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Comparative analysis of platelet 5-HT concentrations in Han and Li patients with post-traumatic stress disorder

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ABSTRACT. We investigated the role of serotonin (5-HT) in the pathogenesis of post-traumatic stress disorder (PTSD) by determining the platelet 5-HT concentrations in Li and Han patients with PTSD in Hainan Province, China. Li and Han control groups of the same sample size have no statistical differences in gender and age distribution compared to those in the PTSD groups who were also examined. The platelet 5-HT concentrations were determined by high-performance liquid chromatography. In addition, the patients and controls were evaluated by the impact of event scale-revised (IES-R). IES-R showed that the total and sub-scale scores of three factors (avoidance, intrusion, and hyperarousal) of Li patients with PTSD were significantly higher than those of Han patients with PTSD. Scores of both PTSD groups were higher than those of their respective control groups. The platelet 5-HT concentration of the

Li patients with PTSD (120.56 ± 118.05 ng/10^9 platelets) was lower than that of the Han patients with PTSD (271.43 ± 181.66 ng/10^9 platelets) and that of both Li and Han control groups (338.54 ± 156.46, 350.58 ± 169.19 ng/10^9 platelets, respectively). Differences existed in symptoms of PTSD in terms of avoidance, intrusion, and hyperarousal in the Li and Han patients with PTSD. The diminished 5-HT activity in patients with PTSD may be relevant to biochemical changes in the brain and body. The differences in these factors between ethnic groups could be due to their customs, social status, and culture.

Key words: Li ethic group; Han ethic group; Post-traumatic stress disorder; Platelet 5-HT

INTRODUCTION

Post-traumatic stress disorder (PTSD) is one of the most typical mental illnesses among acute stress psychoses. These negative effects manifest mainly in the recurrence of the traumatic experiences in consciousness or dreams, persistent symptoms of increased vigilance and the avoidance of any scene triggering the traumatic memory. The psychological and social functions of the patients are severely impaired (Flaks et al., 2014). Epidemiological studies have shown that more than half of the patients with PTSD are frequently accompanied with depression, anxiety disorders, and substance abuse (Marin et al., 2011; Javidi and Yadollahie, 2012; Bajor et al., 2013). The suicide rates in patients with PTSD are six times higher than the general population (Panagioti et al., 2009, 2014). This mental disorder severely damages the patients' ability to work. Two recently conducted systematic reviews consistently reported a strong association between a PTSD diagnosis and suicidal behavior (Krysinska and Lester, 2010; Panagioti et al., 2012). More than half of those diagnosed with PTSD report suicidal thoughts (Ferrada-Noli et al., 1998; Oquendo et al., 2003) and as many as a quarter report suicide attempts (Panagioti et al., 2011). Across a series of studies investigating the mechanisms of suicidal behavior in PTSD populations (Tarrier and Gregg, 2004), an increase in the number and severity of PTSD symptoms have been found to be strongly associated with suicidal behavior (Freeman et al., 2000; Zhang et al., 2010; Baumert et al., 2013). Furthermore, there is empirical evidence that the presence and severity of PTSD symptoms are strong predictors of suicidal behavior among subclinical populations experiencing PTSD symptoms but do not fulfill the full criteria for a PTSD diagnosis (Wang et al., 2011; Zhao et al., 2011; Liu et al., 2012). Hence, we have set up programs in Sanya to study patients with PTSD, which are divided into three groups: the Li minority, the Han minority, and the normal control group. We used platelet 5-hydroxytryptamine (5-HT; also known as serotonin) as an indicator to explore the biochemical mechanism of the pathogenesis of PTSD.

MATERIAL AND METHODS

Patient selection

The selected patients with PTSD were determined by employing the impact of event scale-revised (IES-R). The IES-R has 22 entries in three dimensions: avoidance, intrusion, and

vigilance. The symptoms assessed as avoidance are 5, 7, 8, 11, 12, 13, 17, and 22. Symptoms assessed as intrusion are 1, 2, 3, 6, 9, 14, 16, and 20. Symptoms assessed as vigilance are 4, 10, 15, 18, 19, and 21. Tests with scores of 20 or higher (≥20) are considered PTSD positive, while tests with scores lower than (≤20) are considered PTSD negative. The questionnaire was evaluated by experienced professionals with psychological knowledge. The professionals conducted the survey with the consent of the participants.

We selected 30 Li and 30 Han patients with PTSD who visited doctors during the period between August 2010 and September 2011 at the People's Hospital of Sanya. There were 20 men and 10 women in each group, aged 38.2 ± 2.4. The two groups of patients were assessed by professional psychiatrists using DSM-IV Axis I (SCID-I/P), who specifically referenced the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition of the United States. The study excluded patients with other mental or physical diseases, neurological disorders, history of alcoholism and drug dependence, pregnant or nursing females, and drug abusers. All participants did not take hormone drugs for at least a month and did not receive any psychiatric drug treatment. The two control groups, each of 30 individuals of the Li and Han ethnicity, respectively, were volunteers who visited doctors for their physical checkup during the same period. In the Han group, there were 19 males and 11 females (average age 39.61 ± 2.1 years) and in the Li group, there were 20 males and 10 females (average age 37.86 ± 3.4 years). The individuals in the control group did not have a mental illness, family history of mental illness and any major physical disorders. The gender distribution and age differences between the groups are not statistically significant ($P < 0.05$). This study was conducted in accordance with the declaration of Helsinki and with approval from the Ethics Committee of Hainan General Hospital. Written informed consent was obtained from all participants.

Determination of platelet 5-HT concentrations

Six milliliters of venous blood was drawn from each participant, which was then slowly injected through the silicone-coated tubes containing 5% EDTA as an anticoagulant. After gentle shaking, the samples were centrifuged for 30 min at 8°C and 50 *g*. The upper layer, which is platelet-rich plasma, was removed, placed into a small plastic tube, and centrifuged for 20 min at 8°C and 3500 *g*. Pre-cooled blood-cell isotonic solution (2 mL) was added to the decanted supernatant, and the solution was gently whisked. Of this solution, 0.4 mL was removed for platelet count. The remaining 1.6 mL was centrifuged for 20 min at 8°C and 8500 *g*. The supernatant was decanted, platelet hypotonic broken, 190 μL removed, and determination of 5-HT performed on the same day.

Platelet 5-HT concentrations were measured by high-performance liquid chromatography (HPLC) with a combination of LC-10AT HPLC instrument, SPD-10A detector, Japan East Asia KX-21 hematology analyzer (DKK-TOA Corporation, Japan), and standard 5-HT creatinine sulfate (Sigma, USA). After optimization of test conditions, curves were described by the microcomputer and peak height was printed out with each injection sample of 100 μL. We calculated the levels of 5-HT in platelets (ng/10^9 platelets) through comparison with standard curves and those from normal controls.

Statistical analysis

All data were analyzed with the SPSS13.0 software (Chicago, IL, USA). The results

are reported as means ± standard deviation. We adopted multiple-comparison methods including one-way ANOVA and least significant difference to compare IES-R factor scores and platelet 5-HT concentrations between groups. These analyses were detected using two-sided tests with $P < 0.05$ indicating statistical significance.

RESULTS

Evaluation of patients with PTSD by IES-R

Two ethnic groups of patients with PTSD were evaluated by IES-R (Table 1). No statistical difference was observed between the Li and Han control groups, in either IES-R factors (avoidance, intrusion, and hyperarousal) or total score. However, the IES-R score was significantly higher in the PTSD groups than their respective control groups for both Li and Han ethnic groups. Additionally, the PTSD score of all factors and the total score in the Li PTSD group were significantly higher than in the Han PTSD group.

Table 1. Comparison of IES-R factors in PTSD and control groups according to ethnicity.

Factors	Li PTSD (N = 30)	Han PTSD (N = 30)	Han control (N = 30)	Li control (N = 30)
Avoid	21.98 ± 0.65	20.93 ± 0.82▲	15.33 ± 0.39#,△	16.24 ± 0.39•
Intrusion	23.89 ± 0.72	21.05 ± 0.62▲	16.15 ± 0.35#,△	15.83 ± 0.68•
High alert	21.90 ± 0.86	20.04 ± 0.73▲	17.37 ± 0.33#,△	16.18 ± 0.32•
Total average	22.59 ± 0.75	20.67 ± 0.73▲	16.28 ± 0.36#,△	17.26 ± 0.27•

▲Represents comparison between Li PTSD *vs* Han PTSD, $P < 0.05$; #represents comparison between Han *vs* Li control groups, $P < 0.05$; •represents comparison between Li control *vs* Li PTSD groups, $P < 0.05$; △represents comparison between the Han control group *vs* Han PTSD groups, $P < 0.05$.

Platelet 5-HT levels in patients with PTSD

As described above, the platelet 5-HT levels were determined by HPLC (Table 2). There was no difference in platelet 5-HT levels between Han and Li control groups, but the levels decreased significantly in both PTSD groups. Additionally, the platelet 5-HT levels in the Li PTSD group were significantly lower (<50%) than that in the Han PTSD group.

Table 2. Comparison of platelet 5-HT levels.

Groups	No. of cases	Blood platelet 5-HT (ng/10^9 platelets)	F (P)
Li PTSD	30	120.56 ± 118.05	13.4045 (<0.0001)
Han PTSD	30	271.43 ± 181.66▲	
Li control	30	350.58 ± 169.19#△	
Han control	30	338.54 ± 156.46•	

▲Represents comparison between Han PTSD group *vs* Li PTSD group, $P < 0.01$; #represents comparison between Li control group *vs* Han control group, $P < 0.01$; △represents comparison between Li control group *vs* Li PTSD group, $P < 0.01$; •represents comparison between Han control group *vs* Han PTSD group, $P < 0.01$.

DISCUSSION

Specific symptoms of PTSD include occurrence of intrusion, avoidance, and high vigilance. Key symptom clusters encompass the re-experiencing of the trauma in intrusive

memories (criterion B), avoidance of activities, a state of hyperarousal with hypervigilance, an enhanced startle reaction and insomnia (criterion D) (Lin et al., 2011). By comparing the factors of IES-R between the Li and Han PTSD groups in this study, we can conclude that the total factor scores of avoidance, intrusion, and high vigilance in the Li patients with PTSD are higher than that in the Han patients with PTSD. Scores from both PTSD groups are higher than their respective control groups ($P < 0.05$). This discrepancy between Li and Han PTSD groups could be due to the lower socio-economic status, income level, and education of the Li people (Sun et al., 2011), and the fact that the social resources in the Li ethnic areas are lower than those in the Han areas. These factors might largely contribute to hyperarousal in the Li patients with PTSD. At the same time, the unique culture and beliefs of the Li ethnicity could affect the way they deal with traumatic incidences, which affect the occurrence and severity of PTSD. Their recognition and behaviors are more or less marked with cultural imprints, which caused their specific reaction in the event of unexpected incidences. These reactions result in differences in PTSD incidence and symptom reaction.

Irregularities in levels of 5-HT can cause the body to be unable to maintain the stability of the internal environment, which is likely the critical etiological basis of stress-related disorders. The dysfunction of 5-HT in patients with PTSD of the Li and Han groups could be related to differences in individual traumatic experiences. This study also shows a dose-effect relationship between the inherent uncertainty and unpredictability in controlling unconventional emergency stressors and individual stress responses. The symptoms of PTSD occur when individual psychological defense mechanisms are incapable of responding to sudden and strong stimuli resulting in a loss in the ability to control the adverse consequences of the events. In addition to ethnicity and cultural differences, the Li group is under the influence of individual exposure, acculturation, and religious culture. Therefore, levels of platelet 5-HT in the Li patients with PTSD were lower than those in the Han patients with PTSD.

Conflicts of interest

The authors declare no conflict of interest.

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