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### Isolation, aggressiveness and brain 5-hydroxytryptamine turnover

SIR,—Male albino mice submitted to prolonged isolation showed a smaller increase in brain 5-hydroxytryptamine (5-HT) compared with normal animals, when treated with monoamine oxidase inhibitors (Valzelli, 1966). The present report supplies additional quantitative evidence using the method of Tozer, Neff & Brodie (1966) to calculate the turnover of brain 5-HT.

Male Swiss albino mice,  $20 \pm 2$  g, were isolated (1 animal/cage) or grouped (10 animals/cage) for 4 weeks under the conditions previously described (Consolo, Garattini & Valzelli, 1965). At the end of 4 weeks, isolated and grouped animals received an intraperitoneal injection of tranlycypromine (20 mg/kg). Animals were killed at various times after tranlycypromine injection and their brains analysed for 5-HT (Shore, 1959) and for 5-hydroxyindoleacetic acid (5-HIAA) (Giacalone & Valzelli, 1966).

It is evident that while the level of brain 5-HT is comparable in the two experimental conditions (Table 1), there is always a small but significant decrease of brain 5-HIAA in isolated compared with grouped mice.

The administration of tranlycypromine induces an increase of brain 5-HT and a decrease of brain 5-HIAA, which are respectively linear on a normal or on a logarithmic scale (see Fig. 1) in grouped or isolated animals. However the slope of the curves was different, which indicated an increase in the turn-

TABLE 1. LEVELS OF BRAIN 5-HT AND 5-HIAA IN ISOLATED AND GROUPED MICE

| Experiment No. | Isolated mice   |                   | Grouped mice    |                 |
|----------------|-----------------|-------------------|-----------------|-----------------|
|                | 5-HT            | 5-HIAA            | 5-HT            | 5-HIAA          |
| 1              | 0.65 $\pm$ 0.02 | 0.32 $\pm$ 0.01*  | 0.65 $\pm$ 0.03 | 0.41 $\pm$ 0.01 |
| 2              | 0.81 $\pm$ 0.03 | 0.42 $\pm$ 0.02** | 0.80 $\pm$ 0.02 | 0.51 $\pm$ 0.01 |
| 3              | 0.75 $\pm$ 0.01 | 0.41 $\pm$ 0.01*  | 0.76 $\pm$ 0.01 | 0.49 $\pm$ 0.01 |
| 4              | 0.70 $\pm$ 0.02 | 0.34 $\pm$ 0.01** | 0.71 $\pm$ 0.02 | 0.38 $\pm$ 0.01 |

\* =  $P < 0.01$ .

\*\* =  $P < 0.05$ .

Figures represent  $\mu\text{g/g} \pm \text{s.e.}$

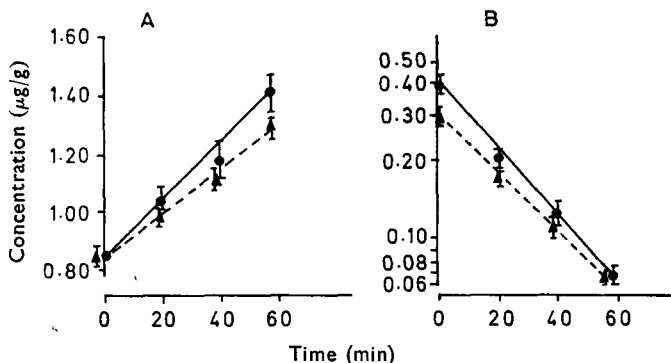


FIG. 1. Increase of brain 5-HT (A) and decrease of brain 5-HIAA (B) after tranlycypromine (20 mg/kg i.p.) in normal (●—●) and in isolated aggressive (▲---▲) mice. On the ordinates the levels of 5-HT or 5-HIAA in µg/g of brain; on the abscissae the time (min) after tranlycypromine administration. The vertical bars represent the standard error of the mean. Each point is based on 8 determinations.

over time of brain 5-HT of about 57% in isolated compared with grouped mice (see Table 2). The reason for this change is probably not related to a different level of tranlycypromine in the brain of isolated or grouped mice (Valzelli, 1966).

TABLE 2. DYNAMIC ASPECTS OF 5-HT METABOLISM IN BRAIN OF ISOLATED AND GROUPED MICE AFTER TRANLYCYPROMINE ADMINISTRATION

|                                      | Isolated mice | Grouped mice |
|--------------------------------------|---------------|--------------|
| [5-HT] <sub>0</sub> µg/g .. .. .     | 0.84 ± 0.02   | 0.84 ± 0.04  |
| [5-HIAA] <sub>0</sub> µg/g .. .. .   | 0.29 ± 0.01*  | 0.38 ± 0.01  |
| Rate constant of 5-HIAA loss .. .. . | 1.42 ± 0.08   | 1.69 ± 0.12  |
| 5-HT turnover rate, µg/g/hr .. .. .  | 0.38          | 0.59         |
| 5-HT turnover time, min .. .. .      | 122           | 79           |

\* =  $P < 0.01$ .

The calculations were made according to Tozer & others (1966).

Since the mice invariably became aggressive after 4 weeks of isolation, the changes observed in brain 5-HT turnover suggest possible correlations between behavioural changes and central metabolism of 5-HT. The data also show that changes in 5-HT turnover are not necessarily reflected in the level of brain 5-HT.

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