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Research article

Retinal co-mediator acetylcholine evokes muscarinic inhibition of recurrent excitation in frog tectum column

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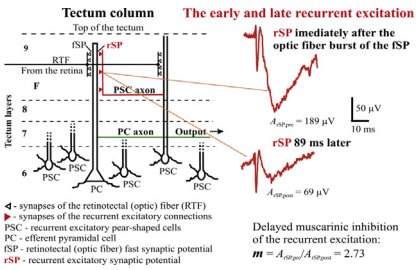
HIGHLIGHTS

- It was shown that recurrent excitatory transmission in the frog tectum column.
- Is inhibited by the endogenous acetylcholine.
- The inhibition occurs with a delay of ~80 ms.
- Muscarinic AChR antagonist atropine eliminates this effect of endogenous ACh.
- Thus, the delayed inhibition is mediated by the activation of muscarinic AChRs.

GRAPHICAL ABSTRACT



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ABSTRACT

Acetylcholine receptors contribute to the control of neuronal and neuronal network activity from insects to humans. We have investigated the action of acetylcholine receptors in the optic tectum of *Rana temporaria* (common frog). Our previous studies have demonstrated that acetylcholine activates presynaptic nicotinic receptors, when released into the frog optic tectum as a co-mediator during firing of a single retinal ganglion cell, and causes: a) potentiation of retinotectal synaptic transmission, and b) facilitation of transition of the tectum column to a higher level of activity. In the present study we have shown that endogenous acetylcholine also activates muscarinic receptors, leading to a delayed inhibition of recurrent excitatory synaptic transmission in the tectum column. The delay of muscarinic inhibition was evaluated to be of ~80 ms, with an extent of inhibition of ~2 times. The inhibition of the recurrent excitation determines transition of the tectum column back to its resting state, giving a functional sense for the inhibition.

1. Introduction

Acetylcholine modulates neuronal network activity by activating both nicotinic and muscarinic receptors located pre- and postsynaptically [7,9,21].

Activation of nicotinic ACh receptors usually leads to an enhanced neuronal network activity. For instance, it leads to a presynaptic potentiation of excitatory synaptic transmission [4,9,13]. The action of ACh through nicotinic receptors develops fast, within a few milliseconds [4,9].

Abbreviations: Art, stimulus artefact; AP, individual retinotectal action potential; fSP, individual retinotectal fast synaptic potential; sNW, slow negative wave; A_{sNW}, magnitude of the sNW; T_{sNW}, duration of the sNW; sNP, slow negative potential; A_{sNP}, amplitude of the sNP; $t_{min,sNP}$, delay of the sNP; rSP, recurrent synaptic potential; $\bar{A}_{rSP,pre}$, average amplitude of the rSPs occurring before the time moment $t_{min,sNP}$; $\bar{A}_{rSP,post}$, average amplitude of the rSPs occurring after the time moment $t_{min,sNP}$; $m = \bar{A}_{rSP,pre}/\bar{A}_{rSP,post}$, muscarinic inhibition of the recurrent excitation.

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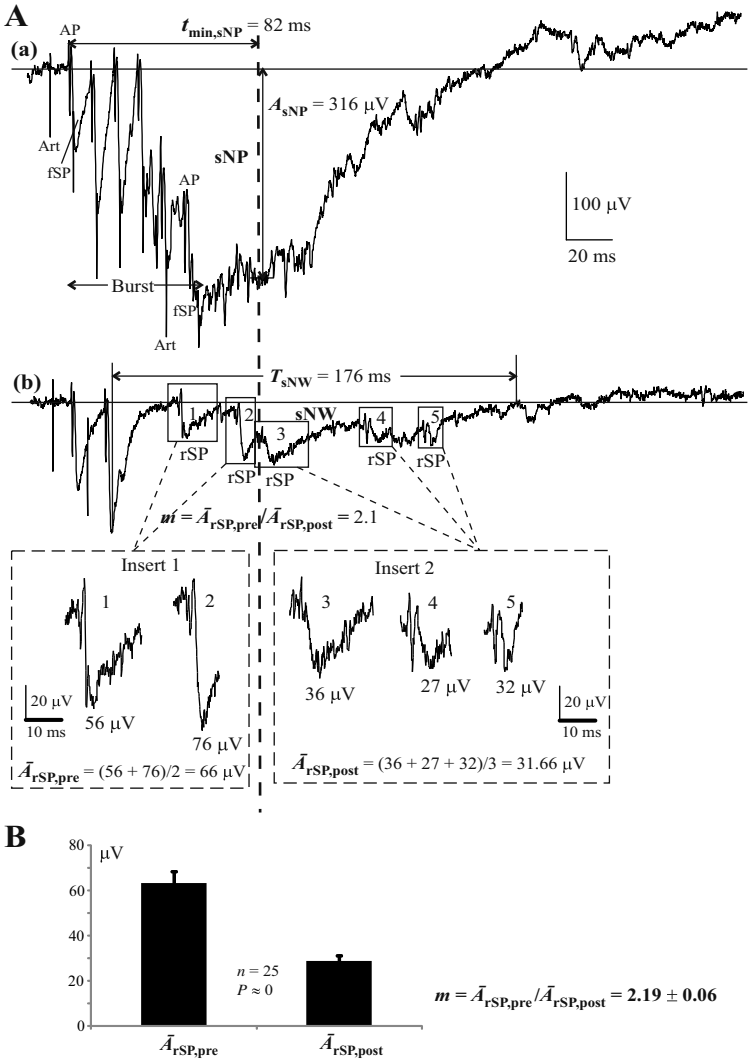

Fig. 1. Delayed inhibition of the recurrent excitation of the frog tectum column.
(A(a)) Response elicited in the tectum by the burst of 6 action potentials of the individual retinotectal (optic) fiber. Art – stimulus artefact. AP – retinotectal individual action potential. fSP – retinotectal individual fast synaptic potential. sNP – slow negative potential. A_{sNP} – amplitude of the sNP. $t_{min,sNP}$ – delay of the sNP (the time interval from the beginning of the response to the time moment when the sNP attains the minimum (maximal absolute value)).
(A(b)) Response elicited in the tectum by the burst of 2 retinotectal action potentials. sNW – slow negative wave. A_{sNW} – amplitude of the sNW. T_{sNW} – duration of the sNW. rSP – recurrent synaptic potential. $\bar{A}_{rSP,pre}$ – average amplitude of the rSPs occurring before the time moment $t_{min,sNP}$. $\bar{A}_{rSP,post}$ – average amplitude of the rSPs occurring after the time moment $t_{min,sNP}$. Ratio $m = \bar{A}_{rSP,pre}/\bar{A}_{rSP,post}$ characterizes the extent of the delayed inhibition of the rSPs. Inserts 1 and 2 displays zoomed in early and late rSPs, respectively, showing, also, the calculation of corresponding averages.
(B) Mean of 25 experiments.

Activation of muscarinic receptors, in contrast, generally leads to a depression of neuronal network activity. For example, it causes a presynaptic inhibition of excitatory synaptic transmission [13–15,19], including the recurrent one [11,20]. The action of ACh through muscarinic receptors develops slowly. The effect occurs with a delay of tens to hundreds milliseconds [10,12,16,18].

Our previous study [5] showed that the exogenous application of ACh receptor agonists causes the inhibition of recurrent excitatory transmission in the *Rana temporaria* (common frog) tectum column (schematic representation of the frog tectum column has been given in [6], figure 5) through the activation of muscarinic ACh receptors. Our group also demonstrated [1] that acetylcholine, as a co-mediator, is released into the frog tectum from glutamatergic terminals of the retinotectal (optic) fiber during firing of a single retinal ganglion cell (darkness or moving edge detector). Lastly, we established in another study [4] that this endogenous acetylcholine activates the presynaptic nicotinic ACh receptors located on the optic fiber terminals, causing after-burst potentiation of the retinotectal transmission. Based on these results, we have proposed that the co-mediator acetylcholine should also activate the muscarinic receptors in the frog tectum column, leading to an inhibition of the recurrent excitatory transmission. In the present study we present evidences in support of this proposition.

2. Material and methods

The experimental procedure has been described in detail in our earlier papers (see, for example, [5]). Here we shortly note on the main points.

2.1. Animals

Experiments were performed in vivo with 23 adult common frogs, *Rana temporaria*. All experiments in this study were carefully carried out in accordance with the "Principles of laboratory animal care" (NIH publication No. 86-23) as well as with the European