Pre- and Postsynaptic Actions of Pancuronium in Spinal Cord - Skeletal Muscle Co-Cultures

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Introduction

In organotypic spinal cord-skeletal muscle co-cultures of mice, functional neuromuscular junctions are forming during the first week in vitro. Thereafter, muscle contractions, driven by the firing of spinal neurons, can be readily observed because drug access to the neuromuscular junction is not limited by diffusion. These co-cultures seem to be a promising tool for the study of compounds modulating neuromuscular transmission directly or indirectly. However, the significance of in vitro studies critically depends on the question of whether the reported drug effect is observed at a clinically relevant concentration. In order to address this issue, we investigated the action of the non-depolarizing muscle relaxant pancuronium.

Results

1. In spinal cord-skeletal muscle co-cultures, spontaneously occurring bursts of action potentials, recorded from neurons in the ventral horn of the spinal cord, are preceding muscle contractions by 1–100 ms.

2. At a clinically relevant concentration of 750 nM, pancuronium attenuates muscle contractions without modifying action potential firing of spinal neurons.

3. The efficacy of pancuronium to block neuromuscular transmission is time-variant, reaching a minimum when ventral horn neurons are firing at their maximal rates.

Methods:

Co-Culturing Spinal Cord and Muscle Cells

Spinal Neurons Trigger Muscle Contractions

Actions of Pancuronium and TTX

- Pancuronium (750 nM)
- TTX (1 μM)

Wash 1

Wash 2

Pen-Spike-Train Muscle Tension: Grand Averages

Burst-Triggered Muscle Activity

Efficacy of Pancuronium in Causing Muscle Relaxation