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Actions of glutamate and kainic acid on the lobster muscle fibre and the frog spinal cord

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As kainic acid (Kai) is a potent glutamate agonist in the mammalian central nervous system (Shinozaki & Konishi, 1970; Johnston, Curtis, Davies & McCulloch, 1974), we have investigated the effect of Kai on two non-mammalian preparations where glutamate is a putative excitatory transmitter (Johnson, 1972). (1) Intracellular recordings were made from single muscle fibres in the lobster walking leg and the effects of Kai and of glutamate were measured as membrane depolarizations. (2) The frog isolated spinal cord preparation was studied according to the method of Mitchell & Phillis (1962) and the spinal acetylcholine (ACh) output was bioassayed every 10 minutes.

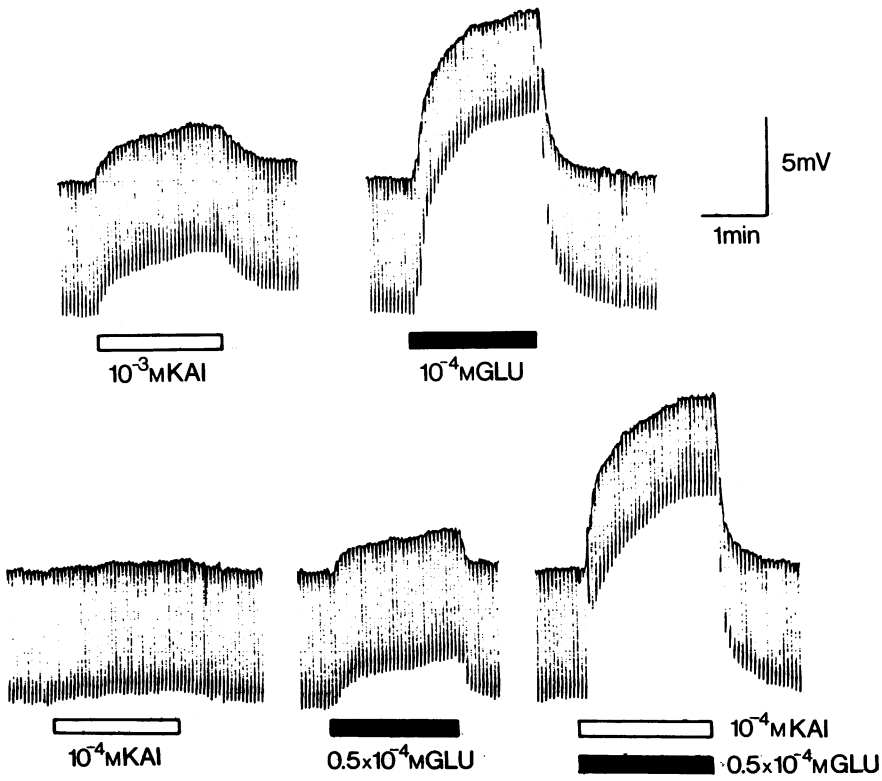

Figure 1 Depolarizations (upward deflections) induced by L-glutamate (GLU: solid bars) and kainic acid (KAI: open bars) in a single lobster muscle fibre. One voltage recording and one current (1.3×10^{-7} A) passing microelectrode were inserted into the middle of the fibre; the resultant electronic potentials were recorded as downward deflections. Concentrations of GLU higher than 1.5×10^{-4} M often caused muscle contraction with microelectrode displacement.

The superfusion of the lobster fibre with glutamate ($0.5\text{-}1.5 \times 10^{-4}$ M) produced membrane depolarizations which reached a maximum within 2 min (Hironaka, 1974). Depolarizations induced by Kai (10^{-4} to 10^{-3} M) were smaller than those caused by glutamate, the action of which was potentiated by Kai in concentrations producing little or no depolarization alone (Figure 1).

In the frog cord, glutamate (5×10^{-5} to 10^{-3} M) and Kai (in lower concentrations of 10^{-5} to 10^{-4} M) evoked spike activity in the ventral roots with initial increase and subsequent depression of ventral root potentials. In the first 10 min glutamate (10^{-4} M) induced a 51% increase in the spinal ACh output while with Kai (10^{-4} M) a 112% rise was found. In still lower concentrations, neither Kai (5×10^{-6} M) nor glutamate (5×10^{-5} M) separately affected ACh output but when added simultaneously raised the ACh output by 30%.

These findings suggest that Kai has more potent effects than glutamate on the frog spinal cord but not on the lobster muscle fibre.

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Actions of γ-aminobutyric acid (GABA) on ganglionic transmission and ganglion cell excitability

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GABA increases Cl^- conductance in rat sympathetic ganglion cells and produces a membrane depolarization, probably because $E_{Cl} < E_m$ (Adams & Brown, 1973). We wish here to consider the consequences for ganglion cell excitability and transmission.

Isolated rat superior cervical ganglia were bathed in flowing oxygenated Krebs' solution at ambient temperature, and neurones impaled with microelectrodes filled with K citrate or acetate. Cells were stimulated directly by passing depolarizing current pulses through the microelectrode or orthodromically through a suction electrode into which the preganglionic trunk was drawn.

On the direct spike GABA (100 μM) (i) reduced the positive overshoot and rate of rise and (ii) increased the threshold depolarizing current. These effects could be explained quantitatively in terms of (a) the increased membrane conductance and (b) increased steady-state Na^+-inactivation during GABA-depolarization (Hodgkin & Huxley, 1952).

In neurones showing minimal impalement shunting (such that the recorded membrane potential exceeded −55 mV (Adams & Brown, 1975)) GABA did not usually block the transmission of single, supramaximal orthodromic stimuli: instead, the amplitude of the orthodromic spike was reduced to an extent comparable with that of the direct spike. This accords with previous observations with extracellular electrodes (De Groat, 1970; Bowery & Brown, unpublished observations). Although the amplitude of the synaptic potential is severely depressed by GABA, transmission does not fail because the synaptic potential is superimposed on a depolarization driving toward E_{Cl} such that the membrane potential attained by the synaptic potential still exceeds the threshold for spike generation.

In contrast, when the impalement leak short-circuited the membrane resistance sufficiently to reduce the resting potential below −55 mV, orthodromic transmission was invariably blocked by GABA. This might be an experimental artefact, reflecting increased Na^+-inactivation during the sustained impalement-depolarization with a consequent rise in the voltage threshold for spike generation. Thus, although attaining a lower absolute membrane potential than in undamaged cells, on adding GABA the synaptic potential is