(Deca-Durabolin®, abbreviated nor-TD) 2.5 mg/kg and 5.0 mg/kg; (4) Ol. arach. 0.1 ml/kg.

The animals were kept in cages over funnels through which the daily urines were collected into bottles. Before the animals were injected with the hormones, the daily urines were collected separately for two days, which provided the control samples for each group. The urine samples were gathered 30 days after each single hormone administration. In each bottle, 5 ml of 5% oxalic acid was added and the bottles were stored in a −15°C refrigerator for serial determination of ascorbic acid (AA). The AA assay was carried out according to the method of SCHAFFERT and KINGSLEY[8].

The daily urinary total AA was 210 μg/100 g body weight in young male rats and 246 μg/100 g in young male rats. The corresponding AA excretion in adult female and male rats was 242 μg/100 g and 453 μg/100 g respectively.

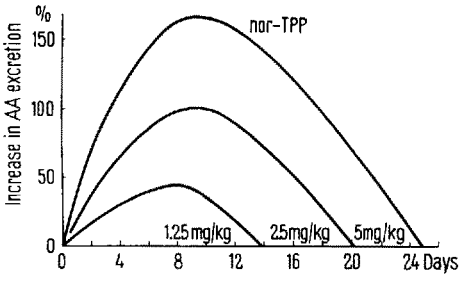
When injected in male adult rats only slight or no response was found after androgenic and anabolic hormones in the daily AA excretion. In young male rats a significant increase was observed. The most significant increase was found in the excretion of AA in female rats. Of these groups also the young female rats were more sensitive in this reaction. After testosterone propionate, the highest values were found on the 3rd and 4th day after its administration. With the doses used, the increase in the excretion of AA was, at its highest, 60–100% above the control values. The basal AA excretion values were restored on the 10th to 12th day.

When the anabolic hormones were injected, a highly significant increase in AA excretion was observed. The highest AA excretion values were found with both substances 8–10 days after their administration. After the top values the AA excretion decreased and the basal excretion was obtained. With nor-TD the basal level was obtained somewhat later than with nor-TPP with same doses.

The results obtained with nor-TPP with three various doses are graphically presented in the Figure. In each group the highest values were reached on the 8th to 10th day. With increasing dosage the AA excretion values are respectively higher and the basal values are obtained later.

The increase in the AA excretion depends on the increase in enzyme action in the liver. Repeated administration of drugs which increases the activity of drug-metabolizing enzymes also stimulates liver growth[9]. This suggests the possibility that the drugs may in some way cause an anabolic effect on protein metabolism in liver. It might be pertinent that testosterone and anabolic hormones which have an enhancing effect on protein metabolism increase also the activity of the microsomal enzymes intimately linked in the AA synthesis in the rat. On the contrary, estrogens which exert a catabolic effect on protein metabolism may have a decreasing effect on AA synthesis.

The effect of androgenic and anabolic hormones on the urinary AA excretion is probably identical with that of pituitary growth hormone[6]. Thus androgenic and anabolic hormones stimulate the synthesis of AA from glucose through the main glucuronic acid pathway as follows: D-glucose → D-glucuronic acid → L-gulonic acid → L-ascorbic acid[10]. In guinea-pigs, which cannot form ascorbic acid, these hormones may cause an increased excretion of glucuronic acid.



The percentage increase in the daily urinary ascorbic acid excretion after nor-TPP administration in three different doses to 2-months-old female rats.

Zusammenfassung. Die Wirkung einiger androgener und anaboler Hormone auf die tägliche urinäre Ascorbinsäureausscheidung junger und erwachsener, sowohl männlicher wie weiblicher Ratten wurde untersucht. Erwachsene männliche Ratten haben von Anfang an eine unabhängig von diesen Hormonen hohe Ascorbinsäureausscheidung. In den andern Gruppen steigern die verwendeten Substanzen die untersuchte Ascorbinsäureausscheidung deutlich.

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Influence of Drugs and Neocortical Spreading Depression on Hippocampal 'Arousal Reaction'

In unanaesthetized, curarized or freely moving rats with implanted electrodes the reversible functional elimination of neocortices by spreading depression (SD) does not influence the regular (4–8/sec) ϑ-activity in the hippocampus evoked by external or reticular stimulation (WEISS and FIFKOVÁ[1]; RÜDIGER, WEISS, and FIFKOVÁ[2]) and Physostigmine administration (BOHDANECKÝ, WEISS, and FIFKOVÁ[3]). This type of activity is highly sensitive to anesthetics (GREEN and ARDUINI[4]; GANGLOFF and MONNIER[5]; BRÜCKE, SAILER, and STUMPF[6]; BRADLEY and NICHOLSON[7] etc.). The question solved in this paper is whether the hippocampal activity after barbiturate and

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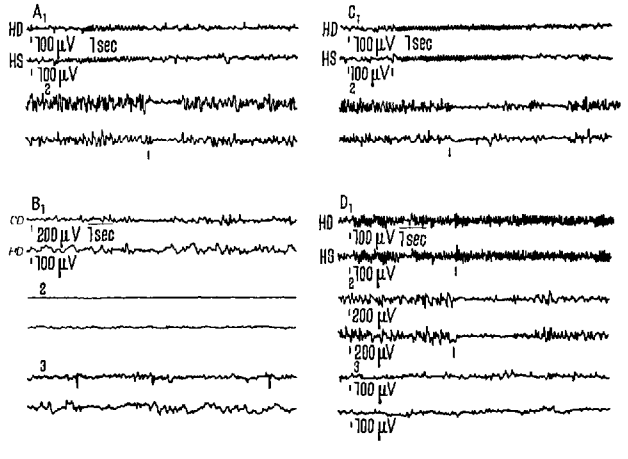
chloralose administration will change during neocortical SD.

Methods. (a) In curarized rats the EEG activity was recorded with bipolar electrodes stereotaxically introduced into dorsal hippocampus, mesencephalic reticular formation and frontal neocortex. (b) In other experiments rats and rabbits with chronically implanted electrodes in the same region were used. The arousal reaction was evoked by external (acoustic or tactile) or reticular stimuli (trains of rectangular pulses 0,5 msec, 400 c/sec). SD was elicited by local application of filter papers (2 × 2 mm) soaked with 10–25% KCl on the dural surface. Barbiturates (Dial, Allobarbital, Thiopental) 40 mg/kg and chloralose 20–40 mg/kg were administered subcutaneously, physostigmine 0,1 mg/kg (in rabbits) intravenously.

Results. (1) In 10 curarized rats the ϑ-activity evoked by external stimuli disappeared after barbiturate administration. In light anaesthesia this type of 'arousal' reaction is replaced by desynchronization of the high-voltage slow-wave activity in the hippocampus (similarly as in the neocortex). During neocortical SD (in contradistinction to unanaesthetized rats) the amplitude of barbiturate activity reversibly decreases in the hippocampus. This reduction lasted approximately as long as the decrease of neocortical activity during SD (Table). During SD the arousal stimuli do not elicit any change in the hippocampogram even when SD was evoked during slight anaesthesia when obviously a desynchronization reaction occurs here. Similar results were obtained in 4 freely moving rats with implanted electrodes in which the reticular formation was stimulated electrically (Figure).

(2) In 9 unrestrained rats with implanted electrodes the hippocampal ϑ-activity evoked by reticular stimulation disappeared after chloralose administration and was replaced in light anaesthesia by desynchronization of slow wave activity. Neocortical SD reduced also in these cases the amplitude of hippocampogram reversibly and eliminated the EEG reaction to arousal stimuli (Figure).

(3) In 6 freely moving rabbits with implanted electrodes intravenous physostigmine evoked hippocampal ϑ-rhythm under normal conditions. The effect of physostigmine administered on the level of slow wave activity induced by a previous application of 20–30 mg/kg of chloralose i.p. was investigated in this group. We have never seen a desynchronization after physostigmine in the hippocampus. Either ϑ-activity occurred or the slow hippocampal activity did not change at all. We observed only in 1 animal that external stimuli evoked desynchronizations and physostigmine ϑ-rhythm.



A: ϑ-Activity in hippocampus after reticular stimulation with implanted electrodes in freely moving rat. 1—before, 2—soon after administration of Allobarbital. B: Spontaneous activity in hippocampus in a rat anaesthetized by Dial (acute experiment). 1—before, 2—during, 3—after bilateral neocortical SD. C: Similar experiments as A using chloralose. D: 1 and 2—as C1, 2; 3—during bilateral SD evoked immediately after 2. In all records: HD—hippocamp. right, HS—hippocamp. left; arrows—stimulation.

The effect of neocortical SD on spontaneous EEG activity in the hippocampus of the rats anaesthetized with Dial

	(a) Homolateral SD	(b) Bilateral SD
1. Number of experiments (depressions)	10	6
2. Frequency of decrease in amplitude absolutely and in %	10 (100)	6 (100)
3. Average amplitude during SD ± S.E. of the mean stat. significance of the decrease as compared to the initial amplitude (100%)	38.0 ± 3.6 $p = 0.003$	28.3 ± 5.4 $p = 0.01$

Discussion. The above experimental data are supporting our preliminary results (WEISS and FIFKOVA[1]). Simultaneously with the elimination of the reticuloseptohippocampal mechanism inducing the hippocampal ϑ-activity by drugs, the slow-wave generating mechanism (probably thalamo-cortical in origin) prevails. This type of activity may be desynchronized by external and reticular stimuli. It depends on the normal function of neocortex.

The arousal reaction during physiological sleep (phase 1 characterized by generalized slow-wave high-voltage activity) is also accompanied mostly by desynchronization of the hippocampal activity (ROLDÁN, WEISS, and FIFKOVÁ[8]). It remains unclear whether the change of ϑ-'arousal' reaction to desynchronization in course of progressing anaesthesia is due to dissociation of separate ϑ-inducing and desynchronizing mechanisms acting on the hippocampus (YASUKOCHI[9]) by drugs.

Zusammenfassung. In leichter Barbiturat- oder Chloralosenarkose wird die ϑ-Aktivität im Hippocampus, durch äussere oder retikulare Stimulierung induziert, von einer desynchronisierten Hippocampus-Aktivität abgelöst. Die Amplitude dieser durch Anästhetika hervorgerufenen langsamen hohen Wellen wird während der neocortikal sich ausbreitenden Depression reversibel verkleinert.

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