LETTER TO THE EDITOR

EFFECT OF CHOLINOMIMETIC AGENTS ON LEARNING AND MEMORY WHEN ADMINISTERED BY INTRA CEREBROVENTRICULAR (ICV) AND INTRAPERITONIAL (IP) ROUTES

(Received on February 1, 1988)

It has been suggested that cholinergic mechanisms are involved in learning and memory (1, 4). Since cholino-mimetic drugs appear unique in their ability to alter the above parameters, this study study was undertaken to determine if there was any difference in effects on learning and memory between a directly acting drug drug, viz., pilocarpine and an indirectly acting drug, physostigmnie and also to compare the differences, if any between peripheral (ip) and central administration (icv) of these drugs. Passive avoidance tests were employed as the model of testing learning and memory.

Wistar rats of either sex weighing between 125-150 g were used : 8 animals used per group. Passive avoidance tests were conducted in a step-through apparatus, which consisted of a bright chamber illuminated by 00 W electric bulb and a dark chamber provided with iron grid that could be electrified by a stimulator. Each rat was placed in the bright chamber and the shutter between the two chambers was opened after 10 secs of familiarisation. Rats entered the dark chamber within 3 min of opening the shutter due to innate behaviour of preferring darkness. To evaluate the influence of drugs on the learning behaviour-drugs were given 15 min and 30 min before the procedure by icv and ip routes respectively. The percentage of the rats entering the dark chamber within the stipulated time of 3 min was noted. After entering the dark chamber they received a shock of mA just once. To study memory retention, four retest trials were given at intervals of 24 hr, 48 hr, 75 hr and 1 wk after the learning session. The avoidance of shock by staying in the bright chamber indicated the retention of memory (2). Pilocarpine nitrate (Plantex, Israel) and physostigmine sulphate (Burroughs Welcome & Co., London) were given ip in a dose of 5 *mg/kg* and 0.1 *mg/kg* respectively; for icv administration, the doses were 100 μg and 1 μg respectively, in a volume of 0.1 μl (3).

Learning behaviour was not altered by either drugs given icv on ip, but difference in retention of memory was observed. Perusal of Figs. 1 and 2 indicates that only 36% (icv)

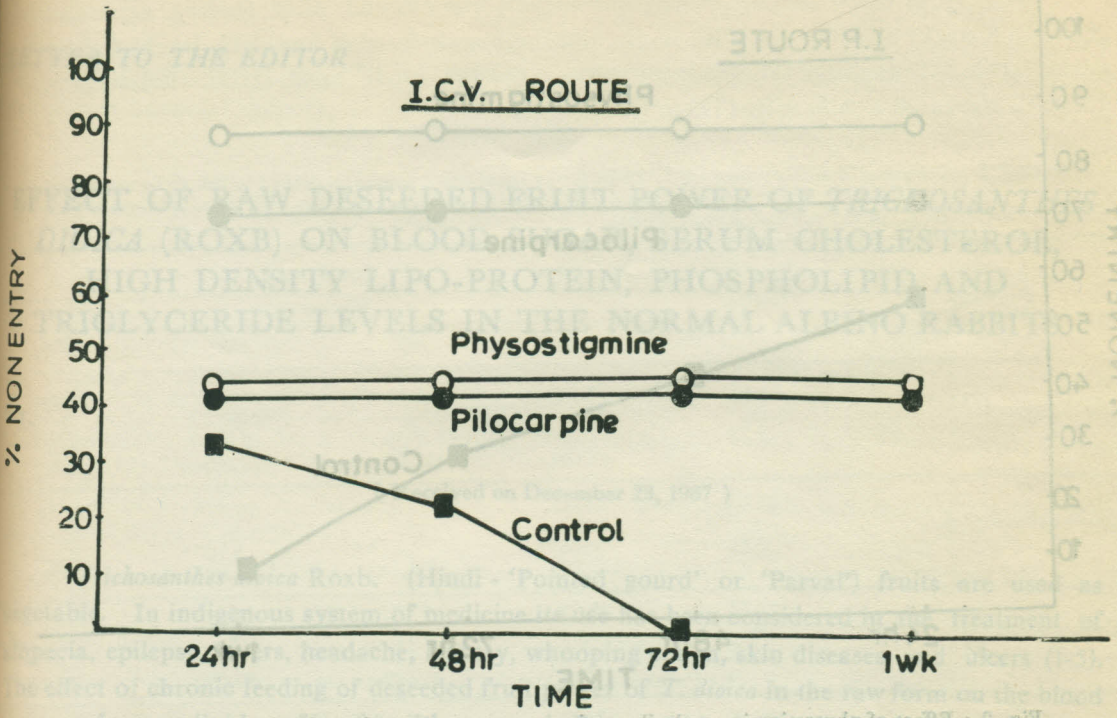

Fig. 1 : Effect of physostigmine and pilocarpine on memory retention after icv administration. % of memory on 'y' axis indicates % of rats remained in the bright chamber.

and 56% (ip) of control rats retained the memory of shock at 24 hr. The percentage of rats retaining the memory gradually reduced and almost all the control rats lost the memory of shock given in the dark chamber by 1 wk. On the other hand memory of the shock was retained throughout the period being significant at one week after pretreatment with pilocarpine whether given icv or ip. Though physostigmine also produced significant memory retention at 1 wk when given icv or ip, the drug when given ip produced significant memory retention at 48 hr and 72 hr also, however, the difference between the effect of pilocarpine and physostigmine per se on memory retention was negligible.

It is, therefore, confirmed that directly and indirectly acting cholinomimetic drugs can facilitate retention of memory and physostigmine seems to be a better drug for this purpose, since it is more effective when given ip which is of practical importance.

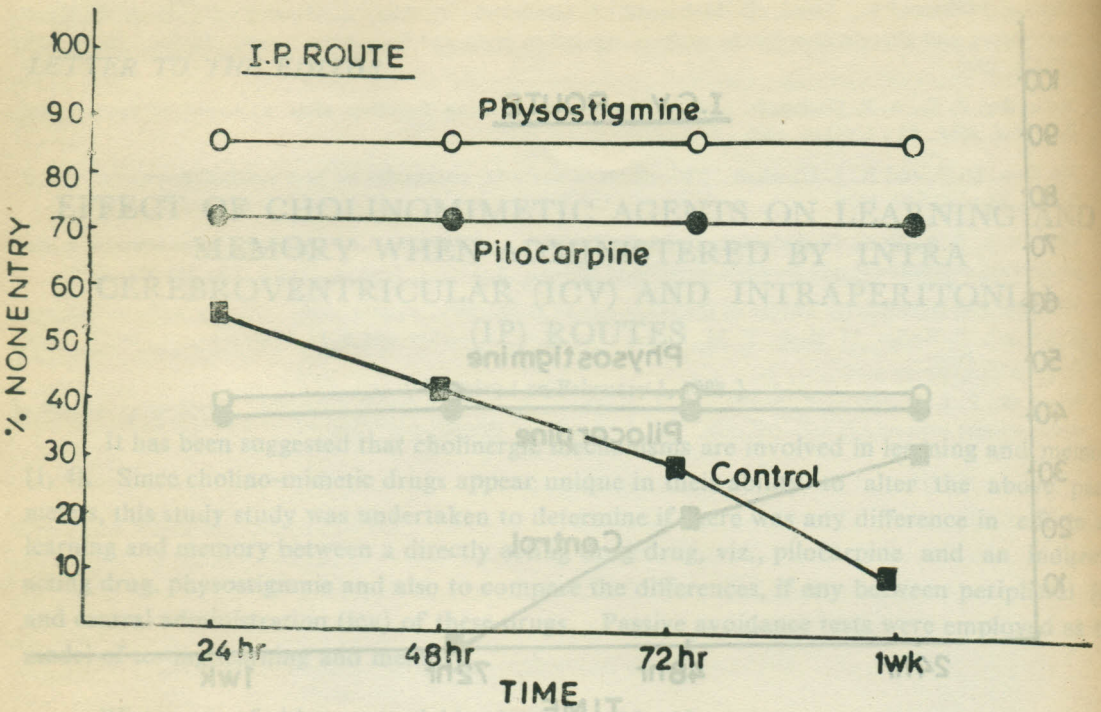

Fig. 2 : Effect of physostigmine and pilocarpine on memory retention after ip administration. % of memory on 'y' axis indicates % of rats remained in the bright chamber.

S. H. KADLIMATTI, B. V. VENKATARAMAN AND THANGAM JOSEPH

Department of Pharmacology,
St. John's Medical College, Bangalore - 560 034

REFERENCES

1. Bures, J., O. Buresova, Z. Bohdanecky and T. Weiss. The effect of physostigmine and atropine on the mechanism of learning. In "Animal Behaviour and Drug Action". Eds. Steinberg, H., de Reuck, A.V.S. and Knight, J. Ciba Foundation Symposium, London, J. and A Churchill Ltd., p 134-143, 1964.
2. Jagdev, N. and F.S.K Barar. Effect of physostigmine and atropine on the single-trial passive avoidance response in rats. *Ind. J. Physiol. Pharmac.*, **26 (3)** : 201-206, 1982.
3. Noble, E. P., R. J. Wurtman and J. Axelord. A simple and rapid method for injecting H^3-norepinephrine into the lateral ventricle of the rat brain. *Life Sci.*, **6** : 281-291, 1967.
4. Squire, L. R. and H. P. Davis. The Pharmacology of memory : A neurobiological perspective. *Ann. Rev. Pharmac. Toxicol.*, **21** : 323-356, 1981.

Reprint request to :. *Dr. B. V Venkataraman, Department of Pharmacology, St. John's Medical College, Bangalore-560 034*