In female rats, persistent cornification of the vaginal epithelium may occur spontaneously in intact individuals[4] or can be induced by transplantation of the testes immediately after birth[5], ligation of oviducts[6], hypothalamic lesions[7,8], and after CCl_4-administration[9]. Hepatotoxicity due to an activation of the sympathetic areas of the central nervous system[10] as well as the adrenal medulla[11] following CCl_4 administration has been documented. Adrenalin (epinephrine) is believed to cause lesions in the liver similar to those seen after CCl_4[12], a constriction of the intrahepatic blood vessels occurs which causes an anoxia in the areas near the central vein and produces centrilobular necrosis accompanied by a fatty infiltration of the parenchymal cells. Fatty liver is known to be directly associated with impaired estrogen inactivation.

Organ weights of adreno-ephedrine-treated experimental and saline-treated control rats (mg/100 g body weight)

Treatment	No. of rats	Adrenals	Pituitary	Uteri
Control	6	18.5 ± 3^a	4.5 ± 0.2^a	191 ± 16^a
Adreno-ephedrine	18	39.0 ± 4	4.6 ± 0.3	300 ± 8

[a] Means $\pm$ S.E.M.

Therefore, from the existing evidence and experimental data it may be assumed that the changes induced after adreno-ephedrine administration are primarily due to hepatic lesions[13].

Zusammenfassung. Adreno-Ephedrin bewirkte bei Ratten Daueröstrus und Zunahme des Gewichts der Uteri und der Nebennieren. Die Ovarien enthielten Follikel verschiedener Grösse, aber keine reifen Corpora lutea. Diese Wirkungen des Adreno-Ephedrins werden auf fettige Infiltration des Leberparenchyms zurückgeführt.

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Brain to Body Relationships in Ontogeny of Canine Brain

Recent studies by Kobayashi[1] have demonstrated the relationship of brain development when compared with body weight to other aspects of neuro-ontogeny in the mouse (Kobayashi et al.[2]). A sudden change in the relationship between log brain:log body weight occurred at 17 days; similar changes occurring at different ages were noted in a review of available data from other species. The significance of these findings has been discussed by Fox[3] in a neuro-ontogenetic study of this species. When the mouse attains 17 days of age (± 1 day) marked changes in behavior also take place, which coincide with the onset of the critical period of socialization as described in the ethological study by Williams and Scott[4].

The present investigation was undertaken to determine if such a phenomenon exists in the dog. Earlier studies (Scott and Marston[5] and Fox[6]) have shown that between 3–4 weeks of age there is a sudden change in the behavior of the neonate dog, which is regarded as the onset of the critical period of socialization for this species (Scott[7]).

Brain to body weight ratios were calculated from 83 dogs of different ages and of various breeds. Subjects were anesthetized with intravenous pentobarbital and the body weight was taken, after which the brain was removed and weighed. A linear relationship was found between the log body:log brain weight from 0.2 to 1.5 kg body weight, at which point there was a 'break' at approximately 37 g brain weight. From this point onward there was again a linear relationship between brain and body weight. Although the subjects were of heterogeneous background differing considerably in physical size, the age range at which the break in the brain:body relationship occurred was at approximately 4 weeks of age (Figure).

Behavioral correlates of this macroparameter of neuro-ontogeny can be made. Fox[8] showed that the canine brain develops most rapidly during 3–6 weeks of age postnatally, while the period from 2–4 weeks of age (Fox[9]) was found to be the time when the most rapid changes in brain size and reduction in cell density occurred. The rate of metabolism in the cortex and caudate nucleus increases rapidly between 3–6 weeks of age, by which time the metabolic rate is within the normal range (Himwich and Fazekas[10]). Also the resistance to anoxia decreases rapidly from birth, and by 4 weeks of age the resistance

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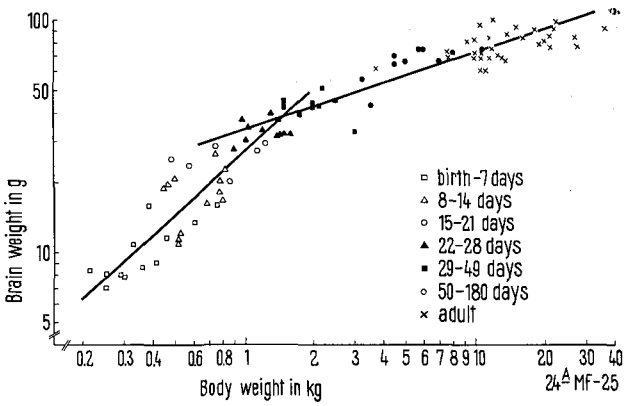
to anoxia is the same as in the adult (Himwich[11]). By 4 weeks of age, stable conditioned responses can first be established[12] and the EEG shows spontaneous activity and many adult characteristics[13,14]. By 4 weeks of age, emotional responses to environmental stimuli appear, and psychological capacities and adult behavioral abilities develop[5] indicative of increased cortical maturation of the later developing higher centers of nervous activity.

These findings show that at approximately 4 weeks of age, when the brain weight is in the region of 37 g and the body weight 1.5 kg, there is a sudden change in the developmental relationships between the brain and body. A critical point in postnatal neuro-ontogeny is therefore evident, which may be correlated with other aspects of CNS development in the dog and supports earlier studies demonstrating a similar phenomenon in the mouse.



Note change in log relationship between brain: body weight occurring abruptly at 1.5 kg body and 37 g brain weight. Nonisogenic subjects were aged from 22–49 days, the median age at this critical point being approximately 4 weeks.

Zusammenfassung. Die Relation Gehirnmasse/Körpergewicht wurde bei 83 Hunden von Geburt bis zum Adultzustand studiert. Ein Bruch in der linearen Relation zwischen den Logarithmen Gehirngewicht und Körpergewicht trat ungefähr im Alter von vier Wochen ein (1,5 kg Körpergewicht zu 37 g Gehirngewicht). Dies betrifft einen kritischen Punkt in der Neuro-Ontogenie, was im Zusammenhang mit anderen Erscheinungen der ZNS- und Verhaltensentwicklung steht.

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Competitive Antagonism Between Norepinephrine and Propranolol

Black et al.[1] first reported that propranolol exerts the β-receptor adrenergic blocking action without any inherent sympathomimetic activity. Since then, several investigators[2–7] have studied the pharmacodynamic effects of these drugs in dogs and human subjects. Very recently, it was found that competitive antagonism exists between isoproterenol and propranolol in anesthetized dogs[4,6]. The present study was undertaken to examine whether such antagonism would also exist between norepinephrine and propranolol in isolated guinea-pig ventricular strip preparations[8].

Twenty guinea-pigs weighing approximately 500 g were killed by cervical dislocation. Their hearts were removed immediately and ventricular strips excised. The strips were washed twice with and then suspended in a bath containing oxygenated Chenoweth Koelle solution[9] (30°C) through which a mixture of 95 % O_2 and 5 % CO_2 (pH 7.35) was bubbled. The frequency of ventricular contraction was kept constant at a rate of 60/min using a Grass stimulator (Model S4). The force of myocardial contraction was measured and recorded continuously using a Grass force displacement transducer (FT-03), and a Grass polygraph (Model 7), respectively. Approximately 45 min after the preparation was completed, the effects of norepinephrine in concentrations ranging between 10^{-7} and $10^{-2}M$ were determined before and after the administration of propranolol in concentrations of 10^{-6} and $10^{-5}M$.

The results of the effect of norepinephrine on myocardial contractile force before and after the administration of propranolol were consistent in all experiments. The average effect of graded doses of norepinephrine is summarized in the Figure. In control ventricular strips, norepinephrine increased myocardial contractile force essentially proportional to the dose. With the administration of increasing doses of propranolol, the effect of given doses of norepinephrine decreased progressively. However, the larger doses of norepinephrine surmounted the blocking

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