wir im Rahmen unserer Methode mit den ECR gleichsetzen, nehmen wir 120 min an. Danach beträgt der ECR an linken 38,15 ± 0,60 und an rechten Vorhöfen 36,63 ± 0,73% Feuchtigewicht.

Wie auch bei der Inulinraumbestimmung sind konstante Temperatur[1,3] und ausreichende Sauerstoffversorgung des Gewebes wesentliche Voraussetzung: mit fallender Temperatur der Inkubationslösung (Figur 2) wird der ECR signifikant kleiner (30 °C $p < 0{,}025$, 20 °C $p < 0{,}005$ und 10 °C $p < 0{,}0005$). Ferner kommt es unter Hypoxiebedingungen zu einer deutlichen Verringerung des ECR (120 min $p < 0{,}0005$ und 180 min $p < 0{,}0005$) – nach 5 Stunden dürfte auch bei diesen Untersuchungen eine beträchtliche Membranschädigung vorliegen.

Diskussion. In der Literatur werden über die Grösse des ECR von Herzmuskelgewebe unterschiedliche Angaben gemacht – sie schwanken von 9%[2] bis 44%[4]. Abgesehen von methodischen Problemen liegen offensichtlich Speziesunterschiede vor, ferner Unterschiede zwischen Vorhof- und Kammermuskulatur[5]. Bei vergleichbaren Versuchsbedingungen ergaben sich für linke Meerschweinchenvorhöfe Werte um 35% FG[1,6–8]; da der Verteilungsraum extracellulärer Kationen nicht unbedingt dem Inulinraum entsprechen braucht, wird sogar ein maximaler ECR von 45% diskutiert[1]. Folglich stehen unsere eigenen vorliegenden Ergebnisse mit den Literaturangaben in guter Übereinstimmung.

^{51}Cr-EDTA erfüllt wesentliche Voraussetzungen, die an eine Substanz zur ECR-Bestimmung zu stellen sind: es dringt nicht in die Zelle ein[9–13] und ist wie Inulin weitgehend inert, es findet also kein Metabolismus statt[14]. Der Komplex hat sich bei verschiedenen Untersuchungen als stabil erwiesen[15], die Plasmabindung ist gering[10,13,14] oder wird vollkommen negiert[12]. Weiterhin garantiert das niedrige Molekulargewicht (343 gegenüber 5100 beim Inulin) eine ausreichend grosse Diffusionsgeschwindigkeit bis zur Einstellung eines Fliessgleichgewichtes. Die Vorteile der Verwendung von ^{51}Cr-EDTA bestehen in der einfachen Messtechnik, in der guten Reproduzierbarkeit, dann in der mit 27,8 Tagen günstigen Halbwertszeit und ferner insbesondere darin, dass man am gleichen Präparat Extracellulärraum und Kationenkonzentration bestimmen kann[16,17].

Summary. The extracellular space of isolated guinea-pig left auricles was studied by using ^{51}Cr-EDTA. Under this condition, we measured the extracellular space as 38.15 ± 0.60% at 35 °C. Under hypothermic and hypoxaemic conditions, we observed significant decrease of the extracellular space.

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Circadian Rhythm in Cerebral Blood Volume of Mouse

The superior cervical ganglion appears to be unique among the sympathetic ganglia in that it receives direct information about environmental lighting conditions via a pathway which, in the rat, is well elucidated[1]. Accordingly, a diurnal rhythm controlled by light has been demonstrated for norepinephrine in the rat pineal[2] and submaxillary[3] glands which are supplied by postganglionic fibres from these ganglia[4–7]. The superior cervical ganglia also give rise to adrenergic nerves innervating the pial and brain vascular beds[8,9]. Estimation of the over-all cerebrovascular response by recording changes in cerebral blood volume (CBV) after sympathetic nerve stimulation and denervation, or after administration of sympathomimetic amines, has revealed a definite adrenergic vasoconstrictor influence on the intracranial vessels[10]. Against this background it could be assumed that the cerebral vascular bed was another region directly influenced by environmental light and, as a first step to test this hypothesis, CBV in mice was measured under various lighting conditions to reveal any diurnal rhythmicity.

Experiments were performed during January-February on 66 adult male NMRI mice (Anticimex, Sweden), approximately 25 g body weigth. They were housed at 21 °C in clear plastic cages with wire top and were fed freely with standard pellet food and tap water. The following groups were studied: a) Animals kept on a 12 h light/12 h darkness schedule during 3 weeks (light source: 40 watt daylight fluorescent tubes giving an animal exposure of 100–150 lux; lights on: 06.00 h; lights off: 18.00 h). The animals were killed at various times during the last dark/light period (Figure). b) Animals maintained in the same way but killed after 6–8 h in the last light period (corresponding to between noon and 14.00 h). c) Animals

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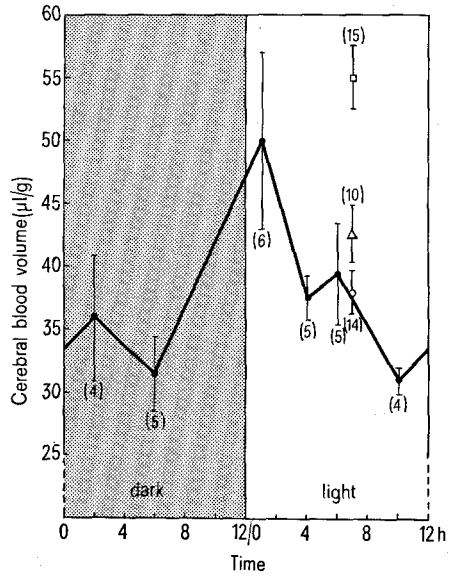
kept for 2 weeks in constant darkness in a photographic dark room provided with light trap. Clearing of the cages was done under a photographic red light source. The animals were killed between noon and 14.00 h. d) Animals kept in constant light (fluorescent light source giving 100–150 lux in the cages) for 2 weeks and then killed between noon and 14.00 h.

CBV was measured as cerebral plasma volume using radio-isotope dilution[11]. A solution (0.1 ml) of human serum albumin (0.3–0.5 mg/ml in 0.9% saline) labelled with ^{131}I (RIHSA) to an activity of 50 µCi/ml was injected into the tail vein of the unanesthetized animal, and after 10 min mixing time the animal was killed by rapid immersion into liquid nitrogen (−196 °C). The entire intracranial content was then dissected out, weighed and placed in a plastic tube. 25 µl blood was drawn from the left ventricle of the heart, collected in another plastic tube to serve as internal reference. All manipulations during dark conditions were performed under a red bulb light. Radioactivity in the samples was measured with an autogamma spectrometer (Packard). CBV was expressed as µl blood per g of brain tissue.

The circadian variation in CBV is presented in the Figure. The CBV values obtained for animals kept for 4–7 h in light (35–40 µl/g) agree with figures previously presented for untreated control animals killed druing the corresponding time of the day[10]. Subsequently, the CBV was significantly reduced (Student's t-test for mean values after 4 h light vs. 10 h light: $P < 0.01$) to reach a minimum level after 10 h in light. A comparatively small CBV was then maintained during the following 8 h after which there was an increase to a maximum CBV of 50 µl/g (6 h darkness vs. 1 h light: $P < 0.05$). CBV then returned to the values measured after 4–7 h in light. The difference between the highest and the lowest CBV levels was statistically significant ($P = 0.02$).



Cerebral blood volume of mice killed throughout the last 24-h cycle of a 12 h darkness/12 h light schedule during 2 weeks. The circadian changes in these untreated animals are indicated by filled circles. Animals maintained for 2 weeks in constant darkness, open square; constant light, open triangle; matching controls on a light-darkness schedule, open circle. Mean values ± standard error of the mean, number of animals within parenthesis.

The CBV measured around noon in animals maintained in constant darkness was significantly higher ($P < 0.001$) than time-matched control animals kept in a light-darkness rhythm. Animals in constant light, however, had a similar CBV as these controls.

It is at present not known whether the marked 24-h variation in the cerebral hemodynamics of mice has resulted from direct changes at the brain level, e.g. intracerebral[12] or autonomic[8–10] neural mechanisms, or whether it is secondary to systemic factors influencing the cerebral circulation, such as fluctuations in arterial carbon dioxide tension or blood pressure[13]. Experiments are in progress to study whether the circadian rhythm in CBV is endogenous or exogenous, i.e. influenced by external lighting conditions. The present results show that at least continuous darkness significantly affects the rhythmic fluctuations. It is notable that the 24-h variation in pineal gland[2] and salivary gland[3] norepinephrine follows a pattern very similar to that of the CBV which would favour a reflex influenced by environmental light: the adrenergic nerves to the intracranial blood vessels as well as to the pineal and salivary glands all arise in the superior cervical sympathetic ganglia[4,5,7] known to receive pathways transmitting external light impulses via the optic tracts[1].

In conclusion, the cerebral blood volume of mice, measured by radioisotope (RIHSA) dilution shows marked circadian variation, with a peak in the early morning and comparatively low levels in the afternoon and evening until midnight. The CBV (measured around noon) of animals kept in constant darkness was significantly higher, that of animals in constant light, however, not altered compared with time-matched control animals on a light-darkness schedule[14].

Zusammenfassung. Mittels I^{131} markiertem Human-Serumalbumin wurde das Blutvolumen im Gehirn von Mäusen zu verschiedenen Tageszeiten gemessen und eine circadiane Rhythmik festgestellt. Andauernder Dunkelaufenthalt führt zu erhöhten Werten des Blutvolumens.

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Réalisation de la différence phasaire du rythme cardiaque chez *Locusta Migratoria* L. I. Vie larvaire

L'Orthoptère Acridien *Locusta migratoria* se présente sous deux formes qui diffèrent par de nombreux caractères[1] et notamment par le rythme cardiaque en fin de vie larvaire et en début de vie imaginale[2].

Nous étudions et comparons ici le rythme cardiaque des Criquets de la phase solitaire et de ceux de la phase grégaire dans des conditions aussi rigoureuses et semblables que possibles pour les deux phases au cours de