Instructor's Response(s) – Discussion Question(s) – Module 6

Discussion Question 1

In an experiment in which cardiac fast action potentials were measured it was observed that administration of a particular drug resulted in a decrease in the duration of phase 2 along with more of a "droop" (negative slope) in phase 2. Please provide a possible explanation for these observations. Answer individually; **post your response to the Discussion Board by 9:00 PM of Day 4 of the module.**

The duration and "droop" (or lack thereof) of phase 2 of the cardiac fast action potential are determined by inward Ca^{2+} current (through, for the most part, L-type Ca^{2+} channels) and outward K^+ currents (I_{K1}, I_{Kr} and I_{Ks}) – see video 2, slide 4 and video 3, slide 4.

So, one way to decrease the duration of phase 2, and to increase its "droop" is to reduce Ca^{2+} entry; this can be accomplished by administering a calcium channel blocker, such as diltiazem – see video 3, slide 3. The potentiation of outward K^+ currents (I_{K1}, I_{Kr} and I_{Ks}) would (also) contribute to the observed effects (would require a drug different then diltiazem though).

Discussion Question 2

What would be the effect of a drug that reduces T-type Ca^{2+} current on the time to reach threshold in a cardiac pacemaker potential? Briefly explain. Answer individually; **post your response to the Discussion Board by 9:00 PM of Day 5 of the module.**

The depolarization (phase 4, video 1, slide 3, panel A) to threshold (video 4, slide 5) of the cardiac pacemaker potential is determined by inward sodium (i_f) and Ca^{2+} currents and an outward K^+ current – see video 4, slides 3 and 4. In particular, there is a T-type Ca^{2+} current that occurs near the end of phase 4 (video 4, slide 4).

So – reducing the T-type Ca^{2+} current present near the end of phase 4 would delay depolarization to threshold (increase the time to reach threshold) in a cardiac pacemaker potential.

Discussion Question 3

What would be the effect of a drug that reduced L-type Ca^{2+} current in AV nodal cells on the timing of the EKG waveform? Briefly explain. Answer individually; **post your response to the Discussion Board by 9:00 PM of Day 7 of the module.**

Conduction velocity in cardiac tissue is proportional to the amplitude of the AP and to the rate of change of membrane potential (V_m) during phase 0 of the AP; higher amplitude and dV_m/dt during phase 0 lead to a higher conduction velocity

Rev 0, 2/27/17 - adapted from Spring 2016
Rev 1, 3/6/17 - correct typo (due day for Q2)
Rev 2, 9/25/17 - change color of text for due dates/times and add refs for B&L[7] to the Q3 response
Rev 3, 7/15/18 - up-date for 601; no content changes
Rev 4, 9/26/19 - change time due from 6:00 PM to 9:00 PM

(B&L[6+], pp 299-300; B&L[7], page 312). A reduction of L-type Ca^{2+} current in AV-nodal cells (e.g., by a calcium channel blocker) will blunt the amplitude of the action potential (B&L[6+], page 304; B&L[7], pp 316-317), thereby reducing conduction velocity through the AV node; the increased delay time through the AV node will be seen on the EKG as a prolonged P-R interval (video 6, slide 7). See also B&L[6+], pp 306-307; B&L[7], pp 318-319.

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