Mechanoreceptors and Adrenergic Nerve Terminals

It is well known that moderate degrees of sympathetic stimulation or small doses of adrenalin or noradrenalin may influence the activity of certain types of mechanoreceptors[1]. There is however so far no conclusive evidence whether this is a direct effect of the catecholamines (CA) on the nerve endings or if it is secondary, e.g. to contraction of adjacent smooth muscles or to changes in the blood flow. It has been shown that sympathetic nerve stimulation or local application of CA may lower the threshold and slow the adaptation of the cutaneous touch receptors in the frog[2] and that sympathomimetic agents may increase the activity of the Pacinian corpuscles of the cat's mesentery[3]. Stimulation of an accessory C fibre penetrating the Pacinian corpuscle[4] has also been shown to facilitate the receptor process[5] under certain conditions.

Using the highly sensitive and specific method of FALCK and HILLARP it is now possible to study the neuronal monoamines at the cellular level[6,7], and in the present investigation this method has been applied in an attempt to establish if adrenergic nerve terminals occur in the immediate vicinity of certain mechanoreceptors. An approach along these lines may throw some new light on the mechanism of sympathetic influence at the receptor level.

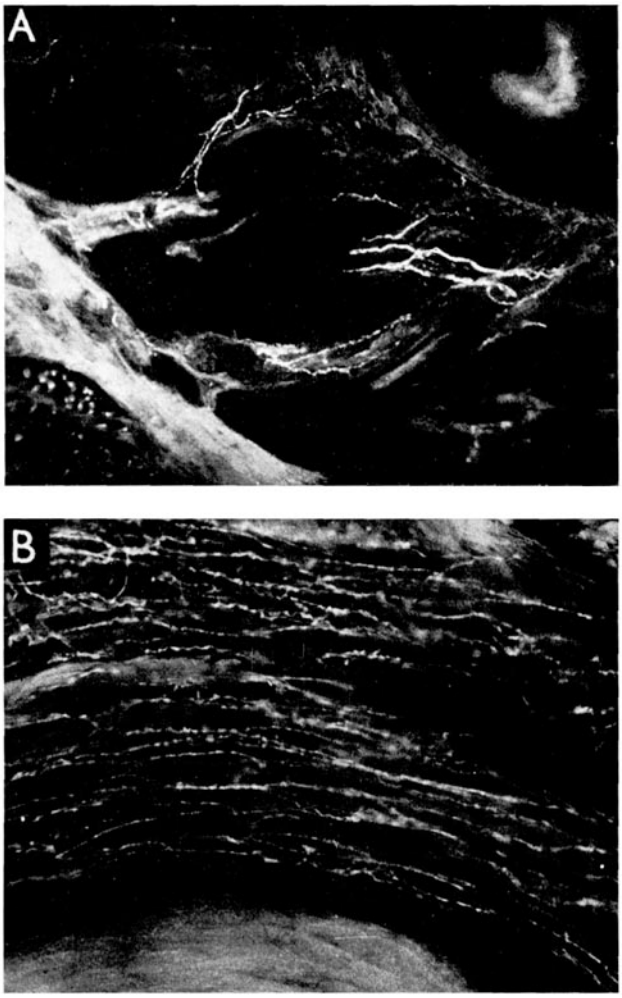
Five frogs (*Rana temporaria*) and five cats were used. In the frogs pieces of skin from the abdomen, dorsum and the extremities were excised. In the cats, two of which were pretreated with reserpine (5 mg/kg i.p.), the carpal tactile hairs[8] and a number of vibrissae were excised along with adjacent tissues. In two of the untreated cats, Pacinian corpuscles from the mesentery were also taken out. All specimens were treated as previously described in detail[7].

Frog. Single scattered adrenergic terminals were found in all skin pieces just beneath the epithelium and sometimes in the basal layer of the epidermis with no certain relation to smooth muscle cells. Since the adrenergic terminals are located in the same skin layer as the unmyelinated free endings serving as mechanoreceptors[9], the CA released may be able to reach the mechanoreceptor terminals. The facilitatory effect of sympathetic stimulation observed in the frog[2] may thus be caused by CA acting directly on the receptors.

Both the arteries and the veins were surrounded by a ground plexus of adrenergic terminals of the same appearance as that previously described in mammals[6,10]. The skin glands were surrounded by a plexus of adrenergic terminals located close to the basal surface of the gland cells. Smooth muscle cells at the mucous glands[11] were not observed in our preparations, but their existence cannot be excluded.

Cat. The Pacinian corpuscles present in the mesenteric tissue studied did not contain any adrenergic terminals. Adrenergic fibres lay scattered in the surrounding adipose tissue without making any close contact with the corpuscles, and a sympathetic influence on these corpuscles through locally released CA is thus not likely.

The adrenergic innervation of the cat's skin has been investigated previously[12]. This study is limited to the carpal tactile hairs and the vibrissae[8], viz. a type of cutaneous sensory organ which judging from its morphological features may be under efferent influence. In the skin pieces containing these carpal tactile hairs adrenergic nerve fibres were found in the trabeculae traversing the vascular sinus; they were also found scattered around the hair sheath where the terminal network of sensory fibres is known to be located (Figure A). In these parts the adrenergic fibres ran freely one by one without making any close contact with other structures. Adrenergic nerve



A, Cross section of carpal tactile hair of cat. Adrenergic nerve fibers reaching hair sheath (upper right) via sinus trabeculae. (Fluorescence microphotograph: × 120.) B, Adrenergic ground plexus in smooth muscles surrounding sinus of carpal tactile hair of cat. Sinus wall with connective tissue exhibiting greenish fluorescence (× 210).

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terminals were also present in the large smooth muscles surrounding the tactile hair forming a typical autonomic ground plexus consisting mainly of strands of several adrenergic nerve terminals (Figure B). The large number of Pacinian corpuscles present close to the carpal tactile hair did not contain any adrenergic nerve terminals.

Around the hair sheath of the vibrissae adrenergic terminals were more thinly scattered. The surrounding striated muscles had no adrenergic innervation. No fluorescent nerve terminals were apparent after treatment with reserpine.

The main morphological difference between the ordinary hair with its fast adapting receptors and the tactile hair with its extremely slowly adapting mechanoreceptors[8,13] is the characteristic vascular sinus around the root proper in the latter. The exact function of this blood sinus is still unknown and its effect on the receptors has been the subject of a great deal of speculation[8]. The adrenergic terminals observed around the hair sheath may exert the same effect on the hair receptors as that suggested above for the adrenergic terminals in frog skin on the touch receptors. The presence of a strong adrenergic plexus innervating the smooth muscles surrounding the sinus of the carpal hairs is also noteworthy in this context. Thus, besides a direct effect of CA released inside the blood sinus, the sympathetic nervous system may also exert an indirect action on the hair receptors through changes in the mechanical properties of the sinus or in the intrasinal pressure[14].

Zusammenfassung. Es ist bekannt, dass gewisse Mechanorezeptoren durch Reizung sympathischer Nerven beeinflusst werden. Histochemisch war es möglich, adrenerge Nerven in Hautschichten des Frosches mit Berührungsrezeptoren nachzuweisen. In Pacinischen Körperchen der Katze wurde keine adrenerge Innervation gefunden, hingegen freie adrenerge Nervenendigungen an den Wurzelscheiden verschiedener Tasthaare.

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Azione dei virus poliomielitico e Coxsackie sulle cellule renali di scimmia (*Macaca mulatta* Shaw)

Vari autori[1-6] hanno potuto constatare che per opera di fattori vari, il nucleolo delle cellule può andare incontro ad apprezzabili modificazioni. In particolare DURYEE[1] ha sostenuto che l'adenocarcinoma di Lucké di *Rana pipiens* è una malattia da virus del nucleolo cellulare, e BOLOGNARI[3,4] ha ammesso che in generale l'organite cellulare che per primo risentirebbe dei fattori oncogeni, sarebbe il nucleolo stesso. Fra i fattori che possono provocare tale azione vanno annoverati appunto i virus, per cui assumono sempre più importanza quelle ricerche dirette ad accertarne l'azione citopatica. Abbiamo voluto pertanto condurre delle indagni per osservare, con l'ausilio di varie tecniche, le manifestazioni cui va incontro il nucleolo in cellule infettate con determinati virus.

Allo scopo ci siamo serviti di colture primarie monostratificate di cellule epiteliali di rene di *Macaca mulatta*, in cui dopo 6–8 giorni di coltura è stata effettuata l'infezione con virus poliomielitico tipo I ceppo Brunhilde e virus Coxsackie B_1.

I gruppi cellulari considerati sono stati: (a) cellule appena tripsinizzate; (b) cellule tenute in coltura per 6–8 giorni; (c) cellule infettate con virus poliomielitico e fissate a 17 h dall'infezione; (d) cellule infettate con virus Coxsackie e fissate a 41 h dall'infezione.

Le colture cellulari sono state fatte sviluppare su vetrini coprioggetti, fissati in Bouin e quindi colorate con il GALGANO I[7] e con il Dominici. Per le osservazioni al microscopio di fluorescenza le colture cellulari sono state fissate in formalina al 10% e trattate con arancio acridina secondo BERTALANFFY[8]. I nucleolini sono stati posti in evidenza dopo fissazione in liquido di Cajal e impregnazione con cloruro di platino[9]. Per le osservazioni al microscopio elettronico le cellule staccate dai tubi di coltura mediante tripsinizzazione, sono state fissate in OsO_4 al 2% secondo Palade e incluse in miscele di metacrilati di butile e di metile (8 parti e 2 parti).

Sono stati ancora misurati i nuclei con relativi nucleoli di 400 cellule per ogni gruppo considerato e costruiti dei diagrammi cartesiani con i logaritmi dei volumi nucleari (in ascissa) e nucleolari (in ordinata). I dati ottenuti sono stati quindi elaborati secondo il metodo di LAMOTTE[10].

Nelle cellule appena tripsinizzate del rene di *Macaca mulatta* il nucleo è apparso piuttosto rotondo, con un piccolo nucleolo posto eccentricamente colorabile col metodo Galgano I in rosso e con il metodo Dominici in azzurro. Nello stesso nucleolo i nucleolini sono risultati quasi sempre assenti, al microscopio di fluorescenza si è notata per lo più fluorescenza rossa. Le stesse cellule tenute in coltura si sono presentate con nucleo notevolmente sviluppato, con nucleolo pur esso voluminoso e di forma estremamente variabile. Sono stati altresì rilevati nucleoli doppi, ora di eguali ora di diverse dimensioni,

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