Accepted Manuscript

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PII: S0301-0511(15)30080-6
DOI: http://dx.doi.org/doi:10.1016/j.biopsycho.2015.11.005
Reference: BIOPSY 7119

To appear in:

Received date: 28-12-2014
Revised date: 20-8-2015
Accepted date: 14-11-2015

EEG alpha frequency correlates of burnout and depression: The role of gender

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Highlights:

- EEG alpha frequency correlates of burnout and depression were analyzed.
- Burnout was associated with alpha power, whereas depression was linked to IAF.
- Notable gender differences were found.
- Neural indicators provide preliminary evidence for establishing burnout as a separate clinical syndrome.

Abstract

EEG alpha frequency band biomarkers of depression are widely explored. Due to their trait-like features, they may help distinguish between depressive and burnout symptomatology, which is often referred to as “work-related depression”. The present correlational study strived to examine whether individual alpha frequency (IAF), power, and coherence in the alpha band can provide evidence for establishing burnout as a separate diagnostic entity. Resting EEG (eyes closed) was recorded in 117 individuals (42 males). In addition, the participants filled-out questionnaires of burnout and depression. Regression analyses highlighted the differential value of IAF and power in predicting burnout and depression. IAF was significantly related to depressive symptomatology, whereas power was linked mostly to burnout. Moreover, seven out of twelve interactions between EEG indicators and gender were significant. Connectivity patterns were significant for depression displaying gender related differences. The results offer tentative support for establishing burnout as a separate clinical syndrome.

Keywords: burnout, depression, EEG, individual alpha frequency, alpha power, coherence

1. Introduction

Burnout and depression represent two major public health concerns (van Luijtelaar, Verbraak, van den Bunt, Keijsers & Arns, 2010; Torker and Biron, 2012), affecting not only employed adults but also students. Among medical students, for instance, the prevalence rate of burnout symptomatology may be as high as 50% (Dyrbye et al., 2008). Similarly, the prevalence of depression among university students varies from 10% to 84.5%, depending on the assessment method, demographic composition of the sample, and place of study (Dyrbye, Thomas & Shanafelt, 2006; Ibrahim, Kelly, Adams & Glazebrook, 2013). Burnout and depression are both defined as negative affective states, however, burnout symptoms are often work-related whereas depression tends to be context-free (Hakanen & Schaufeli, 2012). Symptoms of burnout are thought to include emotional or physical exhaustion, depersonalization or cynicism, and reduced personal accomplishment (Maslach, Schaufeli & Leiter, 2001) and are often reported by people with no history of psychopathology. ICD-10 considers burnout as a state of vital exhaustion with no other specific diagnostic criteria. The latest version of DSM (DSM 5 - APA, 2013) does not even acknowledge burnout as a diagnostic entity. In contrast, major depressive disorder is characterized by depressed mood, diminished interest and pleasure, fatigue and feelings of worthlessness (DSM 5 - APA, 2013; Uher, Payne, Pavlova & Perlis, 2014).

There has been a strong debate over the discriminant validity of the two concepts in the literature (Ahola et al., 2005; Bianchi, Schonfeld & Laurent, 2015a; Hakanen & Schaufeli, 2012). On the one hand, research consistently shows differences between burnout and depression symptomatologies with intecorrelations moderate in size (Ahola & Hakanen, 2007; Hakanen & Schaufeli, 2012; Leiter & Durup, 1994). Several studies even explored the time course and causal order of the two constructs with burnout predicting depression and vice versa (e.g., Ahola & Hakanen, 2007; Torker & Biron, 2012). On the other hand, some studies have reported marked overlap between the concepts and even refer to burnout as work-related depression (e.g., Bianchi, Schonfeld & Laurent, 2014). By using a person-centered approach, Ahola et al. (2014), for instance, found that symptoms of burnout and depression cluster together and develop hand in hand over a course of seven years. Similar results were obtained in a longitudinal study by Bianchi, Schonfeld & Laurent (2015b). A recent review also seriously questioned not only an empirical distinction but also a distinction of theoretical foundations, as not only burnout but also depression may be triggered by job-related factors (Bianchi et al., 2015a). As a result of these inconsistencies, several scholars seriously question whether burnout is a new nosological entity with distinct diagnostic criteria.

1.1. Gender differences in burnout symptomatology and depressive disorders

Aside from the diagnostic ambiguity, one of the crucial points concerning burnout and depressive symptomatologies are gender differences. In general, women are assumed to be more prone to burnout (Maslach et al., 2001), however, empirical evidence on this issue has been inconsistent. A recent meta-analysis involving 183 studies on burnout symptomatology found that women tend to be more emotionally exhausted than men, whereas men report higher levels of depersonalization (Purvanova & Muros, 2010). Overall burnout was found to be higher for women, thus supporting the common held assumption regarding gender differences. It should be noted, however, that the effect sizes for these differences were very limited. In terms of depression, findings on gender differences are more robust. Women are twice as likely as men to suffer from depression and its various forms (for an overview see Kessler, 2005; Piccinelli & Wilkinson, 2000). Authors, however, argue that such gender differences may be inflated due to several artefactual influences (e.g., Parker, Fletcher, Paterson, Anderson & Hong, 2014). Women tend to accentuate reports of depressive symptoms, whereas men tend to attenuate them. In general, reports of depression symptoms may also be biased because of gender-role stereotypes, which make it more socially acceptable to express negative emotions for women (Madden, Barrett & Pietromonaco, 2003). A similar reasoning has also been applied to gender differences in burnout symptomatology (e.g., Purvanova & Muros, 2010).

1.2. EEG-based biomarkers of psychopathology

Electrophysiological studies could help unravel the ambiguity regarding the overlap between burnout and depression as well as clarify whether burnout should be considered a separate diagnostic entity (van Luijtelaar et al., 2010). Moreover, gender-related self-report biases could be eliminated by investigating gender differences in electroencephalographic (EEG) indicators of burnout and depressive symptomatologies. In the past decades, the electroencephalogram (EEG) has been widely used for biomarker research of neuropsychiatric disorders, including major depressive disorder (e.g, Olbrich & Arns, 2013), as it is reliable, noninvasive and cost effective. Knott, Mahoneya, Kennedy & Evans (2001), for instance, argued that the use of EEG in depression research "is based on the belief that major depressions have a biological basis and that glimpses of the determining causes and/or of the factors mediating its expression and relief can be objectively captured by non-invasive neuroelectric probes" (p. 124). A similar argument can be made for other affective psychopathology (e.g., posttraumatic stress disorder; Wahbeh and Oken, 2013; fatigue, Billiot, Budzynski & Andrasik, 1997).

Recently, there has been a surge of interest in EEG-based biomarkers in the alpha frequency range (8-13 Hz) The alpha rhythm has several trait-like properties: (1) it dominates EEG recordings during relaxed wakefulness (Klimesch, 1999), (2) it is stable over time (Kondacs & Szabó, 1999), and (3) it is under strong genetic control (Smit et al., 2006).Alpha power is thought to reflect the number of neurons that discharge synchronously in integrated cortico-cortical and thalamocortical systems (Hindriks & Putten, 2013). Enhanced alpha power or amplitude is an indicator of cortical hypoactivity and vice versa (e.g., Jaworska, Blier, Fusee & Knott, 2013). The variation of spectral distribution within the alpha range can be quantified via two methods: peak alpha frequency (PAF), which is based on the frequency with the highest magnitude, and individual alpha frequency (IAF), which measures the center of gravity rather than the peak (Angelakis et al., 2004a). Results of both may be used interchangeably when discussing research on neural correlates of different psychological states and disorders. However, IAF is considered to be a more accurate measure of the spectral distribution than PAF. IAF is assumed to be related to the characteristics of white matter structure, like fiber density, axonal diameter, and myelination and captures different neural processes than alpha power (e.g., Jann, Koenig, Dierks, Boesch & Federspiel, 2010). IAF (or PAF) is hypothesized to be an index of cognitive preparedness, which refers to the brain's capacity for higher-level cognitive functioning (Angelakis et al., 2004a). Both alpha power and IAF classify as candidate biomarkers (for an overview on biomarkers see Ritsner & Gottesman, 2009), as they are measured reliably and non-invasively, have trait-like features, and are heritable (Olbirch & Arns, 2013). However, they lack the specificity that is necessary to differentiate psychopathologies (e.g., decreased IAF may be characteristic for a wide range cognitive and emotional symptoms; Graces et al., 2013). In addition, IAF alone may also be of limited diagnostic value (Grandy et al., 2013), as the mean IAF of different patient groups is often found to be slower than that of healthy controls (e.g., Alzheimer's disease and mild cognitive impairment, Graces et al., 2013; schizophrenia, Boutros et al., 2008), yet it still ranges within the IAF distribution of healthy adults. Due to these drawbacks, coherence in the alpha frequency range could complement the previous two indicators. In fact, the most contemporary view on different disorders stresses the importance of connectivity and interactions between different areas of the brain (Fingelkurts et al., 2007; Olbirch & Arns, 2013). Defined as a temporal correlation between spatially distal neurophysiological events (Friston et al., 1993), alterations of functional connectivity (and EEG coherence as a specific measure) can add to diagnostic specificity and may help to discriminate between diseases (for review Greicius, 2008; Whitfield-Gabrieli & Ford, 2012).

1.3. EEG alpha activity in depression

The vast majority of recent work investigating alpha activity in major depressive disorder (MDD) focuses on the relationship between asymmetrical (left versus right) alpha power in prefrontal regions (for a review see Coan & Allen, 2004; Thibodeau, Jorgensen & Kim, 2006). As emphasized by Allen and Cohen (2010), most of these studies suggest that MDD may involve a pattern of stronger relative right frontal cortical activity in a resting state (thus, relatively greater left than right alpha power). In fact, frontal EEG asymmetry based on 8-13 Hz alpha power has proposed to be an endophenotype for depression (Stewart et al., 2010). However, the predictive value of EEG frontal alpha asymmetry is highly sensitive to the severity of depressive symptoms as well as EEG reference montages (Jesulola, Sharpley, Bitsika, Agnew & Wilson, in press; Stewart et al., 2010).

Historically, the “ability to produce good alpha waves” was associated with the affective capacity of the individual (Lemere, 1936). These results were often replicated, as mostly elevated alpha power was found in patients with major depressive disorder (Olbrich & Arns, 2013). The overall hypoactivity in resting EEG, however, was more pronounced in males with major depressive disorder (Jaworska, Blier, Fusee & Knott, 2012). Given that enhanced alpha power has been found in frontal and parietal regions, results point to a more generalized pattern of cortical hypoactivity.

IAF has not been extensively studied with respect to depressive symptomatology and major depressive disorder. As IAF is considered a true endophenotype and was linked to cognitive performance and memory (e.g., Grandy et al., 2013), it has potential utility for the study of depression. The hallmark cognitive symptoms of major depressive disorder are also impaired concentration, inability to think and indecisiveness (e.g., Uher et al., 2014). Furthermore, acute stages of major depressive disorder are associated with attention deficits, memory deficits and impairment in executive functioning (Snyder, 2013). These deficits accompany Alzheimer ’s disease and mild cognitive impairment, for both of which a notably slower or lower IAF has been found compared to healthy controls (Garces et al., 2013).

Several studies also noted that the prefrontal cortex should not be viewed as the only brain area associated with depression. In fact, research shows that major depression is related to a distributed system of functionally connected cortical and subcortical areas (Fingelkurts et al., 2007). For example, Greicius et al. (2007) reported that depressed individuals display increased functional connectivity between the subgenual cingulate cortex and thalamus compared to healthy controls. Despite these findings, there is little research devoted to the relationship between depressive disorders and EEG coherence. For instance, Knott et al. (2001) found that male depressed individuals exhibit reduced inter-hemispheric coherence in delta, theta, alpha, and beta frequency bands compared to controls. Fingelkurts et al. (2007) showed more diverse and specific patterns of functional connectivity in the alpha band related to distance and hemispheric lateralization. In contrast, Hinkus et al. (2009) did not find any significant EEG coherence results between the depressive patients and healthy controls in a female sample. In general, results suggest that EEG connectivity could serve as a potential biomarker which should, due to some inconsistencies, receive even greater research attention (Olbrich & Arns, 2013).

1.4. EEG alpha activity in burnout

Research into neural correlates of burnout symptomatology is emerging (Sokka et al., 2014; van Luijtelaar et al., 2010). In the seminal article by van Luijtelaar et al. (2010), alpha power did not discriminate between the burnout and control groups. There was also no support for frontal EEG asymmetry in burnout patients. However, research on fatigue, which is also characteristic of burnout, points to the direction of higher alpha power value when fatigue is high. For instance, Craig, Tran, Wijesuriya & Nguyen (2012) found increases in alpha power after experimentally inducing fatigue among healthy men and women. Based on these findings, it has been argued that increased alpha power in a fatigue state reflects increased efforts to maintain vigilance and wakefulness (Klimesch, 1999).

Van Luijtelaar et al. (2010) also showed that burnout patients have lower PAF than control subjects. Moreover, decreased PAF has been associated with chronic fatigue syndrome in a study by Billiot et al. (1997) pointing to a state of decreased alertness and cognitive preparedness in burnout symptomatology.

To date, only one study examined connectivity patterns in burnout. Tukaiev et al. (2012) found that in men, (1) decreased alpha 1 subband coherence in left frontal-right parietooccipital zones and in right frontal-parietal zones and (2) alpha 2 subband coherence in right parietal-left temporal and occipital zones were related to burnout symptomatology. For women, these findings could not be confirmed.

1.5. The present study

The primary aim of the present study was to investigate the relation of potential biomarkers in the alpha frequency band (IAF, power, and coherence) with self-report measures of depression and burnout in students. By following the recommendations on biomarker and endophenotypes research (e.g., Ritsner & Gottesman, 2009), we used reliable, cost-effective and heritable biomarkers which jointly can enhance sensitivity for detecting a symptomatology and can increase specificity in discriminating from similar traits. Traditional measures such as IAF and power in the alpha frequency band are heritable and may be more robust biomarkers of burnout and depression as, for instance, frontal asymmetry which has been plagued by certain inconsistencies (e.g., Stewart et al., 2010). Given the finding that major depressive disorder is related to a distributed system of networks (e.g, Fingelkurts et al., 2007; Jesulola et al., in press), alpha power and IAF measures were complemented with EEG coherence measures.

Based on our literature review on alpha activity on burnout and depression, no distinct hypotheses for burnout and depression can be formulated. The previous results on EEG correlates are more in favor of the assumption that burnout and depression are not distinct (e.g., Bianchi et al., 2015). Thus, we hypothesized that elevated alpha power will be linked to increased depression as well as burnout scores (Craig et al., 2012; Jaworska et al., 2012). Given that the majority of studies reported decreased IAF in patients with different yet interrelated mental disorders and also among burnout and depression (e.g., Grandy et al., 2013; van Luijtelaar et al., 2010), we expected that higher burnout and depression scores will be associated with lower IAF. As previous results in EEG studies are more inclined toward accepting burnout as a form of depression, we expected similar coherence patterns for burnout and depression. More precisely, we expected to find a specific pattern of short-range anterior, posterior, and left hemisphere functional connections in the alpha frequency band for depression as well as burnout (Fingelkurts et al., 2007).

A second aim of our research was to examine the moderating role of gender between EEG correlates and burnout/depression. Although this aim was rather exploratory, we believe that such approach is feasible because self-report of burnout and depression may be contaminated by gender-based stereotypes. Moreover, studies on major depressive depression frequently point to gender-specific results (e.g., Stewart et al., 2010). In general, there has also been evidence that men and women differ in terms of alpha power, yet the extent of the differences remains unclear (e.g., Jaušovec & Jaušovec, 2010). Overall, our study strived to test whether burnout and depression are really the same psychopathology based on neuroelectrical activity in both men and women.

2. Method

2.1. Participants and procedure

One-hundred-seventeen students of the University of Maribor, 42 of which were male participated in the study. Both undergraduates and graduates, aged between 19 and 29 (Age:

M_{male} = 22.26, *SD* = 2.34; M_{female} = 22.41, *SD* = 1.81; t(115) = 0.36, p = 0.72) were recruited from a large pool of individuals, who completed both burnout and depression questionnaires. Upon arrival to the lab, they were seated in a reclining chair while their resting eyes closed EEG was recorded for 3 minutes. Afterwards they solved several tasks which were part of different studies (Author, 2014a, b). In line with the Helsinki Declaration (World Medical Association, 2008) and with the institutional ethics commission's guidelines, all students participated in the study on a voluntary basis, were fully briefed about the research goals and were given the possibly to decline or terminate the study. In addition, signed informed consent sheets were obtained.

2.2. Instruments

Burnout was assessed with the student version of the original Maslach Burnout Inventory – General Survey (MBI-SS; Schaufeli, Martínez, Marques Pinto, Salanova & Bakker, 2002). The student version of the inventory consists of three dimensions: exhaustion, cynicism and reduced personal efficiency. Items were rated on a 7-point frequency rating scale ranging from 0 (never) to 6 (always) (Schaufeli et al., 2002; Hu & Schaufeli, 2009). As burnout is conceptualized as a syndrome involving all three dimensions, a total mean score was used as an indicator of burnout (Brenninkmeijer & Van Yperen, 2005). Previous studies supported psychometric properties of the scale in terms of its reliability and validity (Schaufeli et al., 2002; Hu & Schaufeli, 2009). In the present study, Cronbach's alpha was .78 for male participants and .79 for female participants, thus indicating appropriate reliability for both groups.

Depression was assessed using the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977). According to clinical diagnostic criteria, the scale consists of items reflecting negative emotions, the absence of positive emotions and physical symptoms. Due to recent psychometric evidence, the new 14-item revision was used consisted of three sub-dimensions: negative affect, anhedonia, and somatic symptoms (Carleton et al, 2013). All items were measured using a 4-point Likert scale (from 0 = rarely or none of the time to 3 = most or all of the time). In its present form, the scale is superior to other versions in terms of reliability, validity and clinical applicability as well offers an unbiased estimation of depressive symptoms across both genders. The total means score served as an estimate of depression among students (Dyrbye et al., 2006; Radloff, 1997). Appropriate reliability of the scale was found in our samples, as Cronbach's alpha was .90 for male participants and .86 for female participants.

2.3. EEG data acquisition

A Quick-Cap with sintered (Silver/Silver Chloride; 8mm diameter) was fitted to each participant. Using the Ten-twenty Electrode Placement System of the International Federation, the EEG activity was monitored over nineteen scalp locations (Fp1, Fp2, F3, F4, F7, F8, T3, T4, T5, T6, C3, C4, P3, P4, O1, O2, Fz, Cz and Pz). All leads were referenced to linked mastoids (A1 and A2), and a ground electrode was applied to the forehead. Additionally, vertical eye movements were recorded with electrodes placed above and below the left eye. Electrode impedance was maintained below 5 kΩ. EEG was recorded using NeuroScan Acquire Software and a SynAmps RT amplifier (Compumedics, Melbourne Australia), which had a bandpass of 0.15–100.0 Hz. At cutoff frequencies the voltage gain was approximately –6 dB. The 19 EEG traces were digitized online at 1000 Hz with a gain of 10x (accuracy of 29.80 nV/LSB in a 24 bit A to D conversion) and stored on a hard disk.

2.4. EEG analyses

Offline EEG analysis was performed using NeuroScan Scan 4.5 Software (Compumedics, Melbourne, Australia). Comprised were epochs of 2048 data points. Ocular artifact reduction was applied according to the method described in Semlitsch et al. (1986). The data was also visually inspected and areas contaminated by non-cerebral artifacts were rejected. A Fast Fourier Transformation, based on the Cooley and Tukey (1965) method, was performed on artifact-free epochs of data in order to derive estimates of spectral power (μV^2). To reduce spectral leakage, a Hanning window was applied. The epoch duration allowed for a frequency resolution of 0.5 Hz – this precision was sufficient for the purpose of the present study (Jaušovec & Jaušovec, 2000). This method was used in order to draw comparisons with the alpha power studies mentioned in the introduction. On average, 85 epochs (2.3% rejection rate) were used in the analysis. The alpha peak (IAF) was determined according to the method described by Klimesch, Schimke & Pfurtscheller (1993) and Angelakis, Lubar & Stathopoulou (2004b): an automatic peak detection procedure found the highest peak (maximum alpha power) in a 7 to 14 Hz window (Haegens, Cousijn, Wallis, Harrison & Nobre, 2014). This method was used because it is more adequate for studying endophenotipic qualities during resting (eyes closed) EEG sessions (Klimesch et al., 1993; Hooper, 2005) than the peak frequency center of gravity method proposed by Klimesch et al., (1993). IAF was computed for each channel and averaged over the anterior (Fp1, Fp2, F3, F4, F7, F8, Fz), central (T3, T4, C3, C4, Cz) and posterior (T5,T6, P3,P4, O1, O2, Pz) locations. EEG power values in the IAF frequency range (IAF ± 1 Hz) were determined for each channel. IAF was used as an anchor point instead of the common division into two lower alpha bands (below IAF) and one upper alpha band (above IAF) because we were interested in power and coherence values in the individually determined alpha frequency range. This methodological approach, which is similar to the one described by Neuling, Rach & Herrmann (2013), was used because it captures the frequency range of interest with greater precision than the more common division described by Klimesch (1999), where IAF serves as a division point between the lower-2 and upper alpha frequency bands. Raw scores were not normally distributed therefore they were subject to logarithmic transformations (using the base 10 logarithm) and averaged in the same way as the IAF measures.

EEG estimates (power and IAF) were averaged in an anterior-posterior direction for two reasons: first, recent discoveries on the organization of the human cortical connectome have identified three main networks, all of which connect posterior brain regions with anterior brain regions: the salience network, the central executive network, and the default mode network (for a review see Smith, et al., 2013). Second, research on gender differences in resting-state brain activity (i.e. resting state EEG power) showed that the most pronounced differences occurred in the anterior-posterior direction (Jaušovec & Jaušovec, 2010). The aforementioned study did not show similar clustering for coherence, thus we decided to analyze all possible combinations between the 19 electrodes.

Coherence is a frequency dependent measure of the degree of linear relatedness between two channels (Grosse et al., 2002). The resulting metric is similar to a Pearson correlation coefficient, with values between 0 and 1, where values closer to 0 indicate little synchronization and values closer to 1 indicate substantial synchronization. Because of the potential for spurious coherence due to volume conduction effects, EEG coherence should be examined between sites that are widely spaced (>5 cm). In our case, the data analyzed were recorded with few electrodes spaced about 7 cm apart, minimizing the effects of volume conduction, hence, no Laplacian transformation was used (e.g., Babiloni et al. 1995). Coherence values in the IAF frequency range (IAF ± 1 Hz) were estimated for all electrode pairs. In that way, 171 coherence measures were computed using the formula (1):

$$R_{xy}=\frac{\sum_i (x_i-\bar{x})(y_i-\bar{y})^*}{\sqrt{\sum_i (x_i-\bar{x})(x_i-\bar{x})^* \sum_i (y_i-\bar{y})(y_i-\bar{y})^*}} \qquad (1)$$

Subsequently, the Fisher Z-transform was applied to the coherence values. This serves not only to normalize the distributions of values, but also to reduce the difference in confidence intervals between greater and smaller values. In order to obtain brain connectivity patterns related to burnout and depression symptomatology, Pearson's correlations between Fisher-Z transformed coherences and inventory scores were calculated and False Discovery Rate (FDR; $p<0.05$) corrected (Benjamini, Krieger & Yekutieli, 2006).

2.5. Statistical analyses

Hierarchical regression analyses were conducted to test whether IAF and alpha power predict burnout and depression (dependent variables). In addition, the role of gender was examined by testing main and interaction effects. In order to avoid multicollinearity, the predictor variables were centered. To further secure unbiased regression models the three locations (anterior, central, posterior) related to IAF and power measures were entered in separate regression models. Interactions effects were based on computed cross-products of centered IAF / alpha power values and gender which were entered in the second step of the regression analyses (Nieuwenhuis, Forstmann &Wagenmakers, 2011). This approach yielded 6 interaction models for each of the outcomes. To illustrate the interaction effects between EEG indicators and gender, all interactions were plotted using raw data scatterplots with separate regression lines for male and female students separately. Significant interaction effects were followed-up by a simple slope analysis.

3. Results

3.1. Descriptive statistics

As seen in Table 1, more pronounced gender differences were observed only for burnout questionnaire scores. Male participants had a significantly higher score than females ($t(115) = 3.02$, $p = 0.003$). No other significant differences related to gender were observed (Depression: $t(115) = 1.25$, $p = 0.23$; IAF–ant: $t(115) = 1.79$, $p = 0.08$; IAF-cent: $t(115) = 1.74$, $p = 0.09$; IAF-post: $t(115) = 0.09$, $p = 0.93$; log power-ant: $t(115) = 0.72$, $p = 0.47$; log power-cent: $t(115) = 0.88$, $p = 0.38$; log power-post: $t(115) = 0.34$, $p = 0.73$)

IAF significantly correlated only with depression scores. For male students the correlations were positive, whereas for female students they were negative. In contrast, alpha power positively correlated with burnout only in the male sample. The correlations for female students were negative but not statistically significant. Although some of the correlations failed to reach significance, for the male sample a trend of positive correlations between the IAF and power on the one hand, and burnout and depression scores on the other, were observed. In female students the pattern of correlations was reverse. The intercorrelations between burnout and depression are moderate in size for both male and female participants. The correlation between power and IAF at different locations was rather small and mostly not significant, which support the notion that IAF and power provide different information about neural processes.

- Insert Table 1 about here -

3.2. Regression analyses – Burnout

For burnout, the regression analyses showed that gender was a significant predictor (Table 3). Significant positive associations between IAF and burnout were observed in the posterior location. In contrast, power positively correlated with burnout in all three locations. It was further shown that three out of six interaction effects between EEG correlates (IAF, power) and gender were significant (left side Figure 1 & 2). Significant interaction effects were followed-up by a simple slope analysis showing that in male students, power was positively related to burnout (log power – ant: simple slope for male students, $B = 0.55$, $p = 0.009$; simple slope test female students, $B = –0.27$, $p = 0.13$; log power – cent: simple slope for male students, $B = 0.58$, $p = 0.008$; simple slope for female students, $B = – 0.27$, $p = 0.13$, log power – post: simple slope for male students, $B = 0.38$, $p = 0.02$; simple slope for female students, B = – 0.26, $p = 0.07$).

- Insert Figure 1 & Table 2 about here -

3.3. Regression analyses – Depression

The regression analyses for depression showed that gender was not a significant predictor. IAF positively predicted depression at all three locations, whereas power negatively predicted depression only at the posterior location. Four out of six interaction effects were significant (three for IAF and one for power; right side Figure 1 & 2). Simple slope tests revealed that in males IAF positively predicted depression, whereas in females a negative relation was observed in anterior and central locations (IAF – ant: simple slope test for male students, $B = 0.13$, $p = 0.02$; simple slope test for female students, $B = – 0.11$, $p = 0.001$; IAF – cent: simple slope test for male students, $B = 0.16$, $p = 0.02$; simple slope test for female students, $B = – 0.14$, $p = 0.003$; IAF – post: simple slope test for male students, $B = 0.18$, $p = 0.01$; simple slope test for female students, $B = – 0.11$, $p = 0.06$; log power – post: simple slope for male students, $B = 0.19$, $p = 0.11$; simple slope for female students, $B = – 0.18$, $p = 0.08$).

- Insert Figure 2 & Table 3 about here -

3.4. Coherence analyses

The common characteristics of the obtained connectivity patterns were: First, significant correlations were only observed for depression, and second, males and females with high depression scores exhibited increased coherences between different brain areas. Connectivity patterns of males with high depression scores were characterized by increased long distance coherences between hubs located in the left parieto-occipital cortex (electrode positions T5 and O1) and different left and right areas in the frontal and orbito-frontal cortex. In contrast, females scoring high on the depression scale showed increased short distance coherences mainly between a hub in the left parietal cortex (electrode position P3) and central brain areas (Figure 3).

- Insert Figure 3 about here –

4. Discussion

The objective of the study was to investigate whether IAF, power and coherence in the IAF frequency range (IAF ±1 Hz) discriminate between the syndromes of burnout and depression and may, thus, serve as potential biomarkers. Since gender differences have been reported for depression (Kessler, 2005), burnout (Maslach et al., 2001), and neuro-electric measures (Jaušovec & Jaušovec, 2010), gender was included in the analysis as a moderating variable. In contrast to our assumptions, some distinctive features of burnout and depression were found. Salient gender differences were found in EEG correlates of burnout and depression.

4.1. EEG alpha band correlates of burnout and depression

The regression analyses revealed that power in the alpha band was moderately related to burnout inventory scores, whereas IAF was related to depression scale scores. In the light of significant interaction effects, the direction of main effects cannot be interpreted, hence the question why burnout is linked to power, whereas depression is linked to IAF. Based on our findings, depression seems to be more related to the characteristics of white matter structure than to the number of oscillating neurons – gray matter characteristics which may be rather characteristic of burnout. A plausible explanation could be that burnout is frequently related to environmental stressors, whereas depression is assumed to be primarily context-free (Durning et. al., 2013; Hakanen & Schaufeli, 2012). Furthermore, it was reported that stressors either provoked in the laboratory (e.g., errors), or those encountered in the environment (e.g., sustained domestic conflict) had a major influence on EEG power (McFarlane, et al., 2005; Compton, Hofheimer, Kazinka, Levinson & Zheutlin, 2013). Hence, it can be assumed that stressors generating burnout increase the number of firing neurons, which could explain the relationship between burnout symptoms and alpha power observed in our study. Research further suggests that burnout is one of the earlier stages of depression with the later developing over a longer time period (Ahola et al., 2014; Ahola & Hakanen, 2013). It has also been suggested that prolonged maladaptive coping with stressors could result in abnormal functional connectivity of brain networks, which are not static but change as a result of development (Harmelech, & Malach, 2013). This could explain the more pronounced correlations between depression scores and IAF in our study.

Moreover, the results of the coherence analysis suggested that brain connectivity relates to depression but not burnout. Namely, significant correlations between Fisher Z-transformed coherences and inventory scores were only observed for depressive symptomatology. On a general level, our results support the assumption that depression is associated with increased rather than decreased functional connectivity. Our findings correspond with recent discoveries suggesting that abnormal anatomical connectivity and functioning of hub regions relates to depression (Fingelkurts et al., 2007; Greicus et al., 2007). Recent EEG studies by Fingelkurts et al. (2007) and Leuchter, Cook, Hunter & Horvath (2012) as well as an fMRI study by Greicus et al. (2007) revealed increased, rather than decreased functional connectivity among mixed-gender samples with major depression. Overall, our results strengthen the interpretation that in depression, adaptive compensatory mechanisms may strengthen connectivity (Fingelkurts et al., 2007), whereas they oppose the assumption that inter-hemispheric synaptic connections might be reduced (Knott at al., 2001).

Altogether, the result may also point to a specific developmental relationship between burnout and depression where burnout is one of the earlier stages of depression with the later developing over a longer time period (Ahola et al., 2014; Ahola & Hakanen, 2013). However, the results of the present study are just a “snapshot” – an isolated observation of the relatedness among IAF, power, depression and burnout in a sample of young adults, which might have biased the results. Thus, future research should focus on the developmental aspects of these complex relationships. Nevertheless, we can conclude that our findings lend some support for considering burnout as a separate clinical syndrome. The finding that IAF and alpha power capture different neural processes (Jann et al., 2010; 2012) may further corroborate our conclusions.

4.2. The moderating role of gender

Another main finding revealed by the regression analysis was the pronounced influence of gender. Seven out of twelve interactions between neural indicators (i.e., IAF, alpha power) and gender were significant. The trend observed was that in males with high scores on depression, brain activation patterns were faster, whereas with burnout, brain activation patterns were accompanied by lower cortical activity. In females, only a negative relation between IAF and depression was found in specific locations. In terms of alpha power, our hypothesis was only confirmed for burnout in male students. In terms of IAF, support for our assumptions was found only for depression in female students, whereas for male students the results were in opposite direction.

Our results on alpha power are in line with studies examining a mixed gender sample burnout-like states (e.g., fatigue; Craig et al., 2012). They, however, do not correspond to the findings of van Luijtelaar et al. (2010), who did not find any differences between burnout and control group in alpha power. A possible explanation for this divide can be that the authors did not perform a finer-grained analysis based on gender. A recent study examining differences between females under chronic stress (i.e., a condition which may resemble burnout) and control subjects did not find any differences in alpha power (Peng et al., 2013). Tentatively, our results together with previous findings point to possible gender-related differences in burnout-like conditions. We also claim that gender differences can, in fact, account for inconsistent findings in previous studies with respect to alpha power. Future research could benefit from examining resting EEG differences between male and females in a variety of stress-related conditions.

In general, IAF of patients with neurological and psychiatric disorders are often found to be lower than that of healthy controls (Grandy et al., 2013). Such brain activation patterns have only been observed for the female sample in our study. To our knowledge, just one study reported a positive correlation between IAF and posttraumatic stress disorder (PTSD) in male war veterans (Wahbeh & Oken, 2013). It is unclear whether the positive correlation between IAF and PTSD scale scores reflects the relation between IAF and the stress disorder, or is moderated by the variable gender, and would be opposite for a female sample of war veterans. In another study by Knott et al. (2001), although no significant group differences in IAF were found, male depressed individuals exhibited faster total frequency than controls. Because of these findings it is crucial that future research on affective disorders focuses on gender differences.

Differences between males and females were also observed in connectivity patterns. These differences were present only for the depression syndrome. Females with high scores on the depression scale predominantly displayed increased short distance connectivity between left posterior and central locations, whereas males with high scores on the depression scale showed long distance connectivity between left posterior locations and left/right frontal and orbito-frontal locations. Our results are not in line with previous studies from which gender-specific effects can be derived. For instance, Knott et al. (2001) found reduced alpha coherence rather than increased coherence among a male sample, whereas Hinrikus et al. (2009) did not find any specific differences in females with major depressive disorder and health controls in terms of gender. In general, the difference in distances between synchronous oscillating brain areas observed in depressed males and females might tentatively explain why depression in males was accompanied by faster brain activity. Long distance connectivity might depend to a greater degree on the fidelity of white matter structure than short distance connectivity observed in females. Another feature that should be taken into account is the pattern of brain-network organization. A growing body of research has identified several brain-networks including a salience network relevant for attending survival-relevant features in the environment; a central executive network involved in adaptive cognitive control; and a default mode network observed in states of relaxation (Power et al., 2011). The observed connectivity patterns of males somewhat resembled the fronto-parietal network involved in initiating and modulating cognitive control processes. Thus, it could be speculated that males scoring high on the depression scale lack adequate cognitive control, generating rumination – the process of thinking perseveratively about one's feelings and problems (Nolen-Hoeksema, Wisco & Lyubomirsky, 2008). The connectivity patterns of females were to some extent similar to the salience network important for monitoring the salience of external inputs and internal brain events (Van den Heuvel & Sporns, 2013). It may be that depressed females have an impaired perception of the most pertinent subset of available sensory data linking them with inadequate internal events – biased information processing increasing the amount of perceived negative events. It was even suggested that negative life events heighten girls' rates of depression beginning in adolescence and account for the gender difference in depression (Hyde, et al., 2008). This vague explanation should be investigated in future research. In sum, our gender-specific findings in terms of coherence opened up a wide space for discussion. As it is still not clear whether to expect decreased or increased functional connectivity in depressed subjects (e.g., Olbrich & Arns, 2013) and what differences to expect between men and women, future studies should strive to validate our results.

4.3. Limitations and implications

The main limitation of the study was the sample size as well as the unbalanced structure of the sample with respect to gender. As noted previously, this study is cross-sectional which did not allow for more firm conclusions on the developmental aspects of the burnout – depression relationship. From a methodological perspective, a larger sample would also permit analysis of all possible combinations between the variables burnout, depression and gender and their relation to neural indicators (i.e., three-way interactions). This study is further based on relatively healthy students (who do not score excessively high on burnout and depression) which may limit the generalizability across employees from different occupations and clinical samples. There is also the possibility of overlapping burnout and depression in terms of actual symptomatology as well as measurement which could possibly confound our findings. Future research on burnout and depression should overcome these limitations. In the first step, however, agreement on diagnostic criteria should be reached and clinically valid cut-off scores of burnout measures should be established across different countries (e.g., Kleijweg, Verbraak & Van Dijk, 2013). Without these necessary steps, research on these salient issues cannot progress and is limited to correlational studies. Future studies, however, could benefit from contemporary approaches to identifying biomarkers of mental disorders such as the Support Vector Machine enabling a precise identification of subjects with different disorders based on their distinct EEG patterns (e.g., Koelstra et al., 2012; Orrù, Pettersson-Yeo, Marquand, Sartori & Mechelli, 2012).

In conclusion, our findings lend tentative support to the notion that burnout represents a separate diagnostic entity rather than a form of depression. Another important finding is that the relation between neural indicators, on the one hand, and depression and burnout on the other, are moderated by gender. Future research on the neurobiological underpinnings of burnout and depression should consider gender as a moderating variable.

Conflicts of interest: The authors declare no conflict of interest.

Acknowledgements: The present research was supported by ARRS – The Agency of Research Republic of Slovenia.

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Figure Captions

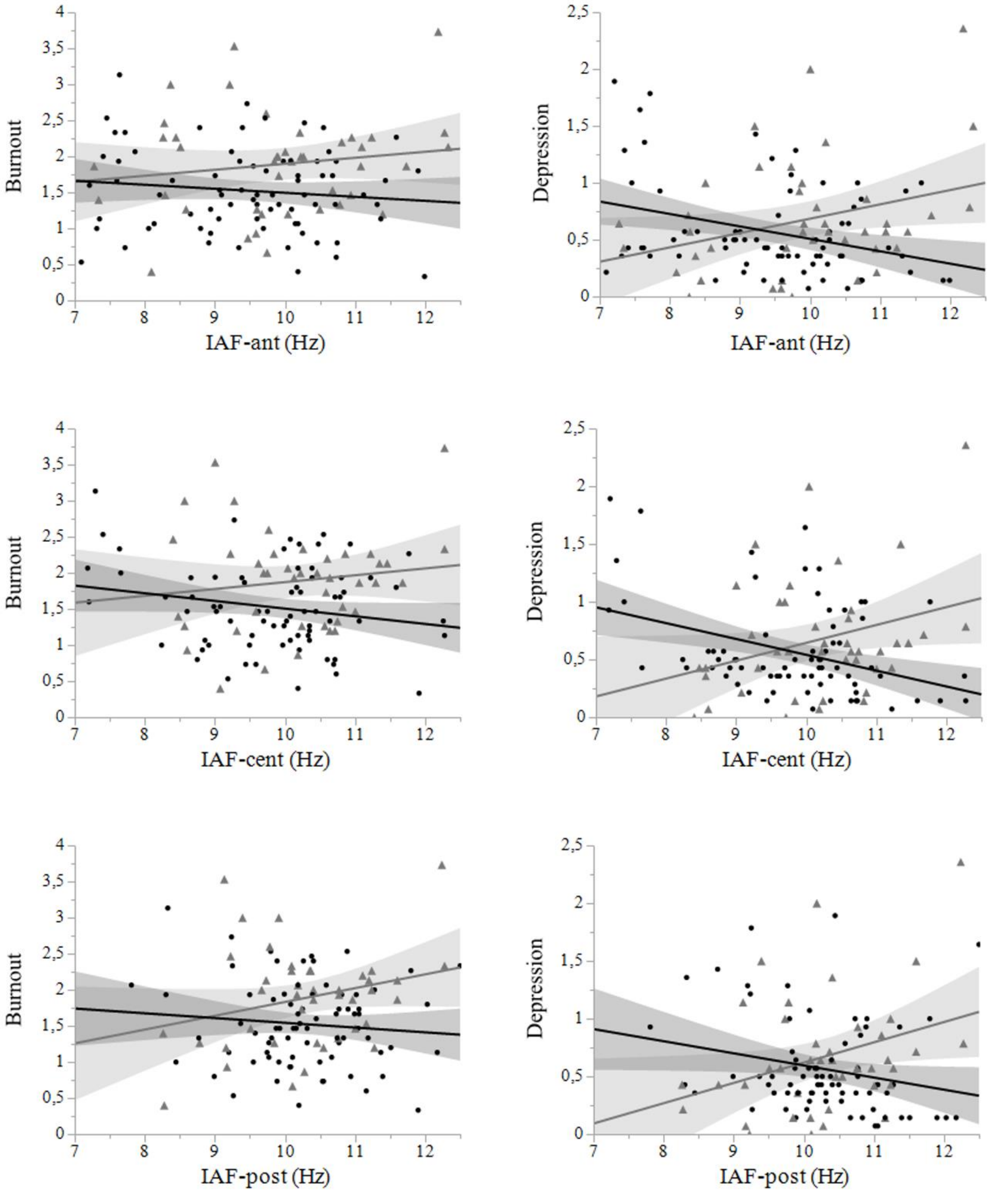

Figure 1. Interactive effects of IAF (anterior, central, posterior) and gender on burnout and depression. Raw values representing the relation between IAF over three scalp location and burnout (left side)/depression (right side) for women are depicted with black circles and for men with gray triangles. Regression line with 95% confidence interval for women is shown in black color and for men in gray color.

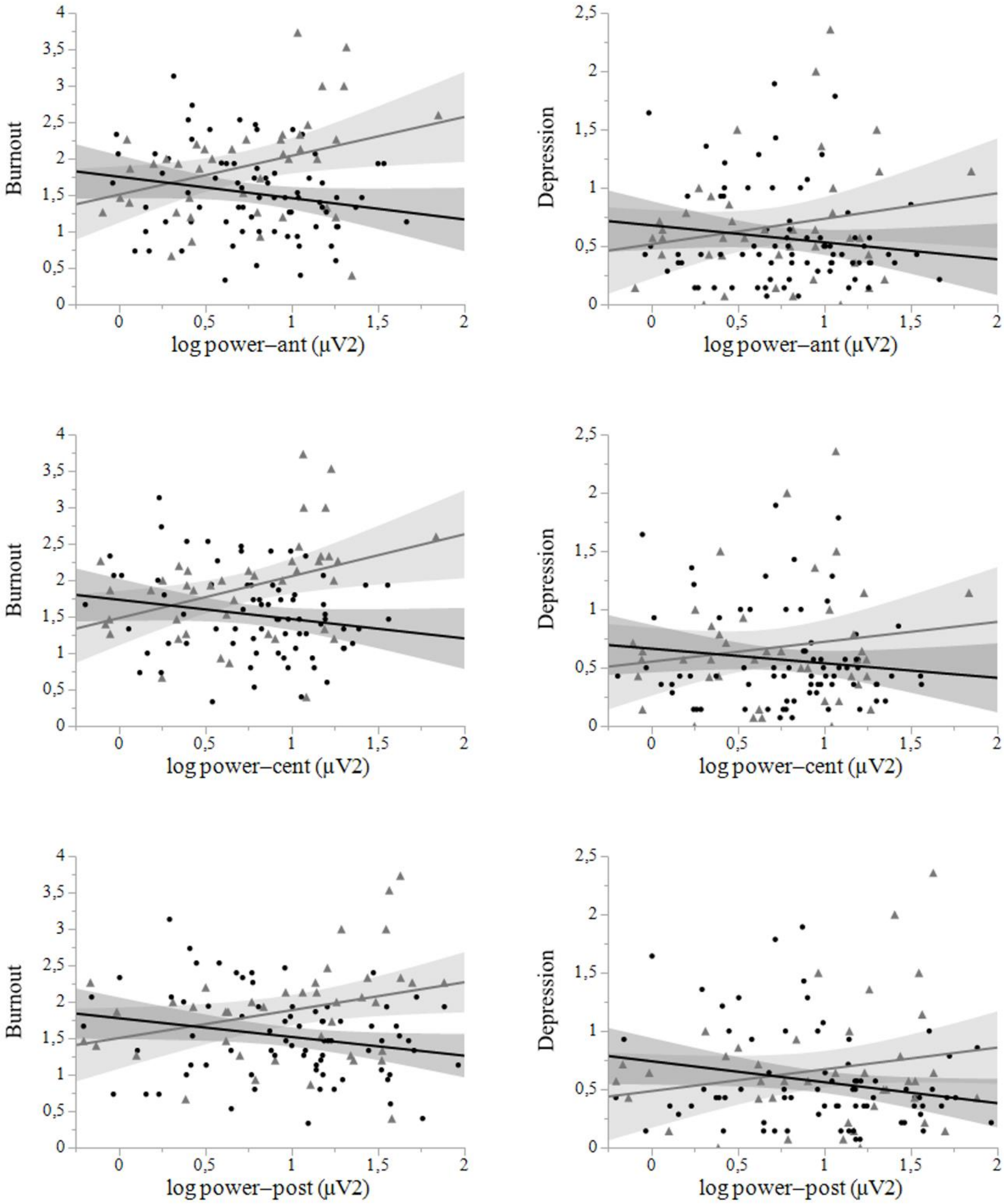

Figure 2. Interactive effects of log transformed alpha power (anterior, central, posterior) and gender on burnout and depression. Raw values representing the relation between alpha power over three scalp location and burnout (left side)/depression (right side) for women are depicted with black circles and for men with gray triangles. Regression line with 95% confidence interval for women is shown in black color and for men in gray color.

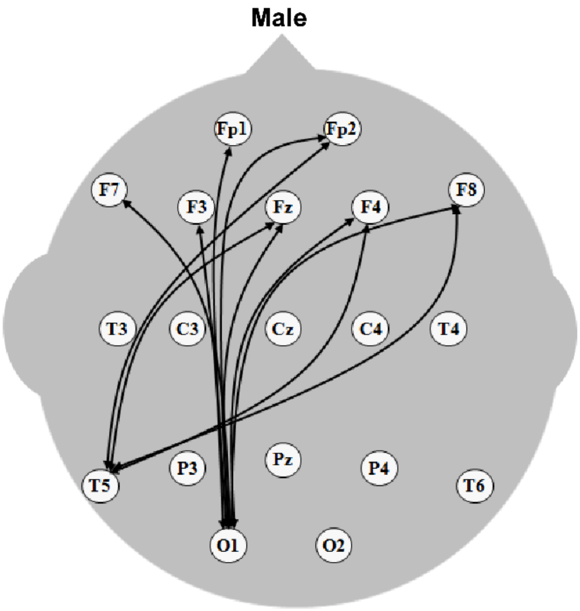

Figure 3. Connectivity maps of significant correlations between Fisher Z-transformed coherences and depression scores in male and female subjects.

Table 1. *Means (M), standard deviations (SD), and zero-order correlations between IAF and log transformed power measures in 3 scalp locations for male and female students*

	1	2	3	4	5	6	7	8	*M*	*SD*
1. Depression	-	0.48 (0.000)	-0.33 (0.004)	-0.38 (0.001)	-0.23 (0.047)	-0.13 (0.230)	-0.14 (0.284)	-0.23 (0.053)	0.57	0.41
2. Burnout	0.60 (0.000)	-	-0.12 (0.318)	-0.20 (0.080)	-0.10 (0.388)	-0.20 (0.089)	-0.19 (0.110)	-0.22 (0.053)	1.52	0.59
3. IAF–ant	0.31 (0.043)	0.15 (0.339)	-	0.77 (0.000)	0.50 (0.000)	0.13 (0.265)	0.16 (0.180)	0.36 (0.002)	9.48	1.23
4. IAF–cent	0.30 (0.051)	0.14 (0.393)	0.78 (0.000)	-	0.62 (0.000)	-0.01 (0.966)	0.04 (0.714)	0.24 (0.037)	9.83	1.12
5. IAF–post	0.32 (0.036)	0.26 (0.100)	0.81 (0.000)	0.88 (0.000)	-	-0.26 (0.025)	-0.24 (0.041)	-0.01 (0.941)	10.29	0.90
6. log power–ant	0.20 (0.210)	0.35 (0.023)	0.051 (0.750)	-0.13 (0.41)	-0.17 (0.275)	-	0.96 (0.000)	0.85 (0.000)	0.78	0.39
7. log power–cent	0.16 (0.321)	0.39 (0.012)	0.15 (0.350)	-0.03 (0.873)	-0.07 (0.652)	0.96 (0.000)	-	0.87 (0.000)	0.79	0.41
8. log power–post	0.22 (0.171)	0.32 (0.038)	0.29 (0.066)	0.11 (0.499)	0.040 (0.799)	0.902 (0.000)	0.95 (0.000)	-	0.98	0.51
M	0.67	1.90	9.91	10.19	10.30	0.72	0.71	1.01		
SD	0.51	0.70	1.27	1.00	0.94	0.46	0.47	0.59		

Note. Correlations for male students (n=42) are presented below the diagonal, and correlations for female students (n = 75) are presented above the diagonal. Means and standard deviations for male students are presented in the vertical columns, and means and standard deviations for female students in the horizontal rows. Numbers in parentheses are *p*-values. ant = anterior; cent = central; and post = posterior.

Table 3. *Regressions results for IAF and log transformed power measures in 3 scalp locations predicting burnout*

Variables	Burnout							
	Step 1				Step 2			
	B	*SE*	β	*p*	*B*	*SE*	β	*p*
IAF–ant	-0.00	0.05	-0.01	0.933	0.08	0.08	0.16	0.283
Gender	-0.37	0.12	-0.27	0.004	-0.35	0.12	-0.26	0.005
IAF–ant X gender					-0.14	0.10	-0.21	0.156
R^2 and ΔR^2			0.07	0.013			0.02	0.156
F for R^2			4.53	0.013			3.73	0.013
IAF–cent	-0.05	0.05	-0.08	0.410	0.10	0.10	0.16	0.334
Gender	-0.38	0.12	-0.28	0.002	-0.36	0.12	-0.27	0.004
IAF – cent X gender					-0.20	0.12	-0.28	0.089
R^2 and ΔR^2			0.08	0.009			0.02	0.089
F for R^2			4.90	0.009			4.30	0.007
IAF–post	0.03	0.06	0.04	0.627	0.19	0.10	0.27	0.067
Gender	-0.36	0.12	-0.27	0.003	-0.36	0.12	-0.27	0.003
IAF–post X gender					-0.26	0.13	-0.28	0.052
R^2 and ΔR^2			0.08	0.011			0.03	0.052
F for R^2			4.65	0.011			4.46	0.005

Gender codes: Male = 0; Female = 1

Table 3. *Continued*

Variables	Burnout							
	Step 1				Step 2			
	B	*SE*	β	*p*	*B*	*SE*	β	*p*
log power–ant	0.06	0.14	0.04	0.661	0.53	0.21	0.34	0.011
Gender	-0.37	0.12	-0.27	0.003	-0.38	0.12	-0.28	0.002
log power–ant X gender					-0.82	0.27	-0.40	0.003
R^2 and ΔR^2			0.08	0.012			0.07	0.003
F for R^2			4.63	0.0.12			6.34	0.001
log power–cent	0.09	0.14	0.06	0.525	0.68	0.20	0.38	0.005
Gender	-0.37	0.12	-0.28	0.003	-0.39	0.12	-0.29	0.001
log power–cent X gender					-0.84	0.27	-0.42	0.002
R^2 and ΔR^2			0.08	0.010			0.08	0.002
F for R^2			4.75	0.010			6.75	0.000
log power–post	0.01	0.11	0.01	0.902	0.38	0.16	0.32	0.020
Gender	-0.37	0.12	-0.27	0.003	-0.36	0.12	-0.27	0.003
log power–post X gender					-0.64	0.21	-0.40	0.003
R^2 and ΔR^2			0.07	0.013			0.07	0.003
F for R^2			4.53	0.013			6.29	0.001

Gender codes: Male = 0; Female = 1

Table 4. *Regressions results for IAF and log transformed power measures in 3 scalp locations predicting depression*

Variables	Depression							
	Step 1				Step 2			
	B	*SE*	β	*p*	*B*	*SE*	β	*p*
IAF–ant	-0.02	0.03	-0.06	0.520	0.13	0.05	0.35	0.018
Gender	-0.12	0.09	-0.13	0.183	-0.09	0.08	-0.10	0.285
IAF–ant X gender					-0.24	0.07	-0.52	0.001
R^2 and ΔR^2			0.02	0.375			0.10	0.001
F for R^2			0.99	0.375			4.92	0.003
IAF–cent	-0.05	0.04	-0.12	0.216	0.16	0.07	0.38	0.022
Gender	-0.13	0.09	-0.14	0.153	-0.09	0.08	-0.10	0.282
IAF–cent X gender					-0.29	0.08	-0.58	0.000
R^2 and ΔR^2			0.03	0.214			0.10	0.000
F for R^2			1.56	0.214			5.63	0.001
IAF– post	0.00	0.05	0.00	0.987	0.18	0.07	0.36	0.016
Gender	-0.11	0.09	-0.12	0.215	-0.11	0.08	-0.12	0.204
IAF–post X gender					-0.28	0.09	-0.45	0.003
R^2 and ΔR^2			0.01	0.462			0.08	0.003
F for R^2			0.78	0.462			3.70	0.014

Gender codes: Male = 0; Female = 1

Table 4. *Continued*

Variables	Depression							
	Step 1				Step 2			
	B	*SE*	β	*p*	*B*	*SE*	β	*p*
log power–ant	0.01	0.10	0.01	0.914	0.22	0.15	0.20	0.151
Gender	-0.11	0.09	-0.12	0.213	-0.11	0.09	-0.12	0.191
log power–ant X gender					-0.36	0.20	-0.26	0.071
R^2 and ΔR^2			0.01	0.459			0.03	0.071
F for R^2			0.78	0.459			1.46	0.185
log power–cent	-0.00	0.10	-0.00	0.990	0.17	0.15	0.16	0.255
Gender	-0.11	0.09	-0.12	0.217	-0.11	0.09	-0.12	0.195
log power–cent X gender					-0.30	0.20	-0.22	0.134
R^2 and ΔR^2			0.01	0.462			0.02	0.134
F for R^2			0.78	0.462			1.29	0.283
log power–post	-0.03	0.08	-0.03	0.748	0.19	0.12	0.22	0.114
Gender	-0.11	0.09	-0.12	0.211	-0.11	0.09	-0.11	0.214
log power–post X gender					-0.37	0.15	-0.33	0.019
R^2 and ΔR^2			0.01	0.438			0.05	0.019
F for R^2			0.83	0.438			2.46	0.066

Gender codes: Male = 0; Female = 1