

## **NEUROCHEMICAL AND BEHAVIOURAL EFFECTS OF LONG TERM INTAKE OF TEA**

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### **ABSTRACT**

Tea consumption in many cases is the main source of caffeine intake in humans. In the present study neurochemical and behavioural effects of long term tea intake are monitored in rats. Long term tea administration did not alter plasma tryptophan (TRP) but significantly attenuated brain TRP and 5-hydroxytryptamine (5-HT, serotonin) levels. Brain 5-hydroxyindole acetic acid (5-HIAA) was comparable in both tea-treated and control rats. An increase in home cage activity was observed after one week in rats taking tea as sole source of liquid, whereas no change on the activity was observed in an open field. Caffeinism has been associated with depression. The decreases of brain monoamine metabolism observed in present study are discussed as lowering of mood observed in tea or coffee consumers.

### **INTRODUCTION**

Caffeine is the most widely used psychoactive drug in the world, It is found in coffee, tea, coca and some soft drinks and is very often used as a social drink to enhance performance and mood (Lieberman H.R., 1987). Administration of caffeine has shown to increase brain 5-HT metabolism (Schlosbeg A.J., 1981), while 24th withdrawal following repeated caffeine ingestion decreases brain 5-HT metabolism (Haleem D.J., 1995). Administration of high doses of caffeine decrease locomotion (Haleem D.J., 1994), whereas increased locomotor activity was observed after administration of low or moderate doses (Buckholtz N.S., 1987). Many studies have been carried out into the physiological and psychological effects of caffeine. The association between depression (Mann J.J., 1996) and caffeine consumption is unclear. However, in light of a role of brain 5-HT in psychiatric illness like depression and reported behavioral changes in coffee consumers (Griffiths R.R., 1990), the present study was carried out to investigate the effects of long term tea administration on locomotor behaviour and brain 5-HT metabolism in rats.

### **MATERIALS AND METHODS**

Locally bred male Wistar rats weighing 200-250gms were caged individually in a quiet room, with free access to cubes of standard rodent diet and water (tap water) at least one week before experimentation.

***Animals and Treatment:***

Tea used as treatment vehicle was prepared by adding 2 table spoons of tea-leaves (Yellow label tea) in one liter of boiling water, 4 table spoons were also added. Tea with sugar was given to test animals for only three days (to avoid taste aversion). Similarly sugar was also added in the tap water of control rats for the same period of time. Tea was given as a sole liquid source to test animals for 4 weeks. Activities of water-treated and tea-treated rats in their home cages and also in an open field were monitored after one week and 4 weeks tea administration. After 4 weeks treatment animals were killed by decapitation using guillotine as described earlier (Haleem D.J., 1994) Brains dissected out immediately were stored at  $-70^{\circ}\text{C}$  for the analysis of monomians by HPLC-EC method (Haleem D.J., 1993). Plasma samples were also collected and stored for the estimation of tryptohan.

**BEHAVIOURAL STUDIES*****Home Cage and Open Field Activity:***

Transparent perspex cages 29x26x2cms size were used to individually cage the animals Activity in the home cage was determined by counting the number of cage crossings for 15 mins as described earlier (Haleem D.J., 1993). Activates of test and control animals were monitored at the same time between 9:00-10:00h to avoid time effect and in a balanced design to avoid order effect. The open field apparatus used in the present study consisted of a square area 76x76 cms with walls 24 cms. high. The floor was divided by lines into 25 equal squares. To determine the open field activity control or test animal was placed for the first time in the center square of the open field. The number of squares crossed were scored for 5 mins as described earlier (Haleem D.J., 1994). The activities of test and control animals were monitored at the same time between 11:00-12:00h and in a balanced design.

***Statistical Analysis***

Behavioral and neurochemical data were analysed by Students t-test.

**RESULTS**

Fig.1 shows the data for plasma TRP, brain TRP, 5HT and 5, HIAA in the control and tea-treated rats. Analysis by t-test revealed a significant decrease of brain TRP ( $p<0.05$ ) and 5-HT ( $p<0.01$ ) in tea-treated rats compared to controls, Decreases in plasma TRP and brain 5-HIAA levels were statistically insignificant.

Fig.2 shows home cage (A) and open field (B) activity of control and tea-treated rats. Data analysed by t-test indicated significant increase ( $p<0.02$ ) in home cage activity following one week of tea intake. These increases were not observed after 4 weeks of tea intake. Open field activities of control and tea treated rats were comparable both after 1 week and 4 weeks of treatment.

Fig.3 shows the possible mechanism involved in the observed decreases of brain 5-HT metabolism following long term tea administration.

## DISCUSSION

Administration of caffeine increases 5-HT metabolism (Schlosberg A.J., 1981), while a decrease in 5-HT metabolism, particularly associated with caffeine withdrawal has been reported previously (Haleem D.J., 1995). Important finding of the present study is that rats given tea to drink for 4 weeks exhibited smaller 5-HT levels in the brain (Fig.1). The decreases of 5-HT observed in the present study are explainable in terms of decreased availability of precursor TRP for 5-HT synthesis because brain TRP levels were also decreased (Fig. 1). Tryptophan hydroxylase, the rate limiting enzyme of 5-HT biosynthesis exists only half saturated with its substrate TRP (Haleem D.J., 1993, 1990). Changes in brain TRP concentration could therefore directly alter 5-HT metabolism.

The uptake of TRP by the brain is brought about by a carrier shared by all large neutral amino acids (LNAAs) (Fernstrom D.J., 1971). The levels of plasma total and free TRP and of LNAAs other than TRP have been shown to alter the transport of TRP from blood to the brain. In the present study the decreases of plasma total TRP (Fig.1) were not significant and therefore do not directly explain brain TRP decreases. Plasma levels of free TRP and of LNAAs other than TRP were not measured in the present study. However, administration of caffeine has been shown to increase plasma free TRP concentration (Schlosberg A.J., 1981) because caffeine like TRP is also ligand for indole site on albumin. It is therefore less likely that changes of plasma free TRP induced by tea could lead to decrease in brain TRP concentration. A possible explanation could be that long term intake of tea decreases insulin secretion leading to a decrease in the utilization of LNAAs (Fernstrom J.D., 1972). TRP is however, prevented from this effect of insulin because a large part of this amino acid exists in protein form (Fernstrom J.D., 1971, 1972)

Caffeine is naturally occurring methylxanthine, which has an effect on the central nervous system. Administration of low doses of caffeine has been shown to increase both home cage and open field activity in rats (Haleem D.J., 1994). Administration of theophylline another alkaloid present in tea also increases locomotor activity. The present study shows that home cage activity is greater in rats given tea as a sole source of water for one week. Open field activity was however not increased in tea-treated rats (Fig.2B). Differences in the effects of tea on home cage and open field activities are explainable in terms of caffeine-induced anxiety in a novel environment. High doses of caffeine have been reported to produce anxiogenic like behaviour in social interaction and plus-maze test (Mumford G.K., 1991). We observed an increase in open field activity following low doses of caffeine and decrease following high doses of caffeine (Haleem D.J., 1994). Thus stress effects of novelty could suppress locomotor enhancing effects of stimulants present in tea resulting in lack of effect on open field activity. Tolerance of caffeine stimulatory effect on CNS is widely used central nervous system (CNS) stimulant. Clinical studies show that work performance and delaying sleep has been noted in humans studies (Holtzman S.G., 1990). Partial tolerance to the locomotor enhancing effects of caffeine also developed following the administration of high doses of caffeine for about a week (Haleem D.J., 1994). The present study shows complete tolerance development in the locomotor enhancing effect of tea. Thus tea induced increases of home cage activity observed after one week of tea administration did not occur after 4 weeks of tea administration (Fig.2A)

Caffeine is widely used central nervous system (CNS) stimulant. Clinical studies show that long term use of caffeine precipitates depressive symptoms in humans (Griffiths R.R., 1990). In the present study monoamine metabolism was decreased following long term tea intake. Since a deficiency of 5-HT is often reported in human depression (Udhe T.W., 1984), the present findings imply that caffeine present in tea may precipitate depression by decreasing brain 5-HT metabolism and functions (Fig. 3).

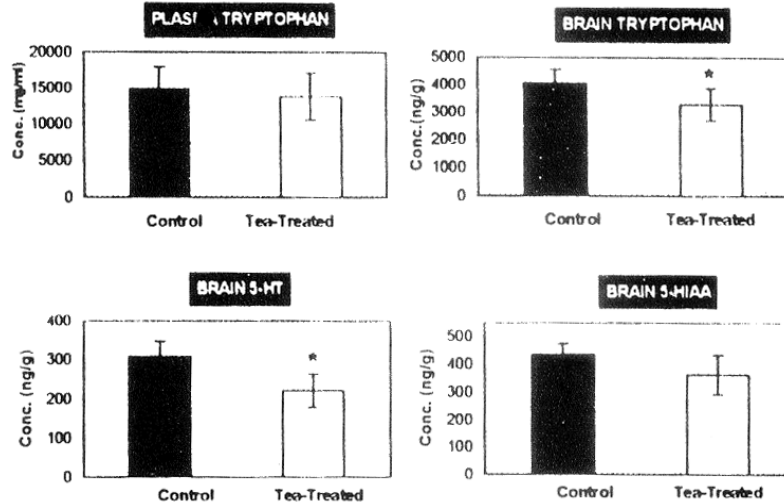


Fig 1: Effect of 4 week tea treatment on plasma TRP, brain TRP, 5-HT and 5-HIAA. Values are mean  $\pm$  SD (nom). Significant difference by Students t-test, \* $p < 0.01$  from controls.

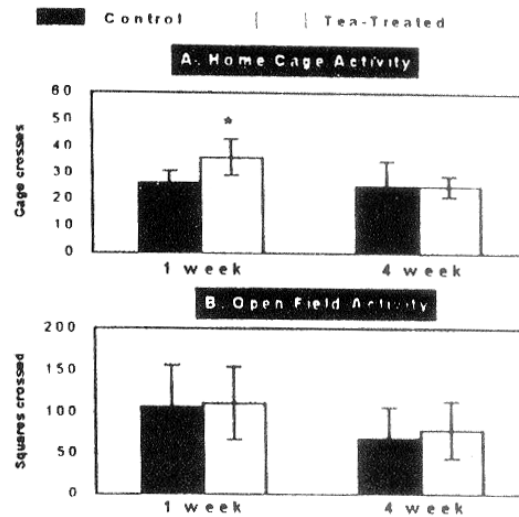


Fig. 2: Effect of 4 week tea treatment on A. Home cage and B. Open field activity. Values are mean  $\pm$  SD. (n=6). Significant differences Students t-test, \* $p < 0.01$  from controls.

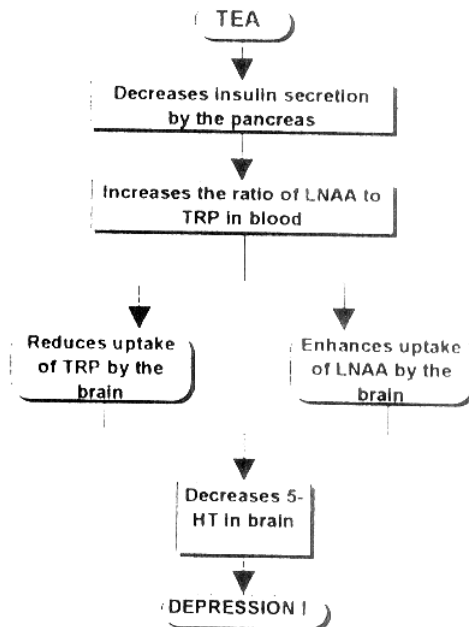


Fig. 3: Possible mechanism involved in the observed decreases of brain 5-HT metabolism following long term tea administration.

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