TITLE: ACETYLCHOLINE RECEPTORS MEDIATE MASSETER MUSCLE RIGIDITY

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Succinylcholine (SCh) induced masseter muscle rigidity (MMR) is a puzzling clinical problem. Not only can it interfere with intubation, but it is sometimes associated with malignant hyperthermia (1). Clinically significant MMR is infrequent, but recent studies show that it occurs commonly at sub-clinical levels in pediatric patients receiving volatile anesthetics (2). We report on our development of a rat model and pharmacologic characterization of MMR.

Male Lewis rats (275-450 g) were anesthetized with 3% halothane in oxygen. Following tracheotomy, mechanical ventilation was established with 1% halothane in oxygen using a small animal ventilator. Right femoral vessels were cannulated for arterial blood pressure monitoring and iv drug administration. Temperature was controlled at 37°C by a heat lamp with a servo mechanism. The head was fixed in a metal clamp. Isometric jaw tension was monitored by a transducer connected to the lower incisors by silk suture. Jaw contraction was produced with bilateral placement of needle electrodes for indirect stimulation. Resting tension was adjusted by maximizing twitch (0.2 Hz) tension. The contracture response to 500 μg/kg SCh was examined in the absence of stimulation. This was preceded by an injection of saline as a control. Since the data were not clearly normally distributed, a nonparametric paired test for significance (Wilcoxin; $P<.05$) was employed.

Saline controls produced no response. In all rats examined (n=6), SCh produced a transient increase in resting tension. The mean peak contracture was 0.97 g (SD=1.1; range=0.2-2.8). The duration, measured as time to 50% recovery, was 30±24 s. Following the contracture, neuromuscular block (greater than 80%) was always detected. A second dose of SCh was administered 45-60 minutes after the first (when there was complete recovery from the previous neuromuscular block) produced contractures of significantly less amplitude (0.28±0.23), often none at all (4 of 6). When a greater than 90% neuromuscular block was achieved by vecuronium (0.8-1.5 mg/kg), contractures could not be detected (n=4) following 500 μg/kg SCh.

We demonstrated that neuromuscular blocking doses of SCh increase jaw tension in rats. As in human MMR, there seems to be a large variability in this contracture response. The antagonism by vecuronium and the tachyphylaxis exhibited by the second dose of SCh are typical of the classical agonist actions of acetylcholine. Therefore, it appears that MMR is mediated by acetylcholine receptors.

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2. Br. J. Anaesth. 64:21-27, 1990

TITLE: MOTOR NERVE TERMINAL EFFECTS OF HALOTHANE (HAL) POTENTIATE CURARE-(DTC) INDUCED NEUROMUSCULAR BLOCK

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The ability of potent inhalation anesthetics to augment the actions of DTC is well known. The mechanism underlying this potentiation is not completely understood. Potent inhalation anesthetics cause blockade of the acetylcholine activated ion channel resulting in decreased miniature endplate current (MEPC) amplitude which appears to be additive to that produced by curare. The combined effects of curare and halothane on evoked neurotransmitter release (endplate current-EPC) have not been reported.

Methods: All studies were performed in the frog (R. Pipiens) sciatic nerve sartorius muscle preparation. EPC's were recorded using the two micro-electrode voltage clamp. A recording electrode was inserted close to an endplate region. If satisfactory MEPP's were recorded a second (current passing) electrode was inserted within 100μm of the first. MEPC's having a growth phase of <0.5 msec indicated adequate recording conditions. EPC's were elicited at 0.4 and 40 Hz. Currents were observed on an oscilloscope. Satisfactory the currents were digitized and isolated using a window discriminator. EPC's were stored and analyzed off line. DTC was dissolved Ringer's solution while HAL was applied by passing compressed air through a calibrated vaporizer whose output was bubbled through the DTC containing solution at appropriate time. Drugs were applied for a minimum of 15 min. After control determinations, DTC followed by DTC plus HAL were applied. EPC's were recorded after each. Results are expressed as percent of control value. The largest of the first five EPC's (EPCL) and the mean value of the last ten EPC's were used for comparison.

Results: Following the application of DTC (10^{-6}M) the amplitude of EPCL was reduced to 33% of control. With the combined application of HAL (1%) amplitude decreased to 13% of the control value. The corresponding tau (time constant of decay) values decreased to 65 and 52% respectively. With no drug application, the mean value of the amplitude of the last ten EPC's was 79% of the control value while tau was 95% of control. Using the amplitude of EPCL as control the mean value of the last ten EPC's after the administration of curare was 28% of the control value while tau was 66%. With the addition of halothane these values were further decreased to 15 and 55% respectively.

Discussion: This study documents the potentiation of the neuromuscular blocking effects of curare by halothane. The potentiation occurred primarily as a result of halothane induced decrease in transmitter release along with some decrease in tau suggesting a primary effect on the motor nerve terminal.