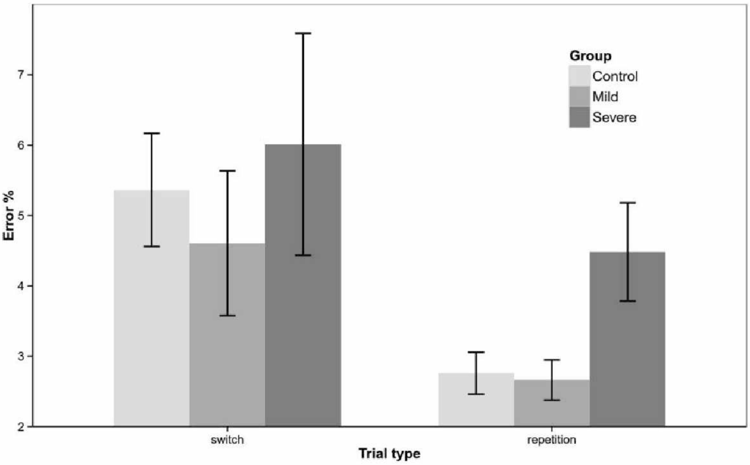


Figure 13. Group mean error rates for the switch and repetition trials in all study groups. Error bars represent standard error of the means.

4.4.2 ERP data

As seen in Figure 14, the P3 response had two distinct phases for task switch trials: the first peaking around 200-250 ms and the second about 100 ms later. According to scalp potential distribution mapping, the two phases had a similar distribution of the maximum amplitude over parietal scalp regions (Figure 15). The P3 responses were more pronounced on switch trials than on repetition trials as also seen in Figures 14 and 15.

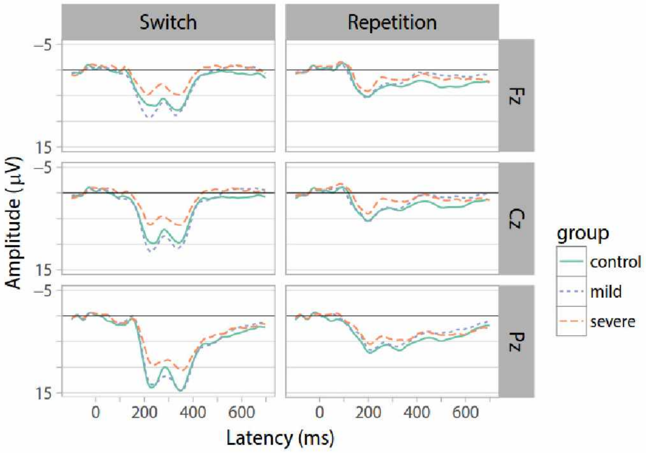


Figure 14. Grand average ERPs for each group from the switch and repetition trials at electrode sites Fz, Cz, and Pz.

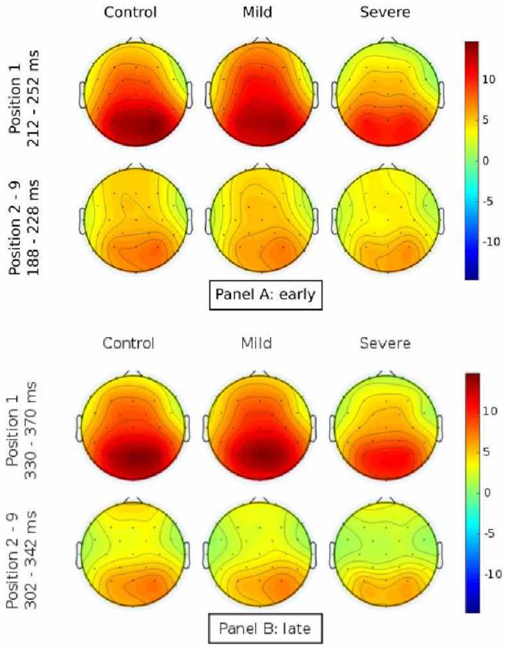


Figure 15. Voltage distribution over the scalp for both phases of the P3 response for each group (panel A: early; panel B: late).

Statistical analysis comparing group differences showed that the mean amplitudes of both the early and the late phase of P3 response were larger on switch than repetition trials (main effect of Trial Type: $F_{1,54} = 95.73$, $p < 0.001$, $\eta^2 = 0.17$; $F_{1,54} = 227.05$, $p < 0.001$, $\eta^2 = 0.28$, for early and late phases, respectively; Figure 16). The main effects of Electrode Position were also significant (early phase: $F_{2,108} = 54.99$, $p < 0.001$, $\varepsilon = 0.68$, $\eta^2 = 0.15$; late phase: $F_{2,108} = 101.14$, $p < 0.001$, $\varepsilon = 0.75$, $\eta^2 = 0.24$), showing that the amplitudes for both phases were the largest at posterior sites (anterior < central < posterior, $p < 0.001$). Notably, the Group × Trial Type interaction was significant for both phases of P3 (early phase: $F_{2,54} = 4.37$, $p = 0.017$, $\eta^2 = 0.02$; late phase: $F_{2,54} = 5.01$, $p = 0.01$, $\eta^2 = 0.02$), with the amplitudes being the smallest in the severe burnout group, and mostly comparable between the mild burnout and control groups (Table 5).

Table 5. Pairwise comparisons for the Group × Trial Type interactions for the mean amplitudes of both phases of P3.

		control vs. mild burnout	control vs. severe burnout	mild burnout vs. severe burnout
early phase	switch	0.01	< 0.001	< 0.001
	repetition	0.41	< 0.001	< 0.001
late phase	switch	0.12	< 0.001	< 0.001
	repetition	0.15	< 0.001	0.02

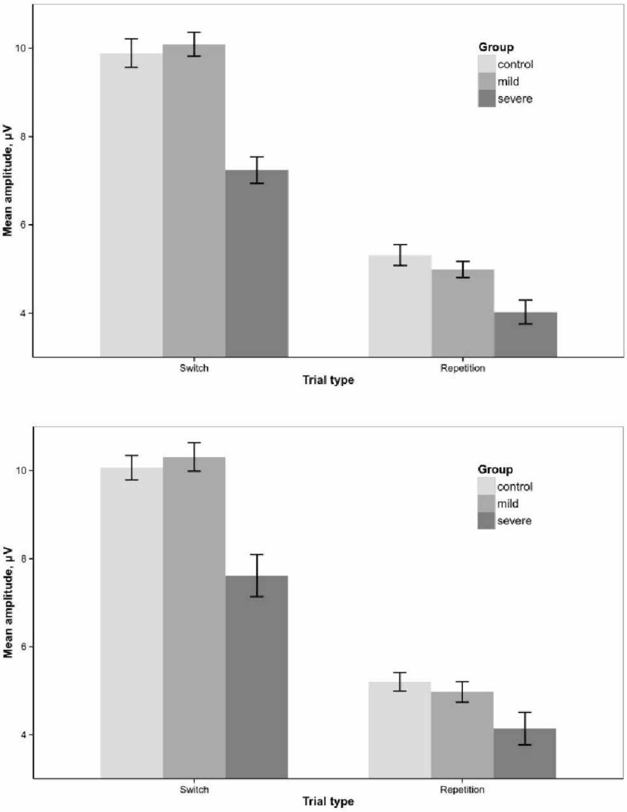


Figure 16. Bar plots showing the group mean amplitudes (μV) with standard error of means of the early (upper figure), and late (lower figure) phase of the P3 for each group at posterior scalp.

In summary, the results of Study IV suggest that severe burnout is associated with inadequate processing when rapid shifting of attention between tasks is required. This is indicated by a decreased P3 amplitude and less accurate performance in the severe burnout group compared to the mild burnout and control groups.

5 Discussion

The four studies reported here investigated attentional mechanisms and cognitive control processes associated with job burnout. Specifically, ERP recordings and questionnaires were performed on 67 currently working employees with burnout symptoms to explore the association of burnout with pre-attentive auditory change-detection processing and attention capture towards emotionally uttered speech (Study II), performance on a working-memory task with varying loads, and involuntary orienting of attention to novel, unexpected sounds during task performance (Study III), as well as shifting of attentional set (Study IV). In Study I, a variant of the multi-feature paradigm was developed to be applied in Study II.

The key finding was that burnout is associated with alterations in attention-related auditory and visual ERP responses. More specifically, we observed burnout-related alterations in momentary involuntary capture of attention to emotionally valenced speech, even when the symptoms are relatively mild (Study II). In addition, burnout was associated with ineffective orienting of attention to novel and potentially important events in the auditory environment during visual task performance, as well as dysfunctional cognitive control processes at fronto-parietal regions needed to monitor and update information in working-memory (Study III). Furthermore, severe burnout was associated with inadequate shifting of attention between task sets, resulting in less accurate performance (Study IV). Taken together, Studies II-IV showed burnout-related susceptibility of the P3 response. Such susceptibility has also been observed in high stress (Shackman et al., 2011), sleep deprivation (Polich & Kok, 1995), and depression (Bruder et al., 1995, 2009; Cavanagh & Geisler, 2006). In the following sections, six topics relevant to the studies will be discussed in more detail: 1) processing of emotionally uttered speech and its alterations in burnout, 2) dysfunctions in attentional control mechanisms in burnout 3) inadequate shifting of attentional set in severe burnout, 4) burnout as a subject for brain research, 5) clinical considerations, and 6) future directions.

5.1 Processing of emotionally uttered speech and its alterations in burnout

In Studies I and II, the ERP waveforms observed in the N1, MMN, and P3a latency ranges were affected by the acoustical properties of the stimuli. For example, the MMN amplitudes were larger for the emotional utterances, and for the location and spectral density deviants than for most other deviants. This reflects the fact that the MMN signal is larger with increasing magnitude of sound change (Pakarinen et al., 2007; Sams, Paavilainen, Alho, & Näätänen, 1985; Tiitinen, May, Reinikainen, & Näätänen, 1994). However, the groups did not differ with respect to the N1 and MMN signals. These highly similar response patterns suggest that an accurate memory trace is constructed for the invariant sound features of the auditory input and that the change-detection processes for speech sounds are similar in both groups (Näätänen et al., 2004; Näätänen, 1992; Pakarinen et al., 2009; Thönnessen et al., 2010).

The emotional utterances generated significant P3a responses, consistent with the involuntary attention capture triggered to novel, unexpected auditory stimuli (Escera et al., 1998; Friedman et al., 2001; Soltani & Knight, 2000), enabling rapid shifts of attention towards potentially important cues, including those which may carry socially relevant information. The P3a responses were elicited even though the emotional utterances in our study were not novel as such, but rarely occurring novelty-like variants of the standard. In terms of processing the emotional contents of the stimuli, there is evidence suggesting that the emotional meaning of prosodic features can be rapidly and systematically registered and identified in an accurate, differentiated categorical manner during speech processing (Jaywant & Pell, 2012; Laukka, 2005; Pell et al., 2015; Pell, Jaywant, Monetta, & Kotz, 2011; Pell & Kotz, 2011; Pell, 2006). Perhaps, emotional prosody is encoded in memory in the form of prototype expressions that correspond to basic emotions (Laukka, 2005).

Importantly, the P3a latencies were found to vary between the groups according to the type of emotional stimuli in the following way: The P3a latencies were significantly shorter to angrily uttered speech sounds, and slower to happy utterances for the burnout group compared to the control group. When interpreting the P3a responses to the emotional utterances, one should take into account that the P3a responses reflect not only the novelty or the emotional content of the stimuli but also the physical deviation, the saliency from the standard (Escera et al., 1998; Polich, 2007). Therefore, for valid conclusions the P3a responses need to be considered in relation to the N1 and MMN signals. The fact that the N1 and MMN responses were comparable in both groups suggests that the divergent P3a latencies towards negative and positive emotions between the groups might be due to the emotional properties of the novelty-like stimuli, and not the mere detection of basic sound features alone. Thus, the results suggest that in our sample of burnout participants, there was an attention capture tendency that is faster for negative, and slower for positive emotions compared to that of the control participants. Given the essential role of the prefrontal cortex in processing emotions and regulating attention together with the anterior cingulate cortex and the amygdala (e.g., Ochsner & Gross, 2005), the present results are in accordance with recent findings of dysfunctional cortico-limbic connectivity in burnout suggesting alterations in the processing of emotionally stressful stimuli (Golkar et al., 2014). In a similar vein, increased neurophysiological activity to salient negative stimuli has been shown in association with high levels of depression (McNeely et al., 2008), and anxiety (Bishop et al., 2004; Bishop, 2007). Importantly, however, the group differences remained significant after self-reported depressive symptoms were statistically controlled for in the analyses.

The notable advantage of the multi-feature paradigms is that in virtually the same recording time as with the traditional single- or two-deviant oddball paradigm, one can obtain a profile of a wide spectrum of auditory feature discrimination processes. This new configuration of stimuli results in ~45% shorter recording time than the multi-feature paradigm with alternating standard sounds (Näätänen et al., 2004; Pakarinen et al., 2009), and the ERP signals well reflect the perceptual properties of these sounds.

5.2 Dysfunctions in attentional control mechanisms in burnout

The novel sounds in Study III elicited a P3a response with two phases reflecting involuntary orienting of attention to these sounds, however being smaller in amplitude in the burnout group. More specifically, the auditory early P3a was smaller in the burnout group when the cognitive load of the visual working-memory task was high whereas the late P3a was reduced across all task loads.

Moreover, the magnitude of the auditory P3a was modulated by the complexity of the visual task so that when the task load increased, the late phase of the P3a to the distracting sounds attenuated in both groups. This is in accordance with previous studies suggesting that involuntary attention switching to distracting auditory stimulation is modulated by top-down mechanisms (Berti & Schröger, 2003; Escera & Corral, 2007; SanMiguel et al., 2008). Importantly, however, the late P3a responses were smaller in the burnout group than in the control group across all memory loads, and the early P3a was reduced with the highest memory load. These results suggest that orienting to task-irrelevant but potentially significant distinct events in the acoustic environment may be insufficient in burnout, as shown in patients with prefrontal lesions (Knight, 1984).

The visual P3b responses elicited for the task-relevant stimuli differed between the groups as a function of the topographical distribution. The burnout group showed a relative attenuation of the P3b at posterior regions while a relative amplification of the P3b was observed at anterior regions. Such frontally enhanced activation in response to task demands has also been observed in older adults (Friedman, Kazmerski, & Fabiani, 1997), and major depression (Harvey et al., 2005). For example, Friedman and colleagues (1997) proposed that older adults still depend on frontal regions for processing stimuli that have already been well encoded in young adults.

Finally, we did not find any difference between the groups in the task performance as indicated by comparable reaction times and error rates, in line with the findings of Harvey and colleagues (2005) in their fMRI study with patients with major depression. Thus, successful task performance in burnout might require additional recruitment of anterior regions to compensate for the decrement in posterior activity. These results suggest that burnout is associated with deficits in cognitive control needed to monitor and update information in working-memory. Furthermore, the more the working-memory is taxed, the more ineffective is the orienting of attention towards potentially significant unexpected sounds in individuals with burnout.

5.3 Inadequate attentional set shifting in severe burnout

In the task switching paradigm applied in Study IV, the key findings were a decreased P3 amplitude in response to the onset of the stimulus and less accurate performance in the severe burnout group compared to the mild burnout and control groups. The observed group differences remained significant after self-reported depressive symptoms, symptoms of anxiety, and sleep disturbances were controlled for in the analysis suggesting that dysfunctions in attentional set shifting were not merely a by-product of the participants in the severe burnout group reporting more intense symptoms of related conditions.

The behavioral results suggest that severe burnout is associated with inadequate processing in cognitive tasks where rapid shifting between tasks is required. Participants in all groups strived to sustain their speed of performance as was stressed in the task instructions. However, in order to do so the accuracy was sacrificed in the severe burnout group. This finding is in accordance with previous behavioral studies suggesting that severe burnout is associated with impaired performance in attention and executive functions as indicated by slower RTs (Kleinsorge, Diestel, Scheil, & Niven, 2014; Oosterholt et al., 2014), higher error rates (Diestel, Cosmar, & Schmidt, 2013), or both (Sandström et al., 2005; van Dam et al., 2011). An increased number of errors related to previously relevant rules has also been observed in mental fatigue as induced by time on task (Lorist et al., 2000) as well as in patients with dorsolateral prefrontal lesions (Barceló & Knight, 2002). Perhaps, the lesions not only impair the mechanisms underlying attentional set shifting but also make it difficult for the patients to keep track of the ongoing task set.

The attenuation of the P3 amplitude in the group of participants experiencing intense symptoms of burnout suggests ineffective shifting of attentional set in burnout. This finding may reflect differences in activation or selection of relevant task sets (Hölig & Berti, 2010; Kieffaber & Hetrick, 2005; Lange et al., 2015; Nicholson et al., 2006; Sohn, Ursu, Anderson, Stenger, & Carter, 2000) suggesting that greater activation associated with switch trials might reflect increased effort in the selection process. Perhaps, selecting what is relevant and what is irrelevant for the task is ineffective in severe burnout as reflected by reduced P3, resulting in more performance errors. Alternatively, the observed smaller P3 in the severe burnout group might reflect reduced ability to maintain spatial information online in working-memory, thereby disrupting working-memory processing and further resulting in less accurate performance. Evidence from neuroimaging studies suggests that orienting attention to a location might functionally overlap with top-down mechanisms such as preparing and executing goal-directed selection of stimuli and responses, thereby recruiting prefrontal cortical areas which together with posterior association cortices are involved in executive control of set shifting (for reviews, see Corbetta & Shulman, 2002; Miller, 2000).

In Study IV, the applied paradigm involves features that complicate the interpretation of the ERP results. First, the interval between correct response to the preceding stimulus and the onset of the subsequent stimulus was very short (150 ms). Second, the cue and the target were only presented simultaneously without manipulation of the cue-target interval. The presentation rate was rapid, and therefore the participants found the task cognitively demanding which was our aim in this study design. However, such features of the paradigm presumably led to temporal overlap of the stimulus-related and response-related processes.

The visual stimuli evoked a pattern of parietally maximal P3 activation with two phases across switch and repetition trials, in accordance with a recent study of Berti (2016) showing a bi-phasic large positive response within 200-400 ms from stimulus onset with more pronounced amplitudes for the switch trials than repetition trials. The two subsequent P3 responses had similar scalp distributions suggesting that they reflect the same P3b response including some contribution presumably from an overlapping parietally maximal negativity related to the response given to the previous stimulus (Karayanidis et al., 2003). Given the short response-to-stimulus interval, the processes related to the preceding response were likely to be still in progress when the subsequent stimulus was presented. In addition, as the cue and the target were presented simultaneously, and the task switches were not predictable, the participants had no opportunity to predict whether the task rule changes, or remains the same. Thus, performance on each trial required both encoding the cue, and selecting and processing of the target character in the stimulus pair. Consequently, there is likely a temporal overlap between cue-related and target-related processes (Nicholson et al., 2005). Unfortunately, the present paradigm limits our possibilities to disentangle these overlapping processes. An experimental paradigm including manipulations of cue-target intervals should be used in the future in order to separate the ERP responses.

While the task performance was comparable between the burnout and control groups in Study III, the severe burnout group performed less accurately than the other groups in Study IV suggesting that in severe burnout, processing is inadequate when rapid shifting between tasks is required. Perhaps, intense burnout symptoms might be required for impaired cognitive task performance to be observed as is the case in a number of previous behavioral studies (e.g., Oosterholt et al., 2014; Sandström et al., 2005; Van der Linden et al., 2005).

5.4 Burnout as a subject for brain research

From a brain research perspective, burnout is a challenging research subject due to the heterogeneity of symptomatology among individuals experiencing burnout (van Dam, 2016). For example, there might be considerable variability between individuals with burnout symptoms in the degree to which working conditions are experienced as stressful (for a review, see Seidler et al., 2014). Thus, the main challenges most obviously relate to the conclusions that could be drawn from the results.

In the present thesis, the sample of participants experiencing symptoms of burnout was heterogeneous and non-clinical in nature. The participants were working-aged (ranging from 27 to 62 years), at work at the time of study, and the participants in the burnout group reported a wide range of burnout symptoms from mild to severe. Based on previous population-based research literature, we considered the sample representative of Finnish working life (Ahola et al., 2006) with the exception of the fact that most of the present participants were females. This may be partly due to the recruitment process or reflect previous burnout research suggesting that women are somewhat more emotionally exhausted than men (Ahola et al., 2006; Purvanova & Muros, 2010). Notably, however, the ratio of female and male participants in all study groups were comparable suggesting that the present results of differences between the groups cannot be easily explained by gender differences. In addition, as the data in all studies of the present thesis were from the same sample of participants (with few exceptions due to exclusion criteria in the ERP analysis), further studies with different samples of participants would be needed in order to be able to increase the generalizability of the results. Furthermore, the present findings need to be considered at a group level since they do not provide a method for patient assessment at an individual level. Significant results with relatively small effect sizes in group comparisons can be considered a representation of this.

The present thesis showed burnout-related dysfunctions in attention and cognitive control processes. Such dysfunctions have been also observed in other conditions such as major depression, generalized anxiety disorder or other stress-related neuropsychiatric conditions (American Psychiatric Association, 2013), and sleep deprivation (Heuer et al., 2004; Kingshott, Cosway, Deary, & Douglas, 2000). Indeed, the burnout participants reported not only burnout symptoms but also a great deal of depressive symptoms, as well as symptoms of anxiety and sleep disturbances. Strong positive correlations were observed between most of these symptoms. In addition, individuals with burnout symptoms showed greater sleepiness during the ERP recording session than the control participants, in accordance with the findings of Ekstedt and colleagues (2006, 2009). Thus, given these overlaps, it is worth discussing to what extent the findings of the present thesis could reflect other overlapping conditions even though the results remained significant after depressive symptoms (Studies II and IV), subjective sleepiness (Study III), symptoms of anxiety (Studies III and IV), and sleep disturbances (Study IV) were statistically controlled for when comparing the burnout and control groups.

Typically, an important prerequisite for valid conclusions from neurophysiological and clinical studies is that the clinical subgroups are defined as precisely as possible. Burnout as a heterogeneous condition does not necessarily meet such a requirement. At the same time, however, one needs to bear in mind the spectrum of depressive and anxiety disorders, too (for reviews, see e.g., Davidson et al., 2002; Hettema, Neale, Kendler, & Ph, 2001; Olatunji, Cisler, & Tolin, 2007; Richards, 2011; Stein, 2009). They may arise from a multitude of causes emerging in broad symptoms, and the underlying mechanisms may also differ. In addition, the more severe the burnout symptoms are, the more common is depression, but notably, all individuals with severe burnout are not diagnosed with depression (Ahola et al., 2005). Consequently, the overlap between the conditions means that studying the neurophysiology of burnout at least to some extent means studying also the neurophysiology of depressive and anxiety disorders. In addition, the questionnaires for assessing symptoms of burnout or depression share similar questions, inevitably leading to strong correlations even at the methodological level. Thus, in the present thesis, although none of the participants were diagnosed with severe clinical depression or anxiety disorder, and the overlapping conditions were in different ways controlled for in the studies, we cannot fully rule out the possibility of some contribution from depressive or anxiety disorders, or sleep disturbances on the results. One could attempt to recruit volunteers who report only burnout symptoms but no symptoms of depression or anxiety, but that would be difficult, and such a sample would also be non-representative of people experiencing job burnout.

Despite the challenges, the present thesis showed that the methods, traditionally used in basic research and clinical settings, can also be applied to study heterogeneous groups of working aged people reporting a wide range of prolonged work-related stress symptoms. Thus, the findings are of value when striving to characterize burnout at a group level amongst related conditions with shared and unique features.

5.5 Clinical considerations

The present thesis raises questions and challenges also from a clinical perspective. First, why do employees with prolonged work fatigue seem to hesitate in contacting the occupational health care due to their symptoms? In the present thesis, approximately only one fifth of the burnout participants entered the study as referred by a health care professional, and the rest of them contacted directly our research group after noticing the study advertisement. Conversations with the participants shed some light on this issue, but in the present thesis the topic remains only speculative. For example, the participants reported worry about a possible label of a mental illness that burnout might bring, worry about keeping one’s job, or worry about the effects their own complaints might have on their work community. Indeed, worry about stigma and the possible harm and misconceptions it would bring have been shown in relation to many mental illnesses (Corrigan & Watson, 2002; Sartorius, 2007). Personality traits might also partly explain this behavior as employee personality, especially conscientiousness and neuroticism, has been suggested to be related to susceptibility to burnout (Alarcon, Eschleman, & Bowling, 2009; Armon, Shirom, & Melamed, 2012). Thus, worry and employee personality may lead to avoidance towards contacting occupational health care when well-being at work is at risk.

Second, behavioral methods assessing cognitive performance may not necessarily be sensitive enough to capture the putative burnout-related impairments, especially when the burnout symptoms are relatively mild. In clinical work, it is thus important to validate the individual's experiences of cognitive disturbances and complaints even though no performance decrement would be observed in a clinical assessment using traditional pen-and-paper methods. In future research, subjective cognitive complaints should be systematically evaluated in order to study whether or not they would correlate with brain research findings on attention and cognitive control processes.

In addition, effort invested in task performance in burnout might warrant further studies with larger sample sizes than in the present thesis. In individual clinical settings, it is typically assessed by the participant or the health care professional. In Study IV, there was a tendency for the mild burnout group to put more effort on the task performance than the severe burnout and control groups as indicated by subjective ratings. This finding may be informative but should be interpreted with caution. One might consider this tendency in light of the attentional control theory by Eysenck, Derakshan, Santos and Calvo (2007). They stated that in anxiety, performance may remain effective when individuals put in compensatory strategies such as enhanced effort to use. Perhaps cognitive performance in mild burnout shares some elements with that of individuals with anxiety symptoms, when participants increase their effort striving to sustain the performance level as good as possible, as also suggested by van Dam (2016). Given that no additional effort was reported in the severe burnout group compared to the control group, the accuracy in the severe burnout group was sacrificed while striving to sustain the performance level.

5.6 Future directions

The present findings may be of help when developing burnout-related interventions in the occupational health care, or preventive actions in workplace settings. However, the relatively large-scale prevalence of burnout potentially leading to considerable economic, social, and psychological costs to employees and employers certainly calls for further studies to contribute to a better understanding of the health and performance consequences of long-term work-related stress. With this regard, applied psychophysiological research methods serving the needs of today's working life might be beneficial in evidence-based health promotion at work. For example, in addition to brain research, other psychophysiological parameters such as heart-rate-variability (e.g., Kemp et al., 2010; Segerstrom & Nes, 2007) or eye blink rate (for a review, see Jongkees & Colzato, 2016) might provide additional value, not only in characterizing burnout features at group level, but also at an individual level in the clinical settings when assessing burnout, or in providing information possibly related to the recovery of burnout.

It should be emphasized that causality cannot be determined in the present thesis. To date, only little is known about the long-term consequences of prolonged work-related stress in terms of behavioral performance and brain mechanisms. A recent behavioral follow-up study showed that after one year from the initial professional care-seeking, performance of the former burnout patients was improved in tasks evaluating executive functions relative to the initial assessment (Eskildsen, Andersen, Pedersen, & Andersen, 2016). However, they still continued to perform worse than their control participants suggesting that cognitive functioning should be taken into account when interventions for alleviating burnout symptoms or return to full-time employment after possible sick leave are planned. These issues should also be considered in interventions that include workplace prevention activities through reducing psychosocial workload and risk factors at work.

Finally, longitudinal studies could provide a better understanding of which individual, interpersonal, or organizational factors contribute to who stays at or returns to work after experienced burnout. These issues will be addressed in a currently ongoing collaborative follow-up study at the Finnish Institute of Occupational Health to which the participants of the present thesis are invited.

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