the dorsal tegmental decussation may be involved in this behavioural response.

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Comparison of the central nervous system actions of taurine and N-pivaloyltaurine

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Biochemical and neurophysiological evidence suggests that taurine functions as an inhibitory neurotransmitter in the central nervous system (Oja & Lähdesmäki, 1974). Taurine is also known to depress motor behaviour and alter cerebral dopamine metabolism (Garcia de Yebenes Prous, Carlsson & Mena Gomez, 1978). Its behavioural and other central nervous system effects are, however, difficult to study, because it only slowly penetrates the blood-brain barrier. This problem could be solved by developing a pro-drug from taurine, i.e. a more lipid soluble derivative which would be converted back to taurine in the brain. For this purpose N-acetyl-, N-propionyl- and N-pivaloyltaurine were synthetized and their actions compared to those of taurine. The derivatives were prepared by applying a modified Schotten-Baumann's method starting from taurine and using a corresponding acid chloride for direct acylation reactions.

Taurine and the derivatives were administered i.p. to white mice weighing 27–31 g. The tests used were: (1) Modification of sleeping time induced by pentobarbitone sodium (40 mg/kg i.v.). (2) Measurement of locomotor activity in Animex Activity Meter at 10 min intervals for 3 h. (3) Modification of morphine (3 mg/kg, s.c.) -induced antinociception (hot plate method). (4) Measurement of cerebral dopamine (DA) concentration in control and α-methyl-*p*-tyrosine (α*M*p*T*; 250 mg/kg, 1 h) -treated mice. Tests 1, 2 and 4 were done in the morning (08–13 h), test 3 in the afternoon (13–16 h).

Taurine (1–10 mmol/kg), N-acetyltaurine (3 mmol/kg) and N-propionyltaurine (0.3–3 mmol/kg) did not significantly lengthen the pentobarbitone sleeping time in the forenoon but N-pivaloyltaurine (0.3–3 mmol/kg) increased it by about 30% ($P < 0.05$); all doses causing about similar increases. Because of the inactivity of N-acetyl- and N-propionyltaurine in this test, their effects were not further studied. Taurine decreased the spontaneous activity of mice during the first 10 min after its administration by 35% (3 mmol/kg; $P < 0.05$) and 44% (10 mmol/kg; $P < 0.001$), but not at any later time point studied. On the other hand, N-pivaloyltaurine (1 mmol/kg) did not alter the activity of mice during the first 10 min after its administration, but reduced it by 40–50% ($P < 0.05$–0.01) at 10–60 min after administration. Taurine (6 mmol/kg) and N-pivaloyltaurine (1 mmol/kg) slightly antagonized the antinociceptive affect of morphine in the hot plate method. N-pivaloyltaurine (10 mmol/kg) increased the brain DA concentration in α*M*p*T*-treated mice (from 0.67 ± 0.02 μg/g to 0.84 ± 0.05 μ/g; mean ± s.e. mean, $n = 4$, $P < 0.02$), and tended to increase it in the control mice, too. Taurine (10 mmol/kg) did not cause any changes in cerebral DA concentration.

Our results suggest that N-pivaloyltaurine penetrates to the brain and is there converted into taurine. Thus N-pivaloyltaurine could be used to study the behavioural and other central nervous system actions of taurine.

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