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Preliminary note

EFFECTS OF DIFFERENT TYPES OF ANTICHOLINESTERASE AGENTS ON IN VIVO HIPPOCAMPAL POPULATION SPIKES IN RATS

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Any anticholinesterase agent, when administered systemically, has widespread and severe physiological and/or toxicological effects. In the central nervous system, acetylcholine is mainly a modulator, responsible e.g. for the ascending control of arousal (McCormick, 1992). In the hippocampus, cholinergic input to CA1 pyramidal neurons from the medial septum (Wainer et al., 1985). Its enhancing effect of synaptic excitation has also been described (Rovira et al., 1983).

Organophosphates (OPs), used as insecticides, are irreversible AChE blockers and their effects on the central nervous activity has been widely studied. While it is obvious to attribute these effects to the AChE blockage, certain data in the literature are not consistent with this (Gralewicz et al., 1991). To see if the OPs studied by us have any non-cholinergic effects we chose the hippocampal population spike (POPSP; Anderson et al., 1971) as a phenomenon under an established cholinergic influence and compared the effect exerted on it by OPs and by physostigmine as a reference AChE blocker. This choice was supported by previous results (Papp et al., 1997).

The experiments were performed on adult male rats weighing ca. 400 g, anaesthetized with 1000 mg/kg urethane i.p. The left hemisphere was exposed and the dura removed. To elicit POPSPs, the perforant path (AP: -6, L: 4.5, V: 4 mm stereotaxic coordinates; Paxinos and Watson, 1982) was stimulated (1 mA, 0.05 ms, 0.1 Hz) via a bipolar needle. A glass recording microelectrode was put in the CA1 region (AP: 3, L: 2.5, V: 2 - 4). Every 10 minutes, a train of 20 stimuli were given and the averaged POPSP was recorded after 1000 x AC amplification in a PC using the pCLAMP sotfware. After 4 or 5 control records, the drug to be studied was given i.p. and further records were taken with the same sequence. The amplitude of the POPSP was measured afterwards and the relative change (treated/control) was calculated and plotted.

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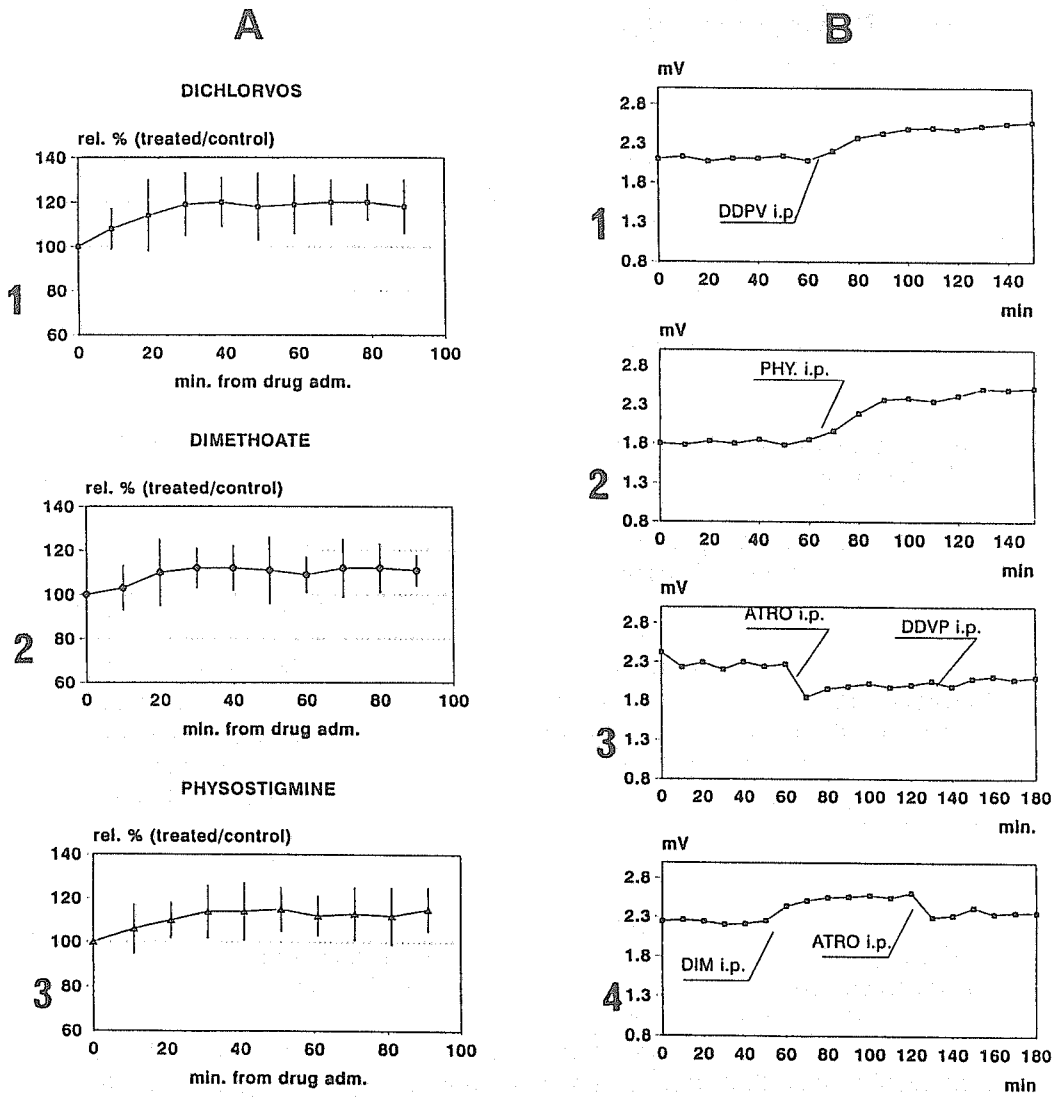

Fig. 1. A: Averaged (n = 10) relative changes of the peak-to-peak amplitude of the population spike caused by dichlorvos (1) dimethoate (2) and physostigmine (3). Error bars represent S.D. B: Time course of the POPSP amplitude in typical single experiments, illustrating the effect of dichlorvos (1), physostigmine (2), atropine and dichlorvos (3) and dimethoate and atropine (4)

The organophosphates, dimethoate (DIM) and dichlorvos (DDVP), were given in 1/5 LD50 dose (45 mg/kg DIM and 0.8 mg/kg DDVP), to keep the results comparable with previous ones (Dési et al., 1991; Nagymajtényi et al. 1994). Physostigmine (PHY) was given in 0.1 mg/kg (based on Lynch and Coon, 1972; Messamore et al., 1993). Both OPs induced an increase in the POPSP amplitude. The increase began within 10 minutes from drug application and was full-blown in ca. 30 min. There was practically no change in the latency of the POPSP peaks. The average relative amplitude change from 10-10 experiments was +19% with DDVP and +12% with DIM (Fig. 1; A/1,2 and B/1). Atropine (ATRO) in 1 mg/kg, given ca. 30 min before OP administration, induced an amplitude decrease which was not reversed by subsequent OP (Fig. 1; B/3,4). PHY as reference substance had the same effect like the OPs. The average amplitude increase of the POPSPs under PHY was +14 % (Fig. 1; A/3, B/2). The effect of atropine pretreatment was also the same as for OPs. The POPSP amplitude increase was significant with each anticholinesterase agent ($p<0.05$, Wilcoxon's signed rank test).

Our results suggest that the effect of OPs on the hippocampal POPSP in rats is a cholinergic one. Septo-hippocampal cholinergic fibres, ending mainly on the pyramidal neurons modulate neuronal activity (Benardo and Prince, 1982) thereby facilitating transmission (Krnjevic and Ropert, 1982). When, by means of the OP-induced AChE blockage, cholinergic influence is increased, a given stimulus can elicit a stronger response - as has been seen by us.

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