with a sharp decline in the corticosterone concentration in plasma, the decrease being particularly marked between 08.00 and 20.00 h on this day. At this time, plasma corticosterone levels in oestrus are comparable with or lower than those noted in the resting phase; this situation is reversed if values between 20.00 and 04.00 h are considered. The corticosterone concentrations are then higher than during the resting phase.

Adrenal corticosterone concentrations (Table II) follow a similar, if not so distinct a pattern. The levels in pro-oestrus are at most times significantly higher than those in the other phases of the sexual cycle. This is not the case, however, at 12.00 h, when neither the values in the resting phase nor those in oestrus are significantly lower, or, as far as the oestrus values are concerned, at 24.00 h or 04.00 h, when the levels are comparable. The cause of this discrepancy needs further elucidation.

Table II. Nychthemeral variations in adrenal corticosterone concentration during the different phases of the sexual cycle in female rats

Time	Resting phase µg/100 mg adrenal	Pro-oestrus µg/100 mg adrenal	Oestrus µg/100 mg adrenal
08.00	4.0 ± 0.43 $n = 27$ $p < 0.01$	6.5 ± 0.56 $n = 14$	3.3 ± 0.95 $n = 9$ $p < 0.01$
12.00	2.7 ± 0.42 $n = 31$ $p < 0.1$	4.3 ± 0.75 $n = 9$	2.4 ± 0.70 $n = 9$ $p < 0.1$
16.00	3.3 ± 0.52 $n = 19$ $p < 0.01$	5.9 ± 0.68 $n = 13$	3.0 ± 0.77 $n = 13$ $p < 0.01$
20.00	3.7 ± 0.74 $n = 9$ $p < 0.01$	7.1 ± 0.6 $n = 9$	4.7 ± 0.78 $n = 9$ $p < 0.05$
24.00	3.8 ± 0.71 $n = 9$ $p < 0.001$	7.4 ± 0.45 $n = 11$	6.1 ± 1.02 $n = 4$ $p < 0.2$
04.00	2.6 ± 0.72 $n = 7$ $p < 0.01$	6.2 ± 0.56 $n = 12$	5.1 ± 0.60 $n = 8$ $p < 0.3$

Significance is calculated by reference to the pro-oestrus values. n = number of animals per group.

Discussion. Corticosterone concentration has been shown to be affected in the normal female rat by nychthemeral rhythm and by the different phases of the sexual cycle. The nychthemeral rhythm of corticosterone in the female rat is fully comparable with that observed in the male rat under similar experimental conditions (see Figure), with the exception that the minimum values in the latter are as a rule lower than with values determined in females during the resting phase.

Sexual activity does not seem to affect the regularity of the nychthemeral rhythm. On the other hand, the pronounced and sustained increase in corticosteroid secretion during the day of the pro-oestrus phase, culminating in very high values in the late afternoon, is noteworthy. It appears that during this critical phase the thalamo-pituitary-adrenal system is subjected to a marked stimulation, which immediately precedes or coincides with ovulation in the rat. It remains to be shown how this burst of adrenocortical activity is related to the different functional changes occurring during this period.

Zusammenfassung. Es wird das physiologische Verhalten von Corticosteron in den einzelnen Zyklusphasen im Plasma und in den Nebennieren normaler weiblicher Ratten untersucht. Die Corticosteronkonzentrationen in Plasma und Nebennieren sind während der Proöstrusphase signifikant höher als während den anderen Zyklusphasen. Der normale Tag-Nacht-Rhythmus bleibt in allen Zyklusphasen aufrechterhalten.

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Experimental Evidence of Inhibitory Control of Pars Intermedia Function and the Rate of Recovery of Function After Denervation in the Teleost *Ictalurus melas*

It is generally agreed that the colour changes in elasmobranchs and amphibians are regulated by the pars intermedia (PI) of the pituitary gland which itself is under the inhibitory control of the brain. Thus any interruptions of the hypothalamo-hypophyseal innervation or transplantation of the gland, i.e. its release from the central control, leads to its hypertrophy and uncontrolled liberation of MSH[1]. Consequently pigment in the skin melanophores becomes either permanently dispersed or remains so for a long time and the ability of the animal to adapt to a white background is totally impaired. The nature of the central control of the PI (meta-adenohypophysis)[2] function in teleosts is, however, obscure. In the only case so far reported (*Poecilia formosa*)[3] the PI, in contrast to elasmobranchs and amphibians, was found to be markedly atrophied in ectopic pituitary transplants. This indicates that in this species the brain has a stimulatory control on PI function. However, the role of MSH in the pigmentation in *Poecilia* has not been experimentally established.

In the present paper the effects of denervation of the PI on the melanophores in *I. melas* (in which MSH plays an important role in the colour changes) are reported with a view to elucidating the nature of the innervation controlling PI function.

Material and method. Denervation of the PI was effected by causing ca. 4 mm deep cuts and lesions by means of a dental drill and a fine probing needle in the exposed hypothalamo-hypophyseal region in between the optic chiasma and the pituitary; in some cases lesions were also made around the gland. In most cases thin rectangular pieces of black plastic (about 2.0×0.7 mm) were vertically inserted into the lesions to prevent the reestablishment of vascular connections. In all, 20 animals (average length 7.0 cm) were operated. Out of these 9 did not survive beyond 14 days (1st casualty after 5 days), 5 lived 27–38 days, 3 50–62 days and 3 were still alive over 143 days. The fish were white-adapted for 3–4 weeks, their mean of melanophore index (MI) before the operation being 1.4, and were replaced on an

The state of melanophores in *I. melas* on illuminated white and black backgrounds at various time intervals following the denervation of the pars intermedia

Time (days)	Background	Mean MI of lower dermal melanophores		Time (days)	Background	Mean MI of lower dermal melanophores	
0	White	5.00	(10)[a]	55	White	3.38 ± 0.35	(6)[a]
2	White	3.77 ± 0.50	(7)	71	White	2.60 ± 0.24	(3)
3	White	3.33 ± 0.71	(7)	95	White	2.40 ± 0.43	(3)
6–8	White	3.20 ± 0.34	(12)	108	White	2.30 ± 0.47	(3)
19	Transferred to black	3.32 ± 0.45	(8)		Transferred to black		
20	Black	5.00	(7)	109	Black	5.00	(3)
38	Returned to white	5.00	(7)	120	Returned to white	5.00	(3)
39	White	3.60 ± 0.36	(7)	121	White	1.73 ± 0.21	(3)
46	White	3.20 ± 0.49	(6)	130	White	1.23 ± 0.20	(3)

[a] Number of animals shown in parentheses. Illumination general ceiling lighting. Temperature 20 ± 1 °C. Melanophore index (MI) readings were recorded from the tail around the vascular arc. Epidermal melanophores always showed slight less dispersion of pigment than the dermal melanophores on a white background.

illuminated white background after the operation (Table). In controls the hypothalamic region was only exposed.

Results and discussion. The results are summarized in the Table. These show 1. the immediate effect of interrupting the hypothalamo-hypophyseal tract on the melanophores of white-adapted animals was of full dispersion of pigment (MI 5.0); 2. 1–3 days after the operation there was a considerable aggregation of pigment and the MI became relatively stable (3.2–3.3); no significant change in the melanophores in the next 2 months was detected and white background adaptation of the animals remained impaired; 3. the animals retained their ability to adapt to a black background; 4. the fish appeared to gradually regain their ability to adapt to a white background about 2 months after the denervation of the PI and in about 4 months they appeared to be able to concentrate their melanophores almost completely (Table). In controls white/black background adaptation was unaffected.

Full dispersion of melanophores immediately following the disruption of the hypothalamo-hypophyseal innervation (result 1) was presumably due to abrupt and uncontrolled release of MSH stored in the PI of white-adapted animals.

The state of partial but significant dispersion of melanophores which lasted for several months on a white background (result 2) could be interpreted in different ways, e.g. a) it might be due to the interruption of stimulatory control of anterior lobe of the pituitary which is supposed to secrete W-hormone[4]. But white background adaptation in this species[5] and in *I. nebulosus*[6] does not appear to depend on the pituitary and is probably controlled by aggregating nerves[7]; b) the nature of the nerves controlling PI function in *Ictalurus*, as in *Poecilia*, could be only stimulatory but this does not explain result 3; c) the possibility of the control being excitory as well as inhibitory also does not seem to offer an entirely satisfactory explanation of results 1–3; d) finally the assumption that the PI function is controlled by an inhibitory innervation appears to provide a simple and logical explanation of result 2. The uncontrolled release of MSH resulting from the denervation of the PI is unable to maintain full dispersion of melanophores on a white background because of the activity of the aggregating nerves. Result 3 is also explainable by this conclusion: MSH released by the denervation is capable of fully dispersing the melanophore pigment on a black background due to the lack of the aggregating activity of the melanophore nerves.

The regaining of the ability of white background adaptation by the operated animals (result 4) appears to be due to a gradual regeneration of the cut nerves after about $2^1/_4$ months, leading ultimately to the reestablishment of the central control on the PI. The slow reestablishment of the control requiring several months indicates that the PI in *I. melas* is controlled by ordinary nerves as reported in the amphibians *Xenopus*, *Bufo*, and *Ambystoma*[8]. Histological changes following denervation of the PI have not been studied as yet[9].

However, the interruption of the hypothalamo-hypophyseal tract by the plastic barrier has been verified by cutting serial sagittal sections of the heads of 10 animals 8 of which lived for at least 14 days following the operation. These include the last 3 animals (see Table) that were killed and fixed after 143 days.

Zusammenfassung. Nachweis, dass beim Teleostier *I. melas*, dessen Sekretion unter der dämpfenden Wirkung des ZNS steht, MSH funktionell relevant ist.

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