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# SHORT COMMUNICATIONS

## The influence of quipazine on the turnover rate of serotonin

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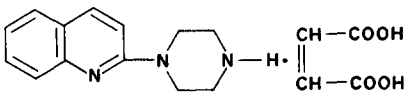
QUIPAZINE (2-(l-piperazinyl)quinoline maleate) is reported to stimulate both peripheral and central serotoninergic receptors.[1–3] The receptor stimulation could result in the elicitation of a feed-back mechanism, causing a compensatory reduction of serotonin utilization leading to a decrease in the concentration of the main serotonin metabolite, 5-hydroxyindoleacetic acid (5-HIAA). LSD, regarded as a stimulant of the serotonin receptor,[4] decreased the brain 5-HIAA level in rats.[5]




2-(1-Piperazinyl) Quinoline maleate

The concentration of serotonin in rat brain was not changed after quipazine administration.[6] We investigated the influence of quipazine on the brain 5-HIAA level and on the turnover rate of serotonin in male Wistar rats (120–160 g). 5-HIAA was estimated by the method of Miller *et al.*[7] The turnover rate of serotonin was calculated from the rate of decline of 5-HIAA in brain after inactivation of monoamine oxidase (MAO).[8]

Quipazine significantly lowered the 5-HIAA level in rat brain (Table 1). This effect may be due to: (a) diminished utilization of serotonin, (b) disturbance in its catabolism, (c) inhibition of reuptake of serotonin into neurons. Quipazine did not affect MAO activity[6] but the inhibition of uptake of labelled serotonin, recently described,[9] should be taken into consideration.

In further experiments we investigated the influence of quipazine on the 5-HIAA concentration in brain of rats pretreated with BOL (D-2 bromolysergic acid diethylamide) or methysergide, both regarded as drugs blocking serotonin receptors.[10–13] No changes in 5-HIAA levels were noticed after quipazine administration under these conditions (Table 1). Similar antagonism against quipazine action was also described in pharmacological and EEG experiments.[1,2,14]

TABLE 1. THE INFLUENCE OF QUIPAZINE ON BRAIN 5-HIAA CONCENTRATION IN NORMAL AND IN SEROTONINOLYTIC-PRETREATED RATS

| Drug treatment (mg/kg) | Time after quipazine or saline administration (min) | 5-HIAA ng/g ± S.E.M. |
|---|---|---|
| Saline | 120 | 672·1 ± 25·5 |
| Quipazine 2·5 | 60 | 486·6 ± 39·2* |
| Quipazine 2·5 | 180 | 534·2 ± 21·9* |
| Quipazine 10·0 | 60 | 484·4 ± 53·3* |
| Quipazine 10·0 | 180 | 372·3 ± 24·6* |
| Saline | 60 | 545·0 ± 10·3 |
| Quipazine 2·5 | 60 | 389·4 ± 12·2† |
| BOL 2·0 + quipazine 2·5 | 60 | 549·0 ± 18·9† ‡ |
| Methysergide 5·0 + quipazine 2·5 | 60 | 536·5 ± 16·5† ‡ |
| BOL 2·0 | — | 542·0 ± 11·4 |
| Methysergide 5·0 | — | 538·9 ± 9·7 |

* $P < 0.01$, † $P < 0.001$.
‡ Statistical significance in comparison with respective quipazine treated group.
Statistical significance was evaluated by the Student's *t*-test.
Each group consisted of 6–8 rats.
BOL and methysergide were administered 20 min before quipazine. All compounds were injected i.p.

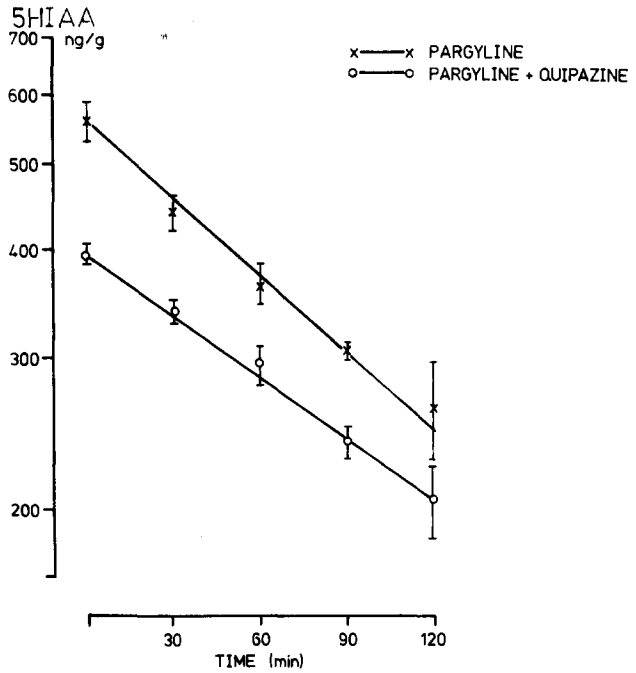



FIG. 1. The influence of quipazine (2·5 mg/kg) on the brain 5-HIAA concentration in rats treated with pargyline (75·0 mg/kg). Each group consisted of eight animals.

To study the synthesis rate of serotonin under the influence of quipazine the latter was given 60 min before the MAO inhibitor pargyline. We found previously that between 60 and 120 min after quipazine administration, 5-HIAA content in brain decreased to about 72 per cent of control value. The results are presented in Fig. 1. The turnover rate and turnover time of serotonin in rats, injected with pargyline alone are 0·236 $\mu g\ g^{-1}\ hr^{-1}$ and 141 min, respectively, while the same values in rats pretreated with quipazine are 0·101 $\mu g\ g^{-1}\ hr^{-1}$ and 234 min.

These results indicate that quipazine reduces the turnover rate of brain serotonin due to the stimulation of central serotoninergic receptors.

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