Indian J Physiol Pharmacol 1995; 39(3): 223-230

# EFFECTS OF SEX STEROIDS ON THE CONCENTRATIONS OF SOME BRAIN NEUROTRANSMITTERS IN MALE AND FEMALE RATS : SOME NEW OBSERVATIONS

A. DAS AND S. K. CHAUDHURI*

*Department of Physiology,*
*Medical College, Calcutta*

**( Received on August 4, 1994 )**

**Abstract**: Concentrations of some neurotransmitters, viz. noradrenaline (NA), 5-hydroxytryptamine (5-HT), dopamine (DA), histamine (H) and gamma aminobutyric acid (GABA) in a part of brain consisting of medulla, pons, mid brain, thalamus and hypothalamus were measured in ovariectomized ($OV_x$), intact (+Te) and castrated male ($Te_x$) rats both without injecting estrogen (E) or E and progesterone (P) as well as after E and E+P administration. Some effects, (which, as far as we are aware of) have not been previously reported, were noted (in addition to other already documented observations). These include : (i) castration in males causes a fall of the level of GABA, NA, 5-HT and DA, (ii) E therapy also causes fall of the levels of GABA, NA and 5-HT and thus E therapy produces similar results like those of bilateral orchidectomy, (iii) P therapy not only reverses the fall of (GABA) but raises it more than the normal value, (iv) P therapy, it appears (although faintly), retrieve to some extent the fall of NA level due to E therapy, (v) Like the $OV_x$ rats, castrated as well as intact rats also showed a fall in the 5-HT level with E treatment but showed a rise when treated by E followed by P, (vi) In between the castrated males and castrated females, the concentrations of all these brain neurotransmitters differ. The probable significances have been discussed.

**Key words:** noradrenaline 5-HT dopamine histamine GABA progesterone castration in males LH surge ovariectomized rats estrogen

## INTRODUCTION

The relationship between the concentrations of some brain neurotransmitters (NTs) and psychiatric disorders or behavioral pattern are now well known. Noradrenaline (NA), dopamine (DA), 5-hydroxytryptamine (5-HT) are thus involved in different psychiatric disorders, like, depression, schizophrenia, mania and so on.

Further, in healthy human females, a recent report from this laboratory (1) showed, exogenous progesterone (P) can influence the psychoanalytical scores of depression, anxiety, mania and schizophrenia.

Nearly 25 years ago, Tonge and Greenglass (2) for the first time showed that concentration of some brain neurotransmitters are influenced by exogenous female sex steroids (FSS) in ovariectomized ($OV_x$) rats. The literature, upto 1982, reporting the relationship between FSS and NT concentrations (NTs), in $OV_x$ rats, has been reviewed by McEwen and Parsons (3). In a recent paper from this laboratory (4), the position in rats with intact ovaries (+OV) was reported.

Despite this somewhat fairly extensive work, certain areas of the field have not received sufficient attention. Such areas of darkness include: (i) the interrelationship between the exogenous FSS and the concentration of gamma amino butyric acid [GABA] in the brain. This is surprising, because GABA is involved in the etiology of anxiety: GABA is also implicated in the etiology of epilepsy and in the mechanism of action of some antiepileptic drugs (eg. valproate

*Corresponding Author and present address: 1/62, Dover Place, Calcutta - 700 019 (West Bengal)

trimethadione). On the other hand P has clinically recognized benificial influence on the epilepsy (5). Common sense logic demands this area should be explored, (ii) The effects of exogenous FSS on males also need attention. In clinical medicine, P is administered in hypernephroma, generalized metastasis in cancer, Pickwickian syndrome, whereas estrogen (E) therapy is popular in carcinoma prostate. That is, males can receive exogenous FSS in different diseases, (iii) Effects of castration, if any, should be studied in males to see whether castration by itself alters the [NTs]. Incidentally, castration alters the metabolism of some NTs in the females (6). (iv) It is well known that there are some differences between male and female behavioral patterns. It will be interesting to see whether there is any difference between the [NTs] in male and female gonadectomized animals.

This work was taken up to throw some light on the above mentioned areas of darkness.

## METHODS

Altogether 531 rats, 351 males and 180 females were used in this study.

*Female rats:* Adult virgin female rats, weighing between 180-200 gms (approx) were taken and ovariectomized. Four weeks after ovariectomy, the animals were divided into 2 groups: Control (Co), and experimental (Ex).

The rats were divided into several batches. Each batch consisted of Co and Ex rats. The Ex rats of every batch received E injection for priming while Co rats received only the vehicle. However, the dose of E used in some batches was usual dose of E (UDE) while in others, it was double dose of E (DDE). Thirty six hrs after E inection, the Ex (but not the Co) rats received P injection. The dose used, in some batches, was usual dose of P (UDP), while in others, it was double dose of P (DDP). The Co rats were given only the vehicle (propylene glycol) instead of P.

Twenty hrs after P or the vehicle injection, rats were sacrificed in a cold room (temp. about 5°C), by breaking the cervical spine (without anesthesia) followed by quick decapitation. The brain was immediately extracted → wiped quickly and a portion of brain, referred as BSH (brain stem-hypothalamus) in this paper, was disseted out. The BSH consisted of medulla+pons+ midbrain + thalami + hypothalamus but no pituitary. From our previous experience (4), we know, administration of FSS can cause terrific enlargement of pituitary. Further we were apprehensive that this enlargement can introduce errors (artefacts) in the results.

The BSH was immediately put into a deep freeze (—20°C) until chemical estimation, which was done on the next day for NA, DA, 5-HT and histamine (H) or 48 hrs after for GABA. In a given BSH either only NA, DA, 5-HT, H were estimated or GABA was estimated. This means, NA, 5-HT, DA, H concentrations were measured from the same BSH while [GABA] were measured from BSHs in which no other estimation was done. Further, in each such batch, there were Co group of rats. This meant, larger number of rats had to be sacrificed. However, this was done to see whether the values of controls in different batches agreed in between themselves closely. A close agreement would ensure that our results were reproducible.

In batches where the effects of P were not studied, rats (both Ex & Co.) were killed after 36 hrs.

*Males:* Rats, weighing between 170 to 185 gm (approx) were divided into 2 major classes, viz those in whom orchidectomy were done ($Te_x$) and others with intact testis (+Te). Each class was divided into several batches. Further, each batch consisted of 2 groups : control (Co) and experimental (Ex),

After gonadectomy, 4 weeks were allowed to pass. Then Co and Ex groups were used. The protocol, including the drug dose (of E and P), in $Te_x$ class of rats were identical with those of $OV_x$ rats. In short, $Te_x$ rats of the Ex were given E, either in UDE or in DDE dose (while the Co rats got only the vehicle) → waited for 36 hrs → P either in UDP or in

DDP dose given in Ex rats alone → sacrificed → concentrtion of NTs in brain estimated as before. For each group of Ex, Co group was ran as usual, the Co rats received only the vehicle.

For +Te rats also, the identical protocol was followed. Where the effects of P were not studied, rats were killed 36 hrs after E or vehicle injection.

For studying the interrelationship between FSS and [GABA] 360 rats were sacrificed. Of these 360 rats, 240 were males (120 were of +Te and the rest 120 were of $Te_x$ groups) and the rest 120 were females (all $OV_x$). For studying the interrelationship between the exogenous FSS and concentration of the other NTs (NA, DA, 5-HT and H), another 171 rats (female 60, male 111) were sacrificed. Of the 111, males 59 were of +Te and 52 were of $Te_x$ groups.

*Drugs* : (1) UDE=200 µg estradiol benzoate in propylene glycol given IP (intraperitoneal) route. (ii) DDE=400 µg of estradiol benzoate in propylene glycol given IP. (iii) UD P = 0.25 mg lynoestrenol (ORGAMETRIL) in 0.5 ml propylene glycol, given IP. DDP = 2 x UDP.

*Chemical estimation* : Of NA, DA, 5-HT and H were made following Sadvongovivad's procedure (7) as was done previously in this laboratory (4). GABA was determined by the technique of Lowe, Robins and Eyerman (8). The fluorescence spectrophotometers used were Hitachi, F4010 (for GABA) and 204A for the others.

Results were expressed in µgms/gm of brain tissue (BSH).

For detection of significance of the differences, Student's 't' test was applied. It will be seen in several instances, the value of *n* was large (eg. Tables IV and V), yet 't' test was used. This is pointed out that 't' test is essentially a more rigid test.

## RESULTS AND DISCUSSION

The results have been presented in the accompanying tables. However, some introductory comments are neccessary:

(1) Instead of examining the whole brain we examined the BSH portion alone. This was because, we saw in a previous work (4) that exogenous FSS, with this protocol, failed to produce a significant change in the [NTs] in the cerebral hemispheres. Further the main trunks of important aminergic tracts, their important sources (like *locus ceruleus*) are situated in the brain stem.

(2) Although the estimations of NA, DA, 5-HT and H were made from the same sample of BSH, for some reason or other, estimation in some samples could not be completed. This explains why the values of *n* have differed in between the same batches during the estimation of NA, DA, 5-HT and H.

**[GABA]**. OVx rats, receiving only E shows a fall in [GABA] in BSH whereas OVx rats receiving P after being primed with E shows a rise in [GABA] in the same area of brain tissue (Table I). The results are consistent. This shows (exogenous) E causes a fall in [GABA] but (exogenous) P not only prevents this fall but causes a definite elevation of [GABA]. This observation fits well with the general conception that P is antiepileptic and on the whole is sedative to the brain (9). The same trend was noted in male rats, whether +Te (Table II) or $Te_x$ (Table III). The results strongly suggest, E causes fall of [GABA] in both male and female brains.

Long ago, Wooley and Timiras (10) showed E treated rats become more prone to experimentally produced seizures whereas P treated rats show the opposite trend. A very recent publication (11) shows that P has a barbiturate like effect on experimental epilepsy in cat. It may be recalled, barbiturates potentiate GABA activity. Further, P has GABA agonist like effect (12).

TABLE I : Effects of progesterone on brain neurotransmitters in OVx rats.

| *OVx* | *GABA* µg/gm | *NA* µg/gm | *Serotonin* µg/gm | *Dopamin* µg/gm | *Histamine* µg/gm |
|---|---|---|---|---|---|
| Control | 353±1.85 n=10 | 0.42±.06 n=6 | 0.53±.001 n=6 | 0.05±.007 n=4 | 0.15±.01 n=4 |
| Vs | 366±2.43 n=10 | 0.26±.02 n=5 | 0.72±.031 n=6 | 0.06±.02 n=4 | 0.18±.02 n=4 |
| Expt. (UDE+UDP) | P < .001 | P < .05 | P < .001 | N.S. | N.S. |
| Control | 345±1.85 n=10 | 0.40±.004 n=6 | 0.54±.056 n=4 | 0.05±.01 n=6 | 0.12±.01 n=4 |
| Vs | 358±2.06 n=10 | 0.24±.028 n=6 | 0.84±.112 n=4 | 0.04±.006 n=6 | 0.13±.004 n=4 |
| Expt. (UDE + 2DP) | P < .001 | P < .05 | P < .02 | N.S. | N.S. |
| Control | 349±1.86 n=10 | 0.41±.063 n=6 | 0.54±.009 n=4 | 0.06±.013 n=4 | 0.12±.01 n=4 |
| Vs | 361±2.03 n=10 | 0.27±.01 n=6 | 0.92±.009 n=4 | 0.07±.016 n=4 | 0.10±.002 n=4 |
| Expt. (2DE+UDP) | P < .001 | P < .05 | P < .02 | N.S. | N.S. |
| Control | 347±1.85 n=10 | 0.40±.007 n=6 | 0.55±.009 n=4 | 0.05±.013 n=6 | 0.15±01 n=4 |
| Vs | 362±2.007 n=10 | 0.26±.005 n=6 | 0.92±.009 n=4 | 0.06±.008 n=6 | 0.20±0.01 n=4 |
| Expt. (2DE+2DP) | P < .001 | P < .05 | P < .01 | N.S. | N.S. |
| Control | 350±1.63 n=10 | 0.48±.005 n=6 | 0.53±.088 n=6 | 0.06±.022 n=6 | 0.16±.031 n=6 |
| Vs | 340±1.45 n=10 | 0.06±.005 n=5 | 0.12±.066 n=6 | 0.05±.006 n=5 | 0.19±.022 n=6 |
| Expt. (UDE) | P < .001 | P < .001 | P < .01 | N.S. | N.S. |
| Control | 350±1.87 n=10 | 0.51±.162 n=6 | 0.50±.045 n=4 | 0.05±.005 n=6 | 0.12±.01 n=4 |
| Vs | 343±1.39 n=10 | 0.03±.005 n=6 | 0.33±.008 n=4 | 0.04±01 n=6 | 0.1±.002 n=4 |
| Expt. (2DE) | P < .01 | P < .02 | P < .02 | N.S. | N.S. |

TABLE II : Effect of progesterone on brain neurotransmitters in testis + in male rats.

| *Testis +* | *GABA* µg/gm | *NA* µg/gm | *Serotonin* µg/gm | *Dopamin* µg/gm | *Histamine* µg/gm |
|---|---|---|---|---|---|
| Control | 780±2.27 n=10 | 0.73±.007 n=6 | 0.72±.009 n=4 | 0.09±.011 n=6 | 0.50±.003 n=6 |
| Vs | 790+1.94 n=10 | 0.56±.012 n=6 | 0.91±.013 n=4 | 0.06±.018 n=5 | 0.47±.006 n=6 |
| Expt. (UDE+UDP) | P < .001 | P < .001 | P < .05 | N.S. | P < .001 |
| Control | 778±1.10 n=10 | 0.71±.024 n=5 | 0.76±.009 n=4 | 0.08±.023 n=5 | 0.47±.018 n=4 |
| Vs | 786±1.01 n=10 | 0.52±.037 n=6 | 0.86±.009 n=4 | 0.06±.018 n=4 | 0.44±.009 n=4 |
| Expt. (UDE + 2DP) | P < .001 | P < .001 | P < .01 | N.S. | N.S. |
| Control | 775±.75 n=10 | 0.71±.03 n=6 | 0.72±.008 n=4 | 0.09±.01 n=6 | 0.47±.009 n=4 |
| Vs | 779±.59 n=10 | 0.53±.08 n=6 | 0.91±.007 n=4 | 0.06±.002 n=4 | 0.44±.007 n=4 |
| Expt. (2DE+UDP) | P < .001 | P < .01 | P < .001 | P < .05 | P < .02 |
| Control | 778±2.36 n=10 | 0.75±.008 n=6 | 0.74±.008 n=4 | 0.07±.011 n=4 | 0.49±.005 n=6 |
| Vs | 791±1.93 n=10 | 0.69±.008 n=5 | 0.93±.007 n=4 | 0.06±.004 n=4 | 0.46±.008 n=5 |
| Expt. (2DE+2DP) | P < .001 | P < .01 | P < .001 | N.S. | P < .02 |
| Control | 783±.57 n=10 | 0.70±.007 n=4 | 0.73±.009 n=4 | 0.09±.024 n=6 | 0.52±.005 n=6 |
| Vs | 778±.98 n=10 | 0.63±.012 n=4 | 0.55±.009 n=4 | 0.06±022 n=6 | 0.50±.005 n=6 |
| Expt. (UDE) | P < .001 | P < .01 | P < .001 | N.S. | P < .05 |
| Control | 781±.82 n=10 | 0.73±.008 n=4 | 0.72±.009 n=4 | 0.09±.003 n=6 | 0.52±.006 n=6 |
| Vs | 776±.58 n=10 | 0.66±.008 n=4 | 0.53±.009 n=4 | 0.11±012 n=6 | 0.49±.008 n=6 |
| Expt. (2DE) | P < .001 | P < .01 | P < .001 | N.S. | P < .02 |

TABLE III : Effect of progesterone on brain neurotransmitters in $Te_X$ rats.

| *Testis +* | *GABA* µg/gm | *NA* µg/gm | *Serotonin* µg/gm | *Dopamin* µg/gm | *Histamine* µg/gm |
|---|---|---|---|---|---|
| Control | 412±1.86 n=10 | 0.25±.009 n=4 | 0.32±.014 n=6 | 0.05±.02 n=4 | 0.72±.009 n=4 |
| Vs | 422+.62 n=10 | 0.13±.009 n=4 | 0.51±.01 n=6 | 0.07±.02 n=4 | 0.69±.009 n=4 |
| Expt. (UDE+UDP) | P < .001 | P < .05 | P < .001 | N.S. | P < .05 |
| Control | 409±.63 n=10 | 0.26±.016 n=4 | 0.31±.008 n=4 | 0.07±.02 n=4 | 0.72±.01 n=4 |
| Vs | 414±.81 n=10 | 0.14±.008 n=4 | 0.52±.008 n=4 | 0.05±.007 n=4 | 0.69±.009 n=4 |
| Expt. (UDE + 2DP) | P < .001 | P < .02 | P < .001 | N.S. | N.S. |
| Control | 407±.87 n=10 | 0.25±.008 n=4 | 0.28±.0001 n=4 | 0.06±.011 n=6 | 0.68±.009 n=4 |
| Vs | 415±2.23 n=10 | 0.10±.004 n=4 | 1.48±.0001 n=4 | 0.06±.013 n=4 | 0.51±.009 n=4 |
| Expt. (2DE+UDP) | P < .001 | P < .01 | N.S. | P < .001 | P < .001 |
| Control | 406±.82 n=10 | 0.25±.005 n=4 | 0.26±.085 n=4 | 0.06±.004 n=4 | 0.74±.009 n=4 |
| Vs | 427±.7 n=10 | 0.13±.007 n=4 | 0.74±.085 n=4 | 0.04±.009 n=4 | 0.68±.009 n=4 |
| Expt. (2DE+2DP) | P < .001 | P < .001 | P < .02 | N.S. | P < .01 |
| Control | 417±.82 n=10 | 0.24±.01 n=4 | 0.22±.009 n=4 | 0.06±.014 n=4 | 0.66±.015 n=4 |
| Vs | 412±.74 n=10 | 0.12±.01 n=4 | 0.12±.009 n=4 | 0.08±.021 n=4 | 0.65±.01 n=4 |
| Expt. (UDE) | P < .001 | P < .01 | P < .01 | N.S. | N.S. |
| Control | 414±.817 n=10 | 0.25±.009 n=4 | 0.25±.009 n=4 | 0.05±.006 n=5 | 0.69±.009 n=4 |
| Vs | 410±.699 n=10 | 0.11±.007 n=4 | 0.13±.009 n=4 | 0.04±.011 n=6 | 0.68±.009 n=4 |
| Expt. (2DE) | P < .001 | P < .001 | P < .001 | N.S. | N.S. |

Excess GABA activity is expected to reduce anxiety (many anxiolytic drugs act via this mechanism). In our previous communication (1), we reported that P has a protective action against anxiety. It is possible, this protective action is GABA mediated.

However, when the values of [GABA] are compared between intact and castrated males as well as between castrated males and females (by interpolating TI, TII and TIII), one is struck with some arresting features: the [GABA] in +Te rats are much higher than those of castrated males (Table IV) or female rats. This suggests that testosterone itself and/or other testicular hormones/chemicals cause elevation of [GABA] in the BSH. Further [GABA] remains higher in castrated male than castrated female rats (Table V).

Hartman and co-workers showed (13) that depression of GABA activity causes a very sharp rise of LH secretion in E primed rats. Sharp rise of LH secretion ("LH surge") occurs just prior to ovulation and LH surge is fundamentally due to sharp elevation of the level of E in the body. One wonders, whether our finding, viz, fall of [GABA] due to E is the link between preovulatory rise of E level and LH surge.

[**NA**]. In OVx rats, E alone or E followed by P caused a fall in noradrenaline concentration in the BSH compared to Co OVx rats not receiving any FSS. Our results, thus tally with those of Tonge and Greenglass (2) who showed similar results in "midbrain" of OVx rats. However, their "midbrain" consisted of hippocampus, hypothalamus, striatum and thalamus. It would be seen that the most important area, the hypothalamus was common to their "midbrain" as well as our BSH.

Apparently at least, in the OVx rats, the fall in NA level is much greater in rats treated with E only, than the same in those treated by E followed by P. However, this difference was not treated statistically because, strictly

TABLE IV : Effects of castration in male rats (values in µgm/gm of BSH).

| | *GABA* | *NA* | *5-HT* | *DA* | *H* |
|---|---|---|---|---|---|
| +Te rats | 779 ± 1.14<br>n = 60 | 0.72 ± .008<br>n = 29 | 0.73 ± .004<br>n = 24 | 0.09 ± .005<br>n = 26 | 0.49 ± .005<br>n = 32 |
| $Te_X$ rats | 411 ± 1.74<br>n = 60<br>P < .001 | 0.25 ± .003<br>n = 24<br>P < .001 | 0.27 ± .008<br>n = 26<br>P < .001 | 0.06 ± .005<br>n = 25<br>P < .001 | 0.70 ± .006<br>n = 24<br>P < .001 |

TABLE V : Castrated male vs. castrated female rats (values in µgm/gm of BSH).

| | *GABA* | *NA* | *5-HT* | *DA* | *H* |
|---|---|---|---|---|---|
| $OV_X$ | 349 ± 1.12<br>n = 60 | 0.41 ± .019<br>n = 36 | 0.53 ± .02<br>n = 28 | 0.05 ± .006<br>n = 32 | 0.14 ± .009<br>n = 26 |
| $Te_X$ | 411 ± 1.74<br>n = 60<br>P < .001 | 0.25 ± .003<br>n = 24<br>P < .001 | 0.27 ± .008<br>n = 26<br>P < .001 | 0.06 ± .005<br>n = 25<br>P < .001 | 0.70 ± .006<br>n = 24<br>P < .001 |

speaking, these two groups were not comparable. (Rats treated by E alone were killed after 36 hrs whereas those treated by E+P survived an additional 20 hrs). Yet the values of NA are so glaringly different that one is tempted to suspect that while E causes a fall of NA level additional treatment of P retrieves the situation to some extent, ie. P acts in the opposite direction to that of P. This suspicion is strengthened by other corroborative evidences: (i) in case of 5-HT levels (see below) the trend is similar (ii) in many other fields P acts in the direction opposite to that of E, (iii) in our previous work (1) we found that P has a protective action against depression (fall of NA is associated with depression). However, beyond this, a firmer committment cannot be made at this stage because, the phenomenon can be explained by other explanations too.

Fall of [NA] was seen also in male rats, both in +Te as well as $Te_X$ series (Tables II and III) in E or E and P treated rats (T II and III). Castration by itself caused a fall of the value of [NA] (Table IV). Further, the [NA] of castrated males have a lower value than that of the castrated females (Table V). We are unable to compare our results with those of anybody else for as far as we have searched the literature, there is no comparable work. As for the human counterpart, it will be interesting to note whether healthy but very old males (ie, males with low androgen value) show any significant behavioral changes from those of the menopausal female, in respect to behaviors where NA plays a part (viz. sleep/depression/anxiety/appetite and so on).

**[5-HT]**. In $OV_X$ rats (Table I) E alone causes a fall in 5-HT level, but E followed by P causes rise of the same. In soft shelled turtles, Mahata and Mahata (14) showed that E causes a fall in 5-HT level in 'pineal and paraphyseal complex' but P caused a rise in 5-HT level. On the other hand, Tonge and Greenglass (2) observed that levels of 5-HT rises following P therapy but E alone has no effect. Incidentally, serotoninergic neurons contain P receptors (15) and one anticipates P should influence the 5-HT level and/or its metabolism. The same trend was maintained in castrated as well as in intact male rats (Table II and III).

Castration itself (Table IV) lowers 5-HT. Further 5-HT level is lower in castrated males than that in castrated females (Table V).

There can be at least two possible significance of rise of 5-HT level (induced by P): female sex behavior (eg. sex receptivity) is known to depend on the 5-HT. A rise of 5-HT level causes development of female sex behavior (16). For the development of female sex behavior fully, together with E, P is also needed (3); thus the P induced rise of 5-HT may be the explanation of the role played by P in the development of female sex behavior. (ii) Fall of NA level (induced by E) should cause depression. In our current work we noted, although subsequent addition of P perhaps retrieves the situation, the NA level still remains lower than the control. It is possible, rise of 5-HT level protects the subject further from developing into depression. Incidentally, fall of 5-HT level can cause depression; also it is well known that some antidepressant drugs act by increasing the local availability of 5-HT in the CNS.

[**DA**]. For practical purposes, FSS does not influence [DA] in $OV_X$ +Te or $Te_X$ rats. This therefore does not support the observation of other workers (2) but support our own previous work (4). However, castration in males causes a fall in DA level (Table IV). Further, castrated males have lower levels in brain than that in castrated females.

[**H**]. Literature on [H] in this field is very meager. In castrated females, FSS have no effect (Table I) on the H level. In males, the H level generally falls in intact ones (Table II) but the trend although present is less consistent in the castrated (Table III) animals. Castration itself raises (Table IV) the level of H in males. The level of H is much higher (Table V) in the brains of castrated males than that in the castrated females. It is not easy to speculate on the significance of the changes of [H] with FSS as the function of H itself is an enigma.

In summary, the major findings of this paper, hitherto (as far as we are aware of) unreported, include : (i) castration in male rats causes a fall of the concentrations of GABA, NA, 5-HT and DA but a rise in H in a part of brain referred as BSH in this paper. (ii) Castrated males have higher concentrations of GABA and H, but lower levels of NA and 5-HT and DA than their female counterparts, in the BSH. (iii) E followed by P treatment causes fall in the concentrations of NA in castrated as well as intact males but produces a rise in [GABA] as well as [5-HT] in $OV_X$ females and males (both +Te and $Te_X$). (4) However, E alone causes fall of [GABA] in [5-HT] in rats of every type ($OV_X$ +Te, $Te_X$).

Note, according to this paper, testicular secretions (presumably testosterone) have some effects which are opposite of those produced by E. In intact males, [GABA], [NA] and [5-HT] are higher than those of their castrated counterparts; also E causes a fall of the level of these very NTs. Obviously, it is logical to conclude testosterone and E have opposite effects on the levels of these NTs in the CNS (and might be the causes of some differences seen between male and female behavioral pattern).

## ACKNOWLEDGEMENTS

The authors thank (i) M/s. Organon Laboratories (Infar) for supplying drugs free of cost and providing laboratory facilities, (ii) Director, Institute of Chemical Biology, Jadavpur for providing laboratory facilities, (iii) Prof (Dr.) M. Chakravorti, Director, School of Tropical Medicine and Prof.-Director of Virology of the same institute for providing various helps including laboratory facilities. The authors also thank (iv) Dr. P.B. Pathak, Principal, Medical College, Calcutta, (v) Dr. H.N. Das, Asstt. Prof. of Biochemistry, Medical College and (vi) Shri Sukdev De Chaudhuri, Laboratory Asstt. Deptt of Physiology for various helps. The authors also thank Mr. A Sen, Proprietor and Mr. N. Radhakrishnan, Composer of New Central Publishing Agency P. Ltd., for various helps in composition.

## REFERENCES


1. Chaudhuri SK, Das A, De KC, Ghosh Malati. Some hitherto unreported findings on the estragenital effects of progesterone. A clinical study. *Indian J Physiol Pharmacol* 1994; 30:174-180.
2. Tonge SR, Greenglass PM. The acute effeccts of estrogen and progesterone on the monoamine levels of the brain of ovariectomized rats. *Psychopharmacologia* 1971; 121:374-381.
3. McEwen BS, Parsons B. Gonadal steroidal action on the brain : neuro chemistry and neuro pharmacology. *Ann Rev Pharmacol Toxicol* 1982; 22:555-598.
4. Chaudhuri SK, Chattopadhyaya RN, Maitra SK, Ray S, Chaudhuri Srabani. Effects of progesterone on some brain neurotransmitters in intact rats. *Indian J Physiol Pharmacol* 1992; 36:255-258.
5. Dichter MA. The epilepsies and convulsive disorders, in *Harrisons's Principals of Internal Medicine* (eds) Wilson JD, Braun Wald E, Isselbacher K, Peterdorsf RG, Martin IB, Fauci AS, Root RK. McGraw Hill, International Edn. 12th Edn, 1991. Chap. 350.
6. Bapna J, Neff NH, Costa E. A method for studying norepinephrine and serotonin metabolism in small regions of rat brain : effect of ovariectomy on amine metabolism in anterior and posterior hypothalamus. *Endocrinlogy* 1971; 89:1345-1350.
7. Sadavongovivad C. Pharmacological significance of biogenic amines in the lung 5-hydroxytryptamine. *Br J Pharmacol* 1970; 38:353-365.
8. Lowe IP, Robins E, Eyerman GS. The flurimetric measurement of glutamate decarboxylase and its distribution in brain. *J Neurochemistry* 1958; 3:8-18.
9. Backstrom T, Bizo M, Hammarback S. Ovarian steroid hormones, effects on mood, behavior and brain excitability. *Acta Obst Gynaecol Scand* 1985; Supple 130:19-24.
10. Wooley D, Timiras PS. The gonad brain relationship: effects of female sex hormones on electroshock convulsions in the rat. *Endocrinology* 1962; 70:196-209.
11. Tauboll E, Lindstrom S. The effect of progesterone and its metabolite 5 alpha-pregnan-3 alpha-01-20 one on focal epileptic seizures in the cat's visual cortex. *Epilepsy Res* 1993; 14:17-30.
12. Finn DA, Gee KW. The influence of estrus cycle on neurosteroid potency at the gamma aminobutyric acid - A receptor complex. *J Pharmacol Exp Ther* 1993; 265:1374-1379.
13. Hartman RD, He JR, Barra Clough CA. Gamma aminobutyric acid - A and - B receptor antagonists increase leuteinizing hormone releasing hormone neuronal responsiveness to intraventricular norepinephrine in ovariectomized estrogen treated rats. *Endocrinology* 1990: 127:1336-1345.
14. Mahata M and Mahata SK. Effects of steroid hormones on serotonin, norepinephrine and epinephrine contents in the pineal paraphyseal complex of the soft shelled turtle. *J Comp Physiol B*. 1992; 162:520-525.
15. Bethea L. Localization of progestin receptors with serotonin in rapheneurons of macaque. *Neuroendocrinology* 1993; 57: 1-6.
16. Wilson CA, Hunter AJ. Progesterone stimulates sexual behaviour in female rats by increasing 5-HT activity on 5-$HT_2$ receptors. *Brain Research* 1985; 333: 223-229.