

Group	<sup>a</sup> LVSA		<sup>b</sup> LVFA		<sup>c</sup> HVSA	
	Frequency (c/sec)	Max. amp. ( $\mu$ v)	Frequency (c/sec)	Max. amp. ( $\mu$ v)	Frequency (c/sec)	Max. amp. ( $\mu$ v)
Non-hibernating control (10)	9.9 $\pm$ 0.41	29 $\pm$ 1.54	25.8 $\pm$ 0.41	12.5 $\pm$ 0.63	Absent	
Non-hibernating exposed (10)	12.7 $\pm$ 0.68 $P < 0.01$	40.4 $\pm$ 0.87 $P < 0.001$	31.2 $\pm$ 0.66 $P < 0.001$	12.5 $\pm$ 0.81	Absent	
Hibernating control (10)	9.8 $\pm$ 0.51	34.6 $\pm$ 0.99	25.8 $\pm$ 0.866	17.9 $\pm$ 0.75	8.9 $\pm$ 0.11	84 $\pm$ 3.48
Hibernating exposed (10)	9.9 $\pm$ 0.69	47.2 $\pm$ 1.31 $P < 0.001$	24.8 $\pm$ 0.94	21.7 $\pm$ 0.82 $P < 0.01$	5.1 $\pm$ 0.525 $P < 0.001$	134.5 $\pm$ 5.65 $P < 0.001$

<sup>a</sup> LVSA, low voltage slow activity. <sup>b</sup> LVFA, low voltage fast activity. <sup>c</sup> HVSA, high voltage slow activity. Figures in parentheses indicate number of animals. The results are Means  $\pm$  S.E.

DAVIS<sup>4</sup> as modified by PINEDA and ADKISSON<sup>5</sup>. The maximum amplitude was calculated according to the method of DEY et al<sup>6</sup>.

**Results.** When compared with non-hibernation control group, the characteristic feature of EEG of hibernation control group consists of an increase in the sequence of occurrence of slower waves and in the slow wave index. Mild high voltage slow activity (HVSA) was also evident. The EEG of the non-hibernation exposed group revealed extreme low voltage fast activity (LVFA) with complete absence of HVSA (Table). The hibernation exposed group demonstrated EEG features, characterized by random to regular HVSA (4–7 c/sec) with about 58% increase in the amplitude and 50% increase in the slow wave index in comparison with the hibernation control group (Figure).

**Discussion.** ECCLES<sup>7</sup> ascribes the cause of synchronised theta activity in nonprimates to the inhibitory neurones acting as pace-makers by periodically inhibiting the ascending afferent pathways. According to GASTAUT and FISCHER-WILLIAMS<sup>8</sup>, this inhibitory system is 'branched off' in a side chain from the thalamo-cortical projection, a system which may actively inhibit the reticular formation of the thalamus (rostral) as well as the caudal brain stem and prevent the discharge of cortical spikes resulting in exclusive HVSA. Thus reticular release may be equally responsible for putting into action the inhibitory system. Naturally the high voltage slow waves do not represent a convulsion wave but a veritable state of neuronal depression linked to a phenomenon of active inhibition. From the present study it appears that, in toads during non-hibernation, the tone of the ascending afferent pathways can be increased by sensory activation (e.g. heat exposure) as revealed by extreme altering response in EEG. Whereas, during hibernation, there is a possibility that some cortical and subcortical inhibitory

mechanisms operate even during prolonged heat exposure, resulting in HVSA in EEG. Moreover, the heightened activity of these inhibitory neurones, according to ECCLES<sup>7</sup>, might be responsible for the conditions of accommodation<sup>9</sup> so as to withstand such a high environmental temperature for a prolonged period.

**Résumé.** L'électroencephalogramme des grenouilles qui ont été exposées à 48°C pendant 8 jours durant la non-hibernation révéla une extrême «low voltage fast activity» avec une absence complète de la «high voltage slow activity» (HVSA). L'hibernation (à 58°C pendant 8 jours) montra un HVSA irrégulier à régulier avec 100% d'augmentation en longueur et quelques mécanismes corticaux et subcorticaux restent actifs même lors d'une prolongation de la chaleur.

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<sup>4</sup> P. A. DAVIS, *J. Neurophysiol.* 4, 92 (1941).

<sup>5</sup> A. PINEDA and M. A. ADKISSON, *Tex. Rep. Biol. Med.* 19, 332 (1961).

<sup>6</sup> C. D. DEY, P. K. DEY and S. R. MUKHERJEE, *Indian J. Physiol. all. Sci.* 19, 13 (1965).

<sup>7</sup> J. C. ECCLES, in *The Physiology of Synapses* (Springer, Berlin 1964).

<sup>8</sup> H. GAUSTAUT and W. M. FISCHER, in *Handbook of Physiology Section I: Neurophysiology*, (Eds. J. FIELD, H. W. MAGOUN and V. E. HILL; American Physiological Society, Washington 1959), vol. 1, p. 344.

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## Depressed Synthesis of DNA in Regenerating Rat Liver after Spinal Cord (C<sub>7</sub>) Transection

Spinal cord transection results in the increase of tryptophan oxygenase and tyrosine aminotransferase activities in rat liver by a process independent of adrenal secretion<sup>1–3</sup>. The enhancement was observed only after C<sub>7</sub> level section, i.e. above the segments which innervate the liver. In an effort to get more information on the possible mechanism of this phenomenon, we studied the effect of spinal cord transection on the synthesis of liver DNA.

**Material and methods.** Groups of 3–4 male albino rats (175 g) kept under standard conditions were used throughout the experiments. Spinal cord transection<sup>1</sup>

and partial hepatectomy<sup>4</sup> were performed under light ether narcosis. In sham-operated animals the spinal cord was exposed only. Synthesis of DNA was measured after i.p. administration of thymidine-2-<sup>14</sup>C (1.5  $\mu$ Ci/0.5  $\mu$ M

<sup>1</sup> K. I. VAPTZAROVA, M. S. DAVIDOV, D. V. MARKOV, P. G. POPOV and G. P. GALABOV, *Life Sci.* 8, 905 (1969).

<sup>2</sup> K. I. VAPTZAROVA, P. G. POPOV, D. STRASHIMIROV and G. P. GALABOV, *C. r. Acad. bulg. Sci.* 26, 567 (1973).

<sup>3</sup> K. I. VAPTZAROVA, P. G. POPOV and G. P. GALABOV, *J. Neurochem.* 21, 291 (1973).

<sup>4</sup> G. M. HIGGINS and R. M. ANDERSON, *Archs Path.* 72, 186 (1931).

per animal) 2 h before killing. The liver was removed, cooled and homogenized in 3 vol of saline and the resulting homogenate was repeatedly extracted with cold 0.2 M  $\text{HClO}_4$  to remove acid-soluble liver pool. The precipitate was subjected to an alkaline hydrolysis (1 M KOH, 18 h, 20°C), neutralized and centrifuged. The sediment was hydrolysed at 100° for 1 h with 70%  $\text{HClO}_4$ . Isolation of spectroscopically pure thymine released from DNA was carried out by paper chromatography, as described previously<sup>5</sup>. The rate of DNA synthesis is expressed as the specific radioactivity of isolated thymine in dpm/ $\mu\text{M}$ . UV-absorbance was assayed using Unicam SP 700 spectrophotometer and the radioactivity was measured in a Packard liquid scintillation counter.

**Results and discussion.** DNA synthesis in regenerating rat liver increases 12 h after operation and reaches the maximum at 24 h of regeneration<sup>6,7</sup>. Spinal cord transection at  $\text{C}_7$  in partially hepatectomized animals results in the depression of thymine incorporation into hepatic DNA (Figure). This effect is especially pronounced when transection is carried out immediately after partial hepatectomy. Also in animals at 16 h after hepatectomy, spinal cord transection depresses the already enhanced DNA synthesis. In the liver of intact animals, it is

difficult to compare the data obtained after cord section with those of controls (Table). Morphology of the liver 24 h after  $\text{C}_7$ -level spinal cord section excludes the changed peritoneal resorption<sup>8</sup>.

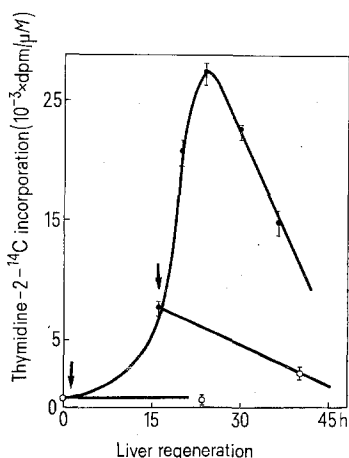
Results similar to our own were obtained by MAROS et al.<sup>9</sup> according to which liver regeneration in rats is markedly inhibited by a mid-thoracic transection of the spinal cord. CLERICI et al.<sup>10</sup>, however, did not find changed metabolic activity of regenerating rat livers (fat and glycogen content, and the capacity to incorporate leucine) on blocking the sympathetic nervous system by the alcoholization of the coeliac and superior mesenteric ganglia followed by partial hepatectomy. On the other hand, CALVERT and BRODY<sup>11</sup> observed that the characteristic hepatic changes seen after the administration of carbon tetrachloride could also be prevented by the pretreatment of animals with reserpine or adrenergic blocking agents, as well as by a high- or mid-thoracic spinal cord transection.

Recently we have found that the administration of reserpine to partially hepatectomized rats decreases the rate of thymidine uptake into liver DNA in a way similar to that observed after  $\text{C}_7$ -level spinal cord section<sup>12</sup>. Reserpine causes the depletion of noradrenaline from sympathetic ganglia and fibres resulting in the decrease of the peripheral sympathetic activity<sup>13,14</sup>. Also phenoxybenzamine, an alpha-adrenergic blocker, given after partial hepatectomy, prolongs the lag phase preceding the peak of DNA synthesis<sup>15</sup>. It seems that transection of the spinal cord above the segments innervating the liver and consequent interruption of descending neural activity to the relevant preganglionic sympathetic neurons results in the depletion of catecholamine content followed by the depression of DNA synthesis.<sup>16</sup>

**Zusammenfassung.** Nachweis, dass Querschnittläsion des Rückenmarkes in der Höhe  $\text{C}_7$  bei Ratten nach partieller Hepatektomie zu bedeutender Hemmung der Auswertung von Thymidin für die DNS-Synthese in der regenerierenden Leber führt.

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Effect of spinal cord  $\text{C}_7$  transection on DNA synthesis in regenerating rat liver. Groups of 3–4 male rats were injected i.p. at different time intervals after partial hepatectomy and/or spinal cord section (arrow) 2 h before killing with thymidine-2- $^{14}\text{C}$  (1.5  $\mu\text{Ci}/0.5 \mu\text{M}$  per animal). Rate of DNA synthesis is expressed as a specific radioactivity of isolated thymine in dpm/ $\mu\text{M}$ .

<sup>5</sup> A. ČIHÁK and J. VESELÝ, *Biochem. Pharmac.* 21, 3257 (1972).

<sup>6</sup> J. W. GRISHAM, *Cancer Res.* 22, 842 (1962).

<sup>7</sup> A. ČIHÁK, M. SEIFERTOVÁ, J. VESELÝ and F. ŠORM, *Int. J. Cancer* 10, 20 (1972).

<sup>8</sup> K. VAPTAROVA, M. DAVIDOV, D. MÄRKOV and G. GALABOV, *Bull. Ass. Anat., Paris* 146, 656 (1971).

<sup>9</sup> T. MAROS, L. SERES-STURM, N. CSIKY and V. KOVACS, *Fegate* 7, 39 (1961).

<sup>10</sup> E. CLERICI, P. MOCARELLI and L. PROVINI, *Expl. molec. Pathol.* 3, 569 (1964).

<sup>11</sup> D. CALVERT and T. M. BRODY, *Am. J. Physiol.* 198, 669 (1960).

<sup>12</sup> A. ČIHÁK and K. I. VAPTAROVA, *Br. J. Pharmac.*, in press.

<sup>13</sup> M. HOLZBAUER and M. VOGT, *J. Neurochem.* 1, 8 (1956).

<sup>14</sup> E. MUSCHOLL and M. VOGT, *J. Physiol.* 141, 132 (1958).

<sup>15</sup> S. THROWER, M. G. ORD and L. A. STOCKEN, *Biochem. Pharmac.* 22, 95 (1973).

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