acting decarboxylase inhibitor[5,6], on the copulatory behaviour of male sluggish rats. Both treatments significantly increased the percentage of animals showing mounts, intromissions and ejaculations.

The aphrodisiac effect of L-DOPA and apomorphine was prevented by the administration of haloperidol, a specific inhibitor of dopamine receptors in brain[7]. In addition, haloperidol completely suppressed the copulatory behaviour spontaneously present in male rats.

The present investigation has shown that the copulatory behaviour of sexually sluggish male animals is stimulated by a combination of L-DOPA with Ro 4-4602 and by apomorphine. Since the administration of L-DOPA to rats treated with Ro 4-4602 has been shown not only to increase the content of brain catecholamines[5], but also to decrease that of serotonin[8], the stimulatory effect on male copulatory behaviour can be ascribed to either mechanism. On the other hand, since apomorphine is considered to act as a direct stimulant of the dopamine receptors in brain[9], the finding that this compound also stimulates the copulatory behaviour in male rats supports the hypothesis that dopamine plays a stimulatory role on male sexual behaviour.

Consistently, the effect of apomorphine and L-DOPA was prevented by haloperidol, a specific inhibitor of dopaminergic receptors in brain[7]. Moreover, this drug also suppressed the spontaneous copulatory behaviour of male rats with high basal level of sexual activity.

Riassunto. L'apomorfina e l'associazione di L-DOPA con Ro 4-4602, un inibitore della decarbossilasi non cerebrale, stimolano il comportamento copulatorio nei ratti maschi con scarsa attività sessuale di base. L'effetto afrodisiaco della L-DOPA e dell'apomorfina è prevenuto dall'aloperidolo.

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Effects of GABA on Presynaptic Nerve Terminals in Bullfrog (*Rana catesbiana*) Sympathetic Ganglia

It is known that the synaptic transmission in mammalian sympathetic ganglia is inhibited by γ-amino-butyric acid (GABA)[1]. The synaptic transmission in bullfrog sympathetic ganglia is also inhibited by the action of this drug. The present communication deals with the presynaptic inhibitory mechanism underlying such an inhibitory action of GABA.

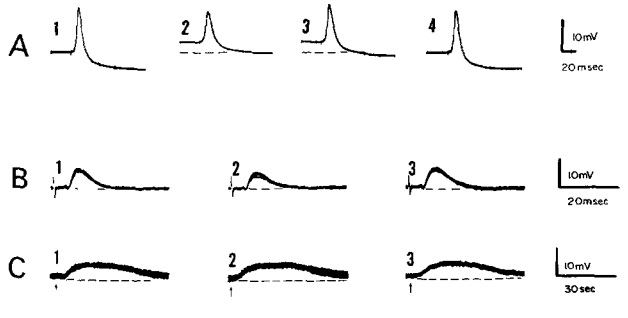

Fig. 1. Effects of 0.1 m*M* GABA on the nicotinic transmission in bullfrog sympathetic ganglia, which was partially blocked by D-tubocurarine (7×10^{-3} m*M*). A) Inhibition of the nicotinic response of ganglion cells. These potentials were recorded by the sucrose-gap method before (1), 1 min (2) and 7 min (3) after an application of GABA, and record 4 was taken 30 min after its withdrawal. Note the original potential level shown by broken lines. B) The fast EPSP recorded from a single ganglion cell before (1) and 1 min (2) after an application of GABA. Record 3 was taken 5 min after its withdrawal. Note the original potential level shown by broken lines. C) The nicotinic ACh depolarization produced by direct applications of ACh before (1) and 1 min (2) after an application of GABA. Record 3 was taken 3 min after its withdrawal. 0.2 cm^3 ACh solution (10 m*M* ACh-Cl in Ringer's solution) was injected into the perfusate at the moments shown by arrows. Note the original potential level shown by broken lines.

Methods. Paravertebral sympathetic ganglion chains of bullfrog (*Rana catesbiana*) were used. The synaptic (nicotinic) transmission mediated by the fast excitatory postsynaptic potential (fast EPSP) was observed by applying supramaximal electrical stimulations (0.5 msec pulses) to preganglionic B nerve fibres[2]. The membrane potentials of preganglionic nerve axons, preganglionic nerve terminals, and ganglion cells were recorded by the sucrose-gap method[3,4]. The intracellular potential of ganglion cells was also recorded[5]. Ionic compositions of the Ringer's solution are as follows: 112 m*M* NaCl, 2 m*M* KCl, 1.8 m*M* $CaCl_2$, and 2 m*M* $NaHCO_3$. Na ions in the Ringer's solution were totally replaced by equimolar *tris* (hydroxymethyl) aminomethane for preparing the Na-free *Tris* solution. Preparations were continuously perfused with a solution flowing through a chamber ($50 \times 5 \times 4$ mm) at the rate of 0.2 cm^3/sec.

Results. The nicotinic transmission in bullfrog sympathetic ganglia was inhibited in the presence of GABA in concentrations of $1\text{–}10^{-2}$ m*M*. Such an inhibition could be observed when GABA was applied to preparations of which nicotinic transmissions were partially blocked by D-tubocurarine (7×10^{-3} m*M*) (Figure 1-A). Sympathetic ganglion cells were depolarized under the effect of GABA[1]. As seen in Figure 1-A, the nicotinic transmission was partially restored, while the depolarization of ganglion cells remained unchanged, when GABA was applied for more than 5–10 min.

In order to clarify the mechanism underlying the inhibition of nicotinic transmission, changes in the fast

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EPSP in single cells were observed by an intracellular microelectrode before and during an application of GABA. The amplitude of fast EPSP was gradually depressed with no detectable (Figure 1-B) or a slight depolarization (less than 3 mV) of the resting membrane under the effect of GABA. The effect of GABA on the acetylcholine (ACh) sensitivity of ganglion cells was studied by recording the nicotinic ACh depolarization produced by direct applications of ACh to the perfusate (Figure 1-C). No detectable changes of the amplitude of the ACh depolarization were observed under the effect of GABA.

The preganglionic nerve terminals were depolarized, whereas the preganglionic nerve axons were not affected, by the action of GABA ($1–10^{-2}$ m*M*) (Figure 2-A). Namely, in preganglionic nerve fibres, their terminal membrane was selectively depolarized by GABA. The depolarization of the preganglionic nerve terminal was partially restored (unlike the depolarization of ganglion cells), when GABA was applied for more than 1 min (Figure 2-A). It has been known that such a depolarization of preganglionic nerve terminals was produced by the action of nicotine[3]. The GABA depolarization disappeared during the nicotine depolarization of preganglionic nerve terminals (Figure 2-B). The GABA depolarization, however, could be produced after a transient nicotine depolarization subsided in the presence of nicotine (Figure 2-B). Furthermore, the GABA depolarization was produced in Ca-deficient (0.1 m*M* $CaCl_2$) Ringer's solution containing 6 m*M* Mg.

The amplitude of GABA depolarizations was decreased (or increased), while nerve terminals were depolarized (or hyperpolarized) by applying a constant cathodal (or anodal) current through a bridge-circuit[3]. This indicated that the GABA depolarization was produced by an increase of the membrane permeability to some ions. The GABA depolarization remained unchanged in the Na-free *Tris* solution.

The GABA depolarization could be inhibited in the presence of picrotoxin (Figure 2-C); when picrotoxin was applied to preparations, no depolarization of nerve terminals was observed. No effect of strychinine on the GABA depolarization was observed. Inhibitions of neither the nicotinic transmission nor the depolarization of presynaptic nerve terminals were observed in the presence of other amino-acids (less than 1 m*M*), such as L-glutamic acid, glycine or β-alanine.

Discussion. According to the present experiment, some kind of membrane receptor which is sensitive to GABA seems to be located at preganglionic nerve terminals. The main cause of the inhibition of the nicotinic transmission in the present preparation was apparently due to a reduction of ACh release from presynaptic nerve endings, being caused by the GABA depolarization at preganglionic nerve terminals.

The present results suggest that the GABA depolarization of preganglionic nerve terminals may be due to an increase in the membrane permeability to certain ions, presumably sodium and/or chloride ions. The fact that no appreciable changes in the GABA depolarization were observed in the Na-free *Tris* solution suggested that the GABA depolarization might be produced by an increase of the membrane permeability to chloride ions.

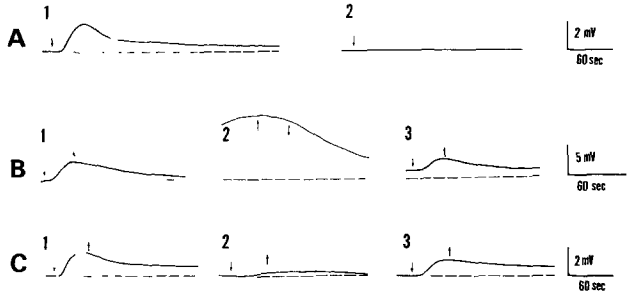

Fig. 2. Depolarizations of preganglionic nerve terminals produced by the action of GABA (0.1 m*M*). These records were taken by the sucrose-gap method. A) Record 1 and 2 were recorded from preganglionic nerve terminals and preganglionic nerve axons, respectively, when GABA was applied (shown by arrows). B) GABA depolarizations produced before (1), 2 min (2) and 10 min (3) after an application of nicotine (0.12 m*M*). GABA was applied for approximately 30–40 sec (shown by arrows). Note the original potential levels shown by broken lines. C) Effect of picrotoxin (0.01 m*M*) on the GABA depolarization. Record 1 and 2 were taken before and 20 min after an application of picrotoxin, respectively, and record 3 was taken 30 min after its withdrawal.

Zusammenfassung. Die hemmende Wirkung von GABA auf die synaptische Transmission wird analysiert und nachgewiesen, dass der Angriffspunkt des GABA offenbar präsynaptisch ist, indem es präsynaptisch zu deutlicher Depolarisation führt.

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Sodium Acetylsalicylate Effectiveness Against Fever Induced by Leukocytic Pyrogen and Prostaglandin E_1 in the Cat[1]

Small quantities of leukocytic pyrogen (LP) placed within the third ventricle[2] or directly into the preoptic/anterior hypothalamic area[3,4] are known to evoke a febrile response in the unanesthetized animal. Sodium acetylsalicylate (NaASA) has been shown to be effective as an antipyretic when administered at the same loci[2,5]. Since prostaglandin E_1 (PGE_1) has also proved to be a potent pyretic agent when discretely applied to the same region of the brain[6–8] and since the synthesis and release of endogenous PGE_1 are inhibited by NaASA[9], Vane has proposed that pyrogen fever may be mediated by PGE_1 in the preoptic/anterior hypothalamic area. The antipyretic action of NaASA against a controlled challenge of exogenous LP and PGE_1 has been utilized here to further examine the hypothesis that local synthesis and release of PGE_1 are implicated in the febrile response to leukocytic pyrogen.

Meterials and methods. Six healthy male cats weighing between 3.6 and 4.1 kg were used in this study. Under halothane anesthesia, cerebral cannulae were implanted stereotaxically to provide access to the third ventricle. Drug tests were begun 1 week after surgery and were conducted at weekly intervals thereafter. Body temperature was assessed with a rectal thermistor and telethermometer and continuously recorded on a polygraph. Normal body temperature was monitored for at least 1 h