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Studies on the plasma tryptophan and urinary 5-hydroxy-3-indoleacetic acid in expedition members residing in Antarctica*

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Abstract In order to clarify the possible relationship between the changes of behavior/personality and metabolic changes of 5-hydroxytryptamine (5-HT) in Antarctic expedition members, plasma tryptophan (Trp) and urinary 5-hydroxy-3-indoleacetic acid (5-HIAA) were studied for 24 winter-over and 19 summer-over members of the 8th and 11th CHINARE respectively. Results showed that plasma Trp decreased significantly after residing 1～3 months at Great Wall Station and did not recover on returning back to Beijing from Antarctica by two weeks travelling. Urinary 5-HIAA increased significantly after residing 6 months at Great Wall Station, and recovered on returning back to Beijing from Antarctica in the winter-over members. The decrease of plasma Trp may be related to the decline of brain 5-HT which might play a role in the changes of behavior/personality . Increase of urinary 5-HIAA might reflect metabolic changes of 5-HT as a whole, but cold weather involving in the release response of platelet should be considered. Therefore, supplement of related food rich in Trp or intervention of L-Trp might be valuable.

Key words Antarctica, expedition member, tryptophan, 5-hydroxy-3-indoleacetic acid.

1 Introduction

Tryptophan (Trp) is one of the necessary amino acids, which can not be synthesized in human bodies but can be taken from the food only. Most of the amino acids exist in plasma as free form, but 90% of the Trp exists in plasma as bound form with plasma proteins. Trp acts as a precursor of 5-HT which is not permeable from peripheral to central, but Trp is permeable to blood-brain barrier (BBB), therefore it

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affords the synthesis of neurotransmitter 5-HT in the brain. The metabolic pathways of central and peripheral 5-HT are in the individual ways. The principal metabolic pathway of 5-HT is as follows: Trp is transformed into 5-hydroxytryptophan (5-HTP) through Trp 5-hydroxylase and then into 5-HT by means of 5-HTP decarboxylase. 5-HT is metabolized through monoamine oxidase (MAO) with the formation of 5-hydroxyindoleacetic acid (5-HIAA), an ultimate product in 5-HT metabolic pathway which is excreted in urine. Wherever in the central or in the peripheral, Trp hydroxylase , a rate-limiting enzyme acting on the pathway from Trp to 5-HT, is normally about half-saturated with Trp. Therefore, the level of 5-HT mainly depends on the concentration of Trp in the blood. Trp is also the precusor of melatonin which is one of the pineal hormones. Both 5-HT and melatonin play a role in mediation of sleep, mood, temperature, pain and memory. Since in Antarctica, dramatic changes of environment around the expedition members occurred, including the seasonal changes, period of polar night, frequent snow storm, etc. , the life and work styles of the expedition members had to be modulated in accompanying with physical as well as psychic effects, then eventually the "winter-over syndrome" appeared. In order to understand such syndrome, the underlying mechanism may be searched by studying the changes of plasma Trp and uninary 5-HIAA which are available in our present conditions. The results showed that plasma Trp levels decreased by 13.3%, 8.8% and 15.0% respectively in 24 winter-over members residing for 1～3 months, half a year and one year in Antarctica. The plasma Trp level decreased by 19.4% in 19 summer-over members residing for 1～3 months. Plasma Trp levels of both winter-over and summer-over members did not recover on returning back to Beijing from Antarctica after 2 weeks travelling. Urinary 5-HIAA excreted increased significantly only after residing for 6 months but more for one year at Great Wall Station, and recovered on returning back to Beijing from Antarctica in the winter-over members.

2 Methods

(1) Subjects. 24 male winter-over members, aged from 24～62 years (average (38.6±9.9) years), included 7 members of the 8th CHINARE and 17 members of the 11th CHINARE, who leaved Beijng in Nov. 1991 and in Nov. 1994 for Great Wall Station respectively. 19 summer-over members, 14 males and 5 females, aged from 27～61 years (average (42.6±9.9) years), included 9 members of the 8th CHINARE and 10 members of the 11th CHINARE. All passed the routine physical examination in qualified hospitals.

(2)Sample collections. Blood and urinary samples were taken from these members before their leaving for Antarctica , as well as after 1～3 months, half a year and one year during their stay in Antarctica, and on returning back to Beijing from Antarctica after 2 weeks travelling. Blood samples collected were centrifuged and the plasmas obtained were stored frozen at −20℃. Total 24 hour urine was collected (HCl was added to keep pH<3) and total volume was recorded. Aliquots of urine were stored frozen at −20℃.

(3) Plasma free Trp was estimated by spectrophotofluorometric method (Duggan and Udenfriend, 1956). Urinary 5-HIAA was estimated using colorimeter by

colour showed with nitritonaphthol (Udenfriend *et al.* 1955). The data in results were presented as $\overline{X}\pm SD$. Statistic analysis was done by Student's t test.

3 Results

3.1 Changes of plasma Trp

The plasma Trp samples taken from 24 winter-over members after residing for 1～3 months, half a year and one year respectively in Antarctica, and on returning back to Beijing from Antarctica were compared with the level before their leaving for Antarctica . The plasma Trp levels were 86.7%, 91.2%, 85.0% and 89.6% of the level before they went to Antarctica. The differences are statistically significant. The levels of plasma Trp were 80.6% and 88.9% respectively in comparing with that before they leaved for Antarctica ($p<0.001$ and 0.05 respectively) in 19 summer-over members (see Table 1).

Table 1. Changes of plasma tryptophan ($(\overline{X}\pm SD)/\mu g\cdot ml^{-1}$) in expedition members

S. t. from	Before going to Antarctica s. t. in B. j.	Residing-time in Antarctica				
		1～3 months		half a year	one year	
		S. t. in Ant.	S. t. in B. j.	S. t. in Ant.	S. t. in Ant.	S. t. in B. j.
Winter-over N=24	11.3±1.8	9.8±1.7***		10.3±1.2*	9.6±1.1**	9.0±1.6***
Summer-over N=19	10.8±2.6	8.7±1.0***	9.6±1.7*			

*; **; *** represent $p<0.05$, 0.01 and 0.001 respectively in comparison with the level before going to Antarctica; N : the number of members tested; S. t. : samples taken; Ant: Antarctica; B. j. : Beijing.

3.2 Changes of urinary 5-HIAA excreted

Urinary 5-HIAA excreted increased significantly from (3.84±1.08) mg/24h (before leaving Beijing) to (4.56±0.83) mg/24h (residing for half a year) and (5.37±3.12) mg/24h (residing for one year) ($p<0.05$). The increases were observed only in samples collected in Antarctica and recovered on their returning back to Beijing. No significant change was noticed in summer-over members (see Table 2).

Table 2. Changes of urinary 5-HIAA ($(\overline{X}\pm SD)/mg\cdot(24h)^{-1}$) in expedition members

S. t. from	Before going to Antarctica s. t. in B. j.	Residing-time in Antarctica				
		1～3 months		half a year	one year	
		S. t. in Ant.	S. t. in B. j.	S. t. In Ant.	S. t. in Ant.	S. t. in B. j.
Winter-over N=24	3.84±1.08	4.43±1.49		4.56±0.83*	5.37±3.12*	3.96±1.89
Summer-over N=17	3.46±1.87	3.20±1.71	3.22±0.79			

* represents $p<0.05$ compared with levels before going to Antarctica; N : the number of members tested; S. t. : samples taken; Ant. :Antarctica; B. j. :Beijing.

4 Discussion

The effects of Antarctic special environment on the expedition members are suggested as follows: (1) Psychic factors (rareness of people, monotonous life, far off one's family and loneliness, etc.) and environmental stresses might lead to the development of the "winter-over syndrome". (2) Physiological and pathological changes may be induced by the extreme cold weather. (3) Some changes were said to be related to Antarctic ozone hole. Studies had shown that the changes of the central 5-HT in case of either too high or too low might be related to the appearance of psychiatric and neurotic disturbances (Davis 1994). It was also reported that the lowering blood Trp and 5-HT in depressive patients without taking medicine were more prominant than that of healthy ones from 8:30 am to 4:30 pm, while the blood 5-HIAA level increased more than that of healthy ones (Pietraszek *et al.* 1991; Eynard *et al.* 1993). Plasma Trp, platelet 5-HT and CSF 5-HIAA decreased in patients with suicidal tendency, depression, insomnia, botheration and the borderline cases as pointed out by Cooper *et al.* (1992) and Quintann (1992).

It is well known that reserpine taken might decrease the central and peripheral 5-HT content, and such changes possibly are related to "depression" of 30% hypertensive patients taking reserpine as treatment for a long course, while such changes were also similar to endogenous depression. Animal experiment also supported the above fact that taking reserpine caused the decrease of 5-HT intrabrain/extrabrain and the increased excretion of 5-HIAA as well . Our results on the metabolic changes of 5-HT obtained from the expedition members did show some similarities to their findings (Table 1 and Table 2), and the results also were coincident with that of Xue *et al.* (1990).

Although plasma Trp reduction might lead to the decrease of 5-HT synthesis both in central and peripheral, but it did not turn up to the original level on returning back to Beijing from Antarctica after two weeks travelling. It seems that the metabolic changes of 5-HT system take time ,which coincides with the recovery period from psychic stress, although without precise evidences from our experimental data. Therefore such causal relationship should be studied further.

In addition, hypothermia might be participated in the pathogenesis of thrombotic diathesis, in turn, a risky factor in cardiovascular events , indicating the increase of releasing response of platelet might be important in such conditions (Escalda *et al.* 1993), although our work did not involve in this special aspect but nearly reflected the part of metabolic changes of 5-HT. Anyhow, such risky factors on thrombotic diathesis are important to be considered especially to those aged or with high cardiovascular susceptibility.

All the results obtained are useful or important as references for further expedition consideration, involving both preventive and therapeutic measures in facing the "winter-over syndrome" and possible cardiac events. L-Trp has been used for thera-

peutic purpose in depressive patients with psychosis and neurosis with an effective rate of 91.5%, together with improving their physiological sleeps (Zang *et al.* 1991). Whether or not, to take some milk or sugar water before going to sleep might be valuable to improve the "winter-over syndrome" for Antarctica expedition members.

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