In some cells, bicuculline clearly antagonized GABA causing either a parallel shift of the dose-response curve to the right or sometimes a depression of the maximum. In other cells, potentiation was seen in the form of a shift to the left of the dose-response curve. Occasionally, both potentiation and antagonism were seen sequentially in the same cell or even within a single dose-response curve when the lower part of the curve was shifted to the left and the maximum was depressed. In all cases, the responses to GABA following termination of the bicuculline application returned rapidly towards control values. In fifty-one out of sixty cells tested, there was either a change in the response of the cell to GABA or a change in the firing rate of the cell in the presence of bicuculline. This indicates that bicuculline was reaching these cells. The responses to GABA were potentiated by bicuculline in twenty cells and antagonized in thirty-one cells. Most of these changes were small, however, being greater than 2-fold in only seven cases of antagonism and nine cases of potentiation.

These results suggest that bicuculline is not a simple GABA antagonist and should be used with caution in the identification of GABA-mimetic compounds or GABA-mediated synapses in the central nervous system.

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Effect of atropine on acetylcholine release from cerebral cortical slices stimulated at different frequencies

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Atropine increases the release of acetylcholine (ACh) from the cerebral cortex *in vivo* (Mitchell, 1963). To determine the effect of atropine on the ACh release mechanism more directly, slabs of rat cortex (300–400 mg) were sliced into strips (0·2 mm thick) and were perfused *in vitro* according to Srinivasan, Neal & Mitchell (1969) with oxygenated Krebs solution containing 2×10^{-4} M eserine and 10^{-5} M choline. After perfusion for 1 h, samples were collected every 2·5 min and their ACh content was assayed on the leech muscle. After four control samples square wave pulses of alternating polarity (5 ms duration, 40 mA) were applied at frequencies of 0·25, 1, 4, 16 and 64/second. The release of ACh remained constant during 40 min of continuous stimulation except at the highest frequency used. Without drugs added to the Krebs solution the minute output rose and the output per volley slowly declined as the frequency of stimulation increased (Fig. 1). In the presence of 3×10^{-7} M atropine the unstimulated output was not any higher than without atropine ((18·4$\pm$1·2 ng/g)/min without atropine, (17·1$\pm$1·7 ng/g)/min with atropine), but atropine greatly enhanced the ACh release evoked by stimulation, especially at low frequencies (Fig. 1). Addition of 3×10^{-7} M atropine or atropine methylnitrate to the perfusion fluid during stimulation immediately increased ACh release.

Atropine, in the concentration used does not affect the inactivation of ACh by uptake processes (Polak, 1969) nor does tetrodotoxin alter the potentiating effect of atropine on ACh release *in vitro* (Molenaar & Polak, 1970). Therefore, the observed

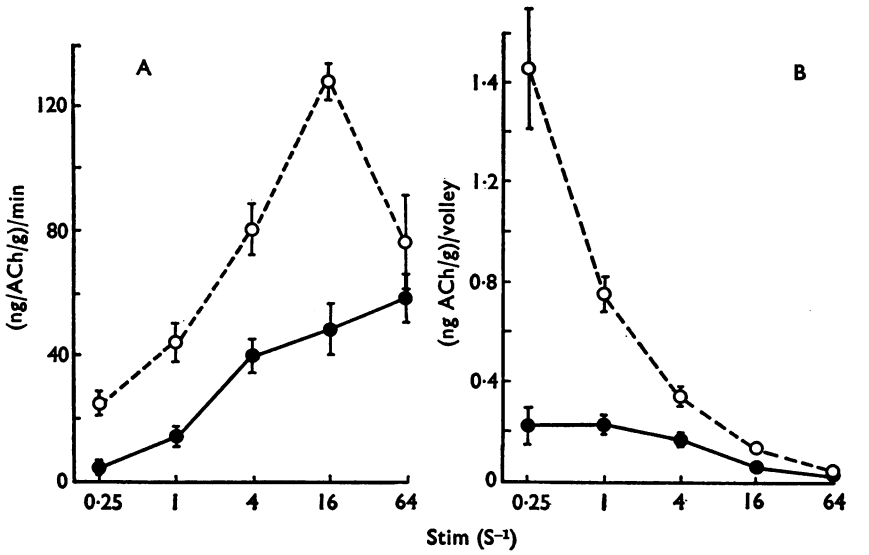

FIG. 1. Release of ACh from cortical slices stimulated at different frequencies. A, Increase in minute output (average minute output during 10 min stimulation minus average minute output during 10 min prestimulation period). B, Volley output (increase in minute output/stimuli per stimulus) ●—● without, ○—○ with 3×10^{-7} M atropine sulphate. Each point is the average ± S.E.M. of three experiments.

potentiation of ACh release by atropine is likely to be due to a presynaptic action which could be an antagonism of a presynaptic inhibitory effect mediated by released ACh.

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Neurally evoked release of noradrenaline from the olfactory bulb

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Previous experiments on the olfactory bulb *in vivo* by Chase & Kopin (1968) have failed to show any specific release of noradrenaline (NA) in response to nervous