**Scientific Basic of Pain**

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**PAIN** is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Pain functions as a Stop Signal. It can be a warning of a threat of possible tissue injury, a basis of learning from experiences (usually want to avoid painful stimuli), and it forces a person to rest

**Terminology**

• Noxious – harmful, injurious

• Noxious stimuli – stimuli that activate nociceptors (pressure, cold/heat extremes, chemicals)

• Nociceptor – nerve receptors that transmits pain impulses

• Pain Threshold – level of noxious stimulus required to alert an individual of a potential threat to tissue

• Pain Tolerance – amount of pain a person is willing or able to tolerate

• Hyperesthesia – abnormal acuteness of sensitivity to touch, pain, or other sensory stimuli

• Paresthesia – abnormal sensation, such as burning, pricking, tingling

• Analgesic – a neurologic or pharmacologic state in which painful stimuli are no longer painful

**Overview of Neural Integration- -Neural pathways**

• Afferent pathways are neural systems where sensory information travels from the sensory receptors through peripheral nerves to the spinal cord and on to the brain

• Efferent pathways are motor commands coming from the cerebral cortex and cerebellum through the brainstem nuclei to motor units in the cranial nerves and spinal cord which continue via the peripheral nerves to effecter organs

**Types of Nerves**

• Afferent (Ascending) – transmit impulses from the periphery to the brain

• First Order neuron - From sensory organ to the CNS

• Second Order neuron - From the CNS input zone to the brainstem

• Third Order neuron - From brainstem to the cerebral cortex

• Efferent (Descending) – transmit impulses from the brain to the periphery

**Sensory receptor**

• Specialized cell or cell process that monitors specific conditions

• Arriving information is a sensation

• Awareness of a sensation is a perception

**Senses**

• General senses

• Pain

• Temperature

• Physical distortion

• Chemical detection

•Receptors for general senses scattered throughout the body

• Special senses

• Located in specific sense organs

• Structurally complex

**Sensory receptors**

• Each receptor cell monitors a specific receptive field

• Transduces the stimulus into an electrical potential change within the receptor cell membrane

• A large enough stimulus changes the receptor potential leading to a generator potential which can lead to an afferent nerve action potential

**Three types of nociceptor**

• Provide information on pain as related to extremes of temperature

• Provide information on pain as related to extremes of mechanical damage

• Provide information on pain as related to extremes of dissolved chemicals

**Two Types of nociceptor nerve fibers**

• Myelinated type A fibers carry fast pain

• Slower type C fibers carry slow pain

**Thermoceptors and mechaniceptors**

• Found in the dermis

• Mechaniceptors

• Sensitive to distortion of their membrane

• Tactile receptors (six types)

• Baroreceptors

• Proprioceptors (three groups)

**Skin Tactile Receptors- -Sensory Receptors**

• Mechanoreceptors – touch, light or deep pressure

• Meissner’s corpuscles (light touch), Pacinian corpuscles (deep pressure), Merkel’s corpuscles (deep pressure)

• Thermoreceptors - heat, cold

• Krause’s end bulbs ( temp & touch), Ruffini corpuscles (in the skin) – touch, tension, heat; (in joint capsules & ligaments – change of position)

• Proprioceptors – change in length or tension

• Muscle Spindles, Golgi Tendon Organs

• Nociceptors – painful stimuli

• Mechanosensitive and chemosensitive

**Nerve Endings**

• “A nerve ending is the termination of a nerve fiber in a peripheral structure.”

• Nerve endings may be sensory (receptor) or motor (effector).

• Nerve endings may:

• Respond to phasic activity - produce an impulse when the stimulus is changing, but not during sustained stimulus; and adapt to a constant stimulus (Meissner’s corpuscles & Pacinian corpuscles)

• Respond to tonic receptors producing impulses as long as the stimulus is present. (muscle spindles, free n. endings, Krause’s end bulbs)

**Nerve Endings**

• Merkel’s corpuscles/disks -

• Sensitive to touch & vibration

• Slow adapting

• Superficial location

• Most sensitive

• Meissner’s corpuscles –

• Sensitive to light touch & vibrations

• Rapid adapting

• Superficial location

• Pacinian corpuscles -

• Sensitive to deep pressure & vibrations

• Rapid adapting

• Deep subcutaneous tissue location

• Krause’s end bulbs –

• Thermoreceptor

• Ruffini corpuscles/endings

• Thermoreceptor

• Sensitive to touch & tension

• Slow adapting

• **Free nerve endings -**

• Afferent

• Detects pain, touch, temperature, mechanical stimuli

**Nociceptors**

• Sensitive to repeated or prolonged stimulation

• Mechanosensitive – excited by stress & tissue damage

• Chemosensitive – excited by the release of chemical mediators

• Bradykinin, Histamine, Prostaglandins, Arachadonic Acid

• Both types may:

• Hyperalgesia

• Primary Hyperalgesia – due to injury

• Secondary Hyperalgesia – due to spreading of chemical mediators

**First Order Neurons**

• Stimulated by sensory receptors

• End in the dorsal horn of the spinal cord

• Types

• A-alpha – non-pain impulses

• A-beta – non-pain impulses

• Large, myelinated

• Low threshold mechanoreceptor; respond to light touch & low-intensity mechanical info

• A-delta – pain impulses due to mechanical pressure

• Large diameter, thinly myelinated

• Short duration, sharp, fast, bright, localized sensation (prickling, stinging, burning)

• C – pain impulses due to chemicals or mechanical

• Small diameter, unmyelinated

•Delayed onset, diffuse nagging sensation (aching, throbbing)

**Second Order Neurons**

• Receive impulses from the FON in the dorsal horn

• Lamina II, Substantia Gelatinosa (SG) - determines the input sent to T cells from peripheral nerve

•T Cells (transmission cells): transmission cell that connects sensory n. to CNS; neurons that organize stimulus input & transmit stimulus to the brain

• Travel along the spinothalmic tract

• Pass through Reticular Formation

• Types

• Wide range specific

• Receive impulses from A-beta, A-delta, & C

• Nociceptive specific

• Receive impulses from A-delta & C

• Ends in thalamus

**Third Order Neurons**

• Begins in thalamus

• Ends in specific brain centers (cerebral cortex)

• Perceive location, quality, intensity

• Allows to feel pain, integrate past experiences & emotions and determine reaction to stimulus

**Descending Neurons**

• Descending Pain Modulation (Descending Pain Control Mechanism)

• Transmit impulses from the brain (corticospinal tract in the cortex) to the spinal cord (lamina)

• Periaquaductal Gray Area (PGA) – release enkephalins

• Nucleus Raphe Magnus (NRM) – release serotonin

• The release of these neurotransmitters inhibit ascending neurons

• Stimulation of the PGA in the midbrain & NRM in the pons & medulla causes analgesia.

• Endogenous opioid peptides - endorphins & enkephalins

**Neurotransmitters**

• Chemical substances that allow nerve impulses to move from one neuron to another

• Found in synapses

• Substance P

• Thought to be responsible for the transmission of pain-producing impulses

• Acetylcholine

• Responsible for transmitting motor nerve impulses

• Enkephalins

• Reduces pain perception by bonding to pain receptor sites

• Norepinephrine

• Causes vasoconstriction

**Neurotransmitters**

• 2 types of chemical neurotransmitters that mediate pain

• Endorphins

• Morphine-like neurohormone; thought to inhibit pain threshold by binding to receptor sites

• Serotonin

• Substance that causes local vasodilation & increases permeability of capillaries

• Both are generated by noxious stimuli, which activate the inhibition of pain transmission

• Can be either excitatory or inhibitory

**Somatic Sensory Pathways**

• Three major pathways carry sensory information

• Posterior (Dorsal) column pathway

* Conscious Proprioception, Stereognosis, Simple Touch

• Anterolateral pathway

* Pain, Temperature, Pressure, Crude Touch

• Spinocerebellar pathway

* Unconscious Proprioception

**Ascending Tracts in the Spinal Cord- -Posterior column pathway**

• Carries fine touch, pressure and proprioceptive sensations

• Axons ascend within the fasciculus gracilis and fasciculus cuneatus

• Relay information to the thalamus via the medial lemniscus

**Dorsal Columns & Spinothalamic Tracts- -Spinothalamic pathway**

• Carries poorly localized sensations of touch, pressure, pain, and temperature

• Axons decussate in the spinal cord and ascend within the anterior and lateral spinothalamic tracts

• Headed toward the ventral nuclei of the thalamus

**Role of Thalamus**

• Second order neurons transmit pain and temperature signals to thalamus contralateral to stimulated receptor

• VPM processes pain and temperature signals from trigeminal (CNV) analog of spinothalamic system for head and neck

• VPL processes pain and temperature signals from peripheral regions of the body such as viscera, trunk and limbs

• Medial (intralaminar) thalamic nuclei process pain and temperature signals from reticular formation (spinoreticular fibers) such as raphe nuclei and locus coruleus

• Central (thalamic) pain signals cannot be localized (e.g., metastatic cancer) and central (thalamic) pain syndrome is relieved by producing electrical lesions in a thalamotomy procedure

**Role of Cerebral Cortex**

• Pain and temperature signals transmitted from VPL and VPM (specific thalamic nuclei) to somatosensory cortices SI and SII for localization

• Pain and temperature signals transmitted from medial intralaminar (nonspecific) nuclei to all regions of cerebral cortex for “alerting” response, which induce wakefulness and inhibit sleep

• Pain and temperature signals also transmitted from intralaminar nonspecific nuclei to limbic system, hypothalamus and associated structures for emotional, endocrine, stress and autonomic responses which produce fear, suffering, cardiovascular, respiratory, gastrointestinal, urogenital and stress-related hormonal responses

**Where Does Pain Come From?**

• Cutaneous Pain

• Sharp, bright, burning; can have a fast or slow onset

• Deep Somatic Pain

• Stems from tendons, muscles, joints, periosteum, & b. vessels

• Visceral Pain

• Originates from internal organs; diffused at first & later may be localized (i.e. appendicitis)

• Psychogenic Pain

• Individual feels pain but cause is emotional rather than physical

**Types of Pain: Classification by Duration**

• Acute pain

• An unpleasant experience with emotional, cognitive, and sensory features, resulting from tissue trauma

• Usually associated with significant, observable tissue pathology

• Resolves with healing of causative injury

• Protective biological function to protect against further injury; protective reflexes include withdrawal, muscle spasm, and autonomic reactions

• Chronic pain

• Pain lasting beyond expected recovery period and identifiable pathology insufficient to explain the pain state

• Disrupts sleep and normal activities of living

• Does not serve a protective, adaptive function

**Types of Pain: Classification by Etiology**

• Nociceptive pain

• Results from normal function of the nervous system

• Caused when a noxious stimulus (eg, trauma, inflammation, infection) activates A-delta and C nociceptors

—Visceral pain: originates in internal organs

—Somatic pain: originates in skin, muscle, skeletal structures

• Neuropathic pain

• Abnormal nociceptive signaling caused by an impairment of the nervous system

• Serves no functional or adaptive purpose

• Causes and examples

—Metabolic: diabetic neuropathy

—Infectious: herpes zoster

—Trauma: nerve entrapment

**The Neurophysiology of Pain**

• Nociception: process by which information about tissue damage reaches the central nervous system

• Transduction

• Transmission

• Perception

• Modulation

**Pain Transduction**

• Nociceptor = pain receptor: specialized receptor for detecting tissue injury/damage

• Nociceptors do not spontaneously depolarize: they send impulses (action potentials) only when stimulated

• No specialized pain “receptors”

• The receptor region of the nociceptor is the free terminal of the axon

• Ion channels in nerve terminal open in response to noxious stimuli, initiating an action potential, the “pain signal”

• Peripheral sensitization: local tissue injury with release of inflammatory mediators can enhance nociceptor response

• Two classes of nociceptive afferent fibers

• Cutaneous mechanoreceptors

• Respond to nondiscriminative tactile stimuli

• Pinch, rub, stretch, squeeze

• A-delta and C fiber, high-threshold

• Cutaneous thermoreceptors

• Respond to transient change in temperature

• Innocuous ward and cool stimuli

**Small Diameter Afferent Fibers**

• Cutaneous nociceptors – cutaneous pain

• A-delta mechanoreceptors

• Mechanical tissue damage

• C-polymodal nociceptors

•Mechanical tissue damage, noxious thermal stimuli, endogenous algesic chemicals

• C-fiber mechanonociceptors

• A-delta heat thermonociceptors

• A-delta, C-fiber cold thermonociceptors

• C-fiber chemonociceptors – algesic chemicals

**Pain Transmission**

• Nociceptors (primary sensory afferents) have cell body in dorsal root ganglia; synapse to second-order neurons in dorsal horn of spinal cord

• Pain impulses can trigger a withdrawal reflex via connections to motor neurons in the spinal cord

• Impulses ascend to brain via various ascending tracts

**CNS Neurotransmitters of A-delta and C-fibers**

• Substance P (Neuropeptide)

• Calcitonin Gene Related Peptide (CGRP)

• Excitatory amino acids – e.g., glutamate

• Release in ischemia/hypoxia – neurotoxicity

**Pain Perception**

• Perception of and reaction to pain are influenced by social and environmental cues, as well as by cultural norms and personal experience

• Both cortical and limbic systems are involved in conscious awareness (perception) of pain

• Recognition of location, intensity, and quality of pain is mediated by processing of signals from the spinothalamic tract > thalamus > somatosensory cortex

• Pain information processing in the brainstem, midbrain, and limbic system appear to mediate affective, motivational, and behavioral responses to painful stimuli

**Pain Modulation**

• Gate control theory advanced by Melzack and Wall in 1965 focused on descending pathways from the brain to the spinal cord that inhibit pain signaling

• Current view: signals originating in the brain can both inhibit and facilitate pain signal transmission

• Neurotransmitters involved in these pathways include

• Endogenous opiates (enkephalins, dynorphins, beta-endorphins)

• Serotonin

• Norepinephrine

**Pain Control Theories**

• Gate Control Theory

• Central Biasing Theory

• Endogenous Opiates Theory

**Gate Control Theory**

• Melzack & Wall, 1965

• Substantia Gelatinosa (SG) in dorsal horn of spinal cord acts as a ‘gate’ – only allows one type of impulses to connect with the SON

• Transmission Cell (T-cell) – distal end of the SON

• If A-beta neurons are stimulated – SG is activated which closes the gate to A-delta & C neurons

• If A-delta & C neurons are stimulated – SG is blocked which closes the gate to A-beta neurons

**Gate Control Theory**

• Gate - located in the dorsal horn of the spinal cord

• Smaller, slower n. fibers carry pain impulses

• Larger, faster n. fibers carry other sensations

• Impulses from faster fibers arriving at gate 1st inhibit pain impulses (acupuncture/pressure, cold, heat, chem. skin irritation).

**Central Biasing Theory**

• Descending neurons are activated by: stimulation of A-delta & C neurons, cognitive processes, anxiety, depression, previous experiences, expectations

• Cause release of enkephalins (PAG) and serotonin (NRM)

• Enkephalin interneuron in area of the SG blocks A-delta & C neurons

**Endogenous Opiates Theory**

• Least understood of all the theories

• Stimulation of A-delta & C fibers causes release of B-endorphins from the PAG & NRM Or

• ACTH/B-lipotropin is released from the anterior pituitary in response to pain – broken down into B-endorphins and corticosteroids

• Mechanism of action – similar to enkephalins to block ascending nerve impulses

• Examples: TENS (low freq. & long pulse duration)

**Goals in Managing Pain**

• Reduce pain!

• Control acute pain!

• Protect the patient from further injury while encouraging progressive exercise

**Other ways to control pain**

• Encourage central biasing – motivation, relaxation, positive thinking

• Minimize tissue damage

• Maintain communication

• If possible, allow exercise

• Medications

* **Acupuncture!**

**GOD cures, Doctors send the bill!**

**-Mark Twain**