# Microelectrophoretic effects of (±) cis – 1,3-aminocyclohexane carboxylic acid on nigral neurones in control and tetanus toxin treated rats

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The conformationally restricted analogue of γ-aminobutyric acid (GABA), cis-1,3-aminocyclohexane carboxylic acid (ACHC) has been reported to selectively inhibit neuronal GABA transport *in vitro* (Bowery, Jones & Neal, 1976). If local inactivation of GABA does indeed occur via cellular uptake, selective inhibition of GABA transport should result in enhancement and prolongation of its effects after both synaptic release and exogenous administration. To test this hypothesis the effects of microlectrophoretically released ACHC was determined on GABA induced depression and on bicuculline sensitive synaptic inhibition of single substantia nigra neurones in control rats and on GABA-induced depression in tetanus toxin pretreated rats. (Tetanus toxin abolishes bicuculline sensitive synaptic inhibition in the nigra (Davies & Tongroach, 1977).

Experiments were performed on rats anaesthetized with urethane (1.2–1.4 g/kg i.p.). Extracellular recordings were obtained from single spontaneously firing nigral neurones via the centre barrel (4M NaCl) of a 7 barrel microelectrode. The following substances were ejected from the outer barrels using standard microelectrophoretic techniques: GABA (0.5M pH 3.5), glycine (0.5M pH 3.5), ACHC (0.5M pH 3.5) (±)-homocysteate (0.2M pH 7), bicuculline methochloride (0.005M in 0.165M NaCl) and pontamine sky blue. Synaptic inhibition was evoked in the nigra by means of a bipolar stimulating electrode located in the ipsilateral caudate nucleus. Some animals were pretreated with tetanus toxin ($10^2$–$10^3$ mouse MLD). The toxin (0.5–1μl) was introduced into the substantia nigra via a micrometer syringe and glass micropipette (tip dia 20–50μ) 6 h prior to recordings.

In tests on 16 neurones inhibited by caudate stimulation in untreated animals, ACHC (40–100nA mean 68nA) weakly depressed the spontaneous firing of 15 by 10–60% (mean 26%). Lower ejecting currents of ACHC (2–50nA mean 25nA) enhanced submaximal GABA induced depressions of 10 of 11 neurones by 20–70% (mean 50%) whereas glycine induced depressions were unaffected. ACHC had no observable effect on caudate evoked inhibition.

In toxin treated rats synaptic inhibition was absent in 15 of 18 neurones, whereas the depressant effects of GABA and glycine were similar to those observed in control animals. In tests on these 15 neurones, only 4 were weakly depressed by ACHC (60–100nA mean 73nA) and GABA induced depression was only enhanced in 1 of 7 of these cells.

Since tetanus toxin does not affect neuronal GABA uptake (Davies, Neal & Tongroach, unpublished observations) inhibition of uptake by ACHC does not explain either the direct depressant action of ACHC or its enhancement of GABA depression, as such effects were absent in toxin treated rats. However, ACHC is itself taken up by neurones (Bowery & Neal, communication this meeting) and consequently may release endogenous GABA by displacement. Such an effect could account for the present findings particularly as tetanus toxin prevents neuronal GABA release.

## References

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