Blocking by picrotoxin of nigra-evoked inhibition of neurons of ventromedial nucleus of the thalamus[1,2]

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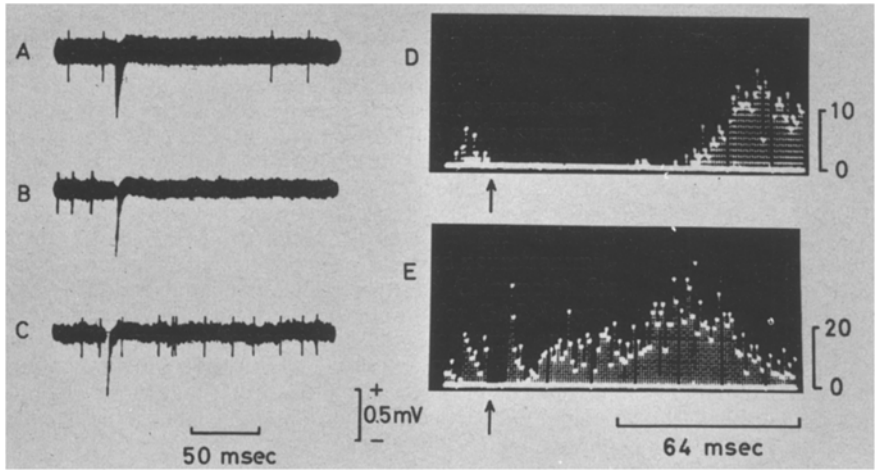
Summary. The transmitter substance released by nigro-thalamic fibres is proposed to be γ-aminobutyric acid, since picrotoxin blocked nigra-evoked monosynaptic inhibition of thalamic neurons.

It has already been shown that caudate efferent fibres exert a monosynaptic inhibitory action on neurons of the internal segment of the globus pallidus[4] and the substantia nigra (SN)[5]; the inhibitory transmitter substance is believed to be GABA[6,7]. Our recent studies revealed that 2 major output systems of the basal ganglia were also inhibitory in nature[8,9]. Stimulation of the pars reticulata of SN monosynaptically (average latency 1.58 msec) produced IPSPs in neurons of the ventromedial (VM) nucleus of the thalamus[8]. It is of interest, therefore, to investigate the transmitter substance mediating this inhibition. GABA-picrotoxin antagonism has been reported at various inhibitory synapses[6,7,10-12]. The present experiment shows that i.v. administration of picrotoxin blocks the inhibitory action of the nigrothalamic fibers on VM neurons.

Materials and methods. Experimental procedures were the same as described in a preceding paper[8]. Cats were anesthetized with sodium pentobarbital, immobilized by i.v. injection of gallamine triethiodide and artificially ventilated. Isotonic sodium chloride solutions of picrotoxin and strychnine nitrate were administered i.v. Extracellular recordings of unitary action potentials from VM were obtained with micropipettes filled with 2 M NaCl solution saturated with fast green-FCF. Recording sites were confirmed by fast green dye marks. Poststimulus time histograms for some units were obtained with a histogram data processor (DAB-5101, Nihonkoden). Spontaneous discharges in the VM area were strongly inhibited by SN stimulation as shown in figure A and B. The spontaneous activity of VM neurons was usually very low. Clear inhibition of spontaneous discharges of a VM neuron produced by SN stimulation is demonstrated in figure D, which was obtained by adding 200 sweeps. The inhibition starts immediately after the stimulation applied to SN and lasts for more than 50 msec, and a rebound increase of the firing is observed. It is reasonable to assume, as shown earlier[8], that this short latency inhibition of the spontaneous firing of the VM neuron is produced by monosynaptic IPSPs. The SN evoked inhibitions shown in figure A, B and D were almost abolished 20 min after i.v. injection of 2.5 mg/kg picrotoxin (figure C and E). I.v. administration of picrotoxin increased the spontaneous firing rate of VM neurons in general. The histogram of figure E, which was obtained by adding 100 sweeps, clearly demonstrates the suppression of the short latency inhibition of the VM neuron shown in figure D. The brief pause of firing seen immediately after the stimulus artifact is due to failure of counting during the stimulus artifact. Furthermore, threshold stimulus intensities for producing SN-evoked inhibition of VM neurons were markedly increased. I.v. injection of 0.6 mg/kg strychnine nitrate failed to produce any significant change in the SN-evoked inhibition of VM neurons. Thus the inhibition exerted by SN on VM neurons is blocked by picrotoxin and resistant to strychnine.

Therefore GABA is likely to be the inhibitory transmitter substance liberated by the nigrothalamic pathway. This hypothesis is supported by the finding; an analysis of the regional distribution of GABA contents within the cat's thalamus showed that the content of GABA in the VM region (ranging from 5 to 6 µmoles/g brain) was significantly higher than in the thalamic region corresponding to the ventrolateral nucleus (2–4 µmoles/g brain)[13].



Effect of picrotoxin on short latency inhibition of spontaneous discharges of VM neurons produced by electrical stimulation of SN. *A* and *B* Inhibition of spontaneous discharges of a VM neuron produced by SN stimulation. *C* Same neuron recorded 20 min after i.v. administration of 2.5 mg/kg picrotoxin. *D* Peristimulus time histogram showing SN-evoked inhibition of discharges of a VM neuron (200 sweeps). *E* Same neuron recorded 25 min after i.v. administration of 2.5 mg/kg picrotoxin (100 sweeps). Arrows in *D* and *E* indicate positions of stimulus artifact.

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