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Job-related burnout is associated with brain neurotransmitter levels in Chinese medical workers: a cross-sectional study

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Abstract

Objective: The aim of the present study was to investigate the relationship between job burnout and neurotransmitter levels in medical staff.

Methods: A total of 80 medical staff were enrolled in the study and assessed for occupational burnout using the Maslach Burnout Inventory – General Survey (MBI-GS). The levels of neurotransmitters in the cerebral cortex were analysed using an SP03 encephalofluctuograph.

Results: The levels of the neurotransmitters γ-aminobutyric acid, 5-hydroxytryptamine (5-HT), norepinephrine (NE), glutamate, acetylcholine (Achl) and dopamine (DA) were significantly lower in men than in women. Medical staff with lower levels of exhaustion had significantly higher neurotransmitter levels than staff with moderate levels of exhaustion. However, there was no significant interaction between sex and exhaustion on neurotransmitter levels. Canonical correlation showed that exhaustion was positively associated with 5-HT and DA, but negatively associated with NE and Achl, regardless of age and sex.

Conclusion: Neurotransmitter levels in the cerebral cortex were associated with job-related burnout in medical staff. The findings suggest that long-term job-related burnout may lead to behavioural and psychiatric disorders.

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Keywords

Burnout, neurotransmitters, medical staff, canonical correlation analysis, 5-hydroxytryptamine, dopamine

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Introduction

Job-related burnout is a cognitive and emotional response to long-term interpersonal stress at work.[1] It can deplete critical neurotransmitters and has similar causes to other types of exhaustion. The stress state is an expression of the imbalance between internal/external demands and brain–body reactions. Research on the molecular mechanisms underlying stress suggests that stress is associated with dysregulation of monoamine neurotransmitters in the brain. For example, studies indicate that rats with chronic stress show significantly decreased dopamine (DA) and γ-aminobutyric acid (GABA) and increased 5-hydroxytryptamine (5-HT) and glutamate (Glu).[2] Although stress increases the activity of serotonergic neurons, reduced serotonin is associated with chronic psychological stress, mood disorders and depressive symptoms.[3] Prolonged stress can lead to an imbalance between excitatory (norepinephrine [NE], DA, Glu) and inhibitory neurotransmitters (GABA). It has been extensively demonstrated that 5-HT, DA, GABA and Glu are involved in learning, memory, emotion and motivation, as well as motor functions.[4]

The hypothalamus–pituitary–adrenal (HPA) axis plays an important role in the stress-induced response. Internal and external stress stimuli can lead to hyperthyroidism and an increase in sympathetic adrenal medulla activity. Monoamine neurotransmitters (such as DA, acetylcholine [Achl], Glu and GABA), as neuron mediators, are also involved in the stress response.[5] Blood and cerebrospinal fluid (CSF) specimens are commonly collected to examine the levels of neurotransmitters in the brain. However, because of the blood–brain barrier, neurotransmitter levels in the blood or CSF may not accurately reflect levels in the brain. In addition, both blood and CSF collection are invasive and involve some discomfort. A recently established, non-invasive approach to brain function detection involves the use of an encephalofluctuograph (EFG) to indirectly measure the levels of brain neurotransmitters.[6]

The EFG was developed to detect brain functions by recording slow brain waves. It not only extracts ultra-slow brain waves (frequency range 1–255 MHz), but also measures the signal magnitude. Many experiments have shown a one-to-one correspondence between ultra-slow brain waves and the activities of neurotransmitters,[7–9] with specific frequencies of ultra-slow waves corresponding to the neurotransmitters GABA, 5-HT, NE, Glu, Achl and DA.[6,10] The EFG measures neurotransmitter levels using electrodes placed on different skull areas; these reflect the activities of the corresponding neurotransmitters GABA, 5-HT, NE, Glu, Achl, DA and other neurotransmitters.

The EFG has been widely used to study neurotransmitter changes in different nervous system diseases, such as neurodegenerative diseases, cerebrovascular diseases and mood disorders.[11–13] Several studies have compared changes in Glu in patients with cerebral infarction using both high performance liquid chromatography on CSF and the EFG. Concentrations of Glu increased significantly after 24 h, reached a peak after 3 days, decreased after 5 days and then were close to normal after 7 days.[14,15] The two methods showed highly similar patterns and magnitudes in Glu changes over the progression of the disease. The results of EFG and plasma 5-HT measurement were consistent in evaluating therapeutic effects on post-stroke depression.[16] The results suggest that EFG measurement of neurotransmitters is reliable.[17,18] In addition, the EFG has been widely used in psychological research.[12,19,20] However, few studies have reported an association between job-related burnout and brain neurotransmitters using the EFG. Thus, the purpose of this study was to investigate the association between job-related burnout and brain neurotransmitter levels using the EFG (Kangli High-Tech Co., Ltd., Shenzhen, China), a non-invasive measure of critical brain chemicals. The aim was to obtain a better understanding of the molecular mechanisms underlying job-related burnout to inform the development of more effective strategies to prevent/treat this type of burnout. To achieve this goal, we used the Maslach Burnout Inventory-General Survey (MBI-GS) to determine the burnout status of occupational groups, and used the EFG to detect the levels of the brain neurotransmitters GABA, 5-HT, NE, Glu, Achl and DA in Chinese medical workers.

Material and methods

Participants

This study included 80 medical workers (41 doctors and 39 nurses) from The Third Hospital of Bijie city, Guizhou province, China, and was conducted from October 2013 to November 2013. All subjects provided written informed consent. The study was approved by the ethics review committee of Xinxiang Medical University.

Maslach Burnout Inventory – General Survey

Burnout syndrome was assessed using the MBI-GS, which was previously translated into Chinese and has shown good reliability and validity in a Chinese sample.[21] The MBI-GS consists of 15 items rated on a Likert scale from 0 to 6 points. The MBI-GS has three subscales: exhaustion (EX, five items), cynicism (CY, four items) and professional efficacy (PE, six items). Higher MBI-GS scores indicate higher levels of burnout. As PE is reverse scored, a person with a higher PE score has a lower professional efficacy. Cronbach's alpha for the scale in this study was 0.812.

Intracerebral neurotransmitter measurement

Before the SP03 EFG was performed, each participant was required to wash his/her head. The EFG appointment time was scheduled between 9–11 am or 3–5 pm. No fasting was required and participants were allowed to follow their usual diet. The participant was required to remain calm and sit quietly with eyes closed during the assessment. The signals were collected using the SP03 EFG for 10 min according to the international standard 12-lead (F3, F4, F7, F8, C3, C4, T5, T6, P3, P4, O1, O2) placement of the electrodes, and were automatically analysed for GABA, 5-HT, NE, Glu, Achl and DA activity.[17,18] During the recording process, electrophysiological artefacts were automatically removed.

Data analysis

Data were input using EpiData 3.1 (EpiData Association, Odense, Denmark) and statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Numerical variables were normally distributed after log transformation, and were thus presented as mean ± standard deviation in log10. A two-tailed test with $P < 0.05$ was considered statistically significant. The t-test was used to test differences in burnout levels of medical staff of different occupations and sex. Two-way analysis of variance was used to test neurotransmitter levels in the cerebral cortex with sex and exhaustion level. Canonical correlation analysis (CCA), a multivariate analysis method that measures the correlations between two sets of variables, was performed to analyse the association between burnout and neurotransmitter levels.[22]

Table 1. Participant characteristics

	Doctors, n (%)		Nurses, n (%)	
Sex				
Men	18	(22.5%)	3	(3.8%)
Women	23	(28.7%)	36	(45.0%)
Age (y)				
<26	7	(8.8%)	15	(18.8%)
26–30	18	(22.4%)	9	(11.2%)
>31	16	(20.0%)	15	(18.8%)

Results

Patient demographics

Table 1 shows the characteristics of the survey subjects. The participants were aged 30.82 ± 8.43 years (range 20–59 years).

Associations of neurotransmitter levels in the cerebral cortex with job position, sex and exhaustion

Neurotransmitter levels in the cerebral cortex, determined using the SP03 EFG, were compared between different demographic variables, and the results are shown in Table 2. There were no significant differences in brain neurotransmitter levels between doctors and nurses. However, sex had significant associations with the levels of all the neurotransmitters, with men showing lower neurotransmitter levels than women ($P < 0.01$).

The possible range of exhaustion scores was 0–6. To examine the associations between neurotransmitter levels and exhaustion, we followed a previous

Table 2. Associations between demographic variables and neurotransmitter levels ($\log_{10}\bar{x} \pm$ standard deviation)

		Neurotransmitter					
Variable	N	GABA	5-HT	Norepinephrine	Glutamate	Acetylcholine	Dopamine
Job							
Doctor	41	1.19±0.70	2.19±0.55	1.91±0.55	1.30±0.70	2.10±0.56	1.71±0.55
Nurse	39	1.41±0.71	2.25±0.59	1.97±0.56	1.47±0.70	2.14±0.60	1.81±0.60
		−1.356	−0.451	−0.499	−1.141	−0.364	−0.732
Sex							
Men	21	0.86±0.69	1.92±0.55	1.66±0.56	1.02±0.67	1.82±0.56	1.42±0.53
Women	59	1.45±0.65	2.33±0.54	2.04±0.52	1.51±0.67	2.22±0.55	1.88±0.55
t		−3.558**	−3.003**	−2.855**	−2.926**	−2.843**	−3.378**
Exhaustion levels							
Low	36	1.49±0.76	2.43±0.64	2.15±0.60	1.61±0.75	2.33±0.65	1.96±0.65
Moderate	44	1.14±0.62	2.05±0.44	1.77±0.45	1.19±0.59	1.95±0.45	1.60±0.45
t		2.298*	3.065**	3.308**	2.790**	3.123**	2.789**

Note: *$P < 0.05$, **$P < 0.01$; GABA: γ-aminobutyric acid; 5-HT: 5-hydroxytryptamine.

method[23] by first categorising participants into three subgroups according to exhaustion score quartiles as the cutoff points; participants scoring less than the lower quartile (<7 points) were defined as showing low exhaustion, those scoring between the lower and upper quartile (7–22 points) had moderate exhaustion and those scoring more than the upper quartile (>22 points) had high exhaustion. Of 80 participants, 36 were categorised as having low exhaustion and 44 were categorised as having moderate exhaustion. No participants were categorised with high exhaustion. The results showed significant differences in all neurotransmitter levels between the low exhaustion and moderate exhaustion groups ($P < 0.05$ or $P < 0.05$); medical staff with low exhaustion had significantly higher neurotransmitter levels than those with moderate exhaustion (Table 2).

Relationship between job-related burnout and neurotransmitter levels in the cerebral cortex

Unlike exhaustion and cynicism, the two dimensions that relate to stress and psychiatric factors in burnout, professional efficacy is associated with job resources and high performance beyond good health. Thus, in the CCA, we omitted professional efficacy to analyse the correlations between mental health (exhaustion and cynicism) and neurotransmitter levels. The results are shown in Tables 3 and 4. In the model including exhaustion and cynicism only, the first canonical correlation coefficient was 0.47 with an explained variance of the correlation of 85.8% (Table 3) ($P = 0.035$). Exhaustion, a predominant variable, was positively associated with 5-HT and DA and negatively associated with NE and Achl. However, the direction of the correlations between cynicism and these neurotransmitter levels were opposite to those between exhaustion and neurotransmitter levels. When we included age and sex in the model, the first canonical correlation coefficient was 0.52 with an explained variance of the correlation of 49.8% ($P = 0.002$). The correlations (and the direction of the correlations) between exhaustion

Table 4. Standardized canonical coefficients for dependent variables and covariates

Independent	Canonical variables: Without age and sex	Canonical variables: With age and sex
Exhaustion (X1)	1.20	0.85
Cynicism (X2)	−0.50	−0.38
Age (X3)		−0.51
Sex (X4)		−0.17
γ-aminobutyric acid (Y1)	−0.26	−0.42
5-hydroxytryptamine (Y2)	1.17	0.76
Norepinephrine (Y3)	−2.33	−2.40
Glutamate (Y4)	0.14	0.37
Acetylcholine (Y5)	−1.04	−1.48
Dopamine (Y6)	1.42	2.38

Table 3. Canonical correlation analysis and dimension reduction analysis

Independent	Proportion (%)	Canonical correlation	Wilks	F	df	P-value
With age and sex						
1	49.8	0.52	0.518	2.12	24	0.002
2	42.2	0.49	0.714	1.70	15	0.053
Without age and sex						
1	85.8	0.47	0.742	1.93	12	0.035
2	14.2	0.21	0.955	0.69	5	0.630

and levels of the neurotransmitters 5-HT, DA, NE and Achl were retained in the second model. In addition, 5-HT, DA and Glu decreased with age, while GABA, NE and Achl increased. Furthermore, age, cynicism and sex (1 man, 2 women) showed negative coefficients, whereas exhaustion showed a positive coefficient. The neurotransmitters 5-HT, DA and Glu showed positive coefficients, whereas GABA, NE and Achl showed negative coefficients.

Discussion

Central GABA is an inhibitory amino acid neurotransmitter and is mainly distributed in neural grey matter; its highest concentrations are found in black matter and the globus pallidus. The HPA axis regulates the neuroendocrine pathway involved in tropism by regulating the levels of cortisol, corticotropin and corticotropin-releasing hormones.[24] NE in the hypothalamus can inhibit the secretion of adrenocorticotropic hormone, thus affecting the HPA axis. 5-HT is an excitatory neurotransmitter released by adrenocorticotropic hormone and can excite the pituitary–adrenocortical system. 5-HT is a central monoamine neurotransmitter and is mainly distributed in the brainstem. It plays an important role in regulating feeding, sexual behaviour, cardiovascular function, the hypothalamus and the anterior pituitary function, and affects sleep and mental activity. DA is also a central monoamine neurotransmitter that occurs throughout the brain; the highest concentration of DA (about 80% of the DA in the brain) is found in the substantia nigra and the striatum. Brain DA plays an important role in influencing general behaviour and mental activity. Glu is the most predominant excitatory neurotransmitter in the brain. Glu and GABA together regulate the function of other neurotransmitters. Loss of Glu and GABA function quickly leads to dysfunction in other neurotransmitters. The present findings indicate that the levels of GABA, 5-HT, NE, Glu, Achl and DA were lower in men than in women. This finding is consistent with a previous animal model study that showed a significant association between sex and neurotransmitter levels in newborns, with women showing higher DA concentrations than men.[25] Taken together, these findings suggest that brain neurotransmitter levels are affected by sex and may reflect differences in hormone types and levels between men and women. However, the mechanisms underlying sex differences in neurotransmitter levels need to be examined further.

Our study found that exhaustion levels had significant effects on NE, Glu and Achl, demonstrating that neurotransmitter levels in the brain were higher in individuals with low exhaustion than in those with moderate exhaustion. Exhaustion was positively associated with 5-HT, Glu and DA but negatively associated with GABA, NE and Achl, regardless of age and sex. These findings are consistent with the results of experimental stress studies previously reported. 5-HT and DA significantly increase during the development of exercise-induced fatigue, and 5-HT plays a dominant role in the dynamic changes of fatigue.[26] Participants with higher levels of chronic stress show lower levels of NE.[27] One study found reduced Achl levels in the hippocampus of stressed mice.[28] Another study on mice showed that exercise-induced exhaustion produced decreased GABA and Glu in the subthalamic nucleus extracellular fluid, as expected.[29] However, although we found a negative association between exhaustion and GABA, there was a positive association between exhaustion and Glu. This discrepancy may be because the type and intensity of different risk factors are differentially associated with exhaustion.

In this study, we also found that exhaustion was positively associated with 5-HT and DA and negatively associated with NE and Achl. It has been shown that increased extracellular DA and 5-HT in the subthalamic nucleus might be an important factor that leads to the development of fatigue during exhausting exercise.[30] However, the direction of the correlations between cynicism and these neurotransmitters were opposite to the associations between exhaustion and the neurotransmitters. This difference in the role of neurotransmitters suggests that exhaustion and cynicism may have different molecular mechanisms, given that exhaustion and cynicism are two different dimensions of burnout. The 'fight or flight' hormone NE is higher in patients who show cynicism or hostility.[31] There is evidence that Achl agonists that inhibit the activity of DA may lead to hostility or cynicism.[32,33] Indicators that incorporate the four indexes of 5-HT, DA, NE and Achl could capture more information and thus be more effective in predicting mental health than a single measure. Neuroendocrine studies have shown that neurotransmitters such as GABA, 5-HT, NE, Glu, Achl and DA are associated with mental, emotional, behavioural, dietary, sleep, learning and memory functions, and with biological rhythms and metabolic activities in mammals,[34] and that levels of monoamine neurotransmitters are correlated with tension levels.[35,36] One study showed that hippocampal 5-HT levels in stressed rats were significantly decreased.[37] A study using a chronic, unpredictable mild stress model of depression found decreased levels of DA, 5-HT and NE in rat plasma.[38] There is also evidence that Achl levels in rats are decreased following chronic unpredictable mild stress.[39] The relationship between stress (especially mental stress) and disease has gained increasing attention in the medical profession. It has been reported that levels of NE, DA 5-HT and other neurotransmitters often change in patients with chronic fatigue syndrome before disease onset.[40]

This finding indicates that we should not ignore the role that neurotransmitters play in mental health. In addition to providing an assessment of the association between two sets of variables, CCA can narrow down, to some extent, the exposure (neurotransmitters) and outcome variables (mental health) that might contribute to the association, based on the variable loadings. For example, we could explore the level of burnout according to neurotransmitter changes. Thus, CCA could be used to identify the most influential factors of both exposure and outcome variables, which may provide more accurate information about the correlation between exposure and outcome and could form the basis for more in-depth research.

We also found a correlation between neurotransmitter levels and age. Our findings reflect previous reports that DA and 5-HT levels, which are associated with cognitive and motor performance, gradually decline with age by approximately 10% each decade from early adulthood.[41] The expression of Glu-positive neurons in the CA3 area of the rat hippocampus gradually decreases with age.[42] One mental illness study found that GABA was significantly and positively correlated with patients' age.[43] These findings indicate that a significant correlation exists between the levels of exhaustion and brain neurotransmitters, and suggests that job-related burnout affects mental activity. Changes in brain neurotransmitter activities may be involved in the physiological processes of job-related burnout.

Conclusion

Aspects of job-related burnout were associated with neurotransmitter levels in the cerebral cortex in Chinese medical workers. Sex had a significant effect on all neurotransmitter levels. The neurotransmitters 5-HT, Glu, DA, GABA, NE and Achl may have different roles in exhaustion and cynicism, reflecting different molecular mechanisms. Furthermore, the findings suggest that long-term job-related burnout may lead to behavioural and psychiatric disorders.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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