Reactions of Hypothalamic Neurons on Stimulation of Neurosecretory Hypothalamic Regions[1]

Electrical stimulation of paraventricular (PV) and supraoptic nuclei (SO) of mammals is known to release neurohormones into both plasm[2,3] and cerebrospinal fluid (CSF)[4]. The PV is assumed to be responsible for oxytocin release, while vasopressin (= ADH) discharge is suggested to be caused by the SO[2–8]. Since, furthermore, the neurohormones oxytocin and vasopressin are know to be capable of influencing the discharge rate of hypothalamic neurons through the blood and/or the CSF[9–11], it was the object of the present investigation to see if there are any changes occurring in the neuronal activity within the hypothalamic region after electrical stimulation of PV and SO.

Materials and methods. 55 rabbits of either sex were used. All experiments were carried out under morphine-urethane anaesthesia. Stimulation of PV and SO was by means of stereotaxically implanted bipolar steel electrodes (electrolytically pointed and coated) using a TR 03-04 squarewave pulse generator (EMG Budapest). The stimulation parameters were 50 cps, 2–5 Volts, 3 msec pulse duration. Time of continuous stimulation was 15 min. The multi-unit activity was recorded contralaterally by means of electrolytically pointed, coated and stereotaxically implanted steel electrodes having a tip diameter of 2–8 μm. The multi-unit activities of SO, PV, medial preoptic area (MPA) and lateral hypothalamic area (LHA) were examined. After preamplification, the impulses were presented on a monitor and their number counted in minute intervals using an automatic counter. All recordings were made over a period of 60 min after stimulation. Then the electrode position in the hypothalamus was marked by means of electromarking and the animals were killed. The exact electrode position was determined by means of HE staining. The changes in neuronal impulse activity were given as a percentage of the initial values to enable the latter (varying for the experiments) to be compared.

Results and discussion. Stimulation of PV (Figure 1, left portion). The contralateral PV (CPV) showed a response as early as 5 min after completion of stimulation, with a decrease in discharge rate of approximately 40%. The most pronounced inhibition of about 75% was observed after 35 min (Figure 2). The contralateral SO (CSO) exhibited a continuous reduction in firing rate, the minimum being reached after 40–45 min. The response to stimulation of LHA and MPA, however, displayed a marked increase in frequency (200–250%). While the impulse counts for MPA show a slight decrease already after 15 min, the latter effect was observed to occur for the neurons of LHA not earlier than after 30 min. The discharge rate of both regions again increased until the 60th min, then remaining markedly increased relative to the initial condition (MPA approx. 400%; LHA approx. 250%).

Stimulation of SO (Figure 1, right portion). The CPV was observed to respond initially to stimulation of the SO with a discontinuous decrease in frequency by approx. 30%. It was not earlier than 30 min after completion of stimulation that the firing rate showed a steep increase (150–170%). The maximum of stimulation effect was attained after 45–50 min. The CSO displayed a maximum in discharge rate (about 350%) as early as 5–10 min after completion of stimulation. Although there was a continuous decrease in the number of spikes over 60 min after stimulation, the discharge rate remained highly increased (about 250%) when compared with the initial position. Within the first 5–10 min after completion of stimulation, the discharge rate of LHA neurons increased to approx. 300% over the original condition, followed by a continuous decrease in impulse counts down to 80% at the end of the observation period. The minimum of impulse frequency was at 45 min. The differences between the reactions of neurons within the individual brain regions after stimulation were also highly significant ($p < 0.001$).

The results reported demonstrate that, after stimulation of PV, the contralateral regions of both PV and SO respond with an inhibition in firing rate, while the neurons of LHA and MPA become activated. The opposite response is observed with the SO being stimulated. Since the discharge rate of SO and PV neurons is know to be capable of being increased by both intraventricular

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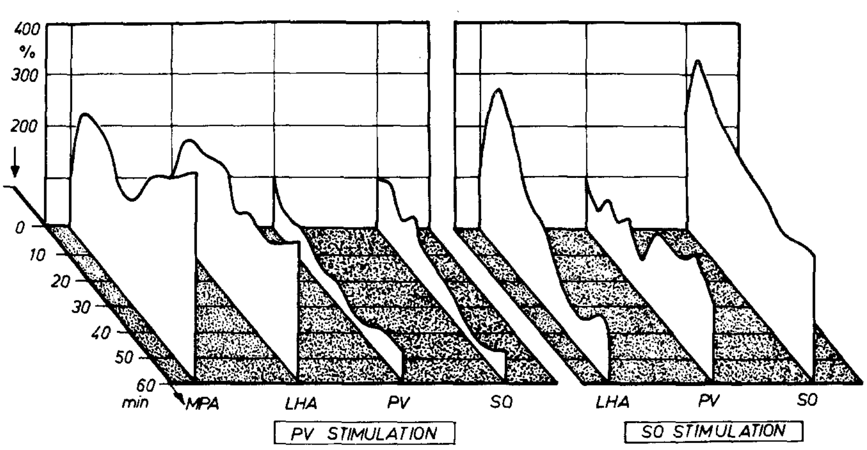

Fig. 1. Three-dimensional representation of modified neuronal activity after electrical stimulation of paraventricular and supraoptic nuclei. Changes of impulse counts over a period of 60 min as a percentage of the initial condition. MPA, medial preoptic area; LHA, lateral hypothalamic area; PV, paraventricular nucleus; SO, supraoptic nucleus; ↓, onset of electrical stimulation.

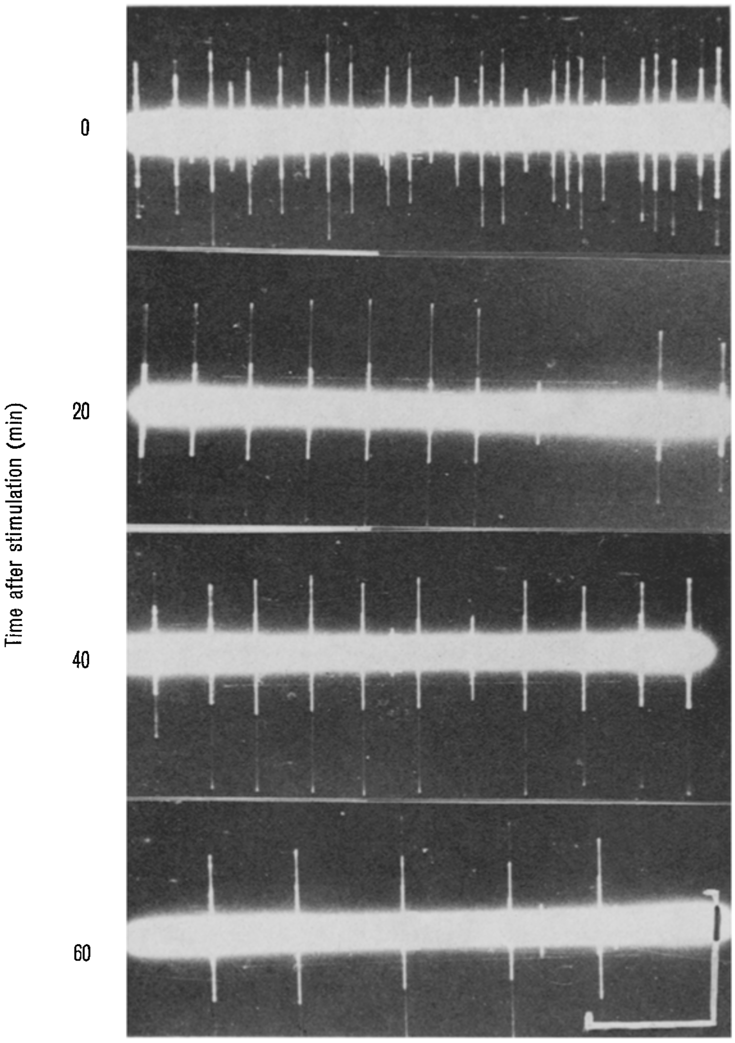

Fig. 2. The effect of electrical stimulation of the paraventricular nucleus (PV) on the multi-unit discharge rate of the controlateral PV. Time marking 0.1 sec; calibration 100 μV.

injection of oxytocin and vasopressin[11], it is reasonable to consider a relation between the changes in neuronal activity occurring after stimulation of diencephalic structures and a release of oxytocin and vasopressin into the CSF, as one possible explanation of the findings. According to our experience, this is suggested by the relatively long latency prior to the occurrence of initial and/or maximum effects, for it is also after intraventricular injection of oxytocin and vasopressin that comparable effects were found[11]. The present findings appear to support the assumption that after stimulation of PV and SO, oyxtocin and vasopressin, respectively, are discharged into the CSF. Thus, a modulating influence on the entire central nervous system through the neurohormones contained in the CSF would be most likely because of their half-life of approx. 30 min.

Zusammenfassung. Elektrische Stimulation neurosekretorischer Kerngebiete des Zwischenhirns führt zu charakteristischen Veränderungen der neuronalen Aktivität angrenzender hypothalamischer Neuronenpopulationen, die einen modulierenden Einfluss von Neurohormonen auf das ZNS vermuten lassen.

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Changes in DBH and Noradrenaline Resulting from Cold Exposure

Dopamine β-hydroxylase (DBH) is the most reliable marker for noradrenaline storage vesicles: it has been shown to be associated with both large and small terminal vesicles[1] as well as the large axonal vesicles[2,3]. In axonal vesicles 18% of the DBH is soluble and releasable by hypo-osmotic shock[3]; the percentage of soluble DBH in small terminal vesicles, the main source of released transmitter[4,5], is not known; it is likely to be less than in the large noradrenaline storage vesicles since the volume to surface ratio decreases steeply with vesicle diameter.

The finding that sympathetic nerve stimulation leads to the appearance of soluble DBH in the perfusate lends support to the hypothesis that noradrenaline is released by exocytosis[6]. However, nothing is known of the sub-