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Kinetics of neurotransmitter release in neuromuscular synapses of newborn and adult rats

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ABSTRACT

The kinetics of the phasic synchronous and delayed asynchronous release of acetylcholine quanta v studied at the neuromuscular junctions of aging rats from infant to mature animals at various frequ cies of rhythmic stimulation of the motor nerve. We found that in infants 6 (P6) and 10 (P10) d after birth a strongly asynchronous phase of quantal release was observed, along with a reduced nu ber of quanta compared to the synapses of adults. The rise time and decay of uni-quantal end-pl currents were significantly longer in infant synapses. The presynaptic immunostaining revealed t the area of the synapses in infants was significantly (up to six times) smaller than in mature junctio The intensity of delayed asynchronous release in infants increased with the frequency of stimulat more than in adults. A blockade of the ryanodine receptors, which can contribute to the formation delayed asynchronous release, had no effect on the kinetics of delayed secretion in the infants unl synapses of adults. Therefore, high degree of asynchrony of quantal release in infants is not associa with the activity of ryanodine receptors and with the liberation of calcium ions from intracellular calci stores.

1. Introduction

During postnatal neuromuscular development, the plasticity of synaptic transmission at the pre-and postsynaptic level is mostly realized by modifications of postsynaptic acetylcholine receptors (Fournier et al., 1991; Zucker and Regehr, 2002; Shi et al., 2012), changing the size and number of acetylcholine (ACh) quanta released by the nerve stimulation (Van der Kloot and Molgó, 1994; Slater, 2008) and also by massive non-quantal ACh release during the synapse elimination period (Vyskočil et al., 2009). Another mechanism for regulating synaptic transmission is the time delay between the presynaptic spike and the release of individual quanta, which accumulate over time to form the final postsynaptic end-plate current (EPC) (Katz and Miledi, 1965; Lin and Faber, 2002). The kinetics of quantal release at the neuromuscular synapses can be regulated by various physiologically active compounds and their receptors (Samigullin et al., 2012), including cholinergic (Nikols et al., 2004), adrenergic (Bukcharaeva et al., 1999; Bukharaeva al., 2002) and purinergic ones (Tsentsevitsky et al., 2011). A the frequency and number of nerve stimulation might influer the synaptic latency of a single quantum release (Kovyazina et 2010). These changes in the kinetics of quanta secretion (or syna tic latencies) affect the amplitude and time course of the integ EPC and modulate the efficiency of synaptic transmission (Slat 2008; Kovyazina et al., 2010).

Presynaptic action potential evokes at least two kinetically d tinguishable modes of neurotransmitter release (Hagler and Go 2001). One is the phasic release of many quanta, which results an almost synchronous activation of the postsynaptic recepto and this is followed by an asynchronous release that occurs up hundreds of ms after nerve stimulation (Katz and Miledi, 196 Goda and Stevens, 1994; Hestrin and Galarreta, 2005).

The initial phasic release is fast but not absolutely synchrono At room temperature, the quantal release usually begins 0.2–0.8 after the peak of the action potential. This shortest 5% of all late cies is called the minimal synaptic latency. Latency distributi then rapidly reaches a maximum at about 3 ms and decays ov the next several milliseconds (Barrett and Stevens, 1972; Van d

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