An In-Depth Patch Clamp Study of HCN2 Channels: Cyclic AMP- A Possible Novel Therapy for the Treatment for the Suppression of the Ih Current by Dexmedetomidine

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Hyperpolarization-activated cyclic nucleotide–gated (HCN) channels are voltage-gated channels in cell membranes of the heart and brain. The Ih current, also called the pacemaker current, plays an important role in cardiac and brain rhythmicity, and impulse transmission. The effect of Dexmedetomidine (DEX), a pre-operative sedative, on the Ih current has not been studied in 688 Wild Type mice thalamus neurons. Tetrodotoxin (TTX) is an agent that blocks all interfering currents, except Ih currents. The purpose of this study was to investigate the effect of DEX (50nM) on Ih currents, in the absence and presence of cyclic adenosine monophosphate (cAMP). Using whole cell patch-clamp technique, a pipette was inserted through cell membranes of 10 single live neurons, and Ih current amplitudes (pA) were measured at a voltage of -100 mV. The procedure was performed in sequential “steps” of 32 seconds each, with the following interventions: TTX (control); DEX+TTX (experimental); and TTX post DEX (“Wash Group”). Normalized Ih current values were significantly lower in the DEX+TTX group, compared to the TTX control, using F-tests and t-tests. Cyclic aMP significantly minimized the reduction of Ih currents, caused by DEX. This research concludes that DEX, a commonly used intravenous sedative, reduces the Ih current, which can result in decreased neuronal excitability, reduced arousal post-anesthesia, and cardiac arrhythmias. Vigilance for these side effects is required when DEX is used for sedation. This study highlights that novel therapy using cAMP can be used in conjunction with DEX, to minimize Ih current reduction and potential side effects.

Awards Won:
Third Award of $1,000