Heart rate and basic principles of circulation

Body mass and heart rate

> Bigger body mass = Larger heart = More cardiac output = Higher stroke volume =Lower heart rate

Heart rate controlled at cellular level.

Sympathetic stimulation

> Speeds up heart rate. Raising cAMP: Noradre or adre bind to beta receptors to raise cAMP. raised cAMP binds to channel for If and increases its current. cAMP activates protein KA which phosphorylates the L type calcium channel, phospholamban and the ryanodine receptor in the sarcoplasmic reticulum (this affects membrane clock as it is affected by Ca2+). Phosphorylation + activating If = increase rate of diastolic depolarisation = increase heart rate..

Parasympathetic stimulation

> Slows down heart rate. Lowering cAMP. Ach binds to muscarinic receptors & directly activates a receptor coupled K channel (Ik(Ach)). Muscarinic receptors also lower the cAMP conc in the cell.

Bradycardic agents

> Non specific: Beta blocks, Non-dihydropyridine L-type Ca channel blockers. Anaesthetics. Anti-arrhythmic agents. Digoxin. Specific bradycardiac agents: Alinidine, Zatebradine and Ivabradine.

Ivabradine

> Only SBA licenced for clinical use. Blocks the funny current.

If

> Plotted going down as it's an inward current.

SA node

Pace makers

> Speed: SA node > AV node > His bundle > purknje fibres. Each have intrinisic rate which is conducted by the SA node (primary pacemaker). Cardiac arrythmias can occur if others fire faster than SA or at randomly.

Movement of impulse

> R.Atrium --> L.Atrium --> Septum --> Ventricular wall

SA node gross anatomy

> Tear drop shape, top of R.Atrium. At junction of SVC & IVC. On one side bounded by Crista terminalis (thick ridge atrial muscle). Heterogenous mix (specialised nodal cells, atrial cells & connective tissue) --> for normal functioning despite age related changes in heart rate. 50-90% connective tissue (depending on age).

SA node microanatomy

> From centre to periphery: Spindle cells, Elongated spindle cell and spinder cell. Gradual + smooth transition from centre to periphery. All have nucleus, lots of membrane and little cytoplasm as needed for AP generation not as muscle cells. P cells in centre: small, poorly differentiated, sparse mitochondria, numerous caveolae (membrane invaginations). Towards periphery: larger, more organised, more muscle filaments and well-defined structure.

SA node (cont)

SA AP

> 1) Diastolic/pacemaker depolarisation/-Phase 4 of AP: sloping baseline between action potentials. 2) Pacemaker potential generated by combo of increasing inward currents & decreasing outward currents. 3) Membrane potential hits threshold & Na+ and/or Ca2+ channels open generating AP. 4) Na+ and Ca2+ channels quickly shut & K+ channels open repolarising membrane down to its min diastolic level. 5) Repeat with regular rhythm

Two theories on SA node clock

> Membrane Clock theory: Cyclic changes in ion currents drive membrane potential to threshold. Calcium clock: Cyclic release of Ca from intracellular store drives membrane potential up and down.

Membrane clock theory

> Funny current (inward current bringing +ve ions into cell) so activates when membrane hyperpolarises. Channel closed during AP. Membrane repolarises and channel slowly opens being +ve into cell. Membrane depolarises till AP can fire. Funny current switches off as channels are inactivated. During diastolic interval some other ionic currents switch on and off. Time & voltage dependent activation of ion currents drives the repetitive clock.

Calcium and membrane clock both important

> Modulate each other. Both stimulated & inhibited by neurotransmitters (NA & Ach). Membrane clock dominate mechanism (as generation of AP needed for pacemaker activity) & Calcium clock fine tunes.

Extra lecture info

Heart rate and life

1. Negative linear relationship between heart rate and life expectancy in animals as higher heart rate means more metabolism so more free radicals (except humans due to chronic diseases)

Heart rate and disease prognosis

1. Heart rate strongly correlated with CV mortality (risk factor or risk indicator?) --> CHD, Myocardial infarction

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