

The morphological and histochemical neurosecretory magnocellular system in the rat after administration of chlorpromazine

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The effect of chlorpromazine (CPZ) on the neurosecretory action of the hypothalamo-hypophyseal system was investigated in 72 male rats. The experimental animals received CPZ in a dose of 0.4 mg, 4.0 mg and 20.0 mg/kg b.w. for 30 days. The rats were sacrificed by decapitation at 24 h and 7 days after the last dose of the drug. The neurosecretory material was stained with paraldehyde fuchsin in the supraoptic nucleus, paraventricular nucleus, eminentia mediana and neurohypophysis, the tigroid was stained with toluidine blue and the acid phosphatase activity was evaluated histoenzymatically. It was found that CPZ reduced the content of the neurosecretory material after 24 h, while an increase was observed 7 days after the last drug administration.

Key words: magnocellular neurosecretory system, chlorpromazine, rat, acid phosphatase, Gomori — positive neurosecretory material

INTRODUCTION

Apart from its beneficial effect, chlorpromazine, as used in psychiatry, induces a number of undesirable symptoms, mainly in the central and peripheral nervous system, circulatory system and endocrine system [2, 3]. Chlorpromazine disturbs the water and electrolyte balance, in which the antidiuretic hormone produced in the magnocellular neurosecretory system is involved. The aim of the study was to detect the morphological and histochemical changes within the supraoptic nucleus (SON), paraventricular nucleus (PVN), medial eminence (ME) and neurohypophysis after administration of various doses of CPZ.

MATERIAL AND METHODS

The study used 72 sexually mature male rats. The experimental animals received chlorpromazine (CPZ) in a dose of 0.4 mg/kg b.w. (I group), 4.0 mg/kg b.w. (II group) and 20.0 mg/kg b.w. (III group). Chlorpro-

mazine was administered intramuscularly every day for 30 days. The control animals were given physiological saline solution. Each group had two subgroups: subgroup I — males dissected after 24 hours; subgroup II — males dissected 7 days after administration of the last drug dose. The animals were decapitated. The brains and pituitaries were fixed in Bock's fluid, Carnoy's fluid and Baker's fluid. Paraffin sections were stained with haematoxylin and eosin, with paraldehyde fuchsin according to Gomori in the Fischer and Haskel modification for neurosecrete [1] and with toluidine blue for the tigroid. Histoenzymatic reaction for acid phosphatase (AP) was carried out according to Gomori.

RESULTS AND DISCUSSION

Supraoptic and paraventricular nucleus cells showed varied neurosecrete content (Fig. 1). Nissl bodies were located around cellular nuclei and on the

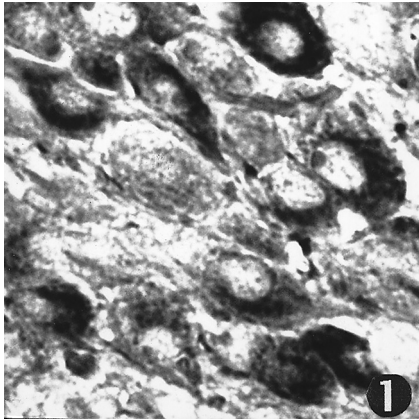


Figure 1. Supraoptic nucleus. Control group. Varied neurosecretory content in cells. Staining according to Fischer and Haskell. Mag. 400 ×.

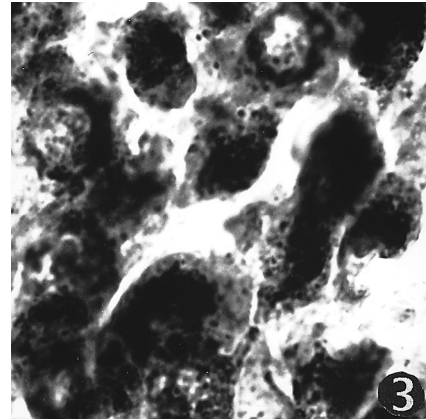


Figure 3. Supraoptic nucleus. Control group. Reaction for acid phosphatase. Staining according to Gomori. Mag. 400 ×.

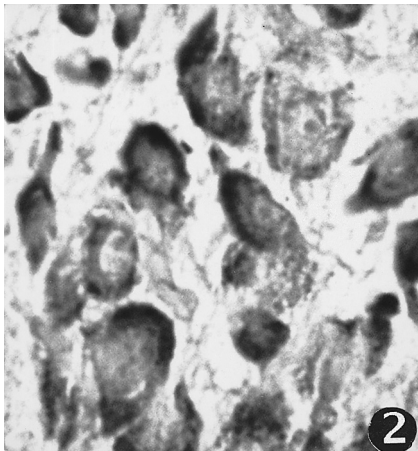


Figure 2. Supraoptic nucleus. Control group. Nissl bodies in the cytoplasm of neurones. Staining with toluidine blue. Mag. 400 ×.

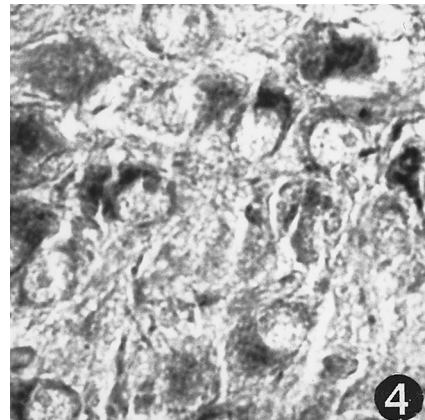


Figure 4. Supraoptic nucleus. Experimental group III. Animals decapitated 24 hours after the last drug dose administration. Reduced neurosecretory content in cells and nerve processes. Staining according to Fischer and Haskell. Mag. 400 ×.

cell periphery (Fig. 2). In EM and in the neurohypophysis, the neurosecretory grains were situated in the fibres in the vicinity of blood vessels. The reaction for AP was characterised by high activity in both SON and PVN (Fig. 3). Administration of CPZ caused a reduction in the neurosecretory content in the cells of SON, PVN, ME and in the nervous part of the pituitary 24 hours after administration of the last drug dose, particularly in the group of animals receiving the highest dose. The neurosecretory content increased 7 days after administration of the last drug dose (Fig. 4). At the same time, the tigroid content in SON and PVN was inversely proportional to the neurosecretory content (Fig. 5). The reaction for AP in SON and PVN became attenuated in all experimental groups after 24 hours (Fig. 6) with an increase after 7 days. The results indicate a pronounced effect of CPZ on all

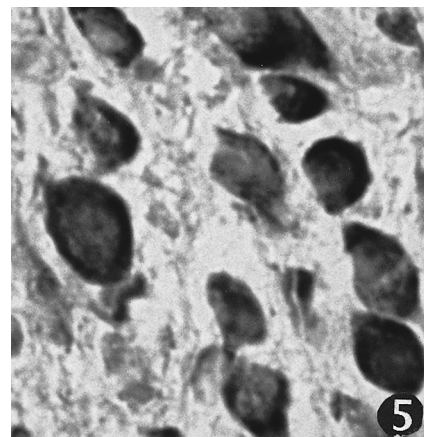


Figure 5. Supraoptic nucleus. Experimental group II. 24 hours after the last drug administration. Marked increase in Nissl substance in nerve cells. Staining according to toluidine blue. Mag. 400 ×.

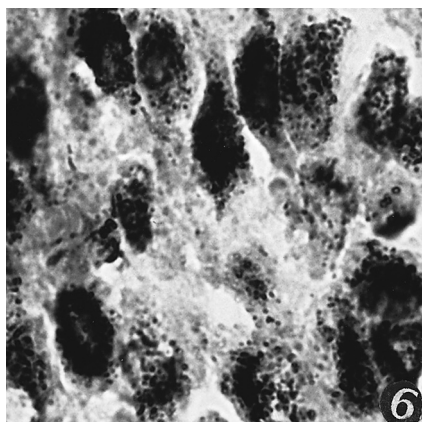


Figure 6. Supraoptic nucleus. Experimental group I. 24 hour after the last drug administration. Attenuated reaction for acid phosphatase. Staining according to Gomori. Mag 400 \times .

the elements of the magnocellular neurosecretory system — SON, PVN, ME and neurohypophysis. Soon after the administration of the last dose the neurosecretory content decreased in all experimental groups both in SON and PVN, with a simultaneous increase in the tigroid content, thus indicating a reduced production of the neurosecretory within the cells of SON and PVN. This may be due to the fact that CPZ inhibits α -adrenergic and dopamine D-2 receptors located in the hypothalamus [4, 5]. Its consequence is a limitation of adenylyl cyclase reactivity and thus a reduction in cyclic AMP level, which leads to biosynthesis attenuation in the cell. Therefore, as hormones produced in the magnocellular neurosecretory system (vasopressin, oxytocin with neurophysine) are protein substances, their synthesis is reduced due to CPZ action, as confirmed by the study of Galfi et al. [4]. Chlorpromazine disturbs the water and electrolyte balance in the organism [2]. These authors report reduced absorption of water in the renal canaliculi after CPZ administration, which may be caused by either direct drug effect on the renal canaliculi or inhibition of vasopressin production within SON and PVN. This is in agreement with our results. According

to Eström et al. [3], CPZ exerts a stimulating effect on neurosecretory release from nerve endings in the pituitary, which was also observed in our study as a reduction in the neurosecretory content in the neurohypophysis. The biological half-life of CPZ in the blood is relatively short (10–20 hours). Seven days after the last drug dose administration we observed an increased neurosecretory content in SON, PVN and the nervous part of the pituitary, only slightly exceeding that noted in the control group. We found attenuation of the reaction for AP in SON and PVN neurones with a simultaneous neurosecretory reduction after 24 hours. A decrease in AP activity indicates CPZ-induced disturbances in cellular metabolism in the hypothalamus, and thus decreased hormone production. Our findings show a slight diffusive reaction for AP, especially in the group III. This may indicate lysosomal membrane injury and the release of enzymes to the cytoplasm of neurocytes, which may be associated with labilisation of lysosomal lipoprotein membranes due to CPZ action [2].

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