Vorderhornzellen konnten hier irgendwelche Veränderungen nachgewiesen werden (Figur c und e).

Hinsichtlich der Strukturveränderungen an den motorischen Vorderhornzellen im Ischaemiebereich waren besonders charakteristisch für die verschiedenen Ischaemiezeiten die Veränderungen der Mitochondrien und des endoplasmatischen Retikulum (Figur b und d). Nach einer Ischaemie von 10 min, die noch im Bereich der Strukturerhaltung liegt, zeigten die Cristae der Mitochondrien kolbenartige Auftreibungen. In der Mitochondrienmatrix waren wolkenartige Substanzverdichtungen zu erkennen. Die Zisternen des endoplasmatischen Retikulums waren deutlich erweitert.

Nach einer Ischaemiedauer von 20 min, bei welcher die Strukturerhaltungszeit der motorischen Vorderhornzellen überschritten ist und die deshalb zu irreversiblen Schädigungen an diesen Zellen führt, waren die Cristae der stark gequollenen Mitochondrien reduziert. Ein Zerfall der Zisternen des endoplasmatischen Retikulum und eine Auflösung der rosettenartigen Gruppierung der Ribosomen sind kennzeichnend für die Veränderungen bei dieser Ischaemiedauer.

Weder vorher noch nachher verabreichtes Silymarin beeinflusste die geschilderten Änderungen der Ultrastruktur.

Schlussfolgerung. Mit einer Funktionsprüfung der motorischen Vorderhornganglienzellen nach BLASIUS und einer elektronenmikroskopischen Untersuchung dieser Zellen nach abgestufter Ischaemie und entsprechenden Kontrollen ist eine umfassende Möglichkeit gegeben, den Einfluss von Substanzen auf die normale und auf die geschädigte Ganglienzellfunktion und -struktur zu bestimmen[11,14,15]. Silymarin übte keinen solchen Einfluss aus. Auch eine schädigende Wirkung durch Silymarin liess sich nicht feststellen, womit alle bisherigen Untersuchungen über die Verträglichkeit des Silymarins bestätigt wurden.

Summary. The effect of Silymarin on the function and structure of lumbar anterior horn cells in the rabbit was studied under graduated ischemia. It was shown that Silymarin has neither useful nor injurious influence on the anterior horn cells examined.

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Depletion of Cerebral Monoamines by *p*-Chlorophenylalanine in the Cat

p-Chlorophenylalanine (*p*CPA) produces a long-lasting depletion of cerebral serotonin (5HT) in several species[1-3]. This effect is related to the inhibition of tryptophan hydroxylase[4]. However, the levels of catecholamines in the brain of rat[1,5,6] and mouse[7] are also affected after a single administration of relatively low doses of the drug. In addition, norepinephrine (NE) has been found to be markedly diminished in various brain areas of the dog after repeated administrations of *p*CPA[1]. In the cat, a single dose of *p*CPA (500 mg/kg i.p.) does not seem to induce any detectable depletion of cerebral catecholamines within 40 h after administration[8].

Recently, the effect of catecholamines on pontogeniculo-occipital spikes induced by *p*CPA was studied in cats[9]. The biochemical findings reported in this investigation indicate that *p*CPA lowers not only the levels of 5HT but also those of the endogenous catecholamines in cat brain.

Methods. Cats of either sex weighing 2–2.5 kg were injected twice with 300 mg/kg of DL-*p*CPA (suspended in saline) i.p. with an interval of 24 h. The animals were killed with 100 mg/kg of nembutal i.p. at various time intervals after the first injection of *p*CPA (see Figure). The brains (without cerebellum) were cut into 2 parts (i.e. forebrain and brain stem) by a prepontine-intercollicular section. One hemisphere of the forebrain and the brain stem were analyzed for their amine content. NE and dopamine (DA) were extracted according to the procedure of ANTON and SAYRE[10] with minor modification (using 2 *M Tris* solution for pH adjustment) and measured spectrophotometrically as described by LAVERTY and TAYLOR[11]. 5HT was extracted by the method of BOGDANSKI et al.[12] and determined according to SNYDER et al.[13]. Saline-treated cats served as controls.

Results. The time course of *p*CPA-induced changes of monoamine levels in the two parts of cat brain is shown in the Figure. In the brain stem, 5HT depletion was almost maximal (reduction to 40% of controls) within 48 h, whereas in the forebrain, a significant decrease (to 60% of controls) was not observed before the 80th h after the first administration of the drug. In the latter brain part, 72 h after the first injection the 5HT content was slightly elevated over the control values.

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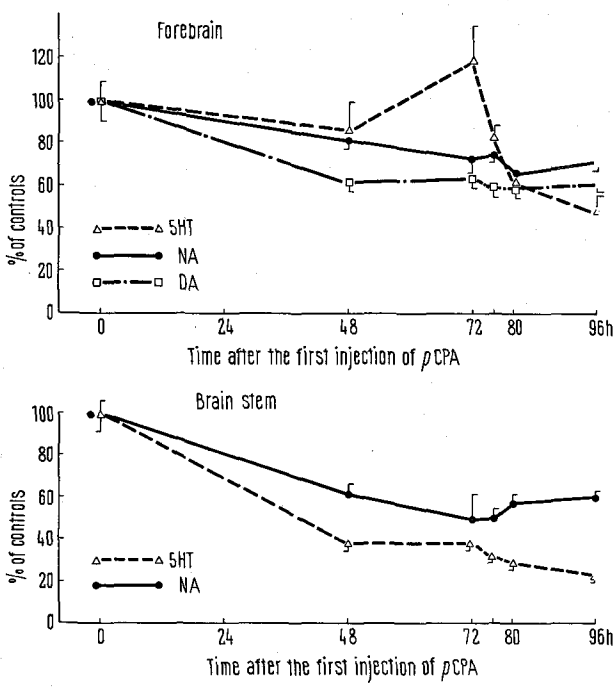
*p*CPA also induced a long-lasting decrease of catecholamines. Both NE and DA were reduced to 60–70% in the forebrain as well as NE in the brain stem (50–60%). The effect on NE seemed to be more pronounced in the brain stem (−50%) than in the forebrain (−34%).



Effect of *p*CPA on endogenous amines in brain stem and forebrain of the cat. The values are expressed in percent of controls and represent means with S.E.M. of 4 double experiments. Control values (μg/g) were 0.35 ± 0.03, 0.25 ± 0.01 and 0.53 ± 0.05 for 5HT, NA and DA in forebrain, 0.80 ± 0.06 and 0.46 ± 0.03 for 5HT and NA in brain stem, respectively.

Discussion. The present results confirm previous findings[1,2]. Thus, *p*CPA markedly reduces the 5HT content of the brain. In addition, these experiments show that the time course of 5HT depletion by *p*CPA is different in the forebrain and in the brain stem. This may suggest different effects of the drug on the synthesis of 5HT in regions which mainly contain nerve cell bodies and short axons (brain stem) from areas containing mainly terminals (forebrain). The slight transient rise of 5HT in the forebrain which precedes the depletion of the amine, is in agreement with previous findings in cat midbrain and diencephalon after a single dose of the drug[2]. However, its mechanism is as yet unclear.

*p*CPA markedly decreases the cerebral endogenous catecholamines in the cat as well as in the rat[6]. The mechanism of this depletion, which seems to be similar for brain stem and forebrain, remains to be elucidated. A direct effect of the drug on tyrosine hydroxylase[5] cannot be excluded. However, this action of *p*CPA might also be mediated by a neuronal mechanism.

In conclusion, these findings indicate that under the experimental conditions described, the depleting action of *p*CPA in cat brain is not selective for 5HT. Accordingly, if the drug is used as a tool for studying the role of 5HT in brain functions, a concomitant effect on catecholamines should be taken into account.

Zusammenfassung. *p*-Chlorphenylalanin, ein Inhibitor der Serotoninbiosynthese, senkte bei Katzen den Serotoningehalt des Gehirns nicht selektiv. Es wurde gleichzeitig eine signifikante und langanhaltende Erniedrigung des Noradrenalin- und Dopamingehalts gefunden.

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Axonal Growth from the Primitive Sympathetic Elements of Human Fetal Adrenal Medulla

The cytoarchitecture of human fetal adrenal medulla serves suitable conditions for isolating tather pure groups of primitive sympathetic cells. According to COUPLAND[1], the adrenomedullary primitive sympathetic elements showed delayed patterns of differentiation and persisted through the first postnatal years. The groups of primitive sympathetic developing AM cells formed tightly packed round to ovoid large cell islands surrounded by a thin connective tissue capsule. Electron microscopy of these cell groups revealed that sympathetic neurones were differentiating in the central region of the clusters while the peripheral zone facing to the cortical elements or medullary venous sinusoids differentiated to catecholamine storing medullary cells (HERVONEN[2]). The purpose of the present work was to develope an organ-culture method which could provide constant conditions for studying different humoral agents possibly exerting an effect on the differentiation of human fetal primitive sympathetic cells.

The adrenal glands of 3–4-month-old human fetuses were removed immediately after the disconnection of the fetomaternal nutritive contact and the medullary region was homogenized by gentle pipetting. The clusters of primitive sympathetic cells were identified under a stereomicroscope and placed on petri dishes for cultivation. The cultivation was performed in Hepes buffered Medium 199. A detailed description of the method will be published elsewhere (HERVONEN and RECHARDT[3]).

A strong fibroblast reaction and rapid monolayer formation by the cells of fetal cortex were the dominating features during the first 2 weeks. After this stage the dedifferentiation and/or degeneration of adrenocortical cells markedly reduced their number. The collections of primitive sympathetic cells were found to be mostly free from surrounding cortical cells. Axons grew rectangularly from the surface of the groups in all directions initially. During the 4th week the growth of the nerve fibres was most marked and complex anastomosing networks of fibres from neighbouring collection of primitive sympathetic elements were observed (Figure). The cells of Schwann were identified along the course of the fibres. The parallell

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