

Correlation Study of Neurotransmitter and Immune Levels in Pre-Hospital Emergency Nurses with Post-Traumatic Stress Disorder

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Abstract

Objective: To investigate the occurrence of PTSD in pre-hospital emergency nurses and its related factors, and to compare the differences of neurotransmitter and immune-related factors between pre-hospital emergency nurses who experienced traumatic events and those who did not develop PTSD and healthy people. **How:** Post-traumatic Stress Disorder Self-Rating Scale (PCL-C) tests were performed on pre-hospital emergency nurses in PTSD group, non-PTSD group and healthy control group, and the plasma monoamine neurotransmitters and serum cytokines were determined by double-antibody sandwich ABC-ELISA assay using enzyme-linked adsorption kit provided by Shanghai Xitang Biotechnology Co., Ltd. **Results:** 1) There were statistically significant differences in PCL-C scores between PTSD group, non-PTSD group and healthy group ($p < 0.05$); 2) There were significant differences in the levels of serum cytokines IL-2, IL-6, IL-10 and TNF- α between PTSD group, non-PTSD group and healthy group ($p < 0.05$); 3) There were significant differences in plasma levels of monoamine neurotransmitters norepinephrine, 5-hydroxytryptamine and dopamine between PTSD group, non-PTSD group and healthy group ($p < 0.05$). **Conclusion:** Pre-hospital emergency nurses should have early psychological intervention and guidance to reduce the occurrence of PTSD in emergency and emergency nurses.

Keywords

Pre-Hospital First Aid, Nurse, Post-Traumatic Stress Disorder, Neuroimmunology

1. Introduction

Post-traumatic Stress Disorder (PTSD) is a delayed and long-term mental disorder caused by unusual, threatening or catastrophic psychological trauma [1], and is an important manifestation of post-disaster mental and behavioral disorders [2]. The main symptoms are reexperiencing the traumatic event, avoidance of trauma-related cues, persistent hyperarousal, selective amnesia and emotional numbing of the traumatic experience. Patients suffer greatly from this. In recent years, with the increase of natural disasters, wars, terrorist incidents, etc., there has been a growing number of studies on post-traumatic stress disorder (PTSD). Compared with the epidemiology of PTSD, the progress in the study of its pathologic pathogenesis is relatively difficult and lagging behind. The particularity of pre-hospital rescue determines that pre-hospital emergency nurses have greater work intensity, higher risk, worse protective measures and more nurse-patient conflicts than ordinary nurses [3]. These traumatic events can cause nurses to have significant negative psychological reactions, which eventually lead to PTSD. The purpose of this study was to compare the differences of neurotransmitter and immune-related factors between pre-hospital emergency nurses who experienced traumatic events and those who did not develop PTSD, and to explore their correlation with the severity of PTSD [4], to provide a better basis for its later treatment, prevention and control and explore more effective treatment methods.

2. Data and Methods

2.1. General Data Inclusion Criteria

All enrolled patients met the diagnostic criteria for PTSD; Aged 22 - 55 years old; All patients were self-aware and signed informed consent forms. Exclusion criteria: Patients with a history of mental illness or depression; Exclude patients with organic diseases; Pregnant and lactating women. Twenty pre-hospital emergency nurses with PTSD who met the above inclusion and exclusion criteria were selected from the Second Affiliated Hospital of Hainan Medical College (Hainan General Hospital of Land Reclamation) and Hainan Provincial People's Hospital from September 2016 to May 2017, and 30 non-post-hospital emergency nurses and 30 healthy people in the control group were enrolled by completely random method.

2.2. Methods

2.2.1. Assessment Methods of PTSD

The PTSD Checklist-Civilian Version (PCL-C) scale is used. The PCL-C scale is designed to evaluate the post-traumatic experience of ordinary people in their daily lives. It asked participants to rate how bothered they were by problems and complaints in the past month on a five-point scale: 1 "not at all", 2 "a little", 3 "moderately", 4 "fairly", and 5 "extremely". It can be divided into 4 factors, namely: increased alertness response; Avoidance response; Traumatic experience re-

current response; Social dysfunction response. The total score of each item (17 - 85) is accumulated. The higher the score, the greater the likelihood of PTSD. This table provides a continuous score based on the number and severity of symptoms, and is a multi-dimensional tool for observing PTSD, which can provide a more detailed description of the main symptoms of PTSD for clinical treatment and nursing. It can also be used as a tool to evaluate the effect of psychological intervention in clinical studies. In the United States, the PCL-C scale is used as a scale for diagnosing PTSD symptoms and evaluating the effectiveness of intervention or treatment for PTSD. PCL-C scores and evaluation results were measured in the above 20 PTSD nurses, 30 non-PTSD nurses and 30 healthy people.

2.2.2. Collection of Patient Specimens and Index Determination

Plasma monoamine neurotransmitter and serum cytokine assay: Using the ELISA kit provided by Shanghai Xitang Biotechnology Co., Ltd., the above 20 nurses with PTSD, 30 nurses without PTSD and 30 healthy people were treated with monoamine neurotransmitters (norepinephrine, dopamine) and cytokines (interleukin IL-2, IL-6, IL-6, IL-6, IL-6, IL-6, IL-6, IL-6, IL-6, IL-6, IL-6, IL-6, IL-6, IL-6, IL-2, IL-6, IL-6, IL-6, and IL-6. IL-10, tumor necrosis factor TNF- α) were measured.

2.3. Statistical Methods

SPSS19.0 statistical software was used for analysis. Measurement data were described using (\pm s), independent sample t test or ANOVA was used for inter-group comparison, and paired t test was used for intra-group comparison. Repeated measurement ANOVA was used to analyze the change of an index in different groups at different time points. The test level was $\alpha = 0.05$, with statistical significance ($p < 0.05$), but without statistical significance ($p > 0.05$).

3. Results

3.1. Comparison of General Data between the Two Groups

There were 55 cases in the PTSD nurse group, 83 cases in the non-PTSD nurse group and 82 cases in the healthy group, including 3 cases in the non-PTSD nurse group and 2 cases in the healthy group, and 80 cases in the non-PTSD nurse group and 80 cases in the healthy group. In the nurse group with PTSD, there were 4 males and 51 females, with an average age of 41.60 ± 8.45 years, and the duration of the disease ranged from 5 weeks to 1.5 years. In the non-PTSD group, there were 5 males and 75 females, with an average age of 38.96 ± 8.57 years. Healthy group: 8 males, 72 females, mean age 35.98 ± 5.80 years old. There were no significant differences in gender and age among the three groups ($p > 0.05$).

3.2. Comparison of PCL-C Scores among the Three Groups

Clinical evaluation: Pre-hospital emergency nurses were assessed with the post-

traumatic Stress Disorder Screening Scale (PCL-C) 1 month after the traumatic event. The assessment was conducted by psychological professionals, and when the total score of PCL-C was greater than or equal to 41 points, it was assessed by two psychiatric clinicians. Results: There were statistically significant differences in PCL-C scores among nurses with PTSD group, nurses without PTSD group and healthy people group ($p < 0.05$). See **Table 1**.

3.3. Comparison of Serum Cytokine Levels

The levels of serum cytokines IL-2, IL-6, IL-10 and TNF- α in PTSD group, non-PTSD group and normal control group were significantly different ($p < 0.05$). See **Table 2**.

3.4. Comparison of Plasma Monoamine Neurotransmitters

There were significant differences in plasma monoamine neurotransmitters (norepinephrine, dopamine) between PTSD group, non-PTSD group and healthy control group ($p < 0.05$). See **Table 3**.

4. Discussion

Post-traumatic stress disorder (PTSD), also known as delayed psychogenic reaction, is a delayed sexual response caused by a stressful event or situation. The

Table 1. Comparison of PCL-C scores between PTSD group, non-PTSD group and healthy group (\pm s).

| Dimension | PTSD nurse group (N = 55) | non-PTSD nurses group (N = 80) | Healthy population group (N = 80) | F | p |
|---------------------|---------------------------|--------------------------------|-----------------------------------|--------|-------|
| PCL-C Total score | 44.58 \pm 11.90 | 33.50 \pm 10.68 | 28.89 \pm 10.07 | 12.86 | 0.000 |
| re-experience | 3.11 \pm 0.75 | 2.13 \pm 0.69 | 1.84 \pm 0.62 | 21.73 | 0.000 |
| Avoidance/numbness | 1.99 \pm 0.78 | 1.69 \pm 0.70 | 1.52 \pm 0.64 | 2.716 | 0.072 |
| Increased alertness | 3.11 \pm 0.92 | 1.92 \pm 0.81 | 1.82 \pm 0.88 | 14.739 | 0.000 |

Table 2. Comparison of IL-2, IL-6, IL-10 and TNF- α levels between PTSD group, non-PTSD group and normal control group (\pm s, pg/mL).

| | PTSD nurse group (N = 55) | non-PTSD nurses group (N = 80) | Healthy population group (N = 80) | F | p |
|---------------|---------------------------|--------------------------------|-----------------------------------|--------|-------|
| IL-2 | 39.83 \pm 13.12 | 33.94 \pm 12.75 | 28.33 \pm 12.12 | 5.052 | 0.009 |
| IL-6 | 56.37 \pm 21.62 | 44.12 \pm 20.86 | 29.65 \pm 22.63 | 9.183 | 0.000 |
| IL-10 | 62.48 \pm 34.19 | 42.56 \pm 24.18 | 13.090 \pm 11.13 | 27.791 | 0.000 |
| TNF- α | 37.61 \pm 4.41 | 39.13 \pm 5.17 | 19.26 \pm 4.32 | 29.08 | 0.000 |

Table 3. Comparison of NE and 5-HT levels between PTSD group, non-PTSD group and normal control group (ng/mL).

| Dimension | PTSD nurse group (N = 55) | non-PTSD nurses group (N = 80) | Healthy population group (N = 80) | F | p |
|-----------|---------------------------|--------------------------------|-----------------------------------|--------|-------|
| NE | 0.96 ± 0.59 | 0.65 ± 0.41 | 0.57 ± 0.36 | 4.711 | 0.012 |
| 5-HT | 627.09 ± 100.81 | 517.03 ± 79.21 | 465.85 ± 80.44 | 26.019 | 0.000 |

diagnosis was first published in the Third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) in 1980. With the continuous accumulation of relevant research results, the diagnostic criteria for PTSD have been significantly modified in DSM-III-R and DSM-IV, and this category is also included in China's CCMD-II-R and the 10th edition of the International Classification of Diseases (ICD-10) published in 1993 (Davidson JRT, 1995; Kessler RC, 1995; Stein MB, 1997). PTSD is a mental disorder that appears late or persists long after an unusually threatening or catastrophic shock. It is mainly manifested by the recurrence of traumatic experiences, which often occur days or even months after the trauma (rarely more than 6 months), and the course of disease can be as long as many years.

J.c. Geuo *et al.* [5] conducted a questionnaire survey among 5500 people who received psychological help in the disaster area of Typhoon Ramasun in Hainan Province. The survey results show that the incidence of post-traumatic stress disorder (PTSD) symptoms after Typhoon Rammasun in Hainan Province is 61.93%, among which 7.8% have obvious PTSD symptoms, indicating that Typhoon Rammasun in Hainan Province has caused relatively large psychological problems to the victims, and the survey found that the prevalence rate is higher among young people and middle-aged people. It shows that young people and middle-aged people are more likely to have psychological symptoms and have lower mental bearing capacity. It suggests that more attention should be paid to young people and middle-aged people when developing mental health services in disaster areas. Some foreign studies have shown that the incidence of PTSD is very high among emergency workers. With the establishment and improvement of China's emergency medical system (EMSS), more and more nurses are engaged in pre-hospital emergency work. The complex climate, illness, bad visual stimulation and various traumatic events in pre-hospital emergency treatment can cause nurses to have obvious negative psychological reactions, and eventually PTSD. A large number of studies have shown [6] that the persistence of PTSD symptoms not only causes physical disorders, but also has a negative impact on the mental aspects of emergency medical personnel, and ultimately leads to the decline of the quality of emergency rescue work. With the establishment and improvement of emergency medical system (EMSS), more and more nurses are engaged in pre-hospital emergency work. Pre-hospital first aid refers to the general term of on-site rescue, transport and en route monitoring of patients with life-threatening emergencies, trauma, poisoning, disaster accidents and other

injuries outside the hospital, that is, the rescue at this stage before the patient becomes ill or injured and begins to seek medical treatment in the hospital. The characteristics of pre-hospital first aid are many emergencies, large randomness, urgent time, complicated and changeable condition of patients, and poor first aid environment. The pre-hospital emergency nurses in the process of rescue because of the environment, rescue objects are very different from the conditions in the hospital. Pre-hospital first aid may face complex climate, difficult traffic channels, crowds, small space, dim light, patients and their families are psychologically anxious, fearful, and the rescue must race against the clock, fully reflecting the characteristics of “time is life”. Especially when a batch of patients appear, pre-hospital emergency nurses must evaluate and judge complex situations in a short time, and deal with different injuries in a timely and reasonable manner. The bad visual stimulation of the body injury at the rescue site, the moan of the patient, the noise of the ambulance, the friction between the nurse and the patient, and even the insult and attack of the family members are all traumatic events that pre-hospital emergency nurses often need to face. The particularity of pre-hospital ambulance determines that pre-hospital emergency nurses have greater work intensity, higher risk, worse protective measures and more nurse-patient conflicts than ordinary nurses. These traumatic events can cause nurses to have significant negative psychological reactions, which eventually lead to PTSD. A large number of studies have shown that [7] the persistence of PTSD symptoms has caused great damage to emergency medical personnel, so that emergency medical personnel are more prone to physical disorders than other personnel, including physical symptoms such as headache, ulcer, high blood pressure, anxiety, depression, insomnia, memory loss, and concentration problems, or sub-health conditions. At the same time, PTSD can also produce other negative effects in mental aspects, such as negative emotions, low job satisfaction, high turnover rate, early retirement or absenteeism, etc., which ultimately lead to the decline of the quality of first aid work. Although the pathogenesis of PTSD is relatively clear among mental disorders, its pathogenesis is still not very clear. Some studies have established animal stress models to induce PTSD to simulate the symptoms of human post-traumatic stress disorder to understand the pathogenesis, while others have studied its pathogenesis from the aspects of biology and imaging based on clinical cases.

Neuroimaging studies have shown that trauma or long-term stressors can cause changes in neuroanatomical structure and neural network function. Based on PTSD neurobiological research has revealed that PTSD is closely related to the hypothalamus-pituitary-adrenal cortical axis (hypothalamic-pituitary-adrenocortical, HPA) and monoamine neurotransmitters such as norepinephrine (norepinephrine, NE) and serotonin (5-hydroxytryptamine, 5-HT), and the latter is characterized by dysregulation. Animal data suggest [8] that chronic stress is associated with reduced availability of norepinephrine transporters in the locus coeruleus (net). However, it is not clear that these models correlate with post-traumatic stress disorder (PTSD), which has been associated with the disorder in humans.

The results showed that PTSD was associated with significantly reduced net availability in the locus coeruleus and greater network availability in this brain region with increased anxiety arousal in patients with PTSD symptom severity. JW Mason *et al.* [9] found that the combined value of the norepinephrine/cortisol (N/C) ratio of two systems provided a measure of distinct post-traumatic stress disorder from other groups of patients during hospitalization. The N/C ratio was more than twice as high in the PTSD group as in the other patient groups after the first sample was hospitalized, the average sample during the hospitalization, and the last sample before discharge. The PTSD group had a mean N/C ratio of 2.54, compared with 99 for the other four groups, with a mean of 81 - 1.18. In the samples they selected, the diagnostic sensitivity was 78% and the specificity was 94%. These preliminary findings further encourage the exploration of multivariate strategies, using hormone ratios or profiles, to improve the diagnostic sensitivity of neuroendocrine criteria in the assessment of patients with psychosis. T Chen *et al.* [10] have shown that the hypothalamic-pituitary-adrenal (HPA) axis plays an important role in the pathogenesis of PTSD patients. Normally, when the brain is stimulated physically or psychologically, it sends a signal to the hypothalamus, the paraventricular nucleus of the hypothalamus releases adrenocorticotropin releasing factor (CRF), which reaches the pituitary gland, Stimulates the pituitary gland to release adreno-cortico-tropic-hormone ACTH, which enters the adrenal glands and promotes the release of cortisol by the adrenal glands. Glucocorticoids bind specifically to the corresponding tissue receptors in the body, activate a series of enzymes, regulate the production and release of a variety of chemical mediators and inflammatory cytokines. Under stress, the body produces a series of protective reactions in order to prevent itself from excessive immune damage. Activated immune cells produce IL-6 and TNF- α , which directly stimulate the synthesis and secretion of hypothalamic corticotrophin-releasing hormone (CRH), and then increase ACTH and cortisol, inhibiting the immune response. Whether the severity of PTSD symptoms is associated with high or low plasma cortisol levels is inconclusive. In the study, the serum levels of IL-2, IL-6, IL-8 and TNF- α in PTSD patients were higher than those in control group. The plasma cortisol concentration was lower than that of the control group. It is speculated that the subjects may have been in a state of stress for a long time (at least 3 months) after experiencing an emotional crisis, so the cortisol concentration may be lower than that of the normal control group. L Li *et al.* [11] explored the role of platelet serotonin in the pathogenesis of PTSD by detecting the concentration of platelet serotonin in the patients with post-traumatic stress disorder (PTSD) of Li nationality and Han nationality in Hainan Province, using LSD for ptwo comparison: The platelet 5-HT levels of PTSD patients of Li nationality and Han nationality and the normal control group were compared pin-ppairs, and the differences were statistically significant ($p < 0.01$). The platelet 5-HT concentration of Li PTSD patients (120.56 ± 118.05) pg/mL was lower than that of Han PTSD patients (271.43 ± 181.66) pg/mL. It was also lower than that in the normal control group of Li nationality (338.54 ± 156.46) pg/mL and

the control group of Han nationality (350.58 ± 169.19) pg/mL, with statistical difference among all groups ($p < 0.01$). There are symptomological differences in avoidance, intrusion and hyperalertness between Li PTSD patients and Han PTSD patients and normal control group. The low serotonin function in PTSD patients may be related to biochemical mechanisms. The ethnic differences in Li PTSD patients are related to ethnic habits, status and culture in tropical areas. Post-traumatic stress disorder (CR-PTSD) is associated with abnormal regulation of various neurotransmitter systems [12]. We assessed thrombocytopenic plasma (PPP) levels of norepinephrine (NE) and serotonin (5-HT) and NE in 17 untreated male outpatients. 24-hour urinary excretion of dopamine (DA) and homovanillic acid (HVA) in chronic CR-PTSD (age 33.1 ± 7.4 years) and 10 normal controls (age 35.8 ± 2.7 years). Compared with the control group, the PTSD patients had significantly lower PPP 5-HT levels, higher PPP NE levels, and significantly higher average 24-hour urinary excretion of all three catecholamines (NE, DA, and HVA).

24-hour urinary HVA values in patients with CR-PTSD were significantly positively correlated with the overall impact of event scale scores and symptom avoidance cluster scores, and PPP 5-HT levels were negatively correlated with Hamilton Anxiety Scale scores. The PPP NE/5-HT ratio in the study group was significantly higher than that in the control group. We believe that this combined enhanced norepinephrine activity and reduced 5-HT activity may be related to the neurobiology of CR-PTSD. J Fan *et al.* [13] studied the correlation between immune function and PTSD in patients with PTSD. Methods 15 patients with PTSD had no physical injury (PCL-C score over 50, score 52 index 79, mean and standard deviation 62 ± 8), 15 patients with PTSD, and trauma cases without PTSD (PCL-C score below 12, score 0 to 11). Serum cytokines (IL-2, IL-6, IL-10, tumor necrosis factor- α) were determined by enzyme-linked immunosorbent assay (ELISA) with mean and standard deviation of 4 ± 4 . Results There were significant differences in IL-2 levels between the two groups ($Z = -2.807$, $p = 0.05$). There was no significant difference in the other three immune indexes ($p > 0.05$). There was no significant correlation between immune indexes and PCL-C scores in 4 cases of PTSD group. Conclusion The biological level of interleukin IL-2 is a disease in patients with post-traumatic stress disorder, and the immunological level and its correlation with PTSD need further study. Research by A Vidovic *et al.* [14] suggests that these changes may be related to the duration of PTSD. The aim of our study was to investigate differences in selected endocrine and immune-related variables between PTSD patients and control subjects, and whether these differences persisted over time. Methods: We evaluated 39 Croatian war veterans with PTSD and 25 healthy volunteers (civilians with no experience of trauma), all men separated at two time points for 5 - 6 years (median; Quartile range: 5.4 - 6.3). Cortisol and prolactin levels were measured by radioimmunoassay, while interleukin-6 and tumor necrosis factor- α were measured by enzyme-linked immunosorbent assay. Immune function was assessed by in vitro natural killer cell cytotoxicity (NKCC). Lymphocyte

count, immunophenotype, and intracellular glucocorticoid receptor expression in various lymphocyte subpopulations were measured by tricolor flow cytometry. The results suggest that the endocrine and immune-related changes observed in PTSD over time may depend on the duration of the abnormal load caused by the disorder and its effect on the interaction between endocrine and stress response-related immune systems. Post-traumatic stress disorder (PTSD) is associated with dysregulation of various neurotransmitter systems [15]. The researchers assessed (24-hour urinary excretion) norepinephrine (NE) and 5 Serotonin (5-ht), NE, dopamine (DA), and homovanillic acid (HVA) showed significant differences in 24-hour urinary excretion of all three catecholamines (NE, DA, and HVA) between the PTSD group and the normal control group. The pathogenesis of PTSD may be related to neurobiology.

5. Conclusion

Foreign scholars have found that medical staff engaged in emergency care in the medical and health industry is a high-risk group of PTSD, and more than 15% of the subjects suffer from PTSD symptoms throughout their life and are unable to live a normal life [16]. Pre-hospital emergency and first aid nurses themselves also have the following susceptibility: indirect mental trauma, psychological violence, verbal violence from rude family members, horizontal violence between colleagues, complex work environment, excessive work load, more than their own capacity, irregular life, low social recognition, gender factors, etc., all of which are possible factors causing PTSD. A large number of studies have shown that PTSD is not only related to the nature and intensity of traumatic events, but also closely related to personality characteristics, cognitive factors, coping styles, attribution styles, social support and other psychosocial factors, all of which play a certain role in the occurrence, development and outcome of PTSD symptoms. Although its pathogenesis is not very clear, most studies support that compared with other changes, its precursor and foundation are neuroendocrine and immune changes, and psychological, neuro-endocrine-immune interaction and linkage effect occur under stress. Therefore, the study on the correlation between neurotransmitters and immune levels in post-traumatic stress disorder is a theoretical study or a scientific exploration, and can also be used as a reference for further research. Therefore, although the results of this study still lack some landmark studies from large samples, at the same time, it still needs to be verified repeatedly by multi-center, multi-orientation and multi-level.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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