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ARTICLES

Effect of Noradrenaline on the Kinetics of Evoked Acetylcholine Secretion in Mouse Neuromuscular Junction[1]

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Abstract—In contrast to frog neuromuscular synapses, where noradrenaline (norepinephrine) and its analogues caused synchronization of the acetylcholine release process, in mouse diaphragm endplates noradrenaline increased the degree of asynchrony of neurosecretion. The effect of noradrenaline on release timing persisted at different levels of external calcium ions (0.25–2.0 mM) and was abolished in presence of both α- and β-adrenoblockers phentolamine and propranolol. The computer reconstruction of multiquantal endplate currents accounting for experimentally observed modification of release kinetics under noradrenaline showed that the rise time of postsynaptic response changes to a greater extent than the amplitude and falling phase of the multiquantal responses. We conclude that there exists a principal difference in the action of noradrenaline in the cholinergic neuromuscular synapses of warm-blooded and cold-blooded animals that can be accounted for by the differences in the type of adrenoreceptors involved in the modulation of synaptic transmission and/or in the involvement of distinct intracellular pathways triggered by receptor activation.

Keywords: neuromuscular junction, endplate current, noradrenaline, acetylcholine, release timing

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INTRODUCTION

It is known that catecholamines, especially noradrenaline (NA) and adrenaline, can exert an influence on the muscular activity in vertebrates affecting both the functional properties of muscle fibers and the process of excitation transmission from nerve to muscle [1–5]. Recent studies provide evidence for colocalization of sympathetic and motor nerve endings in mammals skeletal muscles [6]. The influence of adrenergic compounds particularly on the process of synaptic transmission in the neuromuscular junction has been studied for quite a long period of time. However the results of these studies are often ambiguous because of multiple targets of action of adrenergic agents and the significant role of concomitant factors, such as the degree of cell depolarization, level of extracellular calcium ions etc. For example, it was shown that in rat synapses NA application elevated the endplate potentials amplitude [7–11]. W. Van der Kloot and T. Van der Kloot [12] have revealed that NA, like some other agents, can increase the amplitude of uniquantal responses suggesting that these compounds could influence the size of synaptic vesicles. It was shown also that catecholamines modulate the sensitivity of nicotinic acetylcholine (ACh) receptors in frog endplates [13].

Quite recently, one more mechanism of synaptic transmission modulation was discovered which is associated with a change in kinetics (timing) of secretion of individual acetylcholine quanta in response to nerve stimulation [14–16]. In the frog neuromuscular synapse, it was found that NA produces synchronization of the secretory process without causing any significant increase in the amount of neurotransmitter released [17]. This manifested itself as a decrease of fluctuations in synaptic delays between the peak of the action potential depolarization of the nerve ending and the initiation of the postsynaptic response and as the shortening of the rising phase of the multiquantal signal and increase in the signal amplitude. It was shown that this effect is mediated by activation of β_1 adrenoceptors resulting in elevation of the intracellular cAMP level [18].

It was reasonable to expect that a similar effect could be observed in the neuromusclar synapses of warm-blooded animals. The aim of this study was to investigate the action of NA on the degree of synchrony of acetylcholine quanta secretion from the motor nerve endings in the synapses of mouse diaphragm.

[1] The article was submitted by the authors in English.