Understanding the Electrophysiology of the Heart: The Electrocardiogram and Interpretation of Heart Rate Variability

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Background

Blood flow through the body is sustained by the cardiac output of the heart. Cardiac output, defined as the output of the heart per minute, requires a regular cycle of relaxation and contraction of the atria and ventricles. An electrocardiogram (ECG) monitors the complex electrophysiological events that make up the cardiac rhythm (Becker, 2006).

The heart tissue is composed of two principal cell types: working cells and specialized neural-like conductive cells. Working cells make up the myocardium, or muscle, of the atria and ventricles. The specialized cells are found in the sinoatrial (SA) node, atrioventricular (AV) node, bundle of His, and Purkinje fibers. The specialized cells initiate and conduct electrical impulses through the myocardium. This transmission of electrical signals regulates the rhythm of the cardiac cycle that is essential to maintaining blood volume and contractile strength. The firing rate of the specialized cells is controlled by two sets of autonomic nerves. Sympathetic nerves increase firing rate, while parasympathetic nerves decrease firing rate. The generation of each cardiac cycle begins in the SA node. From the SA node, the signal spreads through the remainder of the conductive tissue into the muscle cells. Abnormalities in the conduction system result in complex cardiac outputs that are referred to as arrhythmias or dysrhythmias (Becker, 2006).

Fundamentals of Electrophysiology

All cardiac muscle cells are positively charged on their outer surfaces. The abundance of cations (positively charged ions) that produces this charge gradient causes cardiac muscle cells to have a resting membrane potential that is relatively positive on the outer surface. The resting membrane potential is maintained by the sodium-potassium pump (Becker, 2006).

When the cell is stimulated, ion channels open and allow an influx of sodium (Na^+) or calcium (Ca^{2+}) ions into the cell. This inward flow of cations decreases the positive charge on the outside of the cell, causing a reversal in resting potential. The period of time during which the membrane potential is reversed is called a depolarization. Depolarizations are very brief because sodium channels close quickly and potassium channels open to restore the resting potential. The potassium channels allow potassium ions (K^+) to leave the cell. At the same time, sodium ions (Na^+) are actively pumped out of the cell. Both processes cause a decrease in positive charge inside the cell and an increase in positive charge outside the cell, reestablishing the resting potential. The reestablishment of the resting potential is called a repolarization. Together, a depolarization and repolarization make up an action potential (AP). Action potentials travel from cell to cell, producing an impulse along the surface of the cardiac tissue (Becker, 2006).

All human cells carry APs, but the purpose of an AP in a given cell depends on that cell's function. In cardiac muscle cells, APs release stored calcium ions, which initiates the contractile process (Becker, 2006).

The Cardiac Impulse

The cells of the heart are special for two reasons. First, the heart cells possess automaticity, which means that they have the ability to initiate electrical impulses spontaneously. Physiologically, this property is explained by the cell membrane's partial permeability to Ca^{2+} and Na^+ ions at rest. This partial permeability allows for a gradual inward "leak" of cations to decrease the resting potential until a threshold is reached, at which point all the channels open and a rapid cation influx depolarizes the membrane, resulting in an AP. Second, cardiac cells, unlike neural tissues, do not release neurotransmitters. Instead of undergoing electrochemical signaling, cardiac cells are in direct contact with cardiac muscle, allowing their APs to directly initiate the depolarization of the myocardium (Becker, 2006).

Cardiac muscle cells are fused together by intercalated discs, which can be thought of as "special attachments." Intercalated discs allow muscle cells to function as a continuous sheet of tissue called a syncytium. The atrial syncytium is separated from the ventricular syncytium by a layer of connective tissue that acts as an insulator (Becker, 2006).

The cardiac impulse begins with the generation of an AP at the SA node. The SA node acts as the "pacemaker of the heart" because it has the fastest rate of spontaneous firing of all the specialized tissues. The generation of this AP causes the depolarization of the atrial muscle. The syncytium acts as an insulator and stops the depolarization from propagating to the ventricles everywhere on the surface of the tissue except at the AV node. The AV node delays and then relays the impulse along the common bundle of His, which penetrates the connective tissue to enter the ventricles. The impulse continues along the common bundle of His until it reaches the Purkinje fibers, which stimulate the ventricular muscle syncytium (Becker, 2006).

The ECG Tracing

The APs of most cells in the human body are very small, but the APs of the heart are large enough to be recorded by surface electrodes. The recording of cardiac impulses produces an ECG tracing. The baseline of the ECG tracing is called the isoelectric line and denotes the resting membrane potential. Deflections from rest are lettered in alphabetical order from P to T. After each deflection from baseline, the tracing returns to the isoelectric point (Becker, 2006).

The normal cardiac pattern can be seen in Figure 1. The first main deflection is called the P wave and represents the depolarization of the atrial muscle cells. It does not reflect the contraction of the muscle or the firing of the SA node. These events may be deducted from the shape and consistency of the P waves. It is assumed that the SA node fires at the start of the P wave and that atrial contraction begins at the peak of the P wave. The ECG recording does not show the repolarization that follows the depolarization in the sequence of the AP (Becker, 2006).

The second main deflection is referred to as the QRS complex. The QRS complex groups together three individual deflections. The Q wave denotes the initial downward deflection that follows the P wave. The R wave follows the Q wave and reflects the initial upward deflection. The peak of the R wave marks the maximum upward deflection of a normal QRS complex. The S wave indicates a return to the isoelectric point. Similarly to the P wave, the QRS complex is not representative of ventricular contraction. The instance of ventricular contraction commences at the peak of the R portion of the complex (Becker, 2006). The deflections that succeeds the QRS complex is called the T wave; it represents the repolarization of the ventricles (Goldenberg, Moss, and Zareba, 2006).
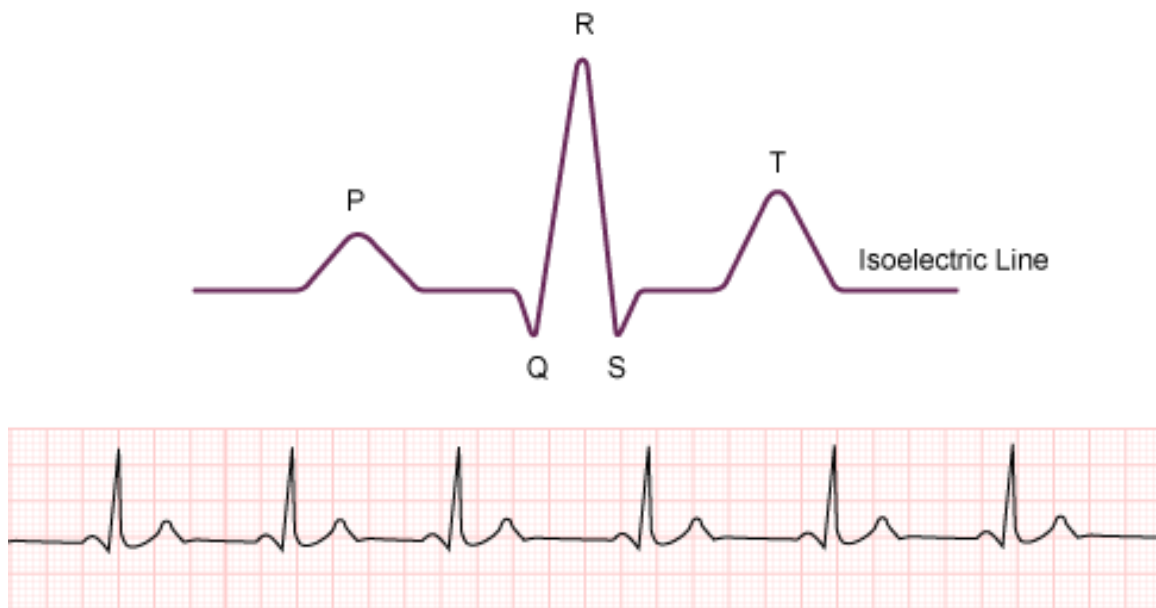

Figure 1. Normal sinus rhythm: P wave, QRS complex, and T wave.

A feature of interest in the ECG tracing is the PR interval. The PR interval reflects the passing of the cardiac impulse through the AV node into the ventricle. This interval is measured from the beginning of the P wave to the beginning of the R portion of the QRS complex. The PR interval commences with the depolarization of the atrial muscle and ends with the start of ventricular depolarization (Becker, 2006).

Basics of Heart Rate Variability

Heart rate variability (HRV) is emerging as an objective measure of regulated emotional responding, which is described as the generation of emotional responses of the appropriate magnitude at the appropriate time (Appelhans & Luecken, 2006). HRV is defined as the temporal variation, or variation in time, between sequences of consecutive heartbeats. On an ECG tracing, the duration of time between two adjacent R wave peaks is called the R-R interval.

The ECG signal requires editing before HRV analysis can be conducted. The editing process requires the removal of all non-sinus-node-originating beats. The resulting periods between QRS complexes result exclusively from SA node depolarizations and are termed N-N (normal-normal) intervals. HRV measures the variability of N-N intervals (Reed, Robertson, & Addison, 2005).

Emotions humans experience while interacting with their environment are associated with varying degrees of physical arousal. The autonomic nervous system (ANS) is responsible for generating physical arousal. The ANS is subdivided into two branches: the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS). The SNS serves an excitatory role, while the role of the PNS is inhibitory. The two branches interact antagonistically to produce varying degrees of physiological arousal. During periods of relative safety and stability, the PNS is dominant and physical arousal is low. In instances of physical or psychological stress, the activity of the SNS becomes dominant and heightens physical arousal (Appelhans & Luecken, 2006).

The SNS and PNS exert regulatory influence on heart rate (HR) by influencing the activity of the SA node. The activation of sympathetic fibers has an excitatory influence on the firing rate of the SA note, increasing HR, and facilitating conduction at the AV node. Parasympathetic activation has inhibitory effects on the SA node, causing a decrease in HR and slowing conduction at the AV node. The two autonomic branches regulate the lengths of time between consecutive heartbeats, called interbeat intervals. A faster HR results in shorter interbeat intervals, while a slower HR results in longer interbeat intervals. Since the two branches act antagonistically, an increase in HR can result from either an increase in sympathetic activity or a decrease in parasympathetic inhibition (vagal withdrawal) (Appelhans & Luecken, 2006).

Physiologically, HRV measures the balance between sympathetic and parasympathetic (vagal) mediation of HR (Reed, Robertson, & Addison, 2005). Both branches exert constant influence over HR, but under normal conditions, the balance between the two favors parasympathetic activity (Appelhans & Luecken, 2006; Reed, Robertson, & Addison, 2005). The PNS influence maintains the resting HR in the range of 60 – 90 beats per minute, well below the intrinsic firing rate of the SA node (Appelhans & Luecken, 2006; Goldenberg, Moss, and Zareba, 2006). HR generally decreases with respiratory expiration (breathing out) and increases with inspiration (breathing in) (Reed, Robertson, & Addison, 2005). The ease with which an individual can transition between low and high states of arousal depends on the ability of the ANS to vary HR. HRV reflects ANS flexibility and is a measure of the interplay between the SNS and PNS. A high HRV is indicative of the ability of the ANS to vary heart rate rapidly, is considered the normal, healthy physiological state (Appelhans & Luecken, 2006).

The two branches of the ANS exhibit different latencies of action, which causes the HR produced by the SNS and PNS to occur at different frequencies. This difference is the basis for frequency-based HRV analysis (Appelhans & Luecken, 2006). Sympathetic mediation exerts its influence on HR over long periods of time and is reflected in the low frequency power (LFP) of the HRV spectrum (0.04 – 0.15 Hz) (Reed, Robertson, & Addison, 2005). Changes in HR due to sympathetic activation occur slowly, with peak effects being observed after approximately 4 s, and a return to baseline occurring after about 20 s (Appelhans & Luecken, 2006). Vagal

mediation exerts its influence on HR more quickly and affects the high frequency power (HFP) of the spectrum (0.15 – 0.4 Hz) (Reed, Robertson, & Addison, 2005). Parasympathetic regulation has a very short latency of response, with peak effects occurring at approximately 0.5 s and a return to baseline occurring within 1 s of initiation (Appelhans & Luecken, 2006).

The LFP to HFP ratio is indicative of sympathetic-vagal balance. Sympathetic-vagal balance follows circadian trends, with higher LFPs occurring during the daytime and higher HFPs occurring at night. In human subjects, exercise, standing, and stress increases sympathetic drive and LFP. In contrast, the stimulation of the face with cold increases parasympathetic drive and HFP (Reed, Robertson, & Addison, 2005).

Monitoring HRV

HRV can be measured in both the time and frequency domains. Of the two, analysis in the time domain is the simplest to perform. To analyze HRV, each N (or R) point is determined in the ECG trace. The mean HR is calculated and the longest and shortest N-N intervals are determined. These values can be used to perform more complex calculations like SDNN and NNSD. The SDNN is the standard deviation of N-N intervals and is representative of overall HRV. The NNSD is the number of adjacent N-N intervals that differ by more than 50 milliseconds (ms). Further analysis can be performed by deriving variables to estimate the short- and long-term components of HRV. The RMSDD is the square root of the mean squared difference between adjacent N-N intervals; it provides a measurement of short-term HRV. SDANN is the standard deviation of the average N-N interval over periods of approximately 5 minutes; it provides an estimate of long-term HRV. Calculating all of these variables allows for the temporal variability of HRV to be quantified (Reed, Robertson, & Addison, 2005).

Signal quality and the elimination of background "noise" is important to accurately analyzing HRV. Analysis is very difficult in patients who are not in sinus rhythm, defined as not having normal ECG tracings, who have extremely irregular HR, or whose tracings contain multiple ectopic beats. Ectopic beats reflect disturbance related to the electrical conduction system and constitute an irregular heart rhythm. Ectopic beats arise from fibers or groups of fibers outside the region of the heart muscle normally responsible for impulse formation. These disturbances can be recognized as deflections from the isoelectric line in the ECG tracing that do not correspond to the P-T wave pattern (Reed, Robertson, & Addison, 2005).

Most studies exclude patients who are not in sinus rhythm, but some authors suggest only excluding ECG signals that display more than 10 ectopic beats per hour. If analyzing a signal with ectopic beats, it is possible to remove ectopic beats and to correct for them by adjusting the positions of the R wave peaks and replacing missing beats midway between pairs of adjacent beats. An editing algorithm can be used to scan the signal and to remove any R-R interval that differs by a certain percentage (20-30%) from its preceding interval (Reed, Robertson, & Addison, 2005).

Measuring Emotional Response using Heart Rate Variability

The influence of the ANS over HRV is regulated by the brain areas that make up the central autonomic network (CAN). The CAN is involved in modulating physiological responses for expressing emotion, responding to environmental stimuli, exhibiting goal-oriented behavior, and regulating homeostasis (Appelhans & Luecken, 2006).

The CAN includes the brainstem and the cortical and limbic systems of the brain. It receives two types of inputs: inputs from visceral afferents carrying information about physical conditions inside the body, and inputs from sensory areas carrying information about the external sensory environment. By processing these inputs, the CAN adjusts physical arousal in accordance to changing situational demands, which allows for the regulation and expression of emotion. The SNS and PNS transmit the output of the CAN to the SA node, which directly influences HR. Consequently, the HRV reflects moment-to-moment output of the CAN (Appelhans & Luecken, 2006).

Empirical Research with HRV

Respiratory sinus arrhythmia is the rhythmic oscillation in HR synchronized with respiration. Breathing air into the lungs temporarily gates off the influence of the PNS on HR, causing an increase in HR and the shortening of the N-N interval, while breathing air out reinstates PNS influence, decreases HR, and elongates the N-N interval (Appelhans & Luecken, 2006). A study conducted by Fabes and Eisenberg found that higher levels of resting respiratory sinus arrhythmia are associated with greater self-reported emotional regulation and use of coping strategies in university students (Fabes & Eisenberg, 1997). The data suggested that individuals with lower resting respiratory sinus arrhythmia experienced greater negative emotional arousal in response to stress, which interfered with their ability to effectively implement coping strategies. In a different study, higher resting respiratory sinus arrhythmia was associated with lower indices of distress in grade school students watching an upsetting film (Fabes, Eisenberg, & Eisenbud, 1993).

Sgofio and colleagues conducted a study to investigate the relationship between cardiac autonomic, endocrine, and behavioral responses to real-life stress episodes. University students underwent two brief social challenges (stress interviews), during which their sympathetic-vagal balance was measured using the time-domain index of HRV. Non-verbal behaviors were also quantified during each social challenge. Psychometric measurements were collected via a SPRAS questionnaire after each stress interview, and samples of saliva were collected to determine cortisol levels before and after the experimental session. The SPRAS questionnaire evaluated submissive behavior. Data showed that individuals with greater levels of sympathetic dominance were characterized by higher scores of submissive behavior, larger cortisol increments, and greater perception of psychophysiological arousal. The results of the study demonstrated a correlation between the level of expression of a number of behavioral patterns and the degree of cardiac autonomic stress. Subjects who exhibited submissive behavior more frequently during the first stress interview were characterized by higher resting HR during the baseline, test, and recovery periods. The HRV of these subjects was lower during all recording

phases. Increased sympathetic influence and/or decreased parasympathetic influence reflect reduced values of HRV, while decreased sympathetic influence and/or increased parasympathetic influence reflect greater values of HRV. This interpretation suggests that subjects who are more prone to submission in stressful social interactions exhibit a greater shift of sympathetic-vagal balance toward sympathetic dominance before, during, and just after the stress episode (Sgofio et al., 2003).

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Figure 1. Normal sinus rhythm: P wave, QRS complex, and T wave. Reprinted from Cardiology Teaching Package, *Practice Learning Resources*, n.d. Retrived October 28, 2015, from http://www.nottingham.ac.uk/nursing/practice/resources/cardiology/function/sinus_rythm.php. Copyright University of Nottingham.

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