Cardiovascular Regulatory Mechanisms
Neural Control of Heart Rate

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Nerve supply to the Heart

1. **Sympathetic nerves**

2. **Parasympathetic nerves**

Sympathetic Innervation

- First five thoracic segments of the spinal cord
- T_1 to T_5
- Arise ➔ Stellate Ganglion

Preganglionic Fibers

- Sympathetic Preganglionic fibers
- From T_1 to T_5 Thoracic segments
- Reach Superior, Middle, Inferior cervical ganglion ➔ Sympathetic chain

Postganglionic fibers

- **Arising :**
- **Superior, Middle, Inferior cervical Ganglion**
- **Innervate: Heart**

Noradrenergic Fibers

- **Terminate ➔ Epicardial region**

Sensation from Heart

- **Carried by ➔ Sympathetic fibers**

Cardiac sympathetic Nerve supplies

1. Sinoatrial (SA) node
2. Atrioventricular (AV) node
3. Muscles of Atria
4. Muscles of Ventricles

Stimulation of sympathetic Nerves to Heart

- *Increase* the Heart Rate (HR) ➔
  - Positive Chronotropic effect
- Increase the Force of contraction ➔
  - Positive Inotropic effect

Stimulation of sympathetic Nerves to Heart

- ***Increase*** **the rate of conduction ➔**
  - **Positive Dromotropic effect**
- ***Increase*** **Excitability➔**
  - **Positive Bathmotropic effect**

Mechanism of Action

- **Sympathetic stimulation ➔**
- **Release Epinephrine (Adrenaline)**

Epinephrine ➔ Inotropic Effect

- Epinephrine ➔ β_1-adrenergic receptors
- Activates ➔Adenyl cyclase
- Enhances ➔ Intracellular cAMP
- cAMP ➔ Opening of Long lasting Ca^{2+} Channels
- Influx of ➔Ca^{2+} ions

Epinephrine ➔ Chronotropic Effect

- Increasing Influx of Ca^{2+} ions ➔ In to SA node
- Increase ➔Rate of spontaneous depolarization
- Reduce ➔ Efflux of K^{+} ions

Epinephrine ➔ AV node

- **Increases rate of impulse transmission**
- **Through AV node**

Clinical Physiology

1. Glucagon
2. Caffeine & Theophylline
3. Digitalis
4. Quinidine, Procainamide, Barbiturates
5. Hypoxia, Hypercapnia, Acidosis

Glucagon ➔ Positive Inotropic effect

- **Increases formation of cAMP**

Caffeine & Theophylline

- **Positive *Inotropic* effect**
- **Prevent breakdown of cAMP**

Digitalis ➔ Positive Inotropic effect

- **Inhibiting Na^+ - K^+ ATPase pump**
- **In myocardium**

Myocardial Contractility

- **Reduced by :**

1. **Quinidine**
2. **Procainamide**
3. **Barbiturates**
4. **Hypoxia, Hypercapnia, Acidosis**

Parasympathetic Innervation

- Through ➔ Vagus nerve (X^{th} CN)
- Preganglionic Parasympathetic fibers ➔
- Vagus nucleus

Parasympathetic Innervation

- Preganglionic Parasympathetic fibers ➔
- Vagus nucleus
- Pass through ➔ Cardiac nerve
- End in ➔ Parasympathetic ganglion in the heart

Parasympathetic Innervation

- Postganglionic Parasympathetic fibers ➔
- Parasympathetic ganglion in the heart
- Innervate ➔ Heart

Noradrenergic Fibers

- **Terminate ➔ Epicardial region**

Vagal fibers

- **End in ➔ Endocardial region**

Right Vagus fibers ➔ Supply

- **SA (Sinoatrial) node ➔**
- **Pacemaker**

Left Vagus fibers ➔ Supply

- **AV (Atrioventricular) node**

No ➔ Parasymapathetic supply

- **Ventricles**

Stimulation of parasympathetic Nerves to Heart

- ***Decrease*** **the Heart Rate (HR) ➔**
  - **Negative Chronotropic effect**
- ***Decrease*** **the Force of contraction ➔**
  - **Negative Inotropic effect**

Stimulation of parasympathetic Nerves to Heart

- ***Decrease*** **the rate of conduction ➔**
  - **Negative Dromotropic effect**
- ***Decrease*** **Excitability➔**
  - **Negative Bathmotropic effect**

Athletes➔Increase in Vagal Tone

- **Increase in Vagal Tone**
- **Reduces ➔ Resting heart rate (HR)**

Mechanism of Action

- **Stimulation of Vagus ➔ Release Acetylcholine**
- **Acetylcholine acts on ➔**
- **Muscarinic receptors**

Ach ➔ Decrease Heart Rate

- Acts ➔ Through ➔ G-Proteins
- Opens ➔ K^+ ion channels
- Promotes ➔Efflux of K^+ ions
- Cause ➔ Hyperpolarization of membrane
- Decreases ➔ Slope of Action Potential
- Reduces ➔Rate of impulse generation in SA node

Left Vagus fibers ➔ AV node

- Stimulation ➔ Left vagus
- Delays conduction of the impulse through
- AV node
- Negative dromotropic

Ach → Reduce force of cardiac muscle contraction (Negative inotropic)

- Reducing → Intracellular cAMP
- Delaying → Opening of Ca^{2+} ion channels
- Reducing → Influx of Ca^{2+} ions
- Reduce force of contraction
- Negative Inotropic

Strong stimulation of Vagus

- **Stops ➔ Heart for short duration**

Vagal escape

- **Heart overcomes ➔**
- **Inhibitory effect on prolonged vagal stimulation**

Vagal escape ➔ Cause

- The Atrioventricular node (AV node)
- Taking over generation of impulse
- After the inhibition of the SA node (Pacemaker)

Moderate tonic discharge

- **Cardiac sympathetic nerves**
- **At rest**

Vagal Tone ➔

- **Considerable**
- **Tonic vagal discharge (Vagal tone)**
- **In humans and other large animals**

Explain what will happen & why…?

- After the administration of
- Muscarinic receptor antagonists
- Such as Atropine

Explain what will happen & why…?

- The heart rate in humans
- Increases from 70 beats/min
- Its normal resting value,
- To 150–180 beats/min

Explain what will happen & why…?

- **Because**

- **The sympathetic tone is unopposed**

Noradrenergic & Cholinergic blocked

- **The heart rate is approximately 100 beats/min**

Clinical Physiology

- **Connections ➔**
- **Reciprocally inhibit ➔**
- **Sympathetic and Parasympathetic systems**

Clinical Physiology

- Acetylcholine (Parasympathetic systems)
- Acting in Presynaptic regions
- Reduces release of
- Norepinephrine (Sympathetic system)

Clinical Physiology

- **Neuropeptide Y ➔**
- **Inhibits release of Acetylcholine (Parasympathetic systems)**
- **From noradrenergic endings**

The normal Heart rate

- 60 to 90 beats / minute
- Average (Mean) heart rate ➔ 72 beats / minute

Neural Regulation of Heart rate

- **Vasomotor centre *(VMC)***
- **Plays a key role**

Vasomotor Centre ➔ Location

- Bilaterally mainly in
- The Reticular substance of the medulla
- & of the Lower 3rd of the Pons

Vasomotor Centre ➔ Transmits

- Parasympathetic impulses
- Through the Vagus (X^{th} - CN)nerves ➔
- To the heart

Vasomotor Centre ➔ Transmits

- Sympathetic impulses
- Through the
- Spinal cord and Peripheral sympathetic nerves
- Arteries, Arterioles, and Veins of the body

Vasomotor Centre ➔ Areas

1. Vasoconstrictor area
2. Vasodilator area
3. Sensory area

Vasoconstrictor area → Location

- Bilaterally in the
- Anterolateral portions
- Of the Upper medulla

Vasoconstrictor area ➔ Neurons

- Originating in this area
- Distribute their fibers
- To all levels of the spinal cord

Vasoconstrictor area ➔Neurons ➔Excite

- Excite
- Preganglionic vasoconstrictor neurons
- Of the ➔ Sympathetic nervous system

Vasodilator area ➔ Location

- Bilaterally in the
- Anterolateral portions of
- The Lower half of the medulla

Vasodilator area ➔ Neurons

- **Originating in this area**
- **Project upward to the vasoconstrictor area**
- ***Inhibit*** **➔ Vasoconstrictor activity of this area**
- **Thus causing ➔** ***Vasodilation***

Sensory area ➔ Location

- **Bilaterally**
- **In the *Nucleus Tractus Solitarius (NTS)***
- ***In the***
- ***Posterolateral portions of***
- ***The Medulla and Lower Pons***

Sensory area → Connections

- Receive → Sensory nerve signals
- From the → Circulatory system
- Mainly through
- The Vagus (X) & Glossopharyngeal nerves (IX)

Sensory area ➔Neurons

- Output signals from sensory area
- Then help to control activities of both
- The Vasoconstrictor and Vasodilator
- Areas of the Vasomotor center (VMC)

Sensory area ➔Neurons

- Providing “Reflex” control of
- Many circulatory functions
- An example is the Baroreceptor reflex
- For controlling Arterial Blood pressure

Control of Heart Activity by VMC

1. **Lateral portion**
2. **Medial portion**

Lateral portion of VMC

- **Transmit ➔ Excitatory impulses**
- **Through the**
- **Sympathetic nerve fibers to ➔ The Heart**

Lateral portion of VMC

- Sympathetic nerve fibers to ➔ The Heart
- When Need to
- Increase heart rate (HR) and contractility

Medial portion of VMC

- **Sends signals to the adjacent**
- ***Dorsal motor nuclei of the vagus nerves***

Dorsal Motor Nucleus of Vagus Nerves

- **Transmit**
- **Parasympathetic impulses through**
- **The vagus (X^{th} - CN)nerves → to the heart**

Medial portion of VMC

- *Dorsal motor nuclei of the vagus nerves*
- **Parasympathetic impulses**
- **The vagus nerves ➔ to the heart**
- **Decrease heart rate and contractility**

Vasomotor centre (VMC)

- **Either**
- **Increase or decrease ➔ Heart activity**

Vasoconstriction ➔ Occur

- Heart rate and
- Strength of heart contraction
- Ordinarily ➔ Increase
- Positive chronotropic & Positive inotropic effect

Vasoconstriction → Inhibited

- Heart rate and Strength of heart contraction
- Ordinarily → Decrease
- Negative chronotropic
- Negative inotropic effect

Control of VMC by Higher nervous centre

- **Large numbers of small neurons**
- **Located throughout**

1. ***Reticular substance of the pons***
2. ***Mesencephalon***
3. ***Diencephalon***

Control of VMC by Higher nervous centre

- Excite
- Or
- Inhibit
- The vasomotor center (VMC)

Reticular substance ➔ Neurons

- More Lateral and Superior portions
- Of the reticular substance
- Cause ➔ Excitation

Reticular substance ➔ Neurons

- More Medial and Inferior portions
- Of the reticular substance
- Cause ➔ Inhibition (RS ➔ M I ➔ Inhibition)

Hypothalamus → Special role

- Controlling the vasoconstrictor system
- Because it can exert powerful
- Excitatory or Inhibitory effects on VMC

Posterolateral portions of the Hypothalamus

- **Posterolateral portion of Hypothalamus**
- **Mainly ➔ Excitation ➔ VMC**

Anterior portions of the Hypothalamus

- Anterior portion either
- Mild excitation or Inhibition ➔VMC
- Depending on the precise part of
- The Anterior hypothalamus that is stimulated

Cerebral cortex

- Excite
- or
- Inhibit
- The vasomotor center (VMC)

Motor cortex ➔ Excite ➔ VMC

- Because of impulses transmitted
- Downward into the hypothalamus ➔
- Then to VMC

Excite or Inhibit → VMC

1. Anterior temporal lobe
2. Orbital areas of the frontal cortex
3. Anterior part of the cingulate gyrus
4. Amygdala, Septum, and Hippocampus

Excite or Inhibit ➔ VMC

- Depending on the precise portions of

1. These areas that are stimulated

2. The intensity of the stimulus

Excite or Inhibit ➔ VMC

- **Basal area of the brain ➔**
- **Can have Profound effects**
- **On cardiovascular function**

Medullary control of CVS

- **Major sources of**
- **Excitatory input to sympathetic nerves**
- **Controlling the vasculature**
- **A group of neurons located**
- ***Near the pial surface of the medulla***

Medullary control of CVS

- *Near the pial surface of the medulla*
- **Rostral Ventro Lateral Medulla**
- **RVLM ➔ Major source of excitatory input**
- **To sympathetic neurons**

Course of Axons of RVLM

- Course ➔ Dorsally and Medially
- Then Descend
- In the Lateral column of the spinal cord
- To Thoracolumbar Intermediolateral cell column (IML)

Axons of RVLM → Neurotransmitter

- *Phenylethanolamine-N-methyltransferase* **(PNMT)**
- *Glutamate* → **Excitatory transmitter** → **Secrete**
- **To activate Preganglionic sympathetic neurons**

Neurovacular compression of RVLM

- **Linked to**
- **Some cases of *Essential hypertension***
- **In humans**

Essential hypertension

- 88% of patients
- With elevated blood pressure
- The cause of the hypertension ➔ Unknown
- They are said to have Essential hypertension

Cardiac Vagal Centre

1. **Nucleus ambiguus (NA)**
2. **Dorsal motor nucleus of the vagus**

- **Cardiac vagal motor neurons**

Control of Heart rate by Vagus nerves

- Cardiac preganglionic parasympathetic
- Nucleus Ambiguus
- Dorsal motor nucleus of vagus nerve

Control of Heart rate by Vagus nerves

- Neurons in the
- Nucleus of the Tractus Solitarius (NTS)
- Project to and excite
- Cardiac Preganglionic Parasympathetic

Medulla ➔ Major site of Origin

- Excitatory input
- To Cardiac vagal motor neurons
- In the Nucleus Ambiguus (NA)

Factors ➔ Accelerate Heart Rate

1. Excitement
2. Anger
3. Most painful stimuli
4. Hypoxia
5. Exercise
6. Thyroid hormones
7. Fever
8. Inspiration

8. Decreased activity of Arterial baroreceptors
9. Increased activity of Atrial stretch receptors

Factors ➔ Slow Heart Rate

1. Expiration
2. Fear
3. Grief
4. Stimulation of Pain fibers in Trigeminal (V^{th} - CN) nerve
5. Increased intracranial pressure (ICT)

Cardiovascular control

- **Neural influences**
- **Coming from Several parts of the**
- **Brainstem**
- **Forebrain**
- **Insular cortex**

Brainstem

- Receives ➔ Feedback
- From sensory receptors in the vasculature
- Baroreceptors and Chemoreceptors

Feedback control mechanism of Brainstem

- An increase in neural output from the brainstem
- To sympathetic nerves leads to
- Decrease in blood vessel diameter
- (Arteriolar vasoconstriction)

Feedback control mechanism of Brainstem

- Increases in stroke volume (SV)
- Increase in Heart rate (HR)
- Which contribute to
- A rise in blood pressure (BP)

Feedback control mechanism of Brainstem

- A rise in blood pressure (BP)
- Increase in Baroreceptor activity
- Which signals ➔The brainstem
- To reduce ➔
- The neural output to sympathetic nerves

Increased Arteriolar constriction accompanied by

- Venoconstriction
- Decrease in the stores of blood
- In the venous reservoirs

Feedback control mechanism of Brainstem

- Changes in the Capacitance vessels
- Do not always parallel
- Changes in the Resistance vessels

Summary ➔ Neural regulation of HR

- Nerve supply to the heart
- M/A of Epinephrine (Adrenaline) on heart
- M/A of Acetylcholine on heart
- Effects of stimulation of sympathetic and parasympathetic on heart

Summary ➔ Neural regulation of HR

- Vasomotor centre
- Role of higher centers on VMC
- Role of Hypothalamus & Cerebral cortex
- Medullary control of CVS through RVLM
- Cardiac vagal centre

Summary ➔ Neural regulation of HR

- Factors increases ➔ Heart rate
- Factors decreases ➔ Heart rate
- Feedback control mechanism of Brainstem