

checked in histological preparations. Details concerning electrode construction and implantation, stimulus measuring and monitoring and electrode position identifying techniques have been published elsewhere²⁻⁴.

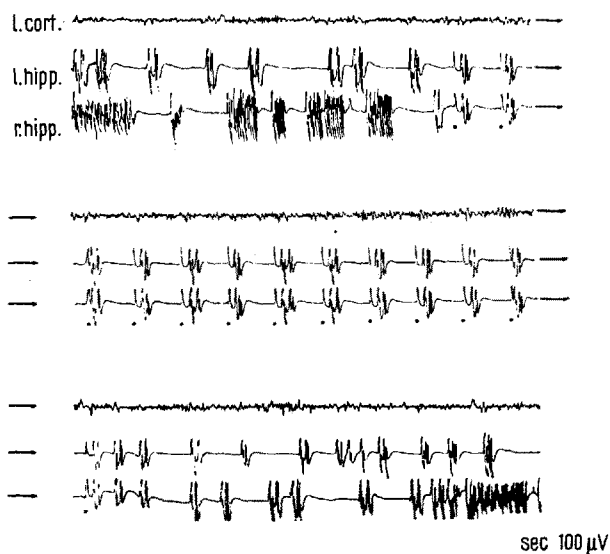
As could be expected, on the grounds of previous experience⁵, 28–30 days after the application of alumina cream, the spontaneous seizure activity appeared, originating first in one and several days later in the other hippocampus as well. The first stage of global, recurring, tonic-clonic hippocampal seizures which, transmitted from the site of origin, involved as a rule the homologous area of the opposite hemisphere, was followed by a long-lasting clonic activity, becoming increasingly more restricted to the corresponding side of origin. Finally, autonomous and persistent focal epileptiform activity could be recorded on both sides of the brain. At this stage of development, the single shock stimuli of an adequate rate (roughly corresponding to the predominating rhythm of the hippocampal discharges) if applied to the thalamic nuclei (N. anterior, N. medialis dorsalis) were invariably found to be effective in driving and synchronizing the rate of otherwise quite independently and asynchronously discharging hippocampal foci. As illustrated in the Figure, the two foci continued to fire synchronously following the cessation of the driving thalamic stimulation, but resumed their own autonomous rates of discharge shortly afterwards.

The general conditions, indispensable in order to control the activity of a primary discharging focus by stimuli applied to a given distant structure, and the possible mechanisms underlying this phenomenon have been extensively discussed elsewhere^{4,6}. In this respect, results of the present work fully support the earlier investigations.

The experiments reported here, clearly demonstrate the important role which the structures constituting the diffuse non-specific thalamo-cortical system⁷ could play in synchronization of activity of the two bilateral and autonomous hippocampal, epileptogenic foci. In addition, if one bears in mind results of the previously published investigations¹, these experiments indicate how multiple, mutually unrelated isocortical and allocortical cerebral areas could be effectively coupled and synchronously subordinated to the thalamic rhythm, when, in the course of convulsive activity, the intralaminar nuclei of the thalamus reach the dominant level of background excitation. Experiments have already been undertaken to check this assumption⁸.

Zusammenfassung. Bei Katzen wurde auf beiden Seiten im Hippocampus je ein epileptischer Fokus (Alumina-paste) geschaffen. In einer zweiten Sitzung wurden Elek-

Cat alu.2



Synchronisation of the clonic activity of the two autonomously discharging hippocampal epileptogenic foci, by single shock stimuli delivered to the thalamus (N. anterior) at the rate of 1/sec. Black dots indicate the stimulus artifacts. L. cort. = left cortex; l. hipp. = left hippocampus; r. hipp. = right hippocampus.

troden in jeden Hippocampus und in die intralaminären Thalamuskern implantiert. Durch Reizung in den letzteren Strukturen konnten die sonst voneinander unabhängigen epileptischen Entladungen der beiden Hippocampi synchronisiert werden.

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² J. M. R. DELGADO, *Yale J. biol. Med.* 24, 351 (1952).

³ LJ. MIHAILOVIĆ and J. M. R. DELGADO, *J. Neurophysiol.* 19, 21 (1956).

⁴ LJ. MIHAILOVIĆ, *Glas de l'Académie Serbe des Sciences* 128, 91 (1959).

⁵ P. PASSOUANT, J. CADILHAC, and LJ. MIHAILOVIĆ, unpublished.

⁶ A. ROSENBLUETH, D. D. BOND, and W. B. CANNON, *Amer. J. Physiol.* 137, 681 (1942).

⁷ H. H. JASPER, *J. EEG clin. Neurophysiol.* 1, 405 (1949).

⁸ This work has been supported by a grant from the Yugoslav Foundation for Scientific Research, Contract No. 490/1.

The Postnatal Development of Homoiothermy and Cold Resistance in Mice

Earlier studies have indicated that the capacity for the regulation of body temperature is relatively poorly developed in newborn mice¹ and rats². On the other hand, the ability to resist low body temperatures is better in newborn rats than in the adult ones³. In order to find out the causal mechanisms of these phenomena, a more detailed study of the time-course of the postnatal development of the homoiothermy and cold resistance is necessary. With this the present study is concerned. The simultaneous

¹ M. S. PEMBREY, *J. Physiol.* 18, 363 (1895). – F. B. SUMNER, *J. exp. Zool.* 15, 315 (1913). – A. GINGLINGER and CH. KAYSER, *Ann. Physiol.* 5, 710 (1929). – L. R. FITZGERALD, *J. exp. Zool.* 124, 415 (1953).

² M. S. PEMBREY, *J. Physiol.* 18, 363 (1895). – B. LEICHTENTRITT, *Z. Biol.* 69 (N.F. 51), 545 (1919). – A. GULICK, *Amer. J. Physiol.* 76, 206 (1926); 119, 322 (1937). – E. D. ANTOSHKINA, *Fisiol. Zhurn. SSSR* 26, 3, 16 (1939). – R. M. HILL, *Amer. J. Physiol.* 149, 651 (1947). – J. FAIRFIELD, *Amer. J. Physiol.* 155, 355 (1948). – S. GELINEO and A. GELINEO, *Bull. Acad. Serbe Sci. Méd.* 3, 119 (1951). – P. HAHN, J. KŘEČEK, and J. KŘEČKOVÁ, *Physiol. Bohemoslov.* 5, 283 (1956). – P. TAYLOR, *J. Physiol.* 154, 113 (1960).

³ E. F. ADOLPH, *Amer. J. Physiol.* 166, 75 (1951).

recording of as many of the relevant variables as possible, as functions of the age and of the environmental temperature, must subsequently also be done in order to elucidate the causes of this development.

The *first series* of experiments consisted of 5900 body temperature measurements and was designed to give a general picture of the development of homoiothermy in mice. The offspring in four inbred litters of two females, belonging to the Swiss albino strain bred in this laboratory, were used as test animals. They were kept at 24°C, the nest temperatures varying usually between 27° and 33.5°C. Daily, one or two of the offspring of each female were weighed and subjected to ambient temperatures of about 31°, 26°, 24°, 19°, 15°, and in some cases also 6°C. The ambient temperatures were measured with a thermocouple kept at a distance of about 1 cm above the animal and the precise values recorded from calibrated galvanometer (El-lab, Copenhagen) readings at intervals of 5 (or 10) min. The skin temperatures were measured by a plastic coated thermocouple (total thickness 0.5 mm) the sensitive point of which was pressed against the skin of the clavicular region and subsequently against the inguinal region of the youngsters. The skin temperatures were measured at intervals of 5 (or 10) min. The measurements were continued until at least two successive measurements agreed well. The skin temperatures of the clavicular and inguinal region thus stabilized were averaged and the mean for the three or four animals tested daily was calculated and plotted against the ambient temperatures. The graphs presented in Figure 1 were obtained thus. The difference between the lowest mean skin temperature achieved and the ambient temperature at 15°, 20°, 24°, and 31°C are presented in Figure 2 as a function of the age of the animals. In several experiments, the lowest colonic temperatures achieved were also recorded. No individual was used for experiments more frequently than at intervals of four days.

Figures 1 and 2 reveal the discontinuous nature of the postnatal development of homoiothermy in mice. The development of the mice of the strain used can be divided in this respect into four periods: (1) The period of poikilothermy, during which the first, probably behavioural thermoregulatory reactions develop (between ages of 0 and 2 days). (2) The period of nearly complete poikilothermy with probably behavioural reactions, which allow for slight deviations from poikilothermy at the middle temperature range (between ages of 2 and 7 days). (3) The period of development of homoiothermy at ambient temperatures between 23° and 33°C (between ages of 7 and 13 days). (4) The period of development of normal homoiothermy of the adult animals, characterized by the achievement of homoiothermy at lower ambient temperatures and the maintenance of normal adult body temperature level with the normal difference between colonic and skin temperatures. During this period, a shift in the neutral temperature probably also takes place (between ages of 13 and 19 days).

The *second series* of experiments consisted of subjecting 200 young mice of different ages to an ambient temperature of -10°C for varying periods. After the decrease in the colonic temperature, this was measured, recorded, and the animal moved to 20°C for recovery. In these experiments, no other means for facilitating the recovery were used. The lowest colonic temperatures achieved by the animals were plotted against their age, those of recovering animals being marked with a circle and those of the moribund animals with a dot. Thus was the Figure 3 constructed.

The development of cold resistance in mice of the strain used can be divided, according to the present material,

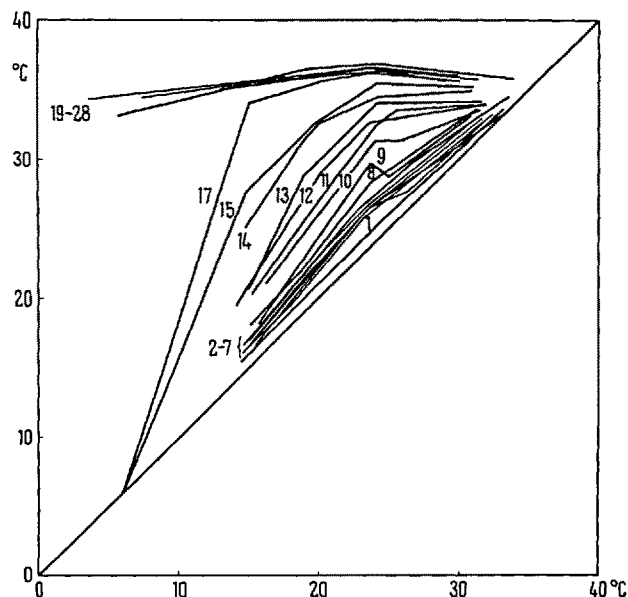


Fig. 1. The stabilized mean skin temperature of mice at different ages as a function of the environmental temperature. Age in days.

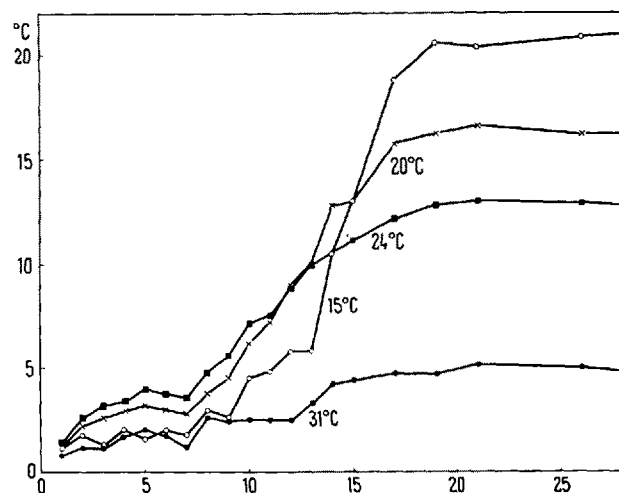


Fig. 2. The difference between stabilized mean skin temperature and environmental temperature at four different environmental temperatures as a function of the age of mice. Age in days.

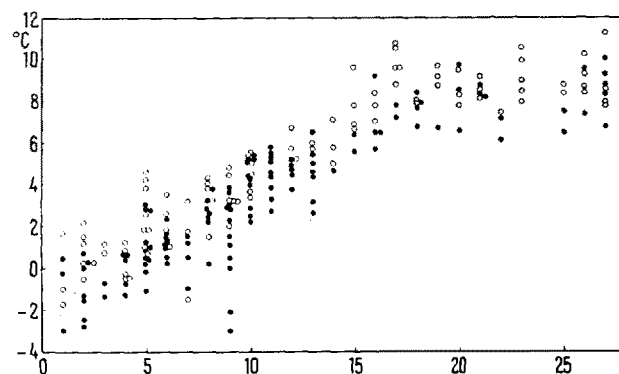


Fig. 3. The lower lethal body temperature of mice as a function of age (in days). The open circles represent lowest body temperature values recorded from surviving individuals, the black dots lowest body temperatures recorded from moribund individuals.

into two periods: (1) The high resistance period of the newborn animals to low body temperatures (the lethal limit being about 0°C) (between ages of 0 and 7 days). (2) The period of decrease in cold resistance (between ages of 7 and 18 days).

After the latter period, cold resistance of the mice is on a rather steady level for at least ten days. At the end of this period, the lethal body temperature is about 9°C, thus being approximately at the adult level.

The present results have been descriptive in character. The correlations found earlier in other animals between the level of thermoregulatory ability and the appearance of muscle shiver in cold, the myelination of hypothalamus, and general metabolic changes have to be subjected to day-to-day studies during the development. The decrease in cold resistance may reflect an increase in vulnerability of the central nervous system through cold or anoxia or the occurrence of general nutritional and metabolic changes in the tissues, as well as the activation of endocrines. These studies may also throw some light on the mechanism of the cold death⁴.

Résumé. Par la mesure des températures dermales stabilisées des souris jeunes exposées aux températures extérieures variées, il a été possible de séparer quatre périodes dans le développement d'homéothermie entre les âges de 0 à 19 jours. La résistance au froid chez les souris jeunes s'amoindrit notamment entre les âges de 7 à 18 jours.

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March 10, 1962.

⁴ The present study is part of a research program supported by research grants from the Finnish Academy of Sciences and the National Science Council of Finland. The technical assistance of Miss HANNA KURPPA is gratefully acknowledged.

Visceral and Vascular Transposition in the Viviparous Toothcarp *Xiphophorus maculatus* (Wagtail Strain)

In some strains of viviparous Toothcarps *situs inversus viscerum*, an anomaly, which is known to occur in about one out of ten thousand human beings, is not uncommon. Recently BAKER-COHEN¹ described this anomaly in 37% of specimens of an inbred line of the domesticated Fury strain of the platyfish *Xiphophorus maculatus*. Personally, we have observed visceral and vascular transposition in the same species, namely an inbred line of the Wagtail strain. 45% of the specimens showed *situs inversus viscerum*, whereas in three other strains of the platyfish, and in the related swordtail species *Xiphophorus helleri* and *Xiphophorus pygmaeus*, the anomaly was not observed or proved to be infrequent. Unborn Wagtail embryos revealed no evidence of a positive correlation between the visceral situs of the mother and the offspring or for twinning in association with visceral and vascular transposition. The asymmetry of the unpaired vena jugularis inferior, occurring in the genus *Xiphophorus*, appeared to be inverted in 10 to 25% of fishes of nearly all strains of *Xiphophorus helleri*, *Xiphophorus pygmaeus*, and *Xiphophorus maculatus*. In animals with *situs inversus viscerum*, an associated inversion of the venous asymmetry was present in most specimens, being consequently mirror images of their normal fellows in both respects. As in

animals with a normal visceral transposition, in about 10 to 25% a relative inversion was observed. In some cases, a double inversion occurred, in this way producing a normal venous asymmetry.

As in the Fury strain¹, so also in the Wagtail strain, both types of inversion were independently genetically determined. However, in neither instance could a simple hypothesis for the mechanism of inheritance be fitted to the available data. The visceral and vascular transposition in the Fury¹ and Wagtail strain of *Xiphophorus maculatus* appeared to be not sex-linked, nor was it maternally influenced. The indications were that it was due to autosomal genes which lacked full expression. As these results correspond very well with those obtained by BAKER-COHEN¹, a more general significance should indubitably be attached to them.

Zusammenfassung. Beschreibung des relativ häufigen *Situs inversus viscerum* beim lebendgebärenden Zahnkarpfen *Xiphophorus maculatus*.

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Department of Histology, Free University, Amsterdam (The Netherlands), February 15, 1962.

¹ K. F. BAKER-COHEN, Amer. J. Anat. 109, 37 (1961).

Die Mitschattierung

Jedes Objekt fällt in seiner Umgebung mehr oder weniger auf. Für Tiere kann beides je nach den Umständen vorteilhaft sein: Kontrastfärbungen dienen allgemein zum Signalisieren und speziell zum Warnen, Tarnfärbungen verbergen das Tier vor seinen Feinden und den Räuber vor seiner Beute.

Von der Umgebung hängt es ab, was (1) möglichst wenig oder (2) möglichst stark auffällt. Wenn man nur zwei Typen unterscheidet, benutzen Tiere (a) in optisch reich gegliederter Umgebung mannigfache Fleckungen, (b) in

optisch eintöniger Umgebung Hell-Dunkel-Schattierung. Entscheidend ist die Grösse des Tieres verglichen mit dem Umgebungsmuster.

(1a) *Tarnen durch Fleckung*: Ein bekanntes Beispiel sind die Plattfische, die ihre Farbe dem Umgebungsmuster sehr weit anpassen können.

(1b) *«Gegenschattierung»*¹: Der dem Licht zugekehrte, das heisst gewöhnlich hell beleuchtete Teil des Tierkörpers ist dunkel, der dem Licht abgewandte, normalerweise im

¹ F. SÜFFERT, Z. Morph. Ökol. Tiere 26, H. 1/2 (1938).