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# MUSCARINIC CHOLINERGIC EFFECTS ON STIMULUS-EVOKED RESPONSES IN RAT PRIMARY SOMATOSENSORY CORTEX. AN ELECTROPHYSIOLOGICAL STUDY*

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Neuron terminals originating from the nucleus basalis magnocellularis (NBM) are the major source of the cortical cholinergic innervation, which is thought to play an essential role in higher brain functions. Electrophysiological studies have shown that activation of muscarinic cholinergic receptors caused a marked enhancement of sensory stimuli onto cortical neurons. Diminished cholinergic innervation of somatosensory cortical areas are manifested in decreased stimulus-evoked activity and impaired performance in a sensory discrimination task. We examined the effects of ACh and its muscarinic agonists on the response properties of layer IV-V barrel cortex neurons evoked by precisely controlled vibrissa deflections. The cholinergic pharmacons displayed their mostly facilitatory effects in latency-dependent manner: In most cases only one latency component of On and/or Off responses were changed.

Keywords: Cholinergic innervation — muscarinic receptors — somatosensory cortex — rat

## Introduction

Several experimental and clinical evidence testify to the important role of cortical cholinergic innervation in maintaining normal cognitive functions. ACh either applied experimentally in the cortex /5/ or released from terminals of stimulated nucleus basalis magnocellularis (NBM) cells in sensory cortical areas /8/ increase the amplitude of responses evoked by sensory stimulation without affecting the background activity. The vibrissa-barrel pathway of the trigeminal system in the rat, firstly anatomically described by Woolsey and Van Der Loos /9/, offers a unique possibility to study the evoked responses in the primary somatosensory cortex induced by a

*Dedicated to Professor György Székely for his 70th birthday.

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controlled and adequate somatosensory stimulation (whisker deflection). In our study we examined the effects of ACh and its agonists on evoked unit activity of cells from identified barrels of the posteriomedial barrel subfield.

## Material and Methods

A total of 36 Sprague-Dawley rats of both sexes were anesthetized with urethane (1.1 g/kg i.p.). After left side craniotomy microelectrode recordings were made at 0.3 mm intervals over the whole barrelfield to find the barrel related to the stimulated whisker. Mostly C1-3 vibrissae were deflected with a multiangular electromechanical stimulator. Stimulus waveforms were ramp-and-hold trapezoids. Details of surgical procedure, stimulation and the description of the recording equipment were published earlier /7/. Within the appropriate barrel the cells were excited quickly (6-10 ms) and powerfully (1-4 spike/stimulus onset and/or offset; On, Off response) by displacement of the related whisker. To the recording electrode filled with 2.5 M NaCl (5-10 MOhm) was adjusted a low impedance micropipette containing the drug. The distance between the electrode tips was not more than 50 μm. The following pharmacons were tested in $10^{-4}$-$10^{-3}$ M concentrations: acetylcholine, acetyl-L-carnitine, carbachol, scopolamine, atropine (the results of antagonist injection are not discussed in this paper). Before penetrations the optimal injection parameters solution were tested (25-40 pl/injection). In every second minutes from 4-6 min prior to the application to 16-20 min following the application peristimulus time histograms (PSTHs, bin width 5 ms) were produced. Activity levels of different latency components of On and Off responses taking from PSTHs figures were plotted versus time.

## Results and Discussion

A total of 16 neurons were examined in detail from 81 isolated neurons in the somatosensory cortices of 36 animals. The results are presented in Table 1. ACh and its agonists increased the activity of at least one component of the On and/or Off responses in 65%. The effect of cholinergic drugs was mostly transient (4-6 min duration), however in some cases the effect was prolonged (up to 20 min or more), which is shown in our first example (Fig. 1). In this case an "unmasking" effect could be observed. After application of acetyl-L-carnitine, one latency component of the previously weak On response increased 6-8 times for 20 min compared to the control, while the first and third components remained unchanged. In most cases our observations were that the cholinergic pharmacons delivered "unmasking" effects on previously weak responses, and moreover, this mostly facilitatory

**Table 1**

ACh and its agonists induced changes of the components of On and Off responses evoked by vibrissa movements

| On | Off | % |
|---|---|---|
| + | + | 49 |
| + | 0 | 7 |
| + | - | 9 |
| 0 | - | 1 |
| - | - | 10 |
| 0 | 0 | 22 |
| 0 | + (§) | 1 |
| + - | 0 (*) | 1 |
| | | 100 |

+: one (in some cases more) of response components increased for longer duration than 4 min after drug injection
-: one (in some cases more) of the response components decreased for longer duration than 4 min after drug injection
0: there was no change (or shorter than 4 min) after drug injection
§: the exceptional case (presented in Fig. 2) when all of the components of an Off response increased after drug injection
*: the exceptional case when all of the components of an On response changed (increased and decreased) after drug injection

effect was manifested in changes of only one latency component of On and/or Off responses consisting of 2-4 components. In a few cases ACh or its agonists modified every component of the On and/or Off responses either in the same (Fig. 2 and §) or in different ways (in Table 1, *).

Although there are plenty of data proving cortical cholinergic effects in the cerebral cortex, their functional mechanisms in sensory processing are not well understood /6/. In rats the major means to explore the environment is the trigeminal system /2/. The major source of cholinergic innervation of the primary somatosensory cortex (SI) is the NBM /1/. Its cortical projecting neurons have restricted arborisation with little collateralisation giving the possibility of fine cholinergic tuning of small and restricted

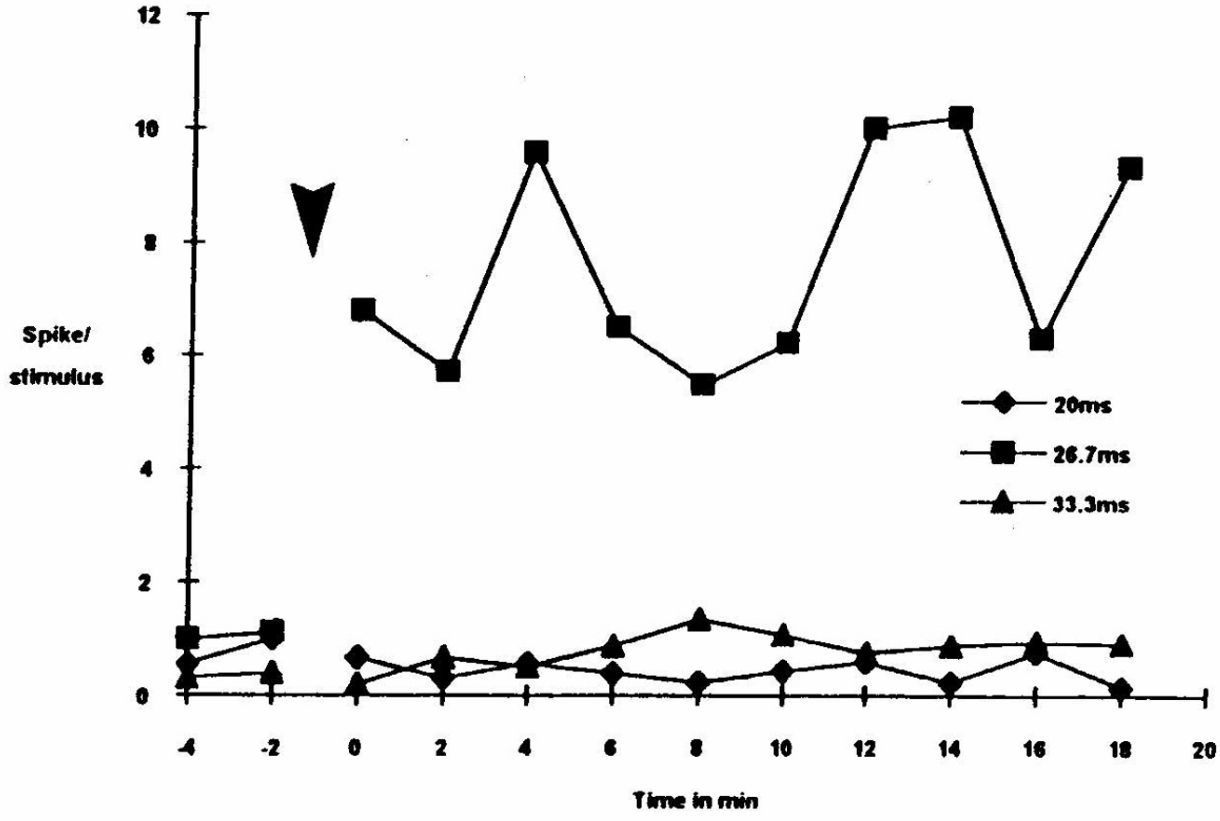


Fig. 1. Acetyl-L-carnitine increased the activity of the second component (with 26.7 ms latency) of the On response 6-8 times compared to the control level, while, the activity of the other two components have not changed at all

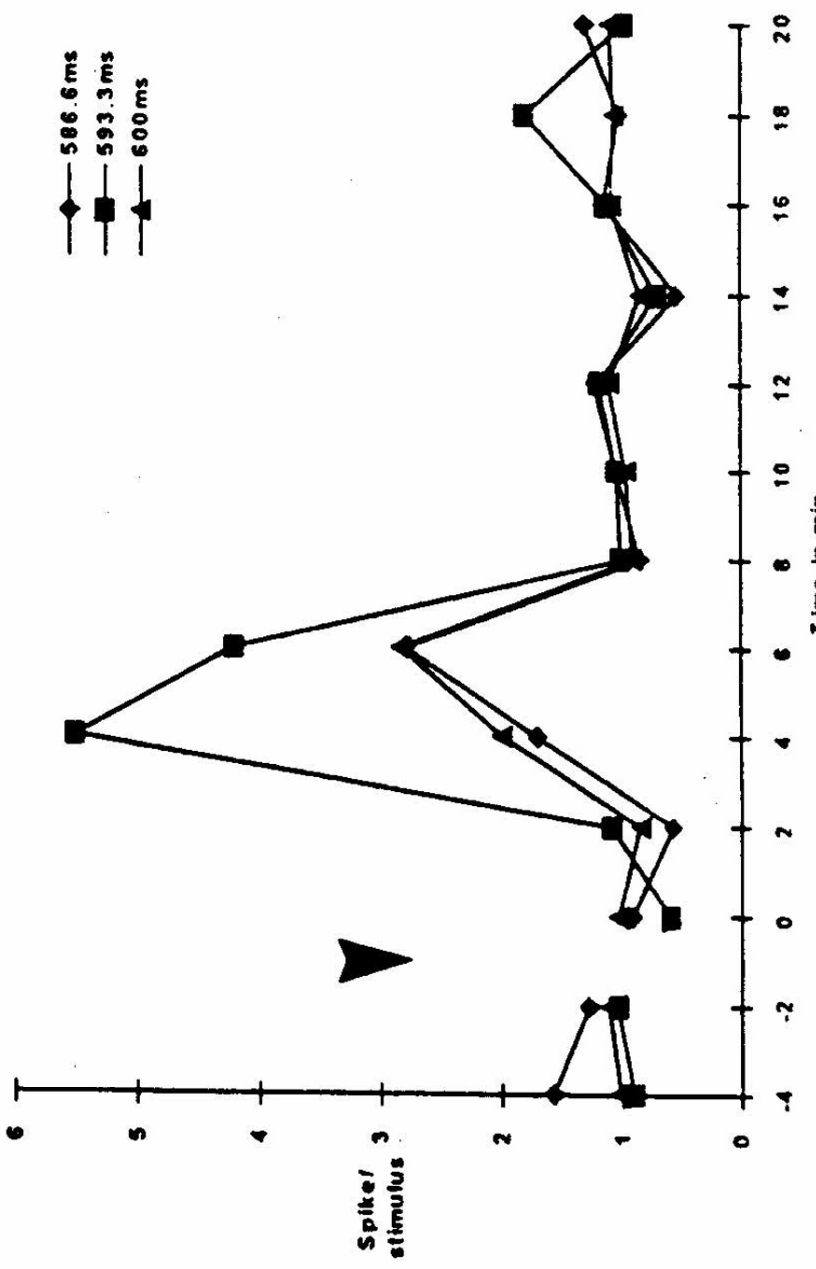


Fig. 2. Carbachol injection increased transiently the activity of all of the tree components of an Off response. This was the exceptional case when all the components of an Off response changed after drug injection

cortical areas of SI. This assumption is assisted by several NBM lesion studies /3, 4/. Decreased stimulus-evoked activity was found in the cholinergically lesioned SI cortex, while metabolic activity remained unchanged /4/. Furthermore, in a recent behavioural study a significant decreased performance in a sensory discrimination task of the NBM lesioned animals was observed because of disrupted sensory information processing /3/. These findings are consistent with our electrophysiological results. The cholinergic drugs developed (in our experiments) their mostly facilitatory action on evoked responses of layer IV-V barrel cortex neurons in a highly latency-dependent manner.

These results may help our understanding on the cholinergic modulation of the sensory processing.

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