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Current Research on the Nature of Cholinergic Receptors

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A review is given of current, mostly biochemical, research on the muscarinic and the nicotinic acetylcholine receptors. The review contains 74 references.

Acetylcholine receptors (AChR) as operational entities have been described for a great many years. They have been localized by iontophoretic application of acetylcholine (ACh) or by binding of ligands. It appeared obvious that they were part of the postsynaptic membrane and their protein nature was early suggested by Nachmansohn. Drug structure-activity studies revealed several kinds of acetylcholine receptors probably requiring different ACh configuration. With the introduction of biospecific chromatography ACh binding molecules could be isolated from postsynaptic membranes of mammalian brain and peripheral tissue and from the electric tissue of certain fishes. Their chemical and physical properties are currently studied. Experiments on membrane reconstitution using isolated AChR are in progress in a number of laboratories, aiming at a clarification of the question if the isolated ACh binding proteins also are responsible for ion translocation or not. While this still is an open question and may turn out to be different in muscarinic and nicotinic systems, isolation of AChR has shown that this molecule differs from that of the ACh hydrolyzing enzyme acetylcholinesterase (AChE).

This review summarizes some of the current biochemical research on the muscarinic (mAChR) and the nicotinic (nAChR) acetylcholine receptor. Some other interesting aspects of current receptor research, such as receptor localization and the nature of the extrajunctional ACh-sensitive sites found after denervation are also touched upon.

MUSCARINIC ACETYLCHOLINE RECEPTOR

Estimates of mAChR levels in brain and peripheral tissue have been made by Rang[1], Burgen[2] and others using either tritiated atropine or atropine-like compounds such as 3-quinuclidinyl benzilate (3-QNB) or tritiated choline mustard derivatives.

Atropine has a low lipid solubility while that of 3-QNB and related compounds is high as is their anticholinergic activity both in the CNS and

in the peripheral nervous system[3,4]. Oxotremorine (100 μM) maximally displaces [^{3}H]-QNB binding[5]. As shown in the following 3-QNB binding mAChR is postsynaptically located. Binding of [^{3}H]-QNB to rat hippocampus was measured after septal lesions which reduced choline acetyltransferase (CAT) activity 65—76% in hippocampal homogenates. Specific binding of [^{3}H]-QNB was hardly altered. Even AChE was reduced by about 70% which confirmed earlier observations[6,7] of an almost exclusively presynaptic location in the hippocampus. 3-QNB binding, however, is postsynaptic. Presynaptic mAChR sites may have different binding properties and not be labelled with 3-QNB or else presynaptic sites, which have been described in the cerebral cortex[8] and are supposed to be involved in ACh-release do not exist in hippocampus. Hippocampus develops no supersensitivity to iontophoretically administered carbamylcholine following septal lesions or to 3-QNB-binding[9]. Binding of [^{3}H]-QNB reaches half-maximal rate of association at 2—3 min and a plateau value in about 10 min. Half maximal binding occurs at about 0.1—0.2 nM 3-QNB and plateaus at about 1 nM. Lesioned and control animals are about equal. Dissociation is slow, $t_{1/2}$ for the 3-QNB receptor complex at 35 °C being about 60 min in both control or lesioned rats. Nonspecific binding is not time dependent and not saturable.

Choline mustard derivatives are potent alkylating muscarinic antagonists as shown in smooth muscle and brain and their binding to mAChR is antagonized by a variety of reversible agonists and antagonists, including ACh. Scatchard plots obtained for guinea pig ileum suggest the presence of two binding sites for ACh with affinities of 1.8×10^8 M^{-1} and 1.6×10^6 M^{-1} in about equal amounts. The total receptor concentration found by ACh inhibition is identical with that found with atropine[2].

The purification of mAChR is a tricky business. Solubilization studies in our laboratories indicate that mAChR is less firmly bound to its membrane than nAChR. The protein, once it is removed from the membrane, is rather unstable. Tritiated benzilylcholine mustard ([^{3}H]-BCM) has been used in some purification experiments. After fractionation the highest specific ligand binding activity was found in the microsomal fraction, together with AChE and 5'nucleotidase. Density and differential centrifugation have been used. Attempts to solubilize mAChR with detergents resulted in a protein unable to bind [^{3}H]-BCM. On SDS gel solubilized protein-marker complexes were found to have apparent Mol. wt. of 23 000 and 30 000. Altogether 12—15 bands were present.

In our laboratories, mAChR is currently purified in collaboration with T. Bartfai[10] and others. While preparing a biospecific adsorbent, we have used conventional methods for a partial purification (Fig. 1). By routine, mAChR is followed with tritiated atropine. Binding equilibrium at 4 °C is only slowly reached, in about 48 hrs. Solubilized receptor looses its ability to bind acetylcholine or atropine rather quickly. Even in a homogenate, 90% of the atropine binding capacity is lost within a week.

Atropine binding is blocked by muscarine but not by tubocurarine or eserine. ACh binding was studied in the presence of anticholinesterases, as so

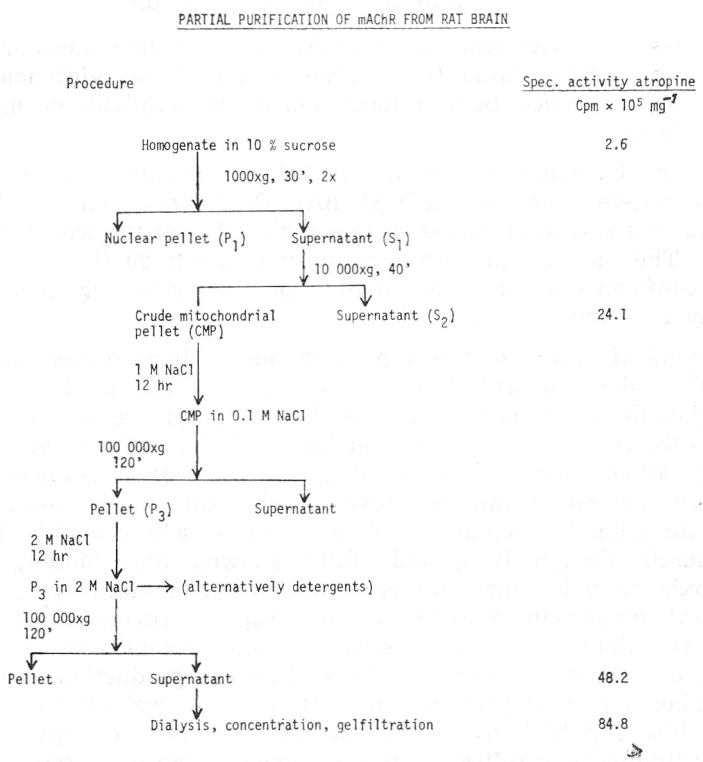

Fig. 1. Steps in partial purification of the muscarinic ACh-receptor from rat brain (unpublished).

far 0.1—0.5% of original acetylcholinesterase activity are found in the receptor preparation. On gelelectrophoresis 3 bands are seen, 2 of which are also present in the esterase. The third band corresponds to mAChR. Gelfiltration of this material gives apparent Mol. wt. of 33 000 and 68 000. mAChR thus seems to be a much smaller functional unit than nAChR. This should perhaps be seen in relation to studies indicating that mAChR might act through guanyl cyclase. Possibly we are here dealing with a regulatory unit. In the preparations guanyl cyclase follows atropine binding in all steps of subcellular fractionation.

It is known that ACh causes accumulation of cGMP in heart, brain and intestinal tissue and ACh as well as muscarinic agonists cause an increase in cGMP levels in rabbit cerebral cortical slices, an action that is abolished by atropine but not by the nicotinic agonist hexamethonium. Nicotinic agonists do, in this system, not affect cGMP levels. The physiological response to mAChR activation may thus be mediated by cGMP which in its turn would be compatible with the slowly developing nature of the responses resulting from activation of mAChR on cerebral neurones. Iontophoretically applied cGMP itself is, however, not acting like ACh on neurones (cat cerebral cortex). It excites cells that are depressed by ACh as well as those which are unaffected by ACh[11].

NICOTINIC ACETYLCHOLINE RECEPTOR

So far the most successful studies of AChR[12–17] at the molecular level have been done on electric tissue from either *Electrophorus electricus, Torpedo marmorata* or *californica*. Some information is also available on nAChR from mammalian tissue.

There may be heterogenicity in nAChR, as indicated *e. g.* by studies on denervated muscle and on purified nAChR. Denervation of the skeletal muscles causes a spread of ACh-sensitive regions[18] over the whole muscle fibre membrane. The increase in ACh sensitivity is about 20 times, a value that has been confirmed by studying binding of radioactive cholinergic ligands, particularly ACh antagonists[18a,19,20].

The chemical nature of the apparently newly formed receptors may not be altogether identical with that of the normal receptors found at neuromuscular junctions. In normal muscle the receptors are almost exclusively confined to the region of the muscle surface underlying the nerve terminal[21,22]. After denervation, the receptors spread though the peak receptor concentration in the extrajunctional membrane never reaches that of the end plate membrane[23,24]. Junctional receptors in denervated muscle resemble those from normal muscle though Berg and Hall[25] showed that binding of α[^{125}I]--bungarotoxin to extrajunctional receptors in organ cultures of denervated (5 days) rat diaphragm muscle is more rapidly reversible than that to junctional receptors of normal muscle. Endplate regions were avoided when testing the denervated muscle. Inhibitors of energy production, such as NaCN or dinitrophenol and of protein synthesis, such as cycloheximide at a concentration blocking 95% of protein synthesis block the rapid loss of the toxin. This finding may reflect a rapid turnover of the toxin-receptor complex in the membrane. Extrajunctional regions of denervated muscle also have a more rapid recovery of ACh sensitivity after α-bungarotoxin blockade as compared to recovery of the end plate regions of normal muscle[26]. This may not to be due to a difference in dissociation constants, but rather to an active metabolic process, probably linked to protein synthesis. The toxin seems to be degraded as radioactivity is found in the medium as iodotyrosin. An intracellular, energy requiring process[27] might be acting and reflect normal receptor turnover in the membrane.

Even normal skeletal muscle nAChR shows heterogenity. Using [^{125}I]α--bungarotoxin (α-bgt) and autoradiography and incubating until no response to nerve stimulation was noticed[28], Fertuck and Salpeter showed that AChR is localized in the postsynaptic membrane nearest the primary cleft (*i. e.* nearest the axon) and not throughout junctional folds. This is in contrast to AChE labelled with [^{3}H]-DFP where the radioactivity is distributed over a broad band coinciding with the junctional fold region[29]. Using electron microscope autoradiography of α-[^{3}H]-bgt binding sites Albuquerque[30] estimated the mean density of nAChR in various skeletal muscles to 8 700 per μm^2 even though the overall size of an endplate ranged from 400 μm^2 to 1 300 μm^2. Highest amounts are found nearest the axon and are about 18 000 α-bgt sites. Only half of them appear to be true active centers of AChR *i. e.* have high affinity for d-tubocurarine and lose all response to ACh upon treatment with α-bgt. The other half is thought likely to be on the ion conductance modulator

component of the receptor system.[31,32] There are few binding sites in the folds compared to the tip and ACh sensitivity seems to be determined by the local density of receptors in the membrane and not by their total number at the endplates. Freeze-etched preparations show 100—140 Å particles, presumed to include receptor-ionic conductance modulator complexes[33].

The area of the postsynaptic membrane may be adapted to the number of quanta needed for synaptic function. The zone of effectiveness of one quantum (10 μM at 1 μm radius from the origin in 0.3 ms) is 3 μm^2 of postsynaptic membrane[34]. 6 000 single channels should be open for the generation of one miniature endplate current. 70% of the surviving part of 10—20 000 ACh molecules is, according to Katz and Miledi, receptor bound, which does not saturate the available receptor sites (~ 30 000 true functional centres). Yet only about 25% of the entire number of functional receptor centers can be removed without diminishing the response to neurally-released ACh[35]. This leads to one, or at the most two, ACh-activated receptor sites per available ion channel.

In cultured skeletal muscle cells clusters of AChR are formed in the absence of neurons and participate probably in synapse formation[36]. AChR might function as determinant of synapse recognition. The average AChR concentration is 9 000 receptors/μm^2 and the receptors resemble those found in electroplax. At other regions the receptor concentration is 900/μm^2. Clusters of AChR on cultured muscle cells were also demonstrated with ferritin-α-bgt conjugates[37], and peaks of sensitivity are also found using focal iontophoresis of ACh[38]. It seems not yet known if receptors in cultures are heterogenous or not.

In the electroplax, the number of toxin binding sites per square micron of cell surface in subsynaptic or extrasynaptic areas was estimated with *Naja nigricollis* α-neurotoxin[38a]. Denervation by destruction of the caudal part of the spinal cord of *Electrophorus electricus* electric organ does not change the number of α-neurotoxin sensitive sites significantly up to 142 days after denervation[38b], but remains 10—20 nmol/g protein. In the normal electroplax no clusters of toxin binding sites are seen except under the nerve endings. These latter binding sites remain even after denervation, though no residual nerve processes are seen. Thus, in the electroplax the ratio of extrasynaptic to subsynaptic α-neurotoxin binding sites does not change for several weeks after denervation. No new receptor sites are appearing.

Using α-bgt the number of receptor sites per g tissue in *Torpedo* electric tissue was estimated[39] to be 6.6×10^{14}. Mouse, rat and frogmuscle endplate have respectively 1.6×10^7, 4.7×10^7, and 1×10^9 sites per endplate[40]. The number of sites is again considerably larger than the number of ACh molecules released by a single nerve impulse (about 3×10^6 in rat diaphragm) indicating many spare receptors[41] or other sites.

Several review articles[12–17] have recently summarized information available about purified nAChR. Therefore the following is rather condensed. Karlin *et al.*[42] have shown that ACh-receptors of electroplaques can be blocked by reagents which reduce S—S bonds to S—H groups and be restored by oxidizing agents. Karlin has purified receptor subunits after affinity labelling (Table I). Another approach was used by Miledi *et al.*[43] who purified

a receptor-α-toxin complex. Others (Table II) have used biospecific chromatography. nAChR is a membrane protein, which has to be solubilized with neutral detergents. Affinity chromatography (Table II) has been performed on flaxedil or choline derivatives[15,43a,44] or on acetylated[45] or native α-neurotoxin from *Naja naja siamensis*[46–48,56] or from *Naja naja naja*[49] bound to a matrix. The isolated acid protein material was shown to bind to Concanavalin A and some other lectins[15], indicating that it is a glycoprotein. Its main sugars are mannose, glucose and galactose[47] (Table III). N-acetylglucose amine is also present. Tests for sialic acid have been negative. The amino acid composition of nAChR has been determined and is different from that of AChE[15,48,59]. Some differences seem to exist between nAChR from *Torpedo* or *Electrophorus*. Some Torpedo data are summarized in Table IV.

TABLE I.

Number and apparent size of nicotinic ACh-receptor subunits as described by various authors

Tissue	nr	Apparent Mol wt.	Ref.
T. marmorata	2	45 000, 50 000	45
	3—4	42 000, ≈ 50 000, ≈ 70 000	59
T. californica	3	28 000, 35 000, 42 000	44
	3	40 000, 50 000, 65 000	64
E. electricus	1	40 000	—
	3	32 000, 40 000, 103 000	42
	2	43 000, 48 000	51
	1	?	48

TABLE II.

Columns used in affinity chromatography of nicotinic ACh-receptor

Tissue	Active part of affinity column	Ref.
T. marmorata	α-toxin *Naja naja siam.*	46, 47, 56
	ac. α-toxin „	45
T. californica	—$NH(CH_2)_5CONH(CH_2)_3N^+(CH_3)_3$	44
E. electricus	α-toxin *Naja naja naja*	49
	α-toxin „ *siam.*	48
	flaxedil analogue	43a 15

TABLE III.

Sugars found in purified nicotinic ACh-receptor[47]
Total carbohydrate: 38 ± 18 μg per mg nAChR.

	Amount of sugar (%)	
	Before DEAE chromatography	After DEAE chromatography
Mannose	80	50—70
Galactose	18	10—20
Glucose	2	10—30
Glucosamine	?	present

TABLE IV.

Summary of data obtained on nAChR from **Torpedo marmorata**[16,45-47,59]

Membrane bound macromolecule, solubilized by neutral detergents
Glycoprotein or glycoproteolipid; mannose, galactose, glucose, glucosamine
Isoelectric point 4.8
Binds ACh, Hill coeff 1 below 10^{-6} M
Amino acid polarity ~ 49, tryptophan, half-cystin
Properties change upon storage
EM size 80—100 Å, pit about 15 Å, 5—6 subunits (?)
Separable into two proteins:
M_{app}: 295 000 ± 30 000; 410 000 ± 40 000 (n = 9); proportion (1.6 ± 0.2) : 1
Both bind acetyl α-neurotoxin, K_D resp. 6×10^{-8} M and 8×10^{-7} M
3 — (4) subunits in SDS, M_{app} 42 000, 51 000, 74 000 and (92 000)
Acetylation gives subunits of about 95 000
Maleylation gives peptides of about 32 amino acids
Antigenic

The isolated glycoprotein appears as one[15] or as two interacting[16,45] macromolecules. Molecular weights are approximative, as detergents are usually bound to the protein. The shape of the protein may be elongated rather than globular[50]. In our laboratory two α-neurotoxin binding macromolecules have been separated and it was recently shown that their binding properties differ. Their amino acid composition seems, however, to be close to identical, while the number of their subunits may differ. None of the two proteins contains any AChE activity at all. It remains to be seen if the proteins are different parts of a binding site — ion translocation unit or different oligomers of the same subunits.

Treatment with SDS in the presence of dithiothreitol results in 1—5 subunits (Table I) depending upon methods and source of electric organ. Subunits are in the range between 25 000 and 70 000. The smallest toxin binding unit is 90 000—140 000 (Table V).

TABLE V.

Size of toxin (1 mol) binding site of purified nAChR

		g	Ref.
T. marmorata	[^{3}H] ac α-toxin *Naja naja*	140 000	46
T. californica	[^{125}I]-α-Bgt	100 000	64
E. electrophorus	calc.		—
	[^{3}H] pyr. α-toxin *Naja naja*	90 000— 180 000	48
	[^{3}H] α-toxin *Naja naja*	150 000	15

Binding of ligands is influenced by the nature and amount of detergent present[16]. It seems therefore meaningless to compare binding data obtained in different laboratories. Upon solubilization nAChR changes its affinity for agonists, while that of antagonists remains approximately as in the membrane[51]. ACh binding is blocked by nicotinic antagonists.

The existence of an nAChR heterogenicity, observed by us, may, however, also be indicated by the different ACh-binding constants found in the literature, though, as also mentioned above, these may be influenced by detergents and by methods used. Moody *et al.*[52], using equilibrium dialysis on purified preparation from *T. californica* found a single dissociation constant $K_D = 2.3$ μM, Elfman and Heilbronn (unpubl. data) found 1 μM using equilibrium dialysis on purified *T. marmorata* nAChR, Weber and Changeux[53] using displacement of radioactive *Naja* toxin from a particulate preparation of *T. marmorata* found $K_D = 8$ nM. Some studies on *T. marmorata* using equilibrium dialysis give Scatchard plots indicating two binding constants of 7 nM and 0.07 μM respectively in a particular preparation[54], 1.4 nM and 0.22 μM in a Lubrol solubilized preparation[55] and 20 nM and 1.97 μM in a highly purified preparation[56]. O'Brien and Gibson[57] found that nAChR purified from stored *T. marmorata* electroplax preparations gives Scatchard plots indicating two ACh binding sites and showed that the high affinity site was heat-labile. The particulate AChR preparations however, are heat-stable. The two ACh sites also have different pH-profiles but both have a typical nicotinic drug profile. Assuming simple competitive binding it was shown that several nicotinic drugs blocked high affinity ACh-binding better than low affinity ACh-binding. This may coincide with our observation[58,59] that the two isolated AChR macromolecules have different affinities for α-neurotoxin. There is also the observation that carbamylcholine releases only about 50% of nAChR from an α-neurotoxin-Sepharose column after incubation for 12 hrs at room temperature. It was assumed that this was due to a secondary reaction between nAChR and α-neurotoxin. A secondary reaction has been described by Klett *et al.*[48]. The amount of irreversibly bound receptor can be reduced considerably

by a shorter incubation time, which seems to underline the explanation given above. Such preparations always yield two nAChR macromolecules, as described earlier in this paper. When discussing binding sites of purified nAChR the possibility that residues of ligands used in affinity columns are bound to the isolated material has also to be kept in mind. This can be checked with immunological methods.

Identification of the isolated material is achieved by binding studies using agonists and antagonists. Further, antibodies to nAChR have been raised in rabbits[45,49,60–62] and these are shown to be able to precipitate nAChR from a solution and to crossreact with nAChR. The antibodies do not react with AChE or with α-neurotoxin used for the purification nor do antibodies to those compounds react with nAChR. Antibodies to nAChR are able to block the response of electroplax to carbamylcholine or that of the dorsal muscle of the leech to ACh. The important question if the isolated glycoprotein is the ACh recognition site only or includes the ion translocation mechanism has not yet been answered. In the electron microscope rosettes of nAChR are seen, having a size of about 80—100 Å and a pit of ~ 15 Å (ref. 15, 16). These rosettes are destroyed[16] by SDS and may represent the nAChR macromolecule with an inner part allowing ion passage. Structures resembling those of the isolated material are seen in the electroplax membrane after freeze-etching[63]. Currently, synthetic lipid vesicles containing AChR (freed from detergent via cholate) are studied[64]. In the presence of carbachol and cholinergic blockers such as the α-neurotoxins these vesicles behave as the microsacs, sealed electroplax membrane vesicles which may be loaded with $^{22}Na^{+}$. This cation is extruded in the presence of an ACh agonist, an effect that is blocked by α-neurotoxin or by *d*-tubocurarine. It is suggested that the synthetic vesicles contain everything necessary for neurotransmitter recognition and ion translocation.

Experiments with AChR in black lipid membranes have shown conductance changes as a function of added cholinergic agonists[65–67]. According to Michaelson *et al.*[64] nAChR contains a neurotransmitter site and a second binding subsite which complexes inorganic cations and bisquaternary cholinergic analogues.

It is obvious that the lipid surroundings of nAChR in the membrane are of importance in receptor function. Using chromatography on LH-20 and chloroform-methanol De Robertis[68] and collaborators have isolated a proteolipid from the electroplax and shown that it had properties of a nicotinic cholinergic receptor and bound ACh. These studies have been criticized because of the utilization of organic solvents in the extraction procedures, which might be expected to denature proteins on the basis of information available from conventional globular proteins. It is possible, however, that the organic solvents still contain sufficient residual water molecules to permit unusual hydrophobic proteins to remain in solution. A recent study by Levinson *et al.*[69] has challenged the procedures used since it was found that chloroform-methanol treatment eliminates the binding activity of whole microsomes (electroplax) and does not solubilize the receptor in active form. It was also claimed that peaks from the LH-20 column capable of ACh binding could be created in the presence of protein-free and receptor-free extract. It was suggested that the binding is nonspecific and that the receptor-ligand interaction may be artifactual. Fiszer

de Plazas and De Robertis[70] have compared their material with detergent--solubilized material and shown α-bgt binding, K_D 4.9×10^{-7} M (1 mol per 37 000 Mol. wt. equiv.). They also showed that the toxin was not replaced by ACh or decamethonium and that, although the toxin could not be extracted into the organic phase the binding activity was lost from the protein residue and appeared in the extract. The quantity of the extracted material resembles that of others ($3—7 \times 10^4$ mol g^{-1} tissue).

We have recently repeated the procedures described by De Robertis *et al.* In one experiment T. marmorata electroplax was used. In the other one the receptor was labelled with [^{3}H]-acetyl α-neurotoxin before chromatography. Two protein peaks were obtained on the LH-20 Sephadex column, extracted with chloroform. Addition of methanol did not elute further material. The label followed the second protein peak (Fig. 2). It was, however, not possible

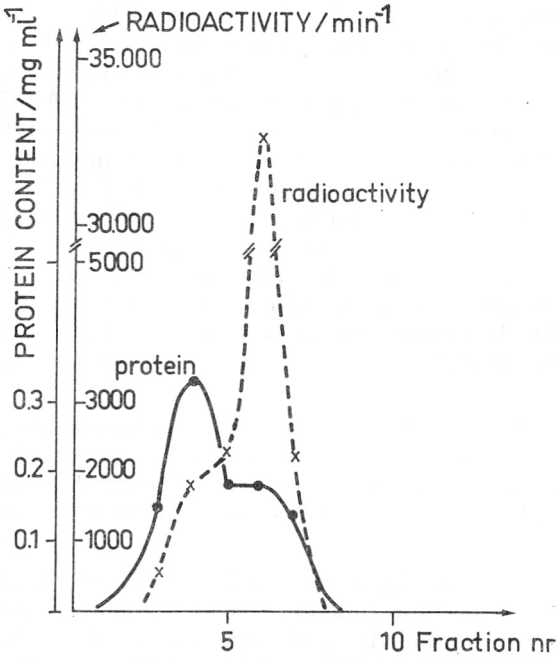

Fig. 2. Elution pattern for neurotoxin-labelled protein or proteolipid from a LH-20 Sephadex column. — protein, ... radioactivity.

to react the nonlabelled isolated proteins with α-neurotoxin nor did these protein fractions react with antibodies to nAChR prepared in our laboratory from immunized rabbits. Cross immunoelectrophoresis was attempted after removal of organic solvents by low temperature evaporation and all proteins were tested after addition of either buffer or buffer containing 1% Triton X-100. The conclusion from this seems to be that proteins prepared by LH-20 chromatography with chloroform-methanol may be denatured and that they cannot react with either acetyl α-neurotoxin or with antibodies to nAChR prepared by the use of detergents, not directly and not after treatment with detergent to break up a possible proteolipid.

Within the frame of this article it has not been possible to review all information available from recent studies on membrane bound or solubilized cholinergic receptors. Mainly biochemical data have been sought out. Other articles from this meeting bring out more information or discuss other aspects. A survey of present knowledge, however, makes it obvious that rapid development is to be expected particularly concerning functional aspects of muscarinic and nicotinic receptors. The mechanism of muscarinic cholinergic transmission may turn out to be rather different from that of nicotinic cholinergic transmission. It is also obvious that the last has not yet been said about the nature of the isolated nicotinic acetylcholine receptor glycoprotein(s).

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DISCUSSION

E. A. Barnard:

With regard to the heterogeneity of neurotoxin binding seen in one of your experiments, is it possible that this arises from the presence of more than one isomer in the acetylated toxin separation that was used? In the case of α-bungarotoxin, we have observed that different isomeric mono-acetyl-derivatives can be separated, which differ somewhat in their affinity between each other (and we used only one of those, which has unchanged affinity). If a mixture of mono-acetylated toxin species was present, its behaviour could differ, perhaps, from one form of the receptor to the other. Has this been excluded?

E. Heilbronn:

According to dr. Karlsson who prepares the acetylated toxin, the acetyl-group is on the N-terminal (isoleucin). Neurotoxins labelled in Lys 23 or Lys 49 have also been used. The affinity of these three derivatives for nAChR in labelling experiment was shown by Libelius to be the same.

M. E. Eldefrawi:

(a) Did I hear you correctly saying that your purified receptor solution is contaminated with bacteria? (b) The results of your ACh binding show 20 nmol/mg protein at saturation, yet your toxin binding saturates below 5 nmol. How do you reconcile the difference between the two numbers?

E. Heilbronn:

(a) When we observed the presence of two AChR oligomers we decided to culture a sample in order to see if any bacteria at all were present. In this sample 1 000 bacteria/ml were found. After this discovery we have been using sodium azide and sterile filtering, with little difference in the isolated proteins. (b) The values you are comparing were not measured on the same AChR sample. However, while toxin binding at saturation does not vary much from sample to sample, ACh-binding at saturation does vary considerably, in fact by as much as up to a factor of 10.

SAŽETAK

Najnovija istraživanja s područja kolinergičnih receptora

Edith Heilbronn

Načinjen je pregled najnovijih, pretežito biokemijskih, istraživanja s područja muskarinskih i nikotinskih receptora acetilkolina. Prikazom je obuhvaćeno 74 referenci.

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