

No potentiation of methamphetamine induced stimulation in the conditioned avoidance test is observed at 20 mg/kg p.o. This test is used to determine antidepressant activity. Tricyclic antidepressants typically cause potentiation of methamphetamine. The compound does not block monoamineoxidase in vitro at  $10^{-3}$  M concentration.

However, in other tests, II retains a selective ability to stimulate the central nervous system. At high doses (150–200 mg/kg i.p.) convulsive side effects and motor tremors occur. The convulsions are manifested as leaping and rolling movements. Convulsions are followed by ataxia, a decrease of respiratory rate (gasping), cyanosis, and diuresis until the animal expires.

At low doses (4 mg/kg) II potentiates apomorphine induced gnawing. Furthermore, II promotes conditioned avoidance learning of the rat. For the majority of the experiments Holtzman rats of varying age groups were used. For each individual set of experiments a total of 12 to 20 animals were used, with half serving as controls and half receiving the drug. Experiments were repeated with fresh groups of rats whenever it was felt that it was desirable to do so. Results were found to be statistically significant.

More specifically, the performance of rats was tested using a number of different testing situations which included: escape response with the animal jumping to the safety of a raised ledge, the pole climbing test, a modification of the test described by COOK and WEIDLEY<sup>3</sup>, and a passive avoidance test of our own design, all using electric foot shock as a negative stimulus. 10 mg/kg of II was given p.o. 1–1½ to 2 h before the test in these experiments. In a typical experiment, avoidance (escape after receiving foot shock) was accomplished within the time limit by 13 control rats which received saline, as compared to 19 rats that had received 10 mg/kg of II ( $n = 26$ ). Conditioned avoidance (escape prior to shock) was achieved by 6 control rats against 14 rats on II. A corridor type maze was used to determine drug effect on performance in a positive reinforced discrimination task. 50 rats were used for the maze experiments, 25 serving as

controls, 15 receiving 10 mg/kg and 10 receiving 20 mg/kg of II. A positive dose response was observed in these trials. The percentage of rats that reached criterion after 4 min was 16% for controls and 29% for rats receiving 10 mg/kg of II and 40% for rats receiving 20 mg/kg of II. Animals were scored by number of errors committed, and total time elapsed to complete the task. Drug effect on retention was determined in the drug and non-drug state of the escape responses, and for the non-drug state in the maze situations.

Positive effects on certain parameters of intellectual performance in man are also observed. Clinical trials on over 100 subjects to date indicate improvement of learning (acquisition of verbal information), short term recall, long term recall and correlation. Learning and short term recall were measured using acquisition and retention of nonsense syllables as criterion. Long term recall and correlation (intellectual speed) were measured through the use of a word completion test.

Full reports of the chemistry and pharmacology of this new agent, and some of its analogues, will be presented in the near future<sup>4</sup>.

*Zusammenfassung.* Es wurde 3-(2-Benzylmethyl-aminoethyl) Benzoessäuremethyl-Ester als neuer Typ einer wirksamen, das Zentralnervensystem aktivierenden Verbindung erkannt. Eine spezifische Wirkung auf Lernvorgang und Gedächtnis wurde festgestellt. Die Verbindung zeigt eine ausgesprochene spasmolytische Wirkung.

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<sup>3</sup> L. COOK and E. WEIDLEY, Ann. N.Y. Acad. Sci. 66, 740 (1957).

<sup>4</sup> Manuscripts in preparation.

## Contractile Filamentous Structures in Sertoli Cells of the Greek Tortoise (*Testudo graeca*)

In recent years increasing interest has been paid to filaments which are supposed to form part of a contractile system in cells not identical with muscle cells. Bundles of filaments, which are assumed to be contractile, have been demonstrated, for example, in fibroblasts of duodenal villi of the rat<sup>1</sup>, myoid cells (myofibroblasts<sup>2</sup>) in the peritubular connective tissue of the mammalian testis<sup>2–5</sup>, and renal parenchymal and interstitial cells<sup>6–9</sup>. Now we have observed conspicuous bundles of filaments in Sertoli cells of *Testudo graeca*, which suggest that this cell type, apart from its overall role in spermatogenesis and maintaining the blood-tubulus barrier<sup>10</sup>, may contribute to the contractility of seminiferous tubules.

Two sexually immature and 2 mature (spermatogenically active) specimens of *Testudo graeca* were perfused with phosphate-buffered glutaraldehyde and phosphate buffer. Testes were removed, postfixed with OsO<sub>4</sub> and embedded for electron microscopy. Thin sections were stained with uranyl acetate and lead citrate.

In immature animals sertoli cells exhibit scattered filaments<sup>10</sup>, which partly insert in semidesmosomes. The peritubular tissue consists of 2–4 layers of elongated cells, which contain numerous free ribosomes, fragments of rough-surfaced ER, mitochondria of the crista-typus

with an electron-dense matrix, but only few filaments. These cells seem to represent an intermediate stage between fibroblasts and myoid cells. They do not form an uninterrupted cellular sheath but only a loose framework which surrounds the seminiferous tubule. In adult, spermatogenically active animals, these cells have changed but little. Filaments are more prominent, but small in-pocketings of the cell membrane, which have been described to be a characteristic feature of peritubular myoid cells<sup>4,5</sup>, are only occasionally seen. Sertoli cells,

<sup>1</sup> F.-H. GÜLDNER, J. R. WOLFF and D. Graf KEYSERLINGK, Z. Zellforsch. 135, 349 (1971).

<sup>2</sup> P. BÖCK, G. BREITENECKER und G. LUNGLMAYR, Z. Zellforsch. 133, 519 (1972).

<sup>3</sup> Y. CLERMONT, Expl. Cell Res. 15, 438 (1958).

<sup>4</sup> M. H. ROSS, Am. J. Anat. 121, 523 (1967).

<sup>5</sup> R. G. MCCORD, Protoplasma 69, 283 (1970).

<sup>6</sup> J. D. NEWSTEAD, J. Ultrastruct. Res. 34, 316 (1971).

<sup>7</sup> M. H. ROSS and E. J. REITH, Am. J. Anat. 129, 399 (1970).

<sup>8</sup> D. C. PEASE, J. Ultrastruct. Res. 23, 304 (1968).

<sup>9</sup> J. ROSTGAARD, B. I. KRISTENSEN and L. E. NIELSEN, Z. Zellforsch. 132, 497 (1972).

<sup>10</sup> M. DYM, Anat. Rec. 175, 639 (1973).

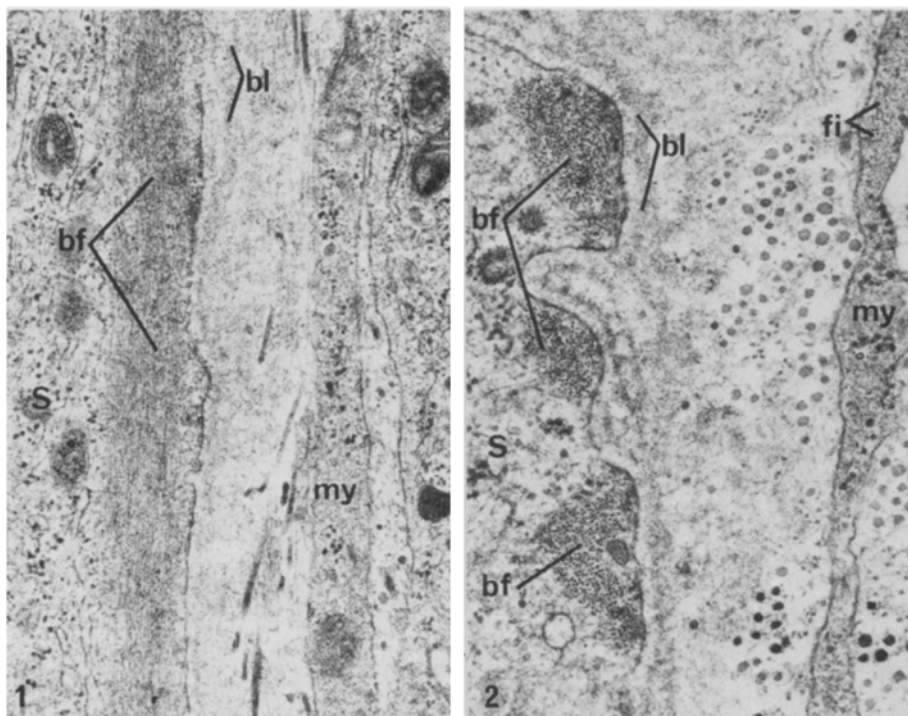


Fig. 1. Bundle of closely packed filaments (bf) near the basal plasmalemma of a Sertoli cell (S) in a spermatogenically active tortoise. Basal lamina (bl) surrounding the seminiferous tubule. Rather undifferentiated myoid cell (my).  $\times 36,000$ .

Fig. 2. Section parallel to the longitudinal axis of a seminiferous tubule. Cross-sectioned bundles of filaments (bf) in foot processes of a Sertoli cell (S). Myoid cell (my) with few filaments (fi). Basal lamina (bl).  $\times 36,000$ .

however, show bundles of closely packed filaments, which fill a  $0.5 \mu\text{m}$  broad zone of the cell near the basal plasmalemma (Figure 1). Filaments are oriented approximately perpendicular to the longitudinal axis of the tubule. In sections parallel to this axis basal foot processes with cross-sectioned bundles of filaments can be observed (Figure 2). Foot processes and bundles of filaments greatly resemble those described in the basal part of proximal tubule cells of rat kidneys<sup>6-9</sup>. Only one type of filament, which is about  $70 \text{ \AA}$  thick, occurs. Contractile activity of seminiferous tubules has already been observed by ROOSEN-RUNGEN<sup>11</sup>, who suggested that this activity was caused by contraction and relaxation of Sertoli cells. Comparison of the tubule boundary structures of the tortoise testis with those of other reptiles<sup>12</sup> reveal distinct differences, which suggest that a general conclusion concerning the involvement of Sertoli cells in tubule motility cannot be made as yet<sup>13</sup>.

**Zusammenfassung.** In basal gelegenen, füsschenartigen Fortsätzen der Sertoli-Zellen von spermatogenetisch aktiven griechischen Landschildkröten (*Testudo graeca*) findet man Filamentbündel, die quer zur Achse der Samenkanälchen verlaufen. Es muss möglicherweise an eine Beteiligung der Sertoli-Zellen beim Transport von Spermien gedacht werden.

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<sup>11</sup> E. C. ROOSEN-RUNGE, Anat. Rec. Suppl. 153, 109 and 413 (1951).

<sup>12</sup> K. UNSICKER, in preparation.

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### Autoradiographische Untersuchungen mit <sup>3</sup>H-Thymidin an der Rattenmilz nach Kryonekrose

In histologischen, histochemischen und autoradiographischen Experimenten sind die zellulären Reaktionen an Leber und Nieren nach Kryonekrosen untersucht worden<sup>1,2</sup>. In Übereinstimmung mit klinischen Befunden<sup>3</sup> wurde festgestellt, dass Kryonekrosen rasch abheilen und nur geringe umschriebene epitheliale und mesenchymale Zellproliferationen auslösen. In den vorliegenden Untersuchungen haben wir geprüft, ob sich das kryochirurgische Verfahren auch an der Milz durchführen lässt und wie sich die Wundheilungsabläufe an diesem Organ nach Kryonekrose verhalten.

An Milzen von 145 g schweren Wistar-Ratten wurden nach einer lokalen Gefrierung ( $-186^{\circ}\text{C}$ , 30 sec) und nach einmaliger i.p. Injektion von <sup>3</sup>H-Thymidin ( $3,0 \mu\text{Ci}/\text{kg}$  Körpergewicht, spezifische Aktivität  $2 \text{ Ci}/\text{mmol}$ , NEN

Chemicals, Boston, USA) in Stripping-Film-Autoradiogrammen (AR 10, Kodak) die Prozentsätze radioaktiv markierter Entzündungszellen (Fibroblasten) im Granulationsgewebe der kryochirurgisch geschädigten Milz bestimmt.

Das mittlere Milzgewicht von 0,5 g änderte sich nicht. Nach 12 h bildete sich eine Koagulationsnekrose aus, an deren Rändern sich nach dem 1. Versuchstag ein zell-

<sup>1</sup> B. HELPAF, H. BREINING and S. LYMBERPOULOS, Naturwissenschaften 59, 369 (1972).

<sup>2</sup> B. HELPAF, H. BREINING und S. LYMBERPOULOS, Beitr. Path. 158, 165 (1973).

<sup>3</sup> H. BREINING, B. HELPAF und S. LYMBERPOULOS, Dt. med. Wschr. 97, 1519 (1972).