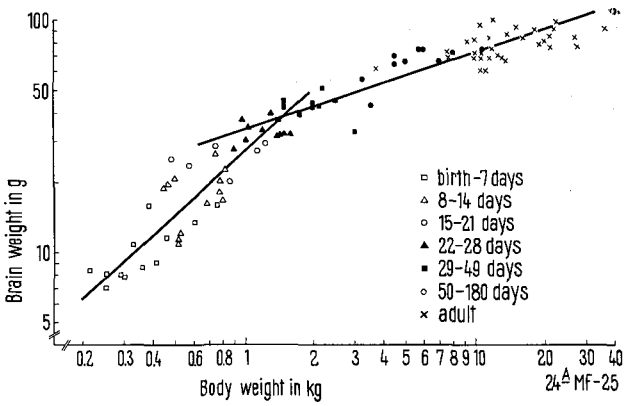
to anoxia is the same as in the adult (Himwich[11]). By 4 weeks of age, stable conditioned responses can first be established[12] and the EEG shows spontaneous activity and many adult characteristics[13,14]. By 4 weeks of age, emotional responses to environmental stimuli appear, and psychological capacities 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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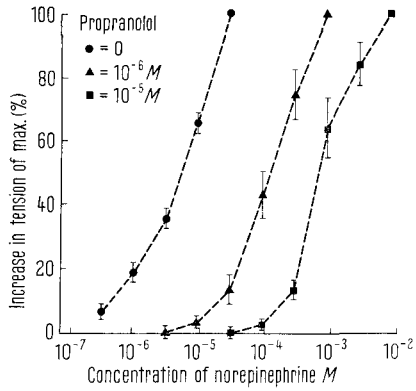
effect of propranolol on myocardial contractile force. As shown in the Figure, each dose-response curve of norepinephrine on myocardial contractile force is shifted progressively to the right, essentially in parallel with each other, as the dose of propranolol increases. This family of dose-response curves appears to satisfy the concept of competitive antagonism between two pharmacological agents, which has been advocated by ARIENS et al.[10] and by SCHILD[11]. Hence, one could conclude that pharmacological competitive antagonism does exist between norepinephrine and propranolol[4,6,12].



Summary of average effect of graded doses of norepinephrine on myocardial contractile force in the guinea-pig ventricular strips. Mean ± S.E.

Zusammenfassung. Der Einfluss von Propranolol, einem neuen β-adrenergischen Blockierungsmittel, auf die Wirkung von Noradrenalin auf die Myokardkontraction wurde an isolierten Meerschweinchenventrikelstreifen studiert. Dabei wurden Indizien für einen kompetitiven Antagonismus beigebracht.

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Persisting Circadian Rhythm in Hepatic Glycogen of Mice during Inanition and Dehydration[1]

CHOSSAT's early data[2] demonstrate that significant circadian periodicity persists in certain birds until the day of their death from starvation and dehydration: statistically significant within-day differences in cloacal temperature of birds completely deprived of food and water as well as in controls (feeding and drinking ad libitum) can be computed from his data published in 1843 (Tables 60 and 68 in [2])[3]. More recently, circadian rhythms in rectal temperature, pinnal mitosis, corticosterone content of serum and adrenal, as well as in pituitary adrenocorticotropic activity, were found to persist in inbred Bagg albino (C) mice deprived of food and water[4,5]. Interest in the question of how long certain other biochemical rhythms demonstrably persist in a mammal deprived of food and water was renewed by problems arising in the construction of a programmed feeding device in preparation for a biosatellite study on rhythms.

Apart from this background, liver glycogen was chosen as a variable for study, since for this function the timing of feeding is still generally regarded as an essential condition of a rhythm. This is done in keeping with a role assigned to nutritional factors already by BERNARD[6] and in line with a report by HIGGINS et al.[7], the pioneering investigations on this subject by ÅGREN et al.[8] notwithstanding. Contrary to the conclusion of ÅGREN et al., the fact that hepatic glycogen drops to very low levels during starvation is misinterpreted for a lack of rhythm. This status quo is not surprising since, with few exceptions, most curves published by students of rhythms more recently on liver glycogen show multiple turning points[9] – a circumstance arising from the failure to 'isolate' a circadian rhythm from other superimposed frequencies (such as the ultradian changes) and 'noise'.

Against this background, the data of the Figure provide a clear view of the persisting circadian rhythm in several groups of animals. Three groups of mice were standardized for periodicity analysis, as described elsewhere[10], but two of these groups were on a modified schedule only in that either all food or all food and water as well was removed 16 h before the starting time of the serially independent sampling here employed.

766 C female mice were singly housed in three separate rooms under conditions of 12 h light (0600 to 1800) alternating with darkness; they were standardized on this regimen for seven days prior to sampling and during the sampling span. Food and water were available ad libitum

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