Veterinary Bioscience: Cardiovascular System

WEEK 1 – STRUCTURE/FUNCTION RELATIONSHIPS IN THE HEART

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Acknowledging the contribution of Prof Liz Tudor for drafting these notes

LECTURE 3 –ELECTRICAL ACTIVITY OF THE HEART

INTENDED LEARNING OUTCOMES

At the end of this lecture you should be able to:

– Describe how the resting membrane potential is created in cardiac myocytes.
– Explain the ionic changes that occur during action potentials in contractile cardiac myocytes and pacemaker cells, including a description of the differences between these
– Identify the refractory period of the cardiac cell electrical cycle, and explain the functional significance of this
– Describe the structural organisation of the pacemaker and conducting tissues of the heart and the normal pathway of action potential conduction through the heart.
– Describe how cardiac sympathetic and parasympathetic nerves alter heart rate and conduction of cardiac action potentials.

KEYWORDS

Atrioventricular node, AV node, autorhythmicity, cardiac myocyte, membrane potential, Purkinje fibre, pacemaker, refractory period, sinoatrial node, SA node.

THE RESTING MEMBRANE POTENTIAL

All cells have an electrical potential across their membranes, because of differences in ionic concentration between the intracellular and interstitial fluid. At rest, cardiac cells membranes are semi-permeable, and selectively permeable to potassium. Large negatively charged intracellular molecules (e.g. proteins) attract positively charged ions and as the membrane is most permeable to K+, this leads to an accumulation of K+ within the cell. However, the electrical forces attracting K+ into the cell are then counterbalanced by the increased concentration gradient, which drives K+ out of the cell.

An equilibrium is reached when these two opposing forces exactly balance. The opposing effect of concentration gradient on electrical gradient means that there are slightly fewer positive charges (in this case K+ ions), moving into the cell than there are negative charges (e.g. proteins). The inside of the cell is therefore negatively charged relative to the outside, and a potential exists across the membrane. If the membrane were permeable only to K+, the membrane potential would be determined purely by the K+ equilibrium potential that can be calculated from the Nernst equation. The K+ equilibrium potential is –90mV.

CARDIAC CELL ION CHANNELS AND GATING

As you have seen previously in other tissues, channels in cell membranes provide for selective movement of ions into the cell down their concentration gradient. Positive ions entering a cell cause an inward current and **depolarisation**. In both cardiac and smooth muscle cells, depolarisation results from opening of channels that allow influx of Na^{+} and Ca^{++} ions. Transition of channel between closed and open state is called **gating**. *Voltage -gated channels* are gated by membrane potential. They are time dependent, and once opened, start to inactivate immediately. Inactivated channels do not allow passage of ions. They are not in closed state as they cannot be re-opened. *Receptor-gated channels* open when a receptor or hormone binds to a receptor

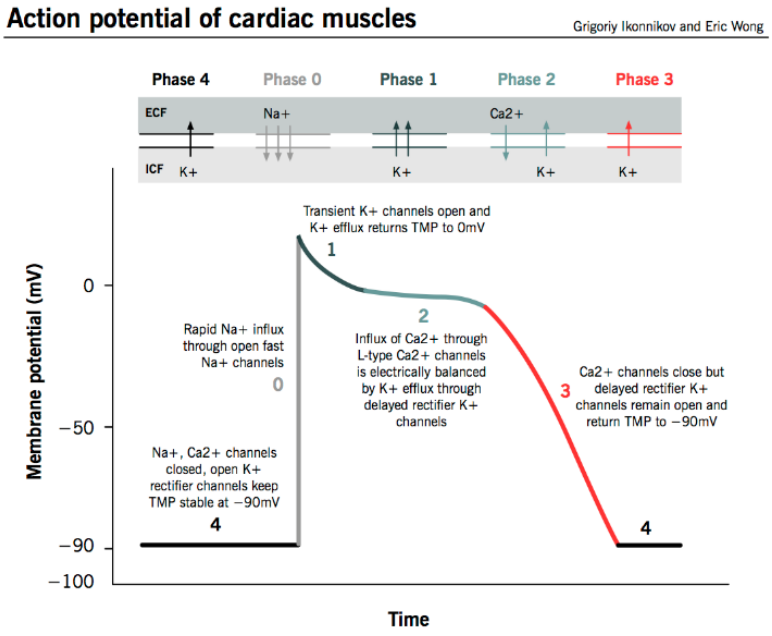
CARDIAC CELL ACTION POTENTIALS - THE ORIGIN OF THE HEART BEAT

One of the intrinsic properties of the heart is 'autorhythmicity', the capacity of the heart to contract as a result of action potentials that it generates by itself. There are two specialised types of cardiac muscle cells; contractile cells (do the mechanical work of pumping), and autorhythmic (non-contractile) cells, also called pacemaker cells. Autorhythmicity is a function of non-contractile cardiac muscle cells (**pacemaker cells**) specialised for initiating and conducting the action potentials responsible for contraction of cardiac muscle cells. Action potentials in pacemaker (autorhythmic) and contractile cardiac cells are distinctly different because of differences in selective movement over time of ions (particularly Ca and Na) into the cell.

IONIC MECHANISM OF THE ACTION POTENTIAL

The action potential can be described in terms of phases corresponding to the movement of specific ions across the cell membrane. In this lecture we will examine these phases and explain why action potentials in pacemaker tissue are distinctly different from those in contracting myocytes.

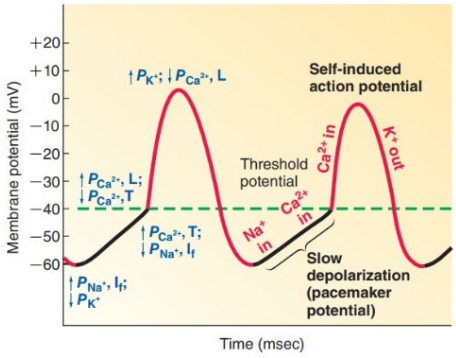
Figure 1: Phases of the contractile cardiac myocyte action potential



(Physiol Rev. 2005 Oct;85(4):1205-53)

The ionic basis of the action potential in pacemaker cells is different.

Figure 2: Pacemaker activity of autorhythmic cells



(Sherwood, 2016)

The initial phase of the slow depolarization to threshold is caused by net Na^+ entry through a type of voltage-gated channel found only in cardiac pacemaker cells.These are sometimes called 'funny' channels or pacemaker channels. They open when the potential becomes more negative at the end of the previous action potential. When they open, there is a net inward current of Na^+ ions, increasing the membrane potential. In pacemaker cells, the permeability to K^+ does not remain constant between action potentials (as for nerve and skeletal muscles). K^+ channels instead slowly close, reducing the outflow of K^+ down its concentration gradient. In the second half of the pacemaker potential stage, voltage-gated calcium channels open, increasing the potential to threshold. These are transient, or T-type Ca channels.

Once threshold is reached, the rising phase occurs due to activation of L-type voltage gated calcium channels. The falling phase is the result of K efflux due to activation of voltage-gated K^+ channels and closure of L-type Ca channels. After the AP is over, there is slow closure of these K^+ channels that contributes to the next slow depolarisation to threshold.

Various autorhythmic cells have different rates of slow depolarisation to threshold. Cell with faster rates will reach threshold more quickly, and therefore generate action potentials more rapidly. The sino atrial (SA) node exhibits the fastest rate of depolarisation. The other autorhythmic tissues are unable to assume their own naturally slower rates, because they are activated by action potentials originating in the SA node before they reach their own threshold. The SA node determines rate at which action potentials are generated, and hence heart rate.

REFRACTORY PERIOD IN CARDIAC MUSCLE CELLS

Cells are in an absolute refractory state during most of the action potential i.e they cannot be stimulated to fire another action potential. This is because Na+ channels are rapidly inactivated in Phase 0, and do not reactivate until the membrane potential becomes more negative than –65mV. The refractory period is almost as long as the period of contraction initiated by the action potential. So cardiac muscle cannot be restimulated until the contract is almost over so summation of contractions, or tetanus, is not possible. This functionally important because pumping blood requires alternate periods of contraction and relaxation . Tetanus of the cardiac muscle would be fatal.

CONTROL OF HEART RATE

Normal rhythmic contractions occur because of the spontaneous electrical pacemaker activity of the sinoatrial (SA) node. The heart beats at an intrinsic rate, dependent on the rate of spontaneous depolarisation to threshold. External influences such as autonomic nerves, hormones and drugs can increase or decrease HR from its intrinsic rate.

Sympathetic and parasympathetic nerves influence heart rate by altering the rate of spontaneous depolarisation of resting potential in the SA node. Parasympathetic fibres (of the vagus nerve) release acetylcholine (ACh) on SA node. ACh increases resting membrane permeability to K^+, causing hyperpolarisation of the membrane potential and slowed rate of spontaneous depolarisation, leading to slowing of heart rate. Sympathetic nerves release noradrenaline, that promotes increased permeability to Na and Ca, increased rate of depolarisation towards threshold and hence increased heart rate.

CONDUCTION OF CARDIAC ACTION POTENTIALS

Cardiac muscle cells are connected to form branching fibres. Adjacent cells are joined by specialised structures called intercalated discs. Within intercalated discs, there are two types of membrane junctions; desmosomes (mechanically holds cells together), and gap junctions (areas of low electrical resistance that enable action potentials to spread between cells). There are no gap junctions between atrial and ventricular contractile cells, and these muscle cells are separated by the nonconductive fibrous skeleton that surrounds the valves. Action potentials are spread from the atria to the ventricles through the conduction system, to ensure synchronisation necessary for pumping. An impulse generated in one part of the heart spreads through the entire heart – all the cardiac muscle cells contract or none of them do.

Conduction velocity is the speed at which an action potential propagates through a region. Conduction velocity varies a lot in different regions of the heart and this allows for coordinated contraction of the heart. The diameter of the conducting fibre is one determinant of conduction speed- small diameter fibres such as the atrioventricular (AV) node conduct more slowly than large diameter fibres such as Purkinje fibres.

STRUCTURAL ARRANGEMENT OF CONDUCTION PATHWAYS IN THE HEART

The spread of cardiac excitation is coordinated to ensure efficient pumping of the heart. As the SA node initiates depolarisation, contraction begins in the atrial muscle. The wave of depolarisation spreads across the atrial muscle, and due to the insulating property of the cardiac skeleton, is directed to the AV node. The slower rate of conduction in the AV node ensures that atrial contraction (and hence emptying of blood into the ventricles) is completed before ventricular contraction begins. From the AV node, conduction continues through the ventricular conduction pathways, the Bundle of His and right and left bundle branches the Purkinje fibres and finally the cardiac myocytes of the ventricles.

THE CARDIAC SKELETON AND ELECTRICAL CONDUCTION

The cardiac skeleton is a fibrous plate- reinforced in some species with cartilage or bone- that serves several functions. It provides for electrical discontinuity between the atria and the ventricles- so that all electrical activity is conducted through the AV node, it provides attachment for the ventricular and atrial muscle, and support for the valves

FURTHER READING

Berne RM & Levy MN, *Cardiovascular Physiology*, 6th Edition 2008.

Dyce, Sack and Wensing, *Textbook of Veterinary Anatomy,* 3rd edition 2002. Sherwood, L, *Human Physiology from Cells to Systems,* 8th Edition 2013.

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