LETTER TO THE EDITOR

EFFECT OF CHLORPROMAZINE AND PROCHLORPERAZINE ON Y-AMINOBUTYRIC ACID (GABA) CONTENT OF RAT BRAIN

Sir,

The administration of phenothiazine tranquillizers produce depression of central nervous system (CNS) (2), but large doses of these drugs show signs of stimulation (4). A significant correlation between Y-aminobutryic acid (GABA) content in brain and excitability has been suggested, a reduction in brain GABA content being accompanied by an increase in brain excitability (9). On the other hand, drugs like phenobarbitone, prominal, primidone, diphenylhydantion, mesantion and diazepam increase GABA content in brain (6, 7, 8). This property has been suggested to be a probable mechanism by which anticonvulsant drugs produce their action (8). There are no reports on the effects of phenothiazine tranquillizers on the GABA content of brain. We have examined the effects of chlorpromazine and prochlorperazine on the GABA content of rat brain.

The determination of GABA was based on the method described by Saad (5).

The mean control GABA content in the rat brain was 391 ± 21 $\mu g/g$ wet tissue. This result is in agreement with previous findings (3,5). The effects of different doses of chlorpromazine or prochlorperazine at 1 hr after i.p. injection on rat brain GABA level is summarized in Table I.

TABLE I: GABA content in the brain of rats 1 hr after i.p. administration of different doses of chlorpromazine (I) or prochlorperazine (II). The results represent mean ± SD of groups of 10 rats for each dose of each drug. Figures in parenthesis indicate % increase or decrease of GABA content in relation to the control level.

Chlorpromazine (I) or prochlorperazine (II) (mg/kg)	*Mean GABA content (μg/g wet tissue)* I	II
0.2	458 ± 42 (17%)*	479 ± 44 (22%)*
0.5	512 ± 46 (30%)*	501 ± 45 (28%)*
2	556 ± 48 (42%)*	458 ± 41 (17%)*
5	578 ± 45 (50%)*	402 ± 34 (3%)*
10	475 ± 43 (21%)*	Not done
25	340 ± 24 (13%)*	287 ± 26 (26%)*
50	318 ± 22 (18%)*	203 ± 11 (48%)*
100	219 ± 10 (43%)*	192 ± 8 (50%)*
Controls		391 ± 21

*Significant difference from the control ($P < 0.001$).

Chlorpromazine in doses of 0.2 to 5 *mg/kg*, and prochlorperazine in doses of 0.2 and 0.5 *mg/kg* significantly increased the normal GABA content of the rat brain (17 to 50% with chlorpromazine, and 22 and 28% with prochlorperazine), but doses of 10 *mg/kg* chlorpromazine, and 2 and 5 *mg/kg* prochlorperazine increased the GABA content by only 21, 17 and 3% respectively over the control level. With still larger doses (25, 50 and 100 *mg/kg*) of chlorpromazine or prochlorperazine, the GABA content of the rat brain was significantly reduced below the normal level.

The alterations in the normal GABA content of rat brain with different doses of chlorpromazine or prochlorperazine seem to reflect the activity of the CNS depending on the size of the dose used. The quantitatively reduced increase of the GABA level with 10 *mg/kg* chlorpromazine or 2 and 5 *mg/kg* prochlorperazine (Table I) compared to 5 *mg/kg* chlorpromazine or 0.5 *mg/kg* prochlorperazine may be indicative of a change in the activity of the CNS.

Chlorpromazine in doses of 20 *mg/kg* has been found to cause high voltage discharges in the hippocampus and amygdala (rhinencephalic seizure activity), and with still larger doses (35 to 40 *mg/kg*), the seizure activity spreads to the cortex (1).

In the light of these observations, the reduction in the brain GABA level below normal with large doses (25 to 100 *mg/kg*) of chlorpromazine or prochlorperazine (Table-I) may indicate a state of stimulation of the CNS.

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