strength of 1.2–1.3 T. On this background of cortical activity, the threshold for inhibition of the MR was never found below 1.5–1.7 T, while the ipsilateral flexion reflex usually occurred at thresholds of 2–3 T.

(2) During *drowsiness or synchronized sleep*, the threshold for the MR was only slightly higher than the values obtained during wakefulness. In some cases, however, there was no change in threshold of the MR, but occasionally a slight decrease in intensity of the muscular reflex response could be detected when stimulus intensities only slightly suprathreshold for the MR were used. The threshold for the ipsilateral flexion reflex also was equal to or slightly higher than the values obtained in the awake animal. Similar values (usually ranging from 3 to 4 T) were also found to be liminal for an arousal reaction. This fact incidentally gives further support to previous findings indicating that the group I*a* afferent volleys do not exert any influence on the ascending activating system, at least as far as it is possible to decide on the basis of the electroencephalographic test[3,4].

(3) During the episodes of *deep, desynchronized sleep* (see [5]), stimulation of the medial gastrocnemius nerve at 1.2–1.4 T did not cause any muscular reflex response even by increasing the duration of the stimulus train (at 100/sec) up to 10 sec, or the rate of stimulation up to 500/sec. This last condition greatly potentiated the MR in the awake cat. On the other hand, when the animal roused spontaneously from sleep or awoke following acoustic stimuli, the MR gradually reappeared. Stimulation of the medial gastrocnemius nerve at 5.8 T, 100/sec, when applied during deep sleep, caused behavioral arousal, which was accompanied by a generalized contraction of both extensor and flexor muscles.

The present experiments clearly show that spinal reflexes are only very slightly affected in the synchronized sleep compared with relaxed wakefulness. On the contrary, during deep sleep there is a complete abolition of the MR and an increase in threshold of the flexion reflex. This response actually comes to light only as a symptom of a generalized motor response occurring during the arousal elicited by stimulating flexion reflex afferents[3,4]. The striking changes of spinal reflexes occurring during the deep stage of sleep may be due to (i) decrease of a facilitatory influence exerted by the brain stem on spinal cord, (ii) descending inhibitory volleys.

Riassunto. Nel gatto integro non anestetizzato il riflesso monosinaptico estensorio e il riflesso polisinaptico flessorio subiscono soltanto lievissime, a volte impercettibili, modificazioni nel passaggio dallo stato di veglia al sonno sincronizzato. Per contro, nel sonno profondo desincronizzato si osserva l'abolizione completa del riflesso monosinaptico e un'elevazione della soglia per il riflesso ipsilaterale flessorio. Per stimoli efficaci a produrre nel sonno profondo questa contrazione flessoria si osserva anche una risposta motoria generalizzata, che si accompagna ad una reazione di risveglio.

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The Effect of Adrenalectomy on the Norepinephrine and Serotonin Content of the Brain and on Reserpine Action in Rats

MONTANARI and STOCKHAM[1] established that reserpine is more toxic 6 days after adrenalectomy than in intact animals. The present experiments were undertaken to investigate the effect of adrenalectomy on the convulsion-facilitating and biogen amine-depleting action of reserpine.

Methods. The experiments were made on Wistar rats. Adrenalectomy was performed under ether anaesthesia and the animals were given saline for drinking. The experiments were carried out the seventh day after the operation. Reserpine was given intravenously and the rats were used for experiment after 4 h. Electroshock (ES) was elicited with bitemporal electrodes and the threshold stimulus was determined on each rat, namely the minimum amount of current which produced tonic extensor seizures. The norepinephrine (NE) determination was carried out according to PAASONEN and KRAYER[2] by blood pressure determination in cats. Serotonin (5-HT) was extracted with acetone[3] and determined on the rat's stomach[4].

Results. The experiments show that adrenalectomy facilitates the effect of reserpine. The convulsion threshold does not differ in rats 7 days after adrenalectomy related to intact animals. 0.15 mg/kg reserpine i.v. has no considerable influence on the seizure threshold in intact animals, but in adrenalectomized rats significant decrease can be observed (Table I).

The augmented effect of reserpine in adrenalectomized rats may be explained by the experiments, which show that the 5-HT content of the brain is significantly lower in adrenalectomized than in intact animals. NE content does not change. The 5-HT content is decreased to 45% of the intact animals and this change can be detected already on the third day after adrenalectomy.

Reserpine has a more marked influence on the 5-HT content of the brain in adrenalectomized than in intact rats. After administration of 0.25 mg/kg reserpine i.v. the

Table I. Convulsive threshold in mA

Treatment	Intact	Adrenalectomized	No. of rats
—	14.5	15.4	10
0.15 mg/kg reserpine i.v.	13.3	11.3	10

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Table II. Brain NE and 5-HT level in intact and adrenalectomized rats

No. of rats	Experimental condition	Treatment	NE γ/g	5-HT γ/g
12	Intact	—	0.270 ± 0.019	0.690 ± 0.101
6	Intact	0.25 mg/kg reserpine i.v.	—	0.231 ± 0.045
10	Adrenalectomy 7 days before	—	0.248 ± 0.031	0.313 ± 0.086
6	Adrenalectomy 3 days before	—	—	0.329 ± 0.097
9	Adrenalectomy 7 days before	0.25 mg/kg reserpine i.v.	—	0.082 ± 0.021

Table III. Brain NE and 5-HT level 10 min after electroschock (ES)

No. of rats	Experimental condition	Treatment	NE γ/g	5-HT γ/g
10	Intact	—	0.270 ± 0.019	0.690 ± 0.101
10	Intact	ES	0.263 ± 0.035	1.030 ± 0.203
10	Adrenalectomized	—	0.248 ± 0.031	0.313 ± 0.086
10	Adrenalectomized	ES	0.244 ± 0.030	0.139 ± 0.032

5-HT content of intact animals decreases to 0.231 γ/g, while in rats adrenalectomized 7 days before to 0.082 γ/g (Table II).

GARATTINI et al.[5] published that after ES the 5-HT content of rat's brain increases. In the present experiments, in intact animals an increase of the 5-HT content of the brain has been found also (there is considerable deviation between the results obtained in single animals), whereas in adrenalectomized rats the 5-HT level shows a further decrease. ES does not change the NE level either in intact or in adrenalectomized rat's brain (Table III).

Further experiments show evidence that the low 5-HT brain level of adrenalectomized rats is not due to an impaired synthesis, since, after administration of 5-HTP, a significant increase can be detected. It is remarkable that Nialamid does not influence the 5-HT content in these animals (Table IV).

When the rats are treated with 2 mg/day hydrocortisone for 7 days after adrenalectomy, the decrease of the brain 5-HT content does not develop. (Acute treatment has no similar effect.) Similar treatment with DOCA does not influence the 5-HT level, whereas DOCA with hydrocortisone restores also the 5-HT level, but this effect does not differ from that obtained when hydrocortisone was given alone (Table V).

Discussion. The results show that adrenalectomy decreases the 5-HT content of rat's brain without changing the NE content. DE MAIO[6] found a marked increase of 5-HT in rat's brain 24 h after adrenalectomy, while TOWNE and SHERMAN[7] could not detect any similar change after 24 h. DE MAIO and MAROBBIO[8], in a later paper, reported that 48 h after adrenalectomy the brain 5-HT content is lower than in intact rats.

In the experiments of GARATTINI et al.[9] the 5-HT content of brain in intact rats was 0.38 ± 0.01 γ/g, whereas 72 h after adrenalectomy it was 0.28 ± 0.01 γ/g.

The data compared with the present results indicate that 24 h after adrenalectomy there is no change in 5-HT level, but the decrease starts after 48–72 h and a significant decrease can be detected after 7 days. This indicates that the adrenals are essential to maintain the normal 5-HT level of the brain, which is supported by the fact that hydrocortisone is able to restore normal levels. Since after 5-HTP administration in the adrenalectomized rats there is 5-HT accumulation in the brain too, it may probably be assumed that the cause of the low 5-HT content in these animals is the inadequate 5-HTP supply, as the substance is formed in the small intestine and not in the brain[10].

The present experiments show that reserpine is not only more toxic after adrenalectomy[1], but its pharmacological action is also augmented because ineffective doses also have a considerable convulsion-facilitating effect in adrenalectomized rats. This may be the explanation of the experiments which show that reserpine reduces the 5-HT level of the brain to a greater degree in adrenalectomized than in intact rats.

Table IV. 5-HT content of brain in adrenalectomized rats

No. of rats	Treatment	Time in h	5-HT γ/g
10	—	—	0.313 ± 0.086
6	75 mg/kg 5-HTP i.v.	0.5	0.728 ± 0.120
6	5 mg/kg Nialamid i.p.	3	0.381 ± 0.093

Table V. 5-HT level of brain in adrenalectomized rats

No. of rats	Treatment	Time in days	5-HT γ/g
10	—	—	0.313 ± 0.086
6	Hydrocortisone 2 mg/rat/day	7	0.512 ± 0.094
6	DOCA 1 mg/rat/day	7	0.368 ± 0.073
6	Hydrocortisone DOCA	7	0.485 ± 0.081

Zusammenfassung. Sieben Tage nach Adrenalektomie ist der 5-HT-Gehalt des Rattengehirns vermindert, während der NA-Gehalt unverändert bleibt. Chronische Hydrocortisonbehandlung restituiert, DOCA-Behandlung bleibt wirkungslos. Nach 5-HTP-Behandlung steigt der 5-HT-Gehalt auch im Gehirn der adrenalektomierten Tiere.

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