exist in the sea trout[6]. Directions of flow across the lamellar surfaces are indicated by arrows. A silver-stained section of ridges and a depression (Figure 2B) shows numerous large cells containing mucous droplets. Some of these cells appear to have spilled their contents onto the ridge surface. WILSON and WESTERMAN[7] reported the presence of many mucous cells of similar appearance in goldfish olfactory lamellae. In the lamellar depressions, the receptor cells appeared quite numerous and densely packed; receptor cells were not observed on the ridges. A similar localization of receptors on the nasal epithelium recently has been reported in the smolt and sea trout[8]. Figure 2B shows that there are cells with cilia on the ridges. The mucus-secreting cells are not found in the depressions on the lamellae, but the olfactory receptors are concentrated there.

TEICHMAN[3] demonstrated that a volume of water flowing through the nasal capsule of the eel circulates past many lamellae consecutively. However, our observations show that in the garfish a volume of water passes over a lamella, and thus over the receptor surface, only once.

Water forced by outside pressure through the nasal capsule would move most rapidly in the bulk solution and more slowly close to the surfaces[9]. The rhythmic action of the cilia ensures that the hydrodynamic situation in fish nasal capsule is quite the reverse. We infer that the ciliary action, making for highest velocity of flow close to the surfaces, provides for efficient delivery of odorant to the receptors.

Résumé. Le cours d'un courant d'eau produit par les cils dans la capsule nasale de *Lepisosteus osseus* est décrit. Un certain volume d'eau ne passe sur l'épithelium nasal qu'une seule fois avant de sortir de la capsule, une situation différente de celle qui s'observe chez l'anguille. L'eau effectue son parcours en 2–9 sec, selon la route suivie à travers la cavité et la condition physiologique du poisson. Des cils sur des lamelles réséquées produisent à la surface un écoulement d'une vitesse moyenne de 2.2 mm par sec.

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Physostigmine Attenuation of Δ^9-Tetrahydrocannabinol Induced Hyperthermia in Rats

Administration of low doses of Δ^9-tetrahydrocannabinol (Δ^9-THC) may produce hyperthermia in rats[1,2]. Hypothermia appears after higher doses[1–3]. A similar dissociation of temperature effects is also reported for morphine[4–6].

A cholinergic link in central body temperature regulation is implied from experiments showing that when central cholinergic transmission is blocked, a rise in temperature appears; the opposite effect appears after acethylcholine (ACh) application[7–9]. That the morphine-induced hyperthermia may result from diminished ACh release has gained experimental support[6]. Physostigmine (0.1 mg/kg) attenuated morphine-induced hyperthermia whereas neostigmine (0.08 mg/kg) did not. Thus, only the centrally active esterase inhibitor exerted the attenuating effect[6].

This finding prompted us to investigate whether physostigmine would also attenuate THC-induced hyperthermia. Administrations of equimolar doses of neostigmine would indicate whether the THC hyperthermia was of central or peripheral origin.

Materials and methods. To answer these questions, male Sprague-Dawley rats, weighting 310–320 g, individually housed with free access to food and water, were treated with 1.0 mg/kg of Δ^9-THC alone or in combination with physostigmine (0.1 and 0.2 mg/kg) or neostigmine (0.08 and 0.16 mg/kg). The effects of the choline esterase inhibitors and the THC vehicle when given alone were also assessed. The drugs were administered in a balanced order according to a Latin square design[10], and the treatments were spaced 5 days apart. The effects of a moderate dose of morphine (2.5 mg/kg) given alone or in combination with physostigmine (0.1 or 0.2 mg/kg) were also studied.

We used 3 latin squares ($2\times5\times5$, Figure A; $2\times5\times5$, Figure B; $2\times3\times3$, Figure C) in order to minimize the number of injections. Physostigmine sulphate, neostigmine bromide, and morphine hydrocloride were dissolved in isotonic saline, whereas Δ^9-THC was given as a suspension of propylene glycol and saline plus Tween-80. Control rats received the THC vehicle. The i.p. route was used throughout and the volume injected was 0.1 ml per 100 g body weight. In the week preceeding the first experimental session, the animals were sham-injected and accustomed to the recording technique.

All recordings were performed in a room varying between 22–24 °C in temperature. The rectal temperature was measured by a thermistor rectal probe, inserted 4 cm into the rectum. Before each session 1 control measure-

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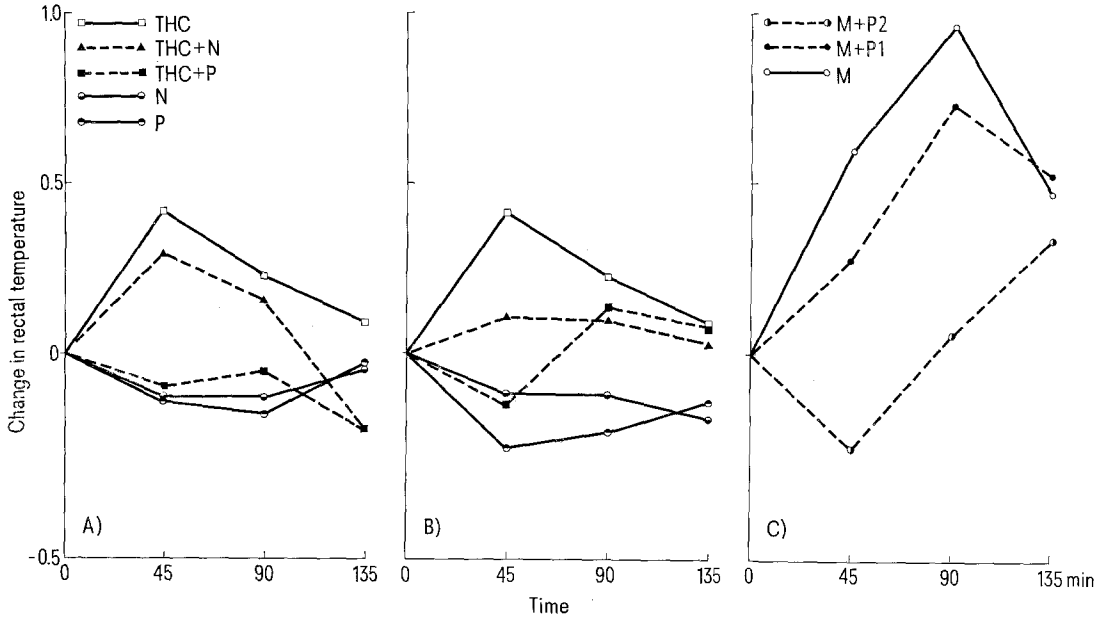

Changes in rectal temperature for rats treated with Δ^9-tetrahydrocannabinol 1.0 mg/kg (THC), physostigmine 0.1 and 0.2 mg/kg (P), neostigmine 0.08 and 0.16 mg/kg (N), THC + P or THC + N. A) The low doses of P and N; B) the high doses of P and N. C) Temperatures changes following administration of morphine 2.5 mg/kg (M), M + physostigmine 0.1 mg/kg (P1) or M + physostigmine 0.20 mg/kg (P2). For each curve in A) and B) $n = 10$; C) $n = 6$. There were no carry-over effects, i.e. the previous injection had not influenced the results of the following session at any point in the present study.

ment was determined 30 min prior to the injections. Rectal temperature was then assessed 45, 90, and 135 min after the drug administrations. To assess the influence of the drugs on rectal temperature, the pre-injection values were subtracted from the respective post injection (p.i.) measurements and then expressed as a difference from the control condition. That is, the controls represent the zero-levels in the Figure. Student's *t*-test and DUNN's multiple comparison procedure[11] were used for the statistical evaluation.

Results and discussion. From the Figure it can the seen that both Δ^9-THC ($p < 0.02$) and morphine ($p < 0.01$) resulted in hyperthermia, the effect being more marked for the latter drug. Our results suggest a shorter action for Δ^9-THC (peak effect, 45 min p.i.) than for morphine (peak effect 90 min p. i.). This is in agreement with previous findings[1,2,6]. An analysis of the combined treatment of Δ^9-THC and the choline esterase inhibitors show that physostigmine attenuated the Δ^9-THC-induced hyperthermia at the time of peak effect ($p < 0.01$), whereas neostigmine did not ($p > 0.05$). The lower doses are depicted in Figure A and the higher doses in Figure B. The effects of treatment with morphine alone or in combination with physostigmine (0.1 and 0.2 mg/kg) are shown in Figure C. There was also an attenuation of morphine-induced hyperthermia. The effect was most marked with the high dose of physostigmine ($p < 0.01$). The separate treatments of the choline esterase inhibitors did not alter the rectal temperature significantly ($p > 0.05$), either when compared with the pre-injection measurements or with the controls. Thus, we may conclude that both Δ^9-THC- and morphine-induced hyperthermia is counteracted by an i.p. injection of physostigmine in a dose that does not in itself bring about any marked temperature changes (cf. Figure A and C).

In the introductory remarks, evidence was presented for the supposition that morphine hyperthermia was accounted for by diminished release of ACh within the brain. If also Δ^9-THC-induced hyperthermia is related to a reduced ACh release, the attenuating effect of physostigmine could be explained. Interference with release of ACh following Δ^9-THC treatment has been reported[12]. Since neostigmine was shown not to influence the Δ^9-THC-induced thermal response significantly, we suggest that Δ^9-THC hyperthermia is primarily of central origin though peripheral influences cannot be excluded.

Although morphine and Δ^9-THC produce similar thermal effects, the underlying mechanisms need not necessarily be the same. Further research is needed to clarify these points[13,14].

Zusammenfassung. Ratten, die mit 1,0 mg/kg Δ^9-THC behandelt wurden, zeigten eine Steigerung der rektalen Temperatur. Dieser Effekt wurde durch Physostigmin, nicht aber durch äquimolare Dosen von Neostigmin vermindert. Temperaturerhöhungen durch Morphium wurden auch durch Physostigmin gehemmt. Aus diesen Resultaten wird geschlossen, dass die thermischen Reaktionen hauptsächlich zentralen Ursprungs sind und in sich ein cholinergisches Glied schliessen.

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