

Winter MCSN Lecture 2023

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Unlocking the Senses: Somatosensation and proprioception

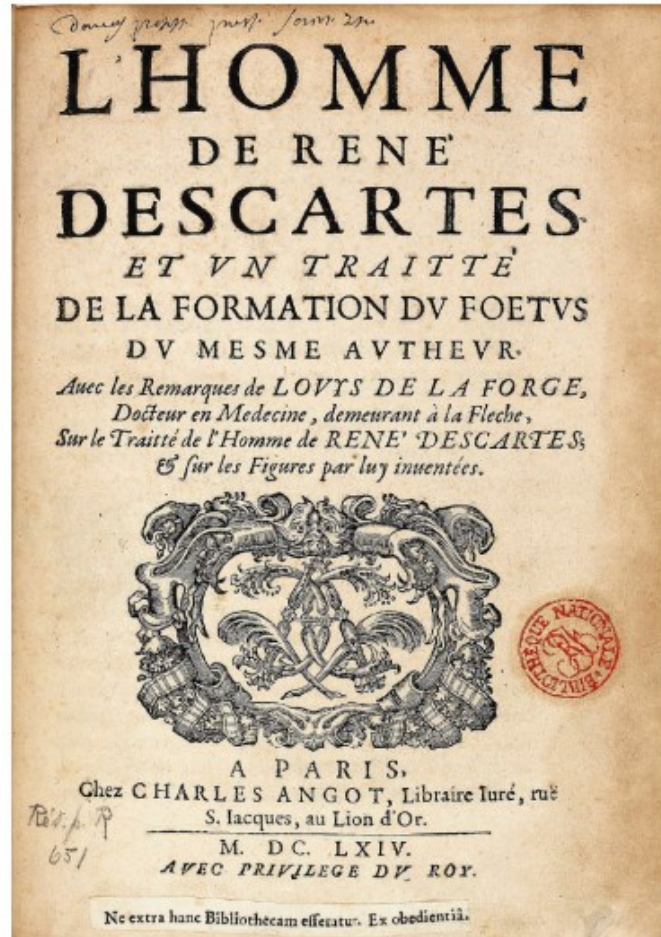
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Navigating the World through Body Awareness

How do we perceive the world?



17th century
Rene Descartes

Sensation



The process of detecting a **stimulus**
(Something that attracts the attention of a sensory organ)

The stimulation of **sensory receptors** and the transition of sensory information to the central nervous system CNS





Sensory receptors are located in the **sensory organs**







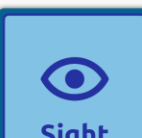

Sensation threshold

Sense	Stimulus	Threshold
 Touch		Feeling a bee's wing falling a distance of 1cm onto your skin


Sensation threshold

Sense	Stimulus	Threshold
 Touch		Feeling a bee's wing falling a distance of 1cm onto your skin
 Hearing		Hearing a clock ticking 20 feet away











Sensation threshold

Sense	Stimulus	Threshold
 Touch		Feeling a bee's wing falling a distance of 1cm onto your skin
 Hearing		Hearing a clock ticking 20 feet away
 Sight		Seeing a candle flame 30 miles away on a clear night

Sensation threshold

Sense	Stimulus	Threshold
 Touch		Feeling a bee's wing falling a distance of 1cm onto your skin
 Hearing		Hearing a clock ticking 20 feet away
 Sight		Seeing a candle flame 30 miles away on a clear night
 Smell		Smelling a single drop of perfume in a three room house

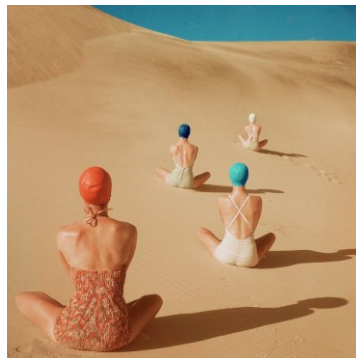
Sensation threshold

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 Smell		Smelling a single drop of perfume in a three room house
 Taste		Tasting a single teaspoon of sugar dissolved in two gallons of water

Sensory adaptation

The process by which we become **less aware** of weak stimuli.

If a stimulus is unchanging, we become **desensitized** to it.



Introduction to Somatosensation



The body's ability to perceive touch, temperature, and pain.

Somatosensation

Somatosensation encompasses the perception of touch, temperature, pain, pressure and hearing.

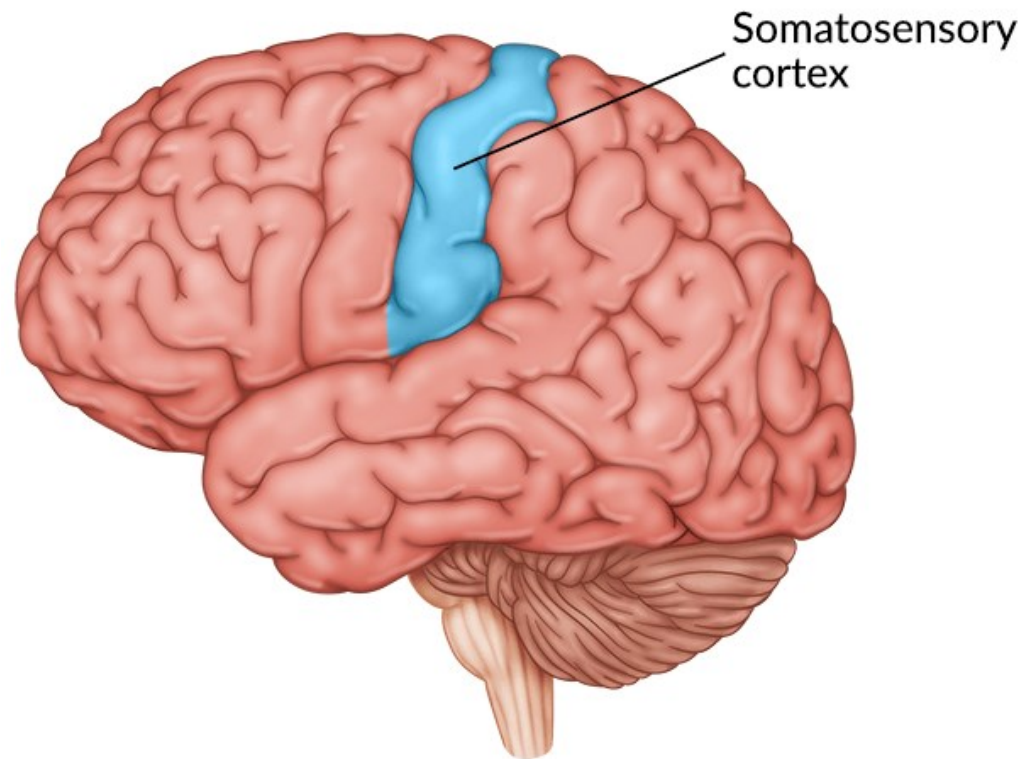
It allows us to engage with the world through our sensory organs and receive essential feedback.

Somatosensation

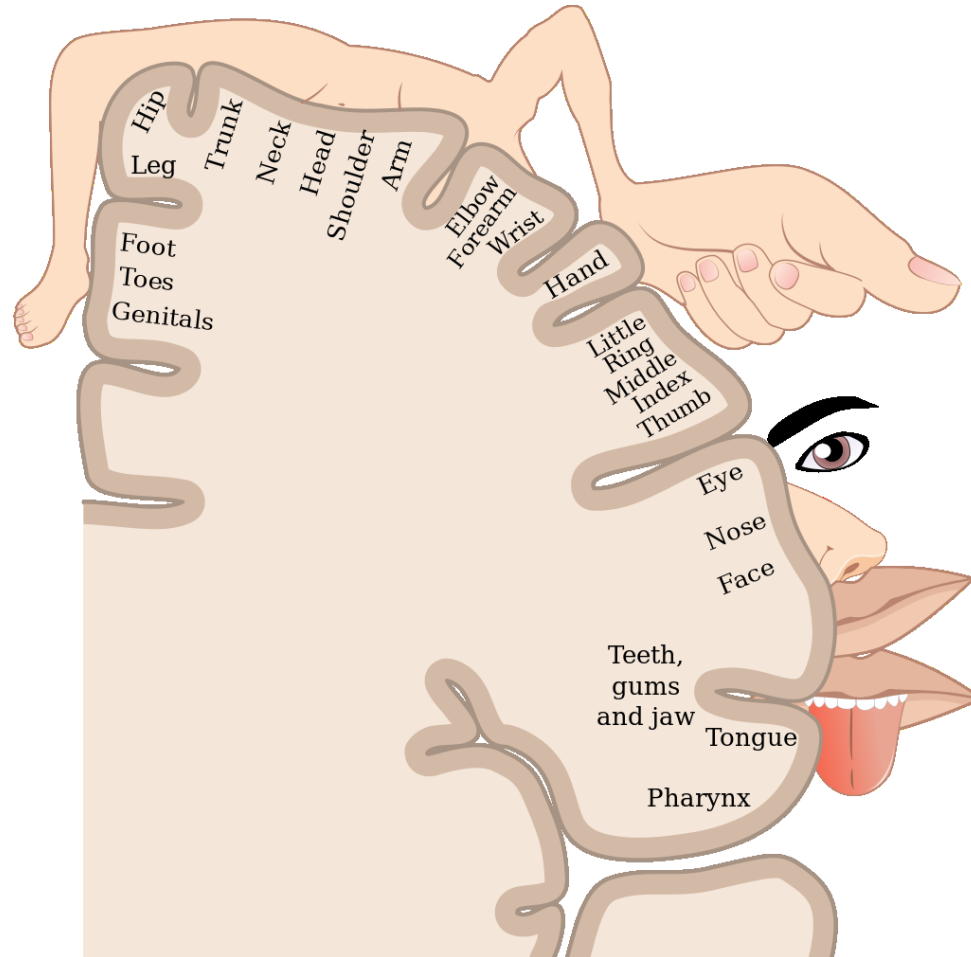
The sensation of the body and its movements.

- Discriminative touch
- Deep pressure
- Cold vs Warm
- Pain
- Itch
- Tickle
- Position and movement of the joints
- Hearing

Sensory organs > Receptors > Nerves > Brain



Homunculus



“Little person”

Organ sizes are enlarged to reflect the relative size of the brain’s motor cortex and sensory cortex devoted to each body part.

Homunculus



“Little person”

Organ sizes are enlarged to reflect the relative size of the brain's motor cortex and sensory cortex devoted to each body part.

Mechanisms of Somatosensation

Sensory Receptors

Somatosensation is the perception of touch, pressure, temperature, and pain.

It is mediated by specialized sensory receptors located in the skin, muscles, and other tissues. These receptors respond to mechanical, thermal, and chemical stimuli and convert them into electrical signals that can be processed by the nervous system.

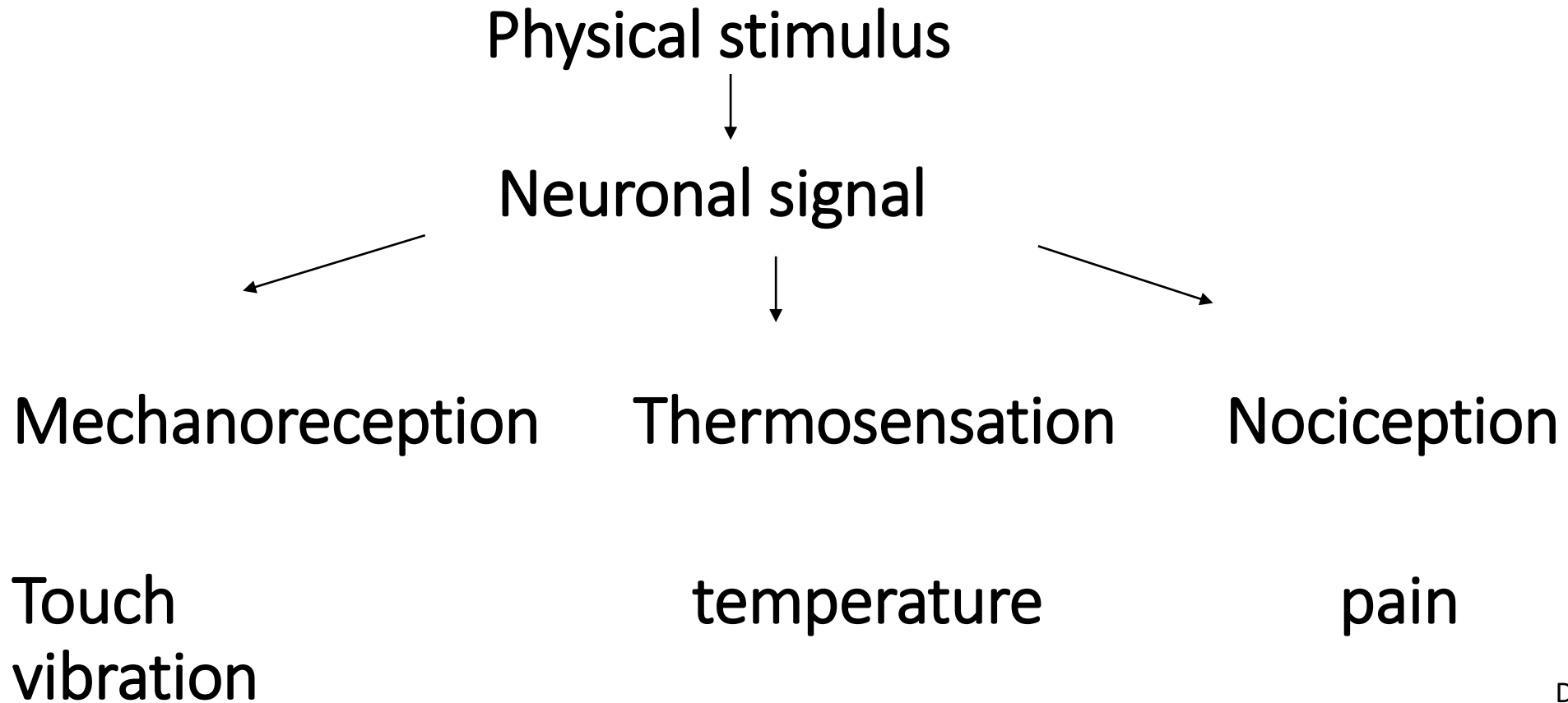
Neural Pathways

The neural pathways involved in somatosensation consist of three main components:

the peripheral nervous system, the spinal cord, and the brain. When a sensory receptor is activated, it sends an electrical signal through the peripheral nerves to the spinal cord.

In the spinal cord, the signal is relayed to the brain via ascending pathways. The brain then processes the signal and generates the perception of touch, pressure, temperature, or pain.

Somatosensation



Somatosensation

Physical stimulus

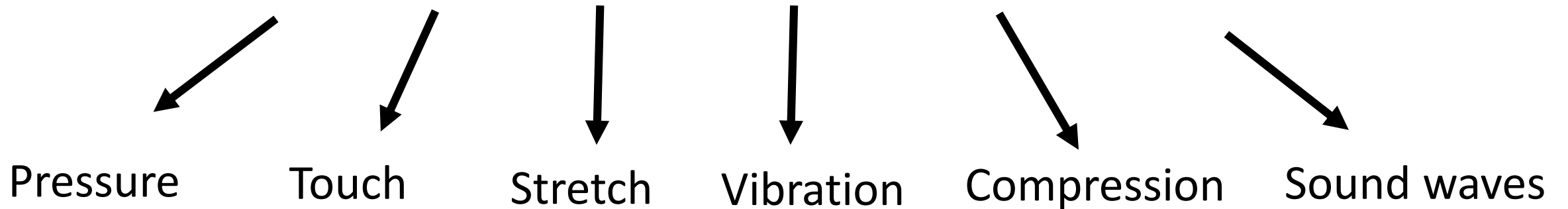


Neuronal signal



Mechanoreception

Mechanoreception

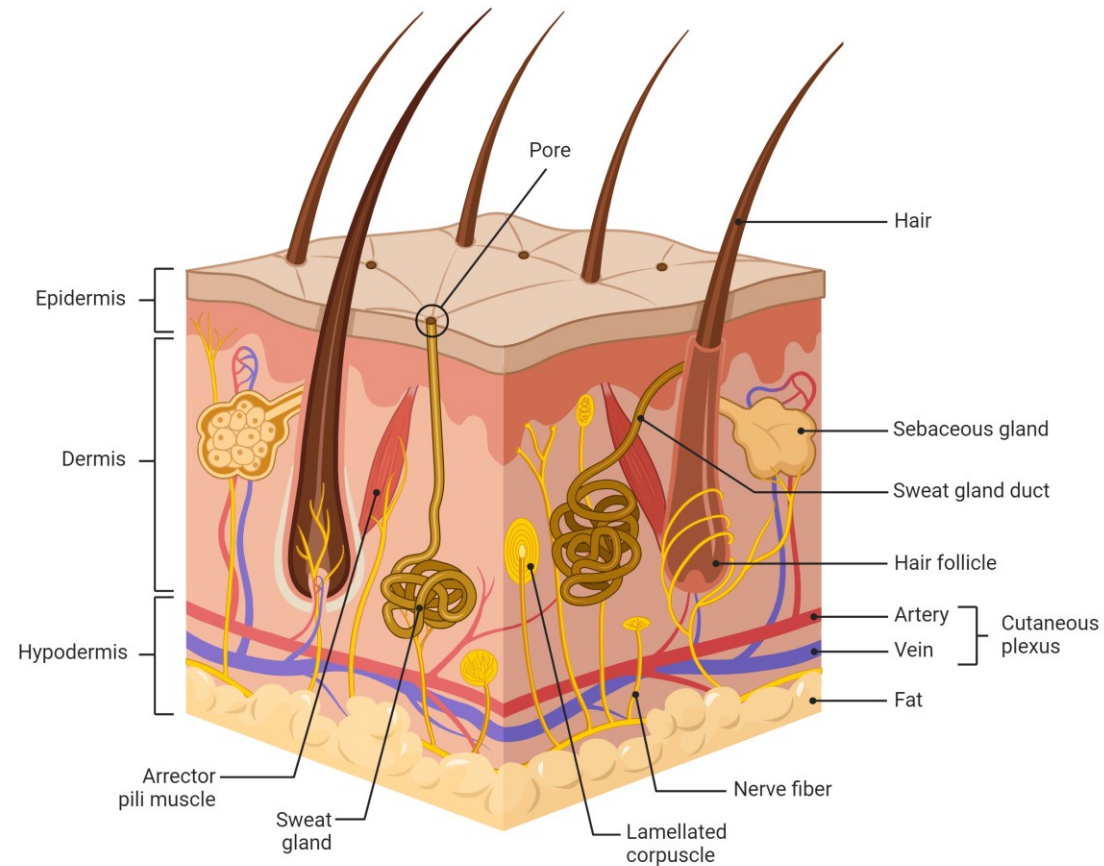


How do we sense?

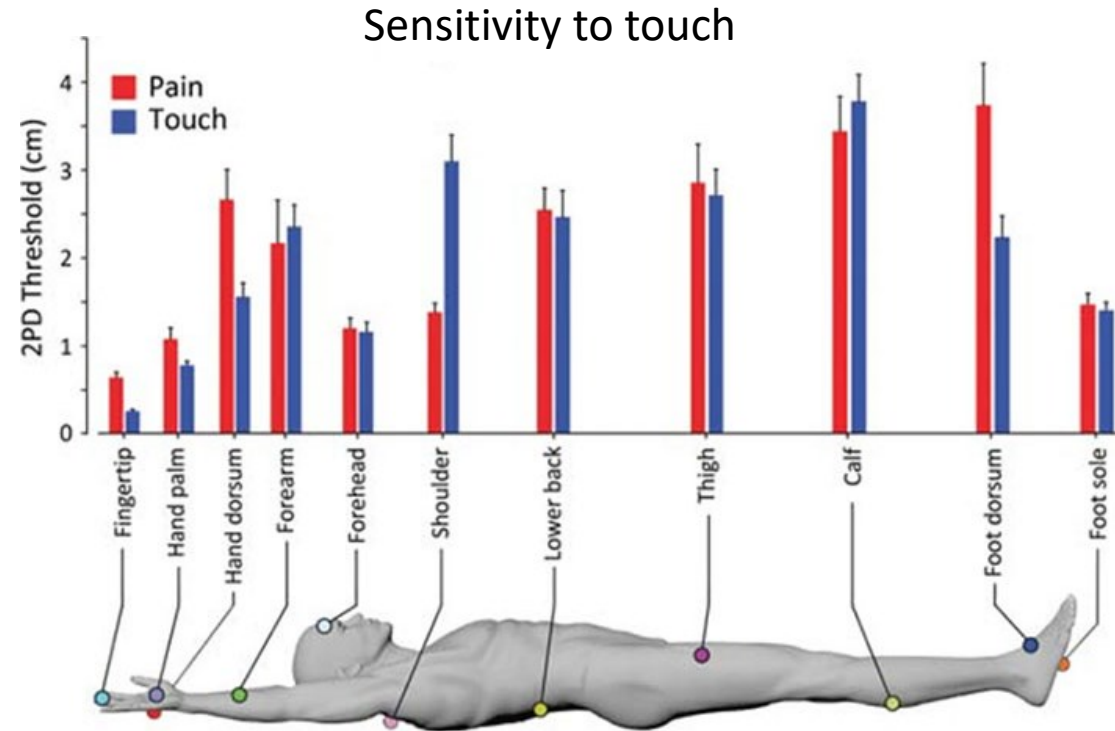
Sensory Organs

Sensory organs – Tactile sensation

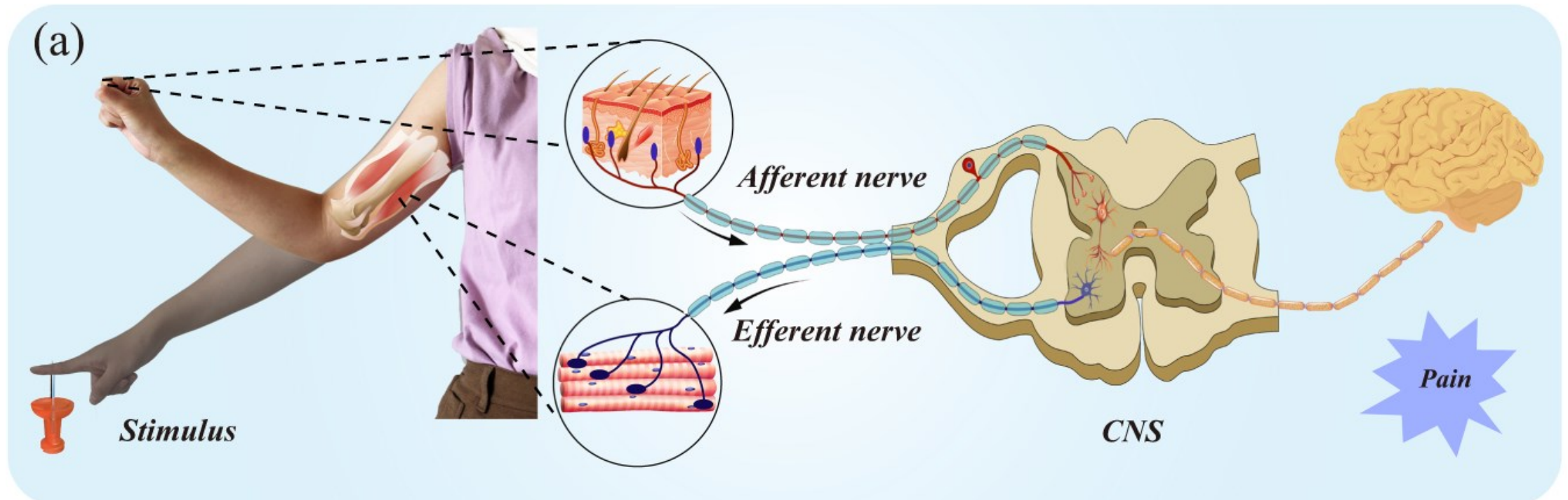
Skin



Sensory organs –Skin

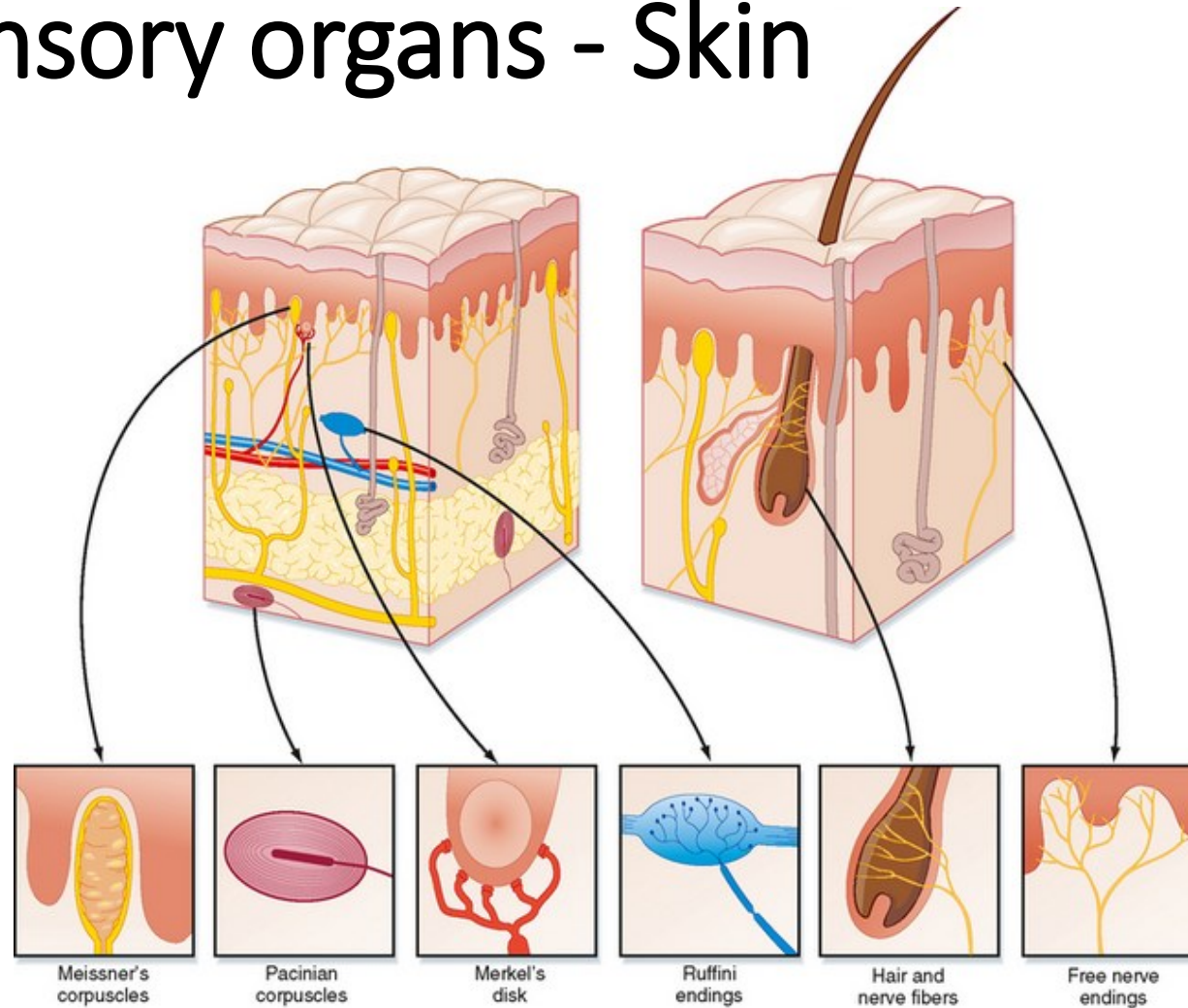


Sensory organs – Tactile sensation Skin



Sun et al., Nature (2022)

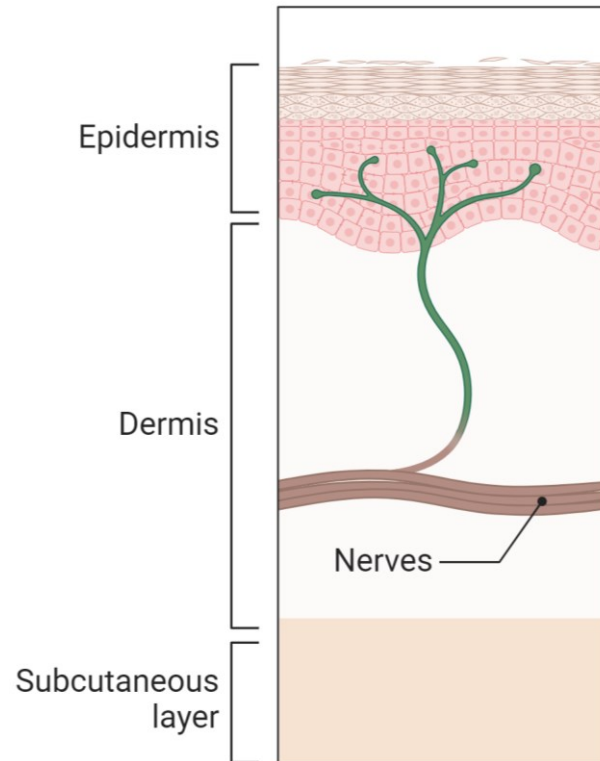
Sensory organs - Skin



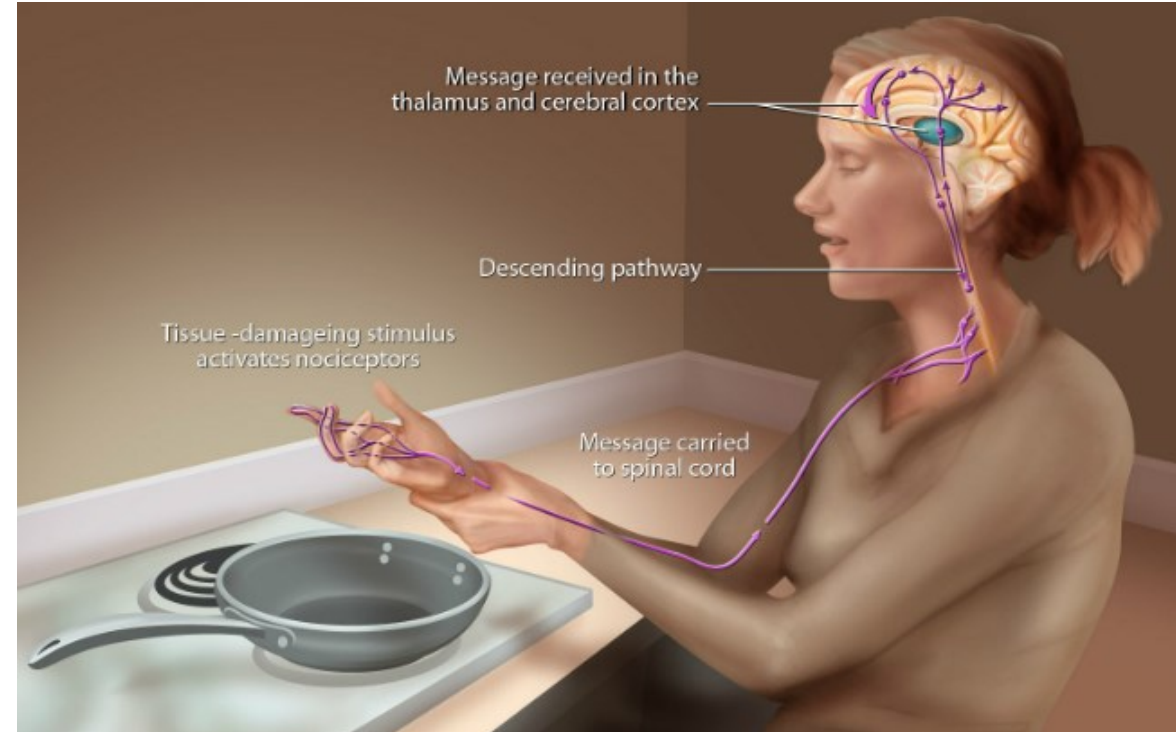


Types of Skin Mechanoreceptors

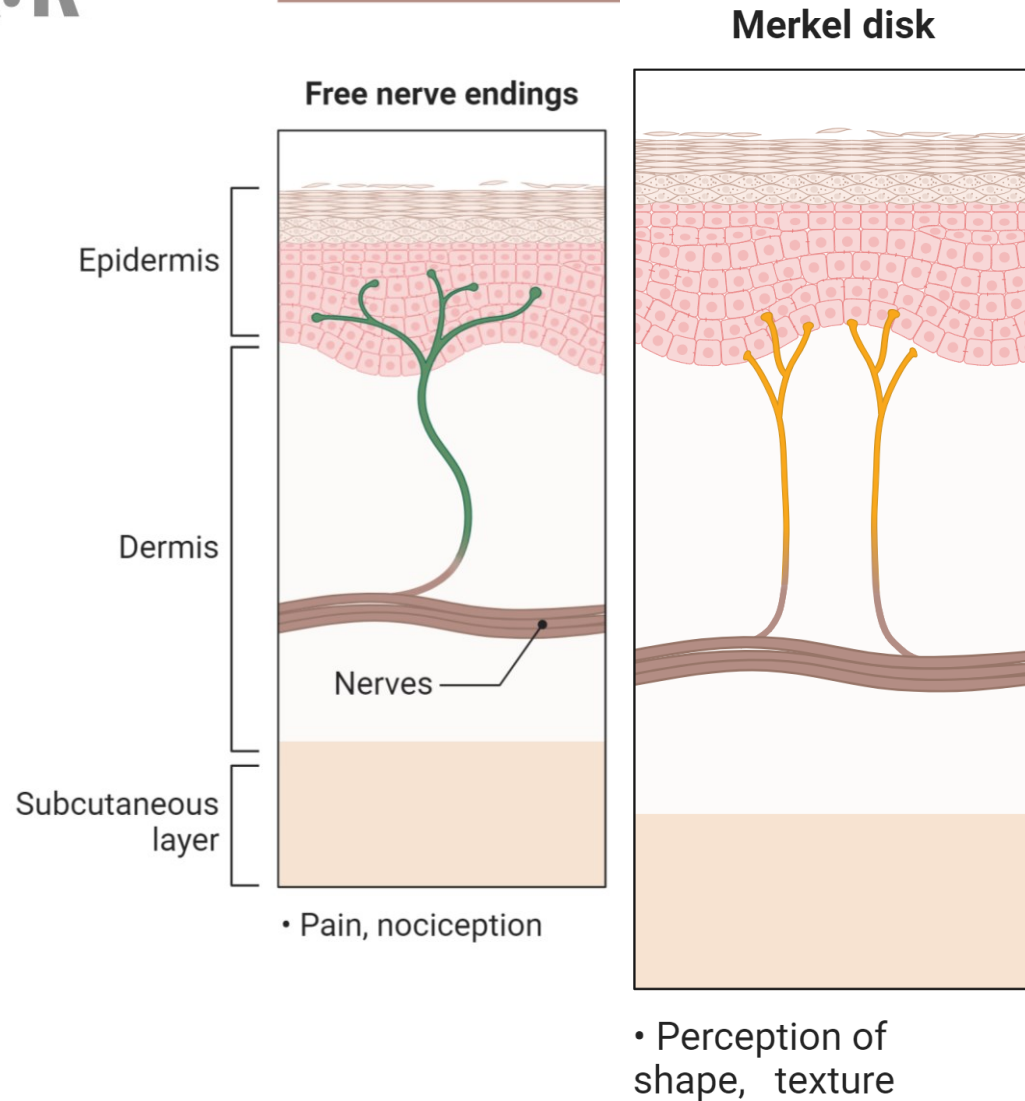
Free nerve endings



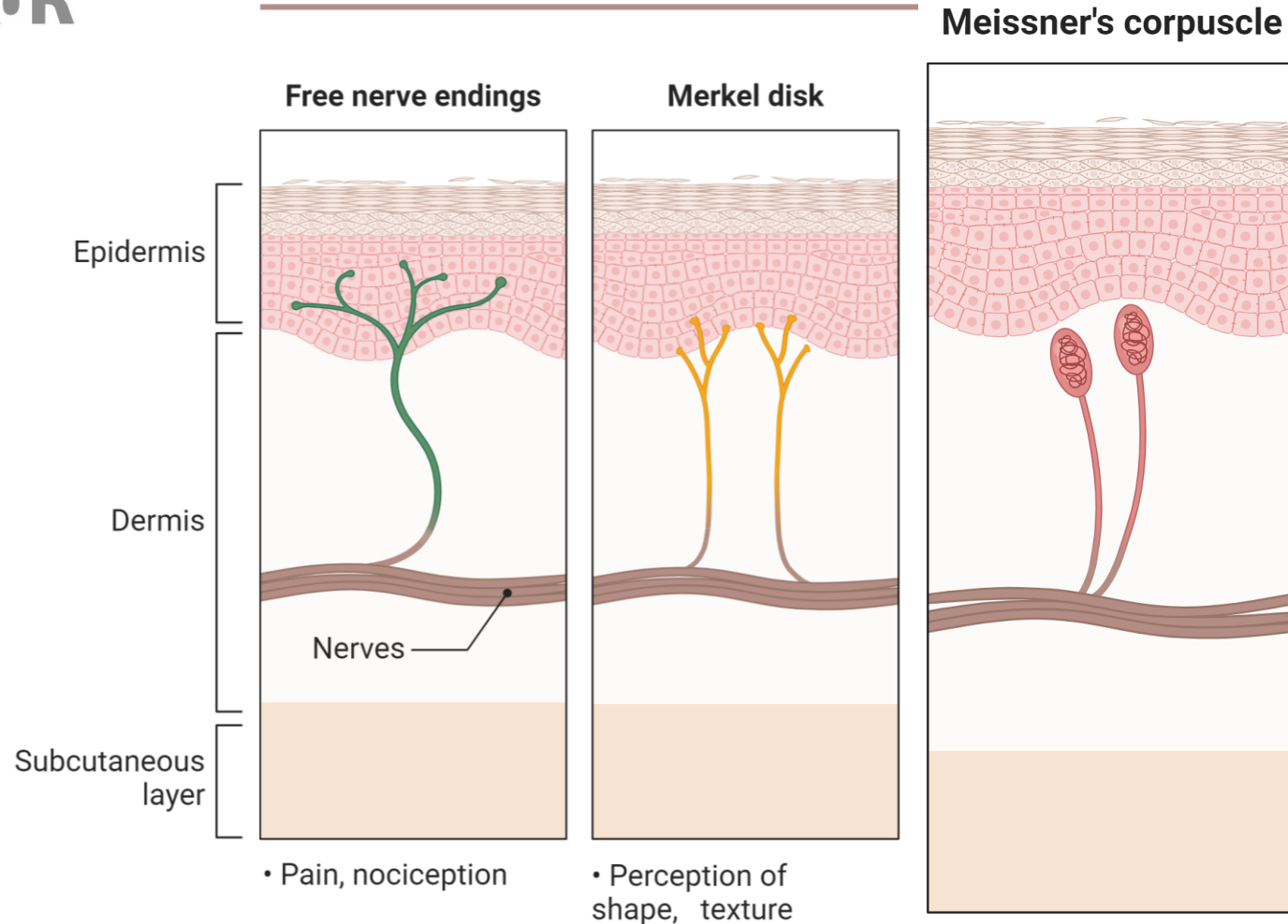
• Pain, nociception



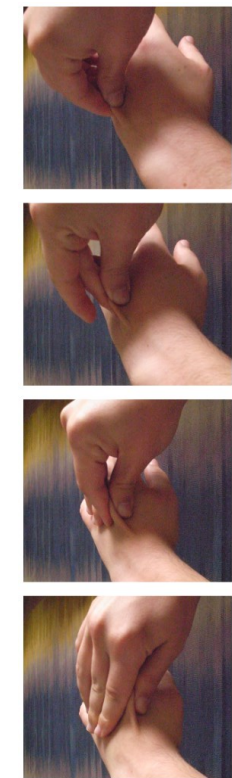
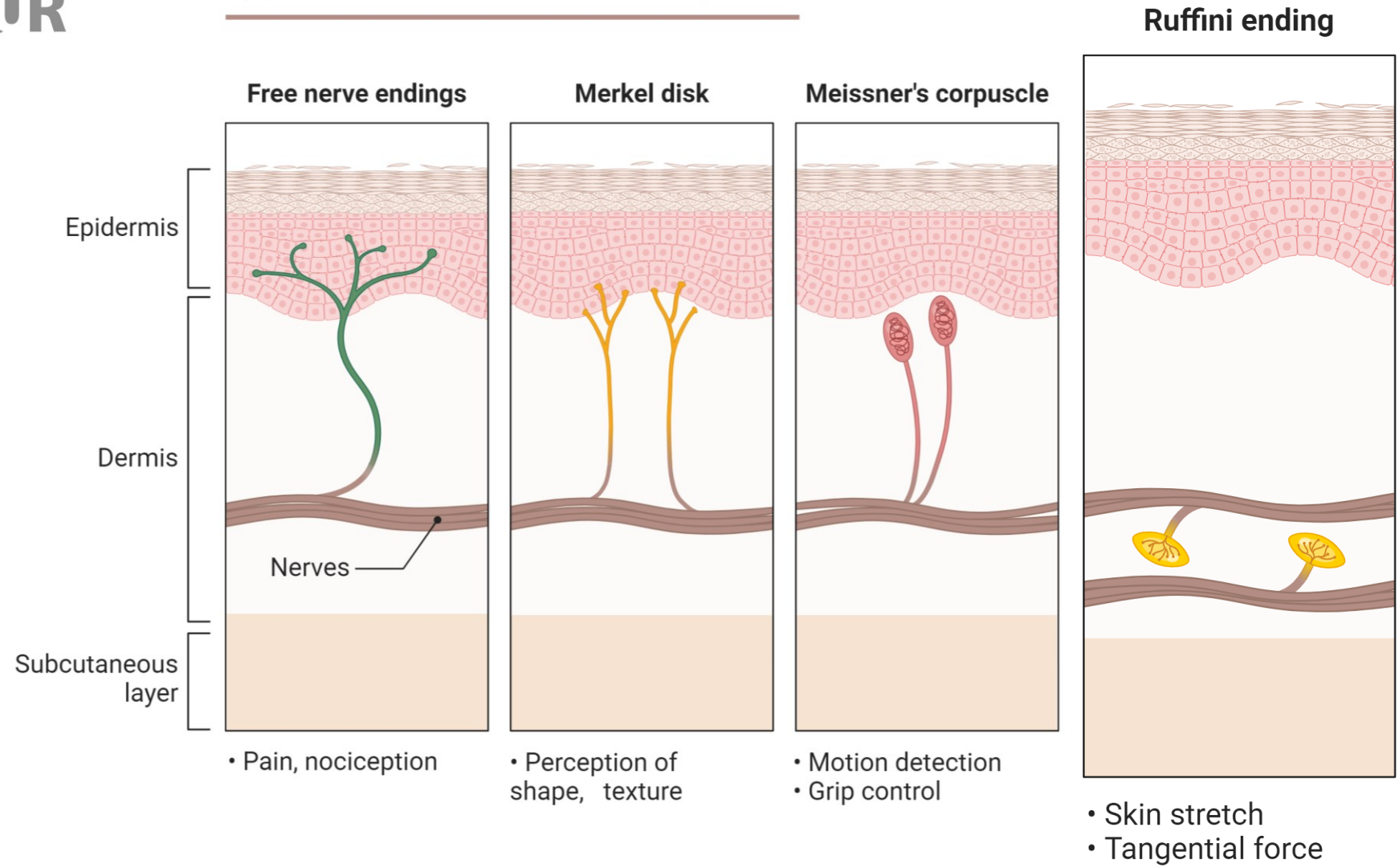
Types of Skin Mechanoreceptors



Types of Skin Mechanoreceptors

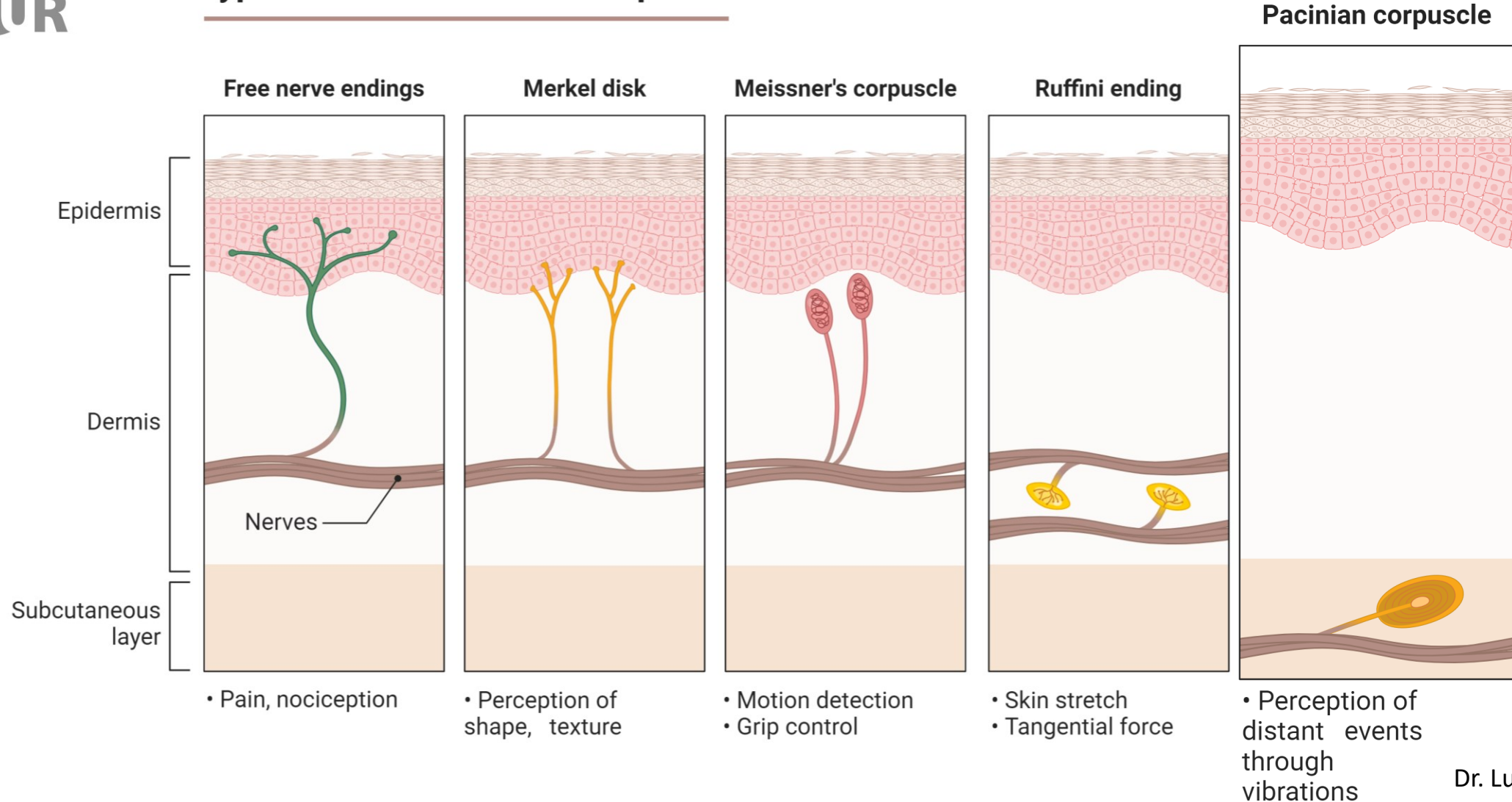


Types of Skin Mechanoreceptors

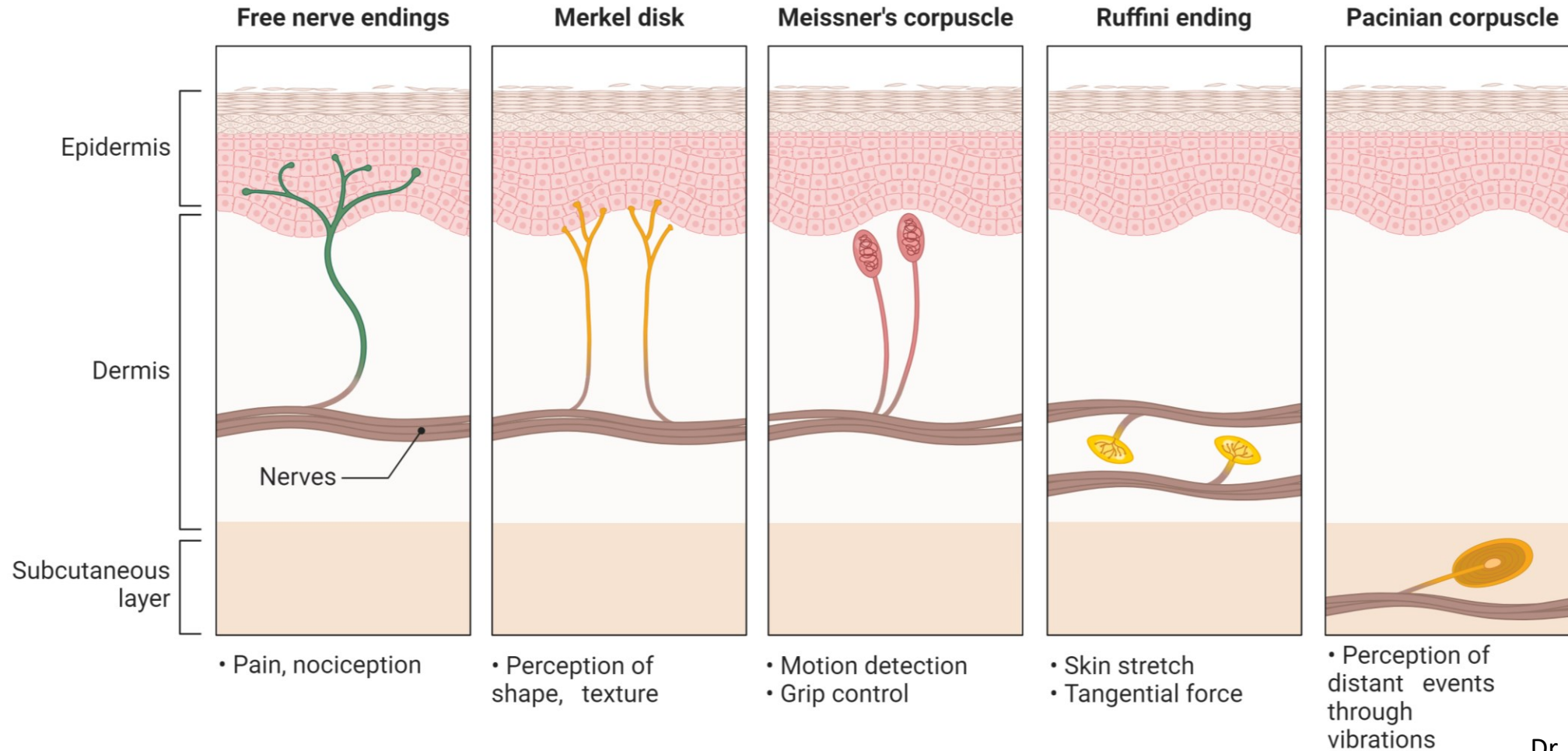




Types of Skin Mechanoreceptors



Types of Skin Mechanoreceptors



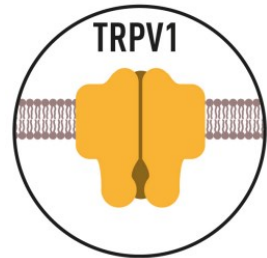
Tickle sensation



- The sensation of tickle is poorly understood.
- We cannot tickle ourselves since the brain compares the resulting stimulation to the “expected” stimulation and generates a weaker somatosensory response.

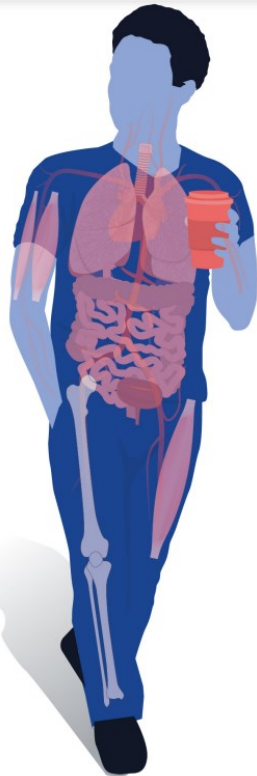


THE 2021 NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE: DISCOVERING HOW WE FEEL HEAT AND TOUCH USING ANIMALS AND CELLS



Temperature
Heat pain

Core body temperature
Inflammatory pain
Neuropathic pain
Visceral pain
Protective reflexes



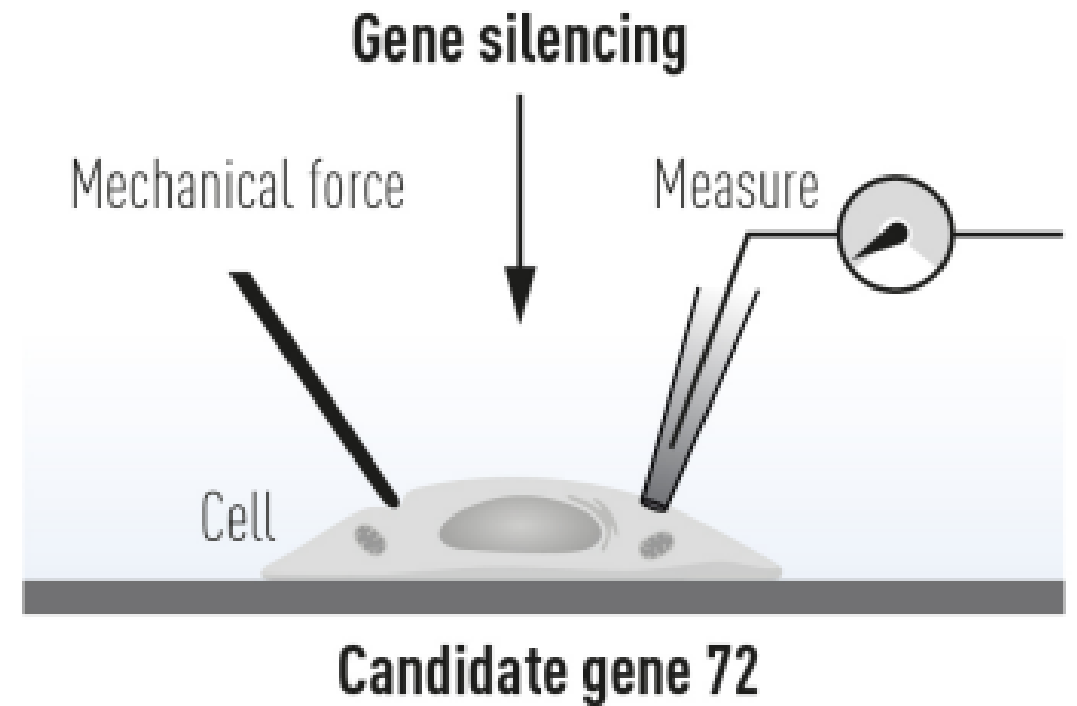
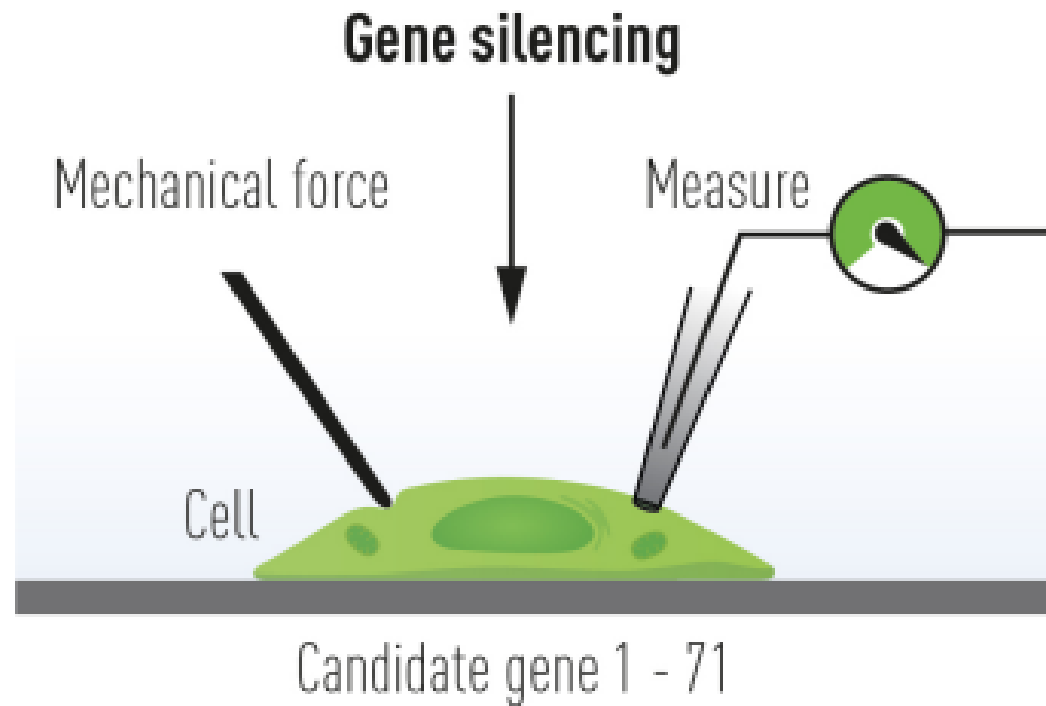
Touch
Proprioception

Mechanical pain
Urination
Respiration
Blood pressure
Skeletal remodeling



Prof. Ardem Patapoutian **Prof. David Julius**

Piezo discovery

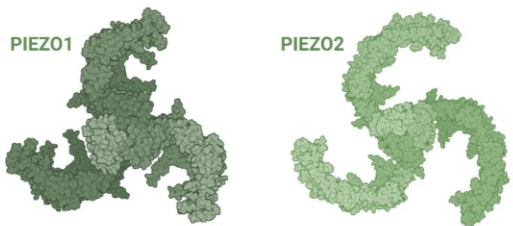




Essential for the Sensation of Touch: PIEZO Channels

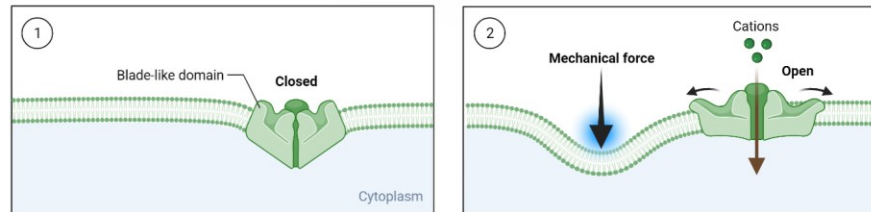


Molecular Structures of PIEZO Channels



Both PIEZO1 and PIEZO2 have a three-bladed, propeller-like structure. Both are homotrimeric - the three subunits come together to form the central membrane-spanning pore. They contain nine repetitive units, each with four transmembrane helices.

PIEZO Channels: How Do They Allow Mechanosensation?



PIEZO1 and PIEZO2 are both **mechanically-activated cation channels**. Based on protein structure, it was predicted that the 'blades' of the PIEZO channels undergo a lever-like flattening motion upon application of mechanical stress. This opens up their central pore, allowing an influx on positive charge. The exact mechanism by which mechanical force leads to the central pore opening is not fully understood.

Summary

Relevance of PIEZO Channels in Physiology and Medicine

Since their discovery, PIEZO1 and PIEZO2 have been proven to be critical mechanosensors throughout the human body, contributing to multiple important physiological processes.



Lungs

PIEZO2 acts as an airway stretch sensor in respiratory tissue and is critical for normal breathing.



Blood pressure

Both PIEZO1 and PIEZO2 act as baroreceptors and are essential in blood pressure regulation.



Vascular cells

PIEZO1 is an important sensor of shear stress in vasculature and required for embryonic vascular development.



Bladder

PIEZO2 is a sensor for stretch in the bladder urothelium and innervating sensory neurons.



Malaria

Polymorphisms and mutations in PIEZO1 have been shown to protect against symptoms of malaria.



Immune cells

PIEZO1 regulates macrophage phagocytic activity and thereby facilitates erythrocyte turnover.



Thermal Somatosensation

The TRP Ion Channels

Our ability to sense heat and cold is crucial for survival. In our daily lives, we perceive millions of sensations that are processed through intricate molecular pathways.

Dr. David Julius has used distinctive molecules from the natural world to understand how signals responsible for temperature and pain sensation are transmitted by transient receptor potential (TRP) channels that activate across different temperature ranges.



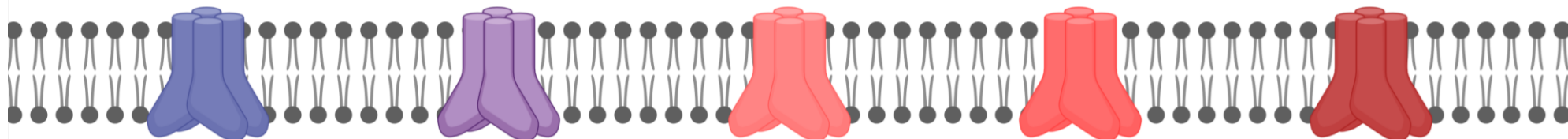
TRP channels are potential targets for a new generation of painkillers / analgesic drugs.



Synthetic design of unique sensory systems could be used as biosensors in industrial applications.



Potential treatment for heat / cold hypersensitivity and hyposensitivity disorders.





Publications

Nobel Prize Outreach AB 2021. Tue. 2 Nov 2021.

Piezo1 and Piezo2 are essential components of distinct mechanically activated cation channels (2010) PMID: 20813920.

Structure-based membrane dome mechanism for Piezo mechanosensitivity (2017), PMID: 29231809.

Structure and mechanogating of the mammalian tactile channel PIEZO2 (2019), PMID: 31435011.

Piezo2 senses airway stretch and mediates lung inflation-induced apnoea (2017) PMID: 28002412.

PIEZOs mediate neuronal sensing of blood pressure and the baroreceptor reflex (2018) PMID: 30361375

Piezo1 integration of vascular architecture with physiological force (2014), PMID: 25119035

Piezo1, a mechanically activated ion channel, is required for vascular development in mice (2014), PMID: 24958852

PIEZO2 in sensory neurons and urothelial cells coordinates urination (2020), PMID: 33057202

Common PIEZO1 Allele in African Populations Causes RBC Dehydration and Attenuates Plasmodium Infection (2018), PMID: 29576450

A common polymorphism in the mechanosensitive ion channel PIEZO1 is associated with protection from severe malaria in humans (2020), PMID: 32265284

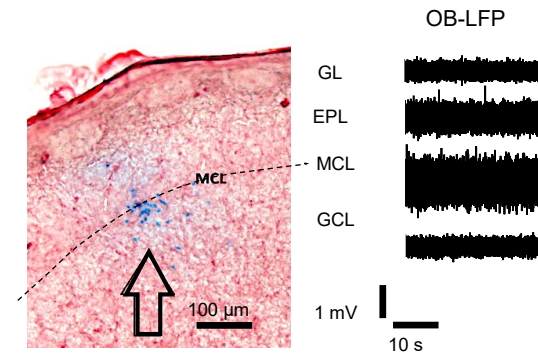
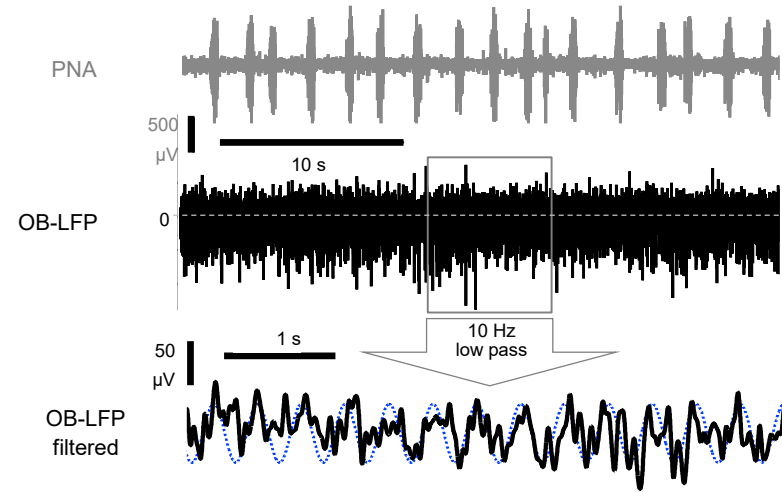
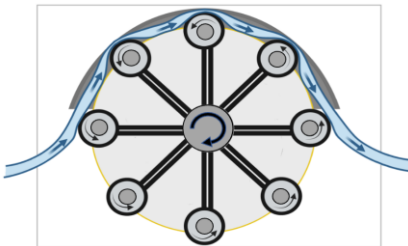
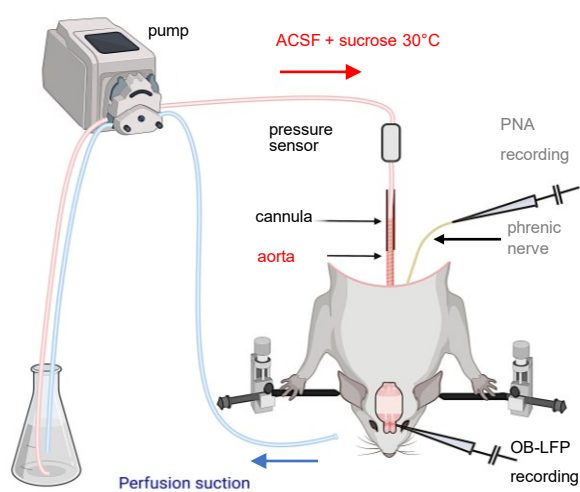
Common PIEZO1 Allele in African Populations Causes RBC Dehydration and Attenuates Plasmodium Infection (2018), PMID: 29576450

A role of PIEZO1 in iron metabolism in mice and humans (2021) PMID: 33571427

**Blood pressure pulsations modulate central neuronal activity via mechanosensitive ion channels
(2023) Salameh et al., Science**



Blood pressure pulsations modulate central neuronal activity via mechanosensitive ion channels

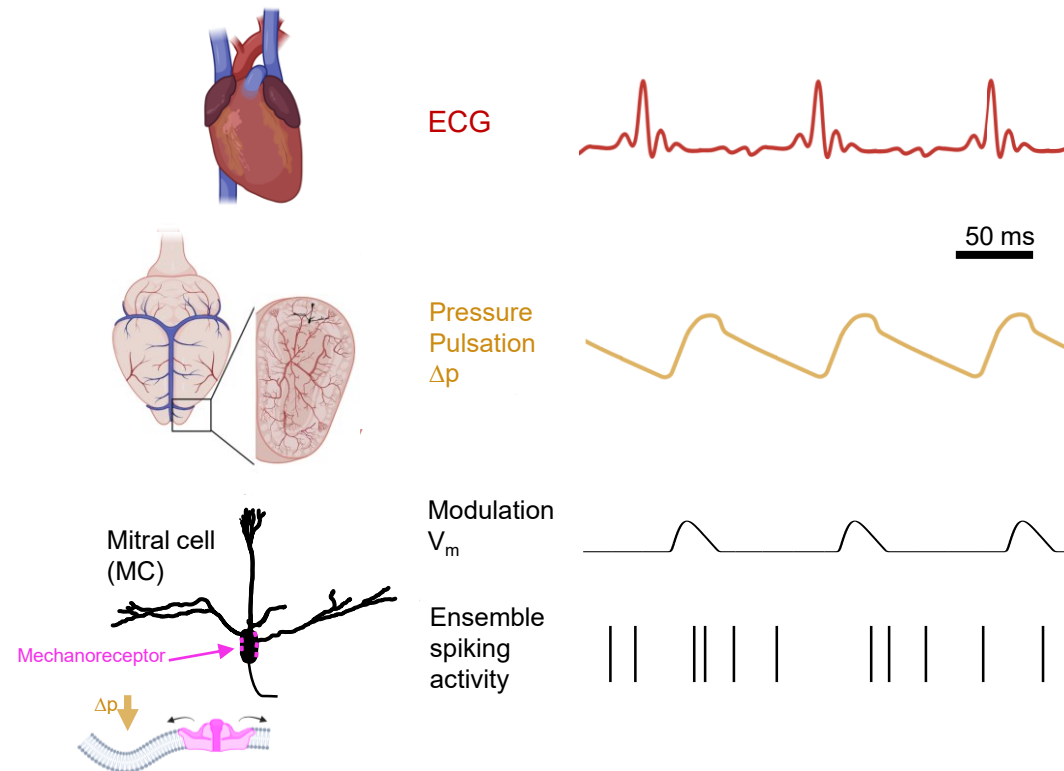


Salameh et al., (2023) Science

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Blood pressure pulsations modulate central neuronal activity via mechanosensitive ion channels

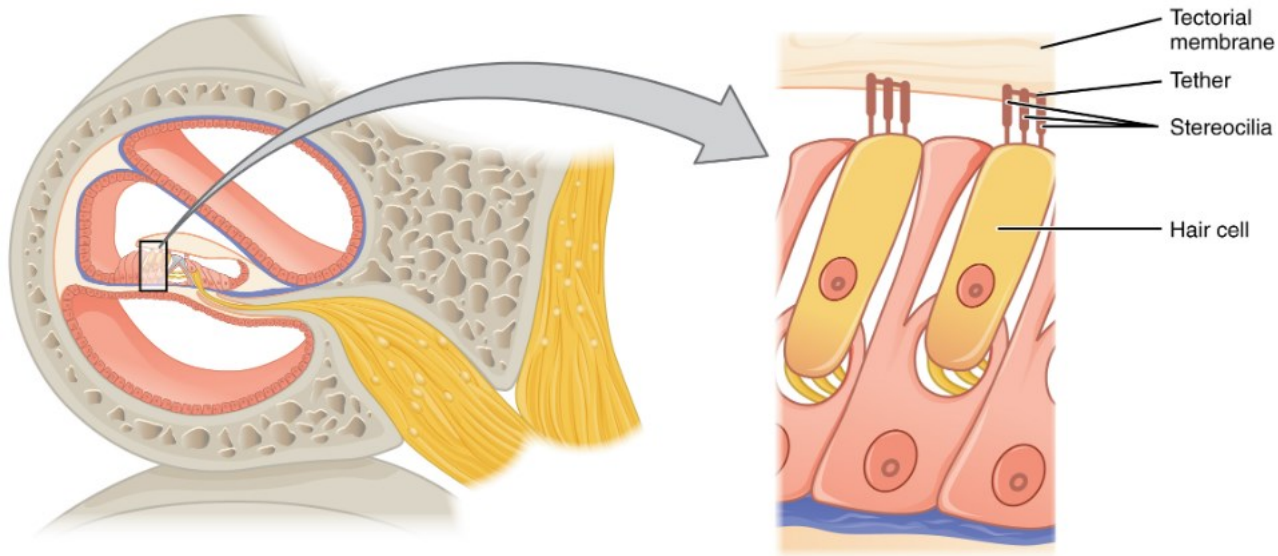


Salameh et al., (2024) Science

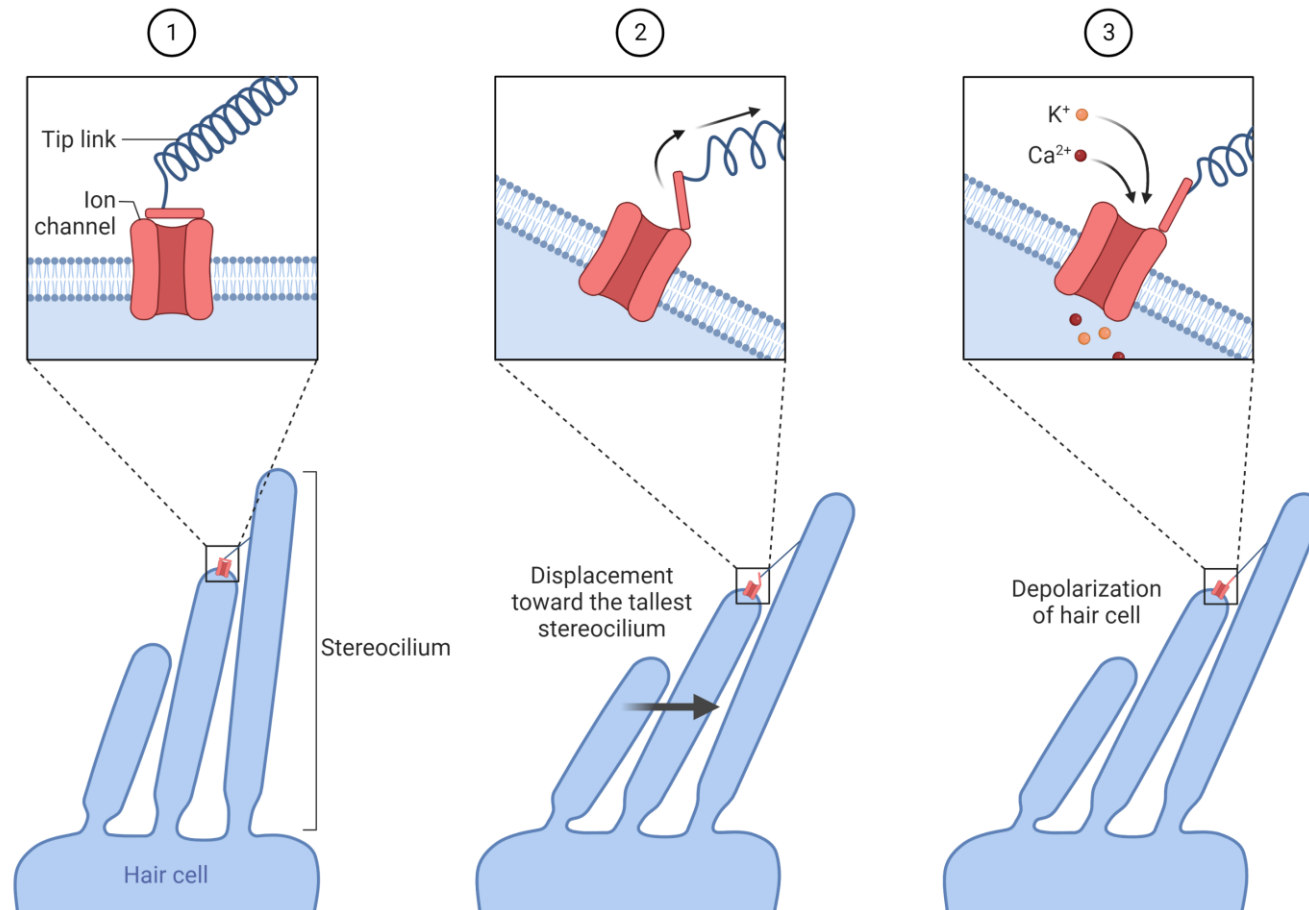
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Sensory organs – Auditory Hair cells

Equilibrium (Balance) and Hearing rely on the physical movement response of the hair cells.

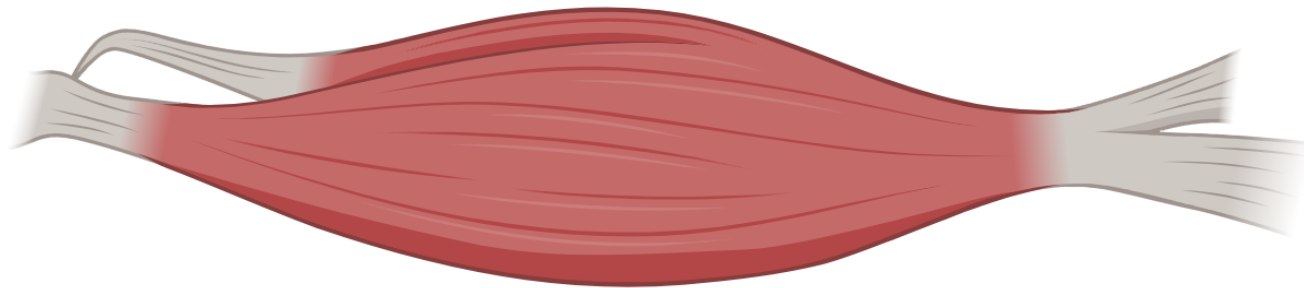


Mechanoelectrical transduction in Hair cells

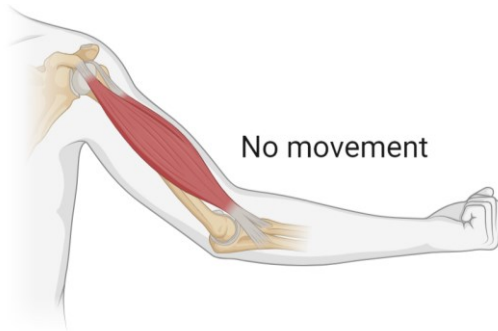


Sensory organs

Muscle Spindles

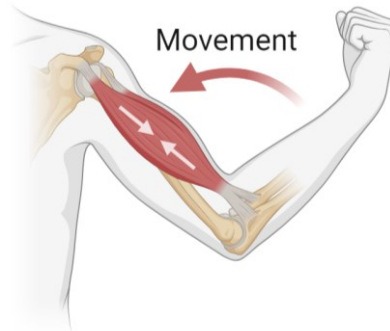


Muscle spindle Joint mechanoreceptors



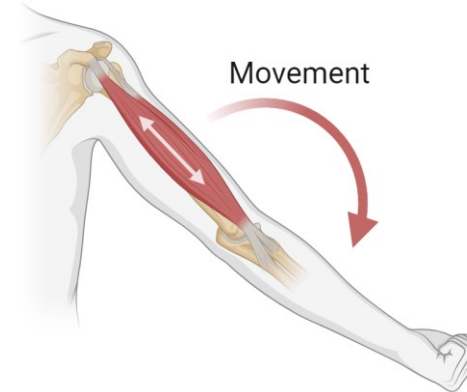
Isometric contraction

Muscle fibers do not change in length



Concentric contraction

Muscle fibers shorten



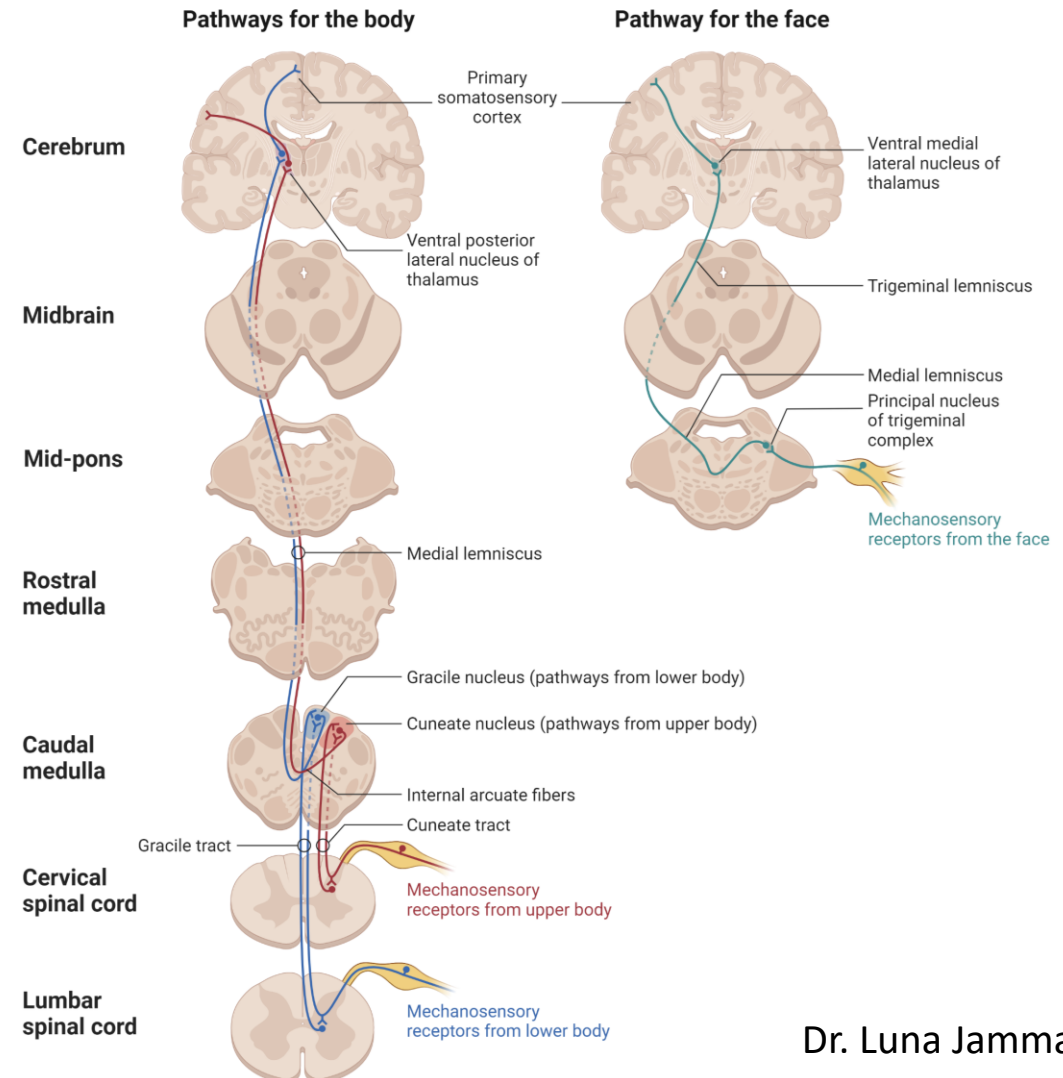
Eccentric contraction

Muscle fibers lengthen

How is the signal transmitted to the Brain?

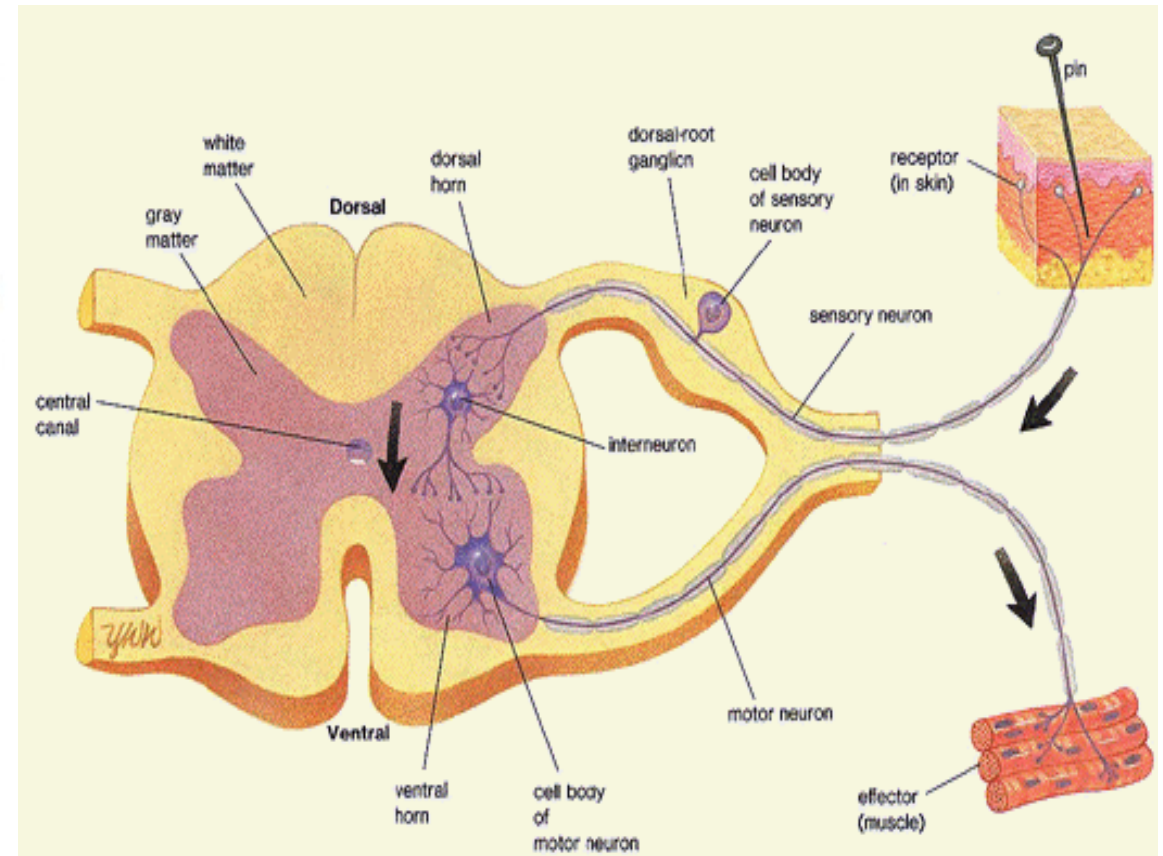
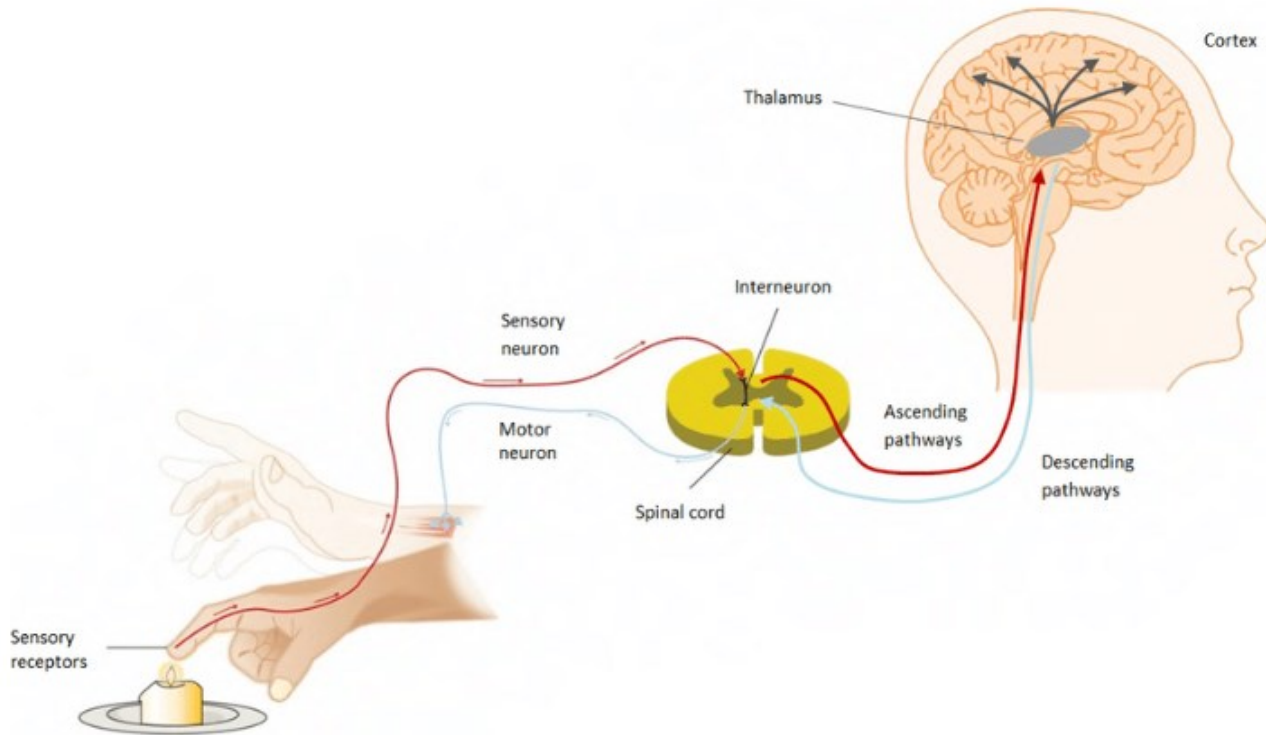
Dorsal Column-Medial Lemniscal Pathway

The Main Touch Pathways



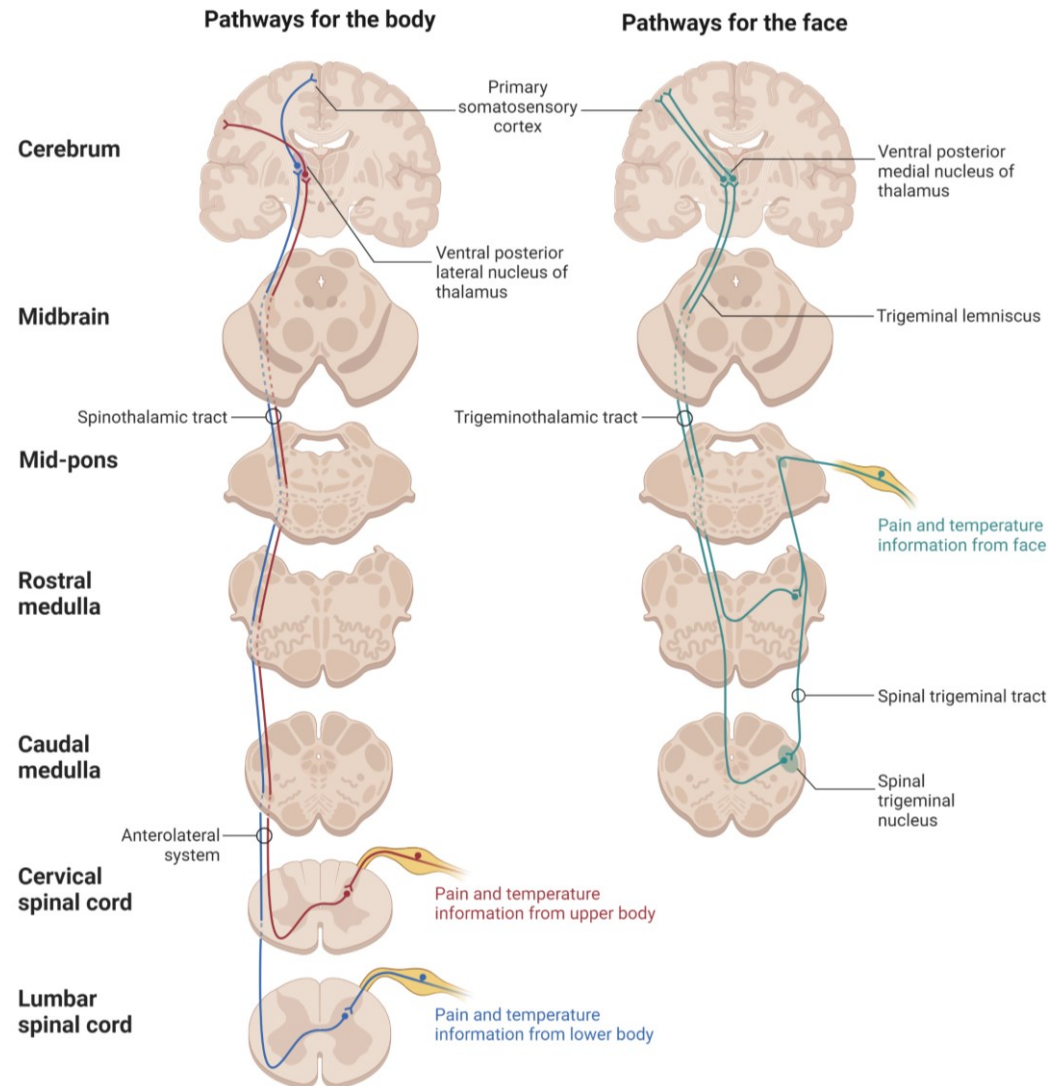


Spinothalamic Pathway

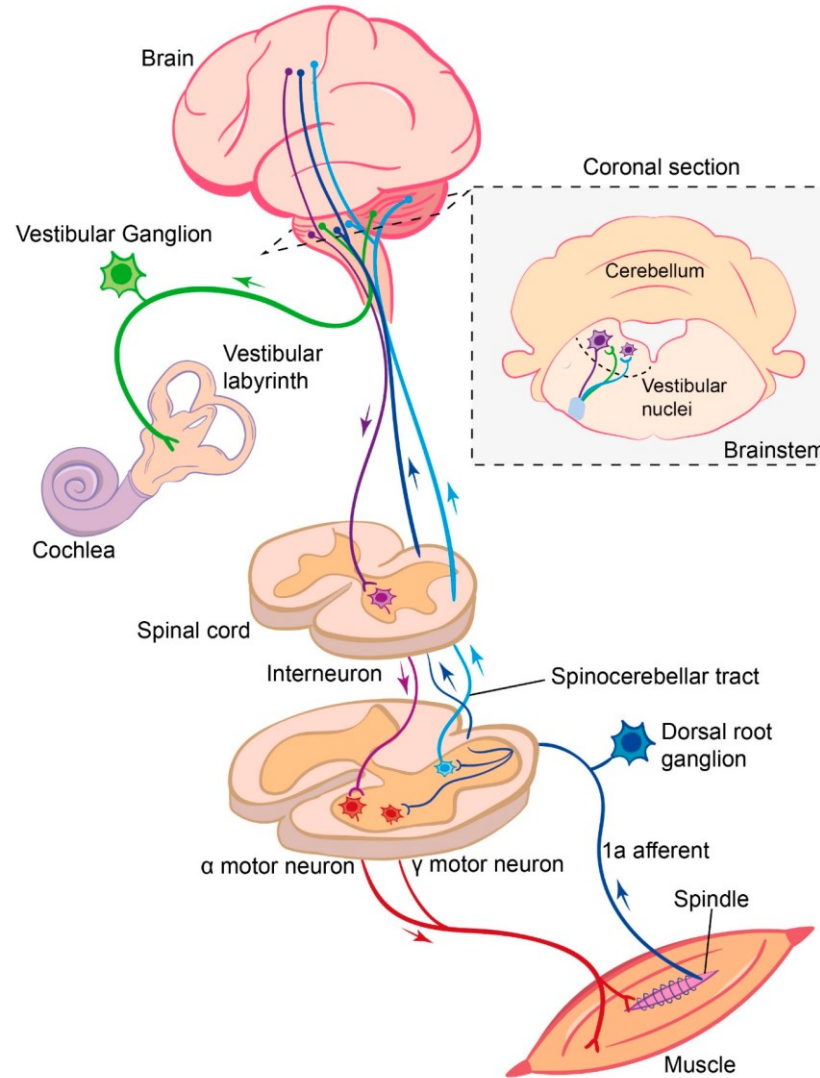


Spinothalamic Pathway

Discriminative Pain Pathways



Spinocerebellar Pathway



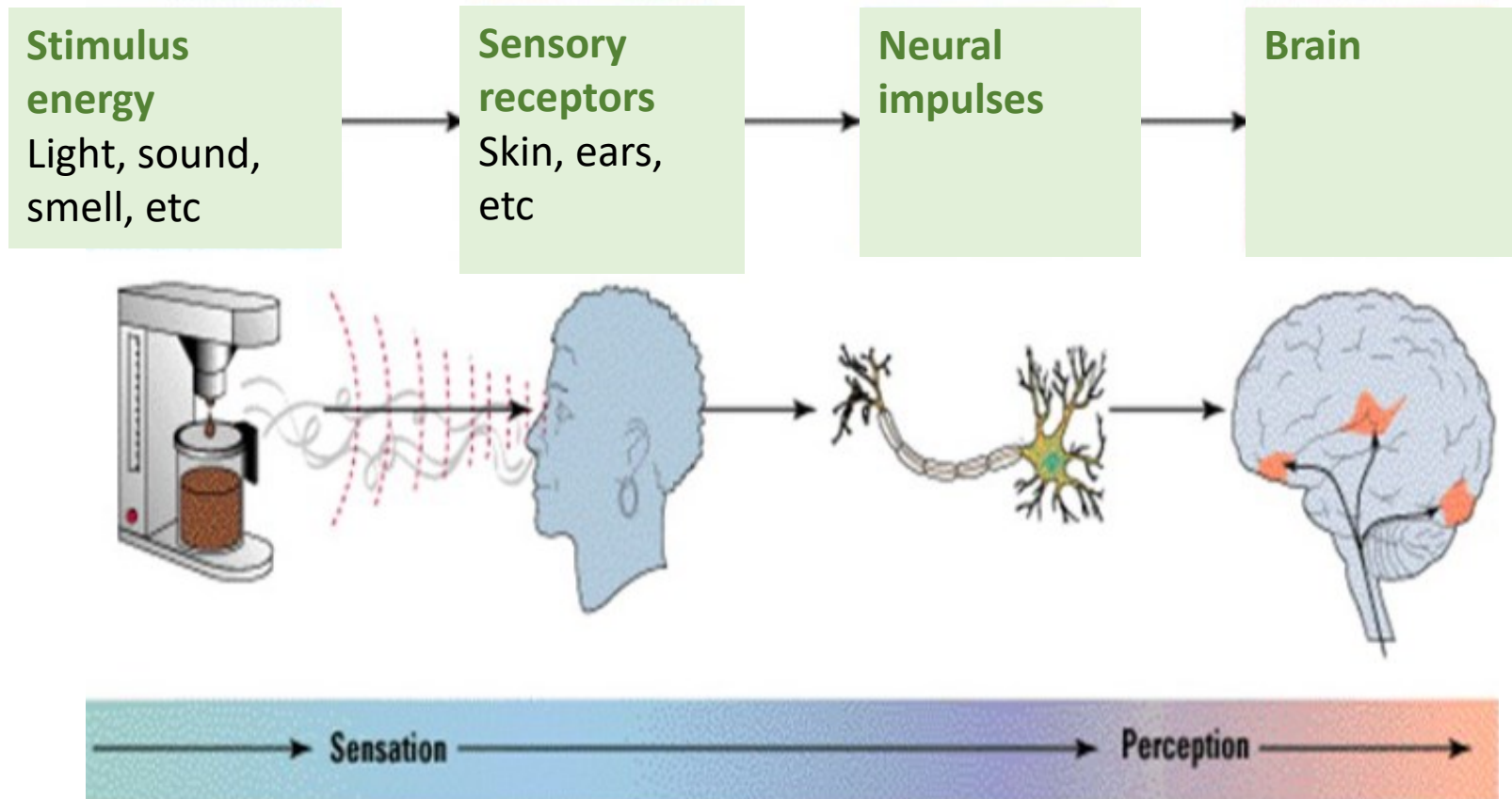
Perception

The process by which the brain organizes and interprets sensory information

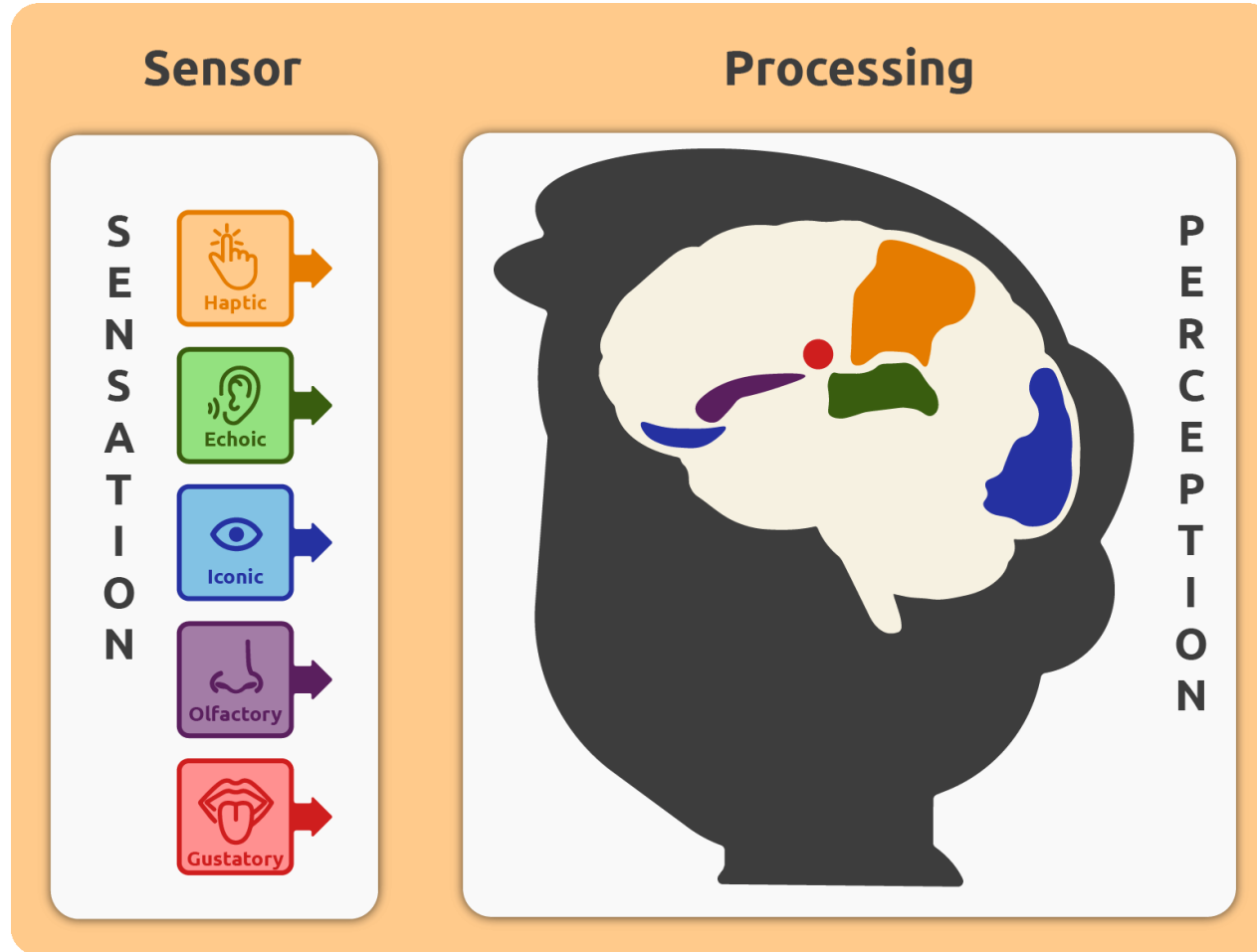
Using sensory information to form a meaningful pattern

Final, organized, meaningful experience of sensory information

The process



The process



Influences on Perception

Our **needs** affect our perception because we are more likely to perceive something we need.

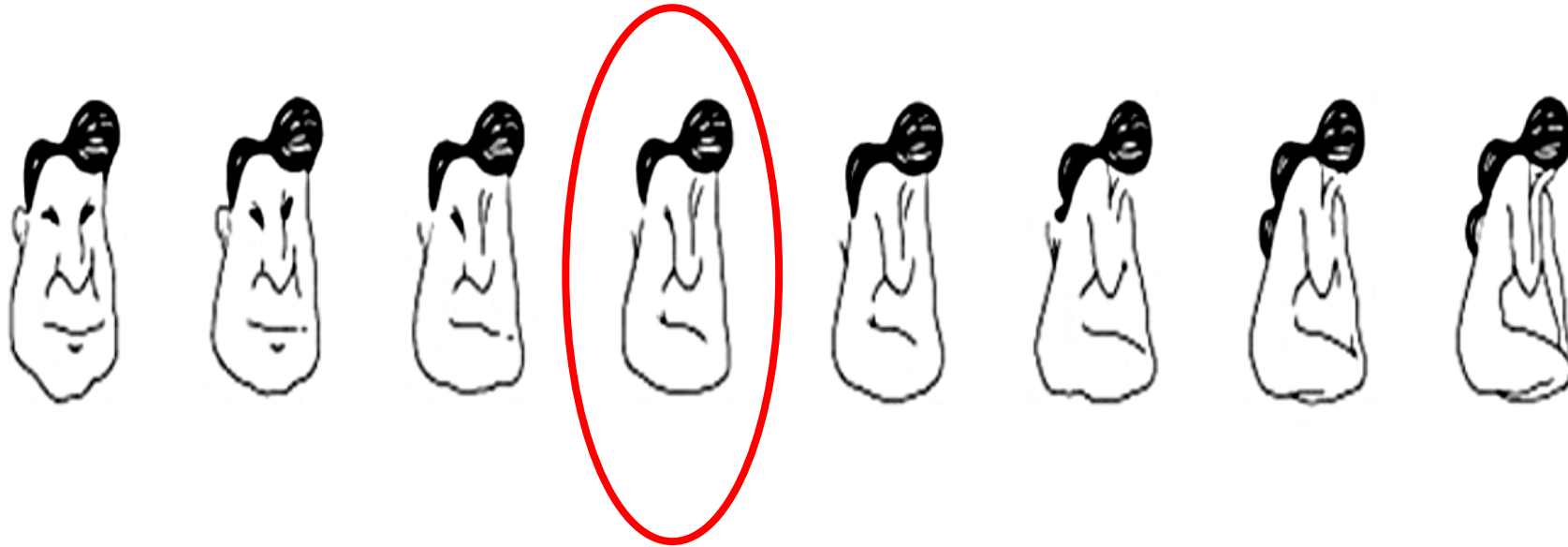
Our **beliefs** can affect what we perceive.

Emotions such as fear, can influence perception of sensory information.

Our **Culture** influences our perception.

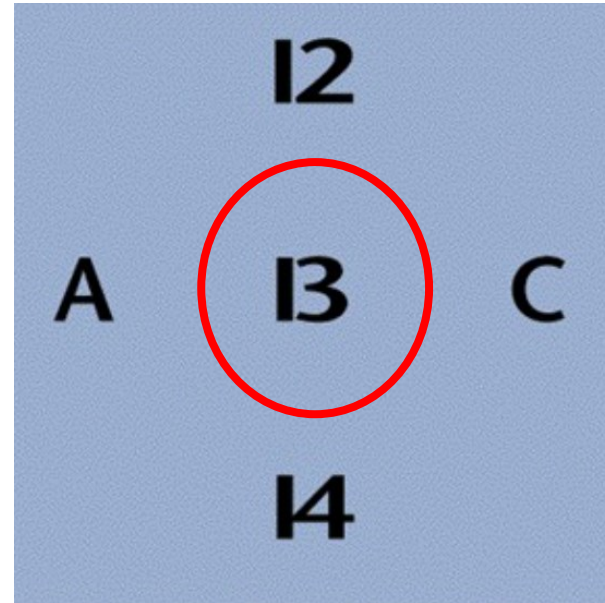
Expectations based on our **previous experiences** influence how we perceive the world.

Perceptual set



What do you see?

Perceptual set



What do you see?

Summary

Sensation refers to the process of receiving information through the senses, perception refers to the way your brain interprets these sensations. If and how you perceive things, depends on your absolute, differential and terminal threshold. If you would like to improve your perception, you can improve your lifestyle and train your perception with exercises.

Perception is the interpretation your brain makes based on what you see, hear, smell, feel, taste and the information that is already stored within your memory. Perception is important because it helps you to understand the world around you.

Proprioception - Kinaesthesia

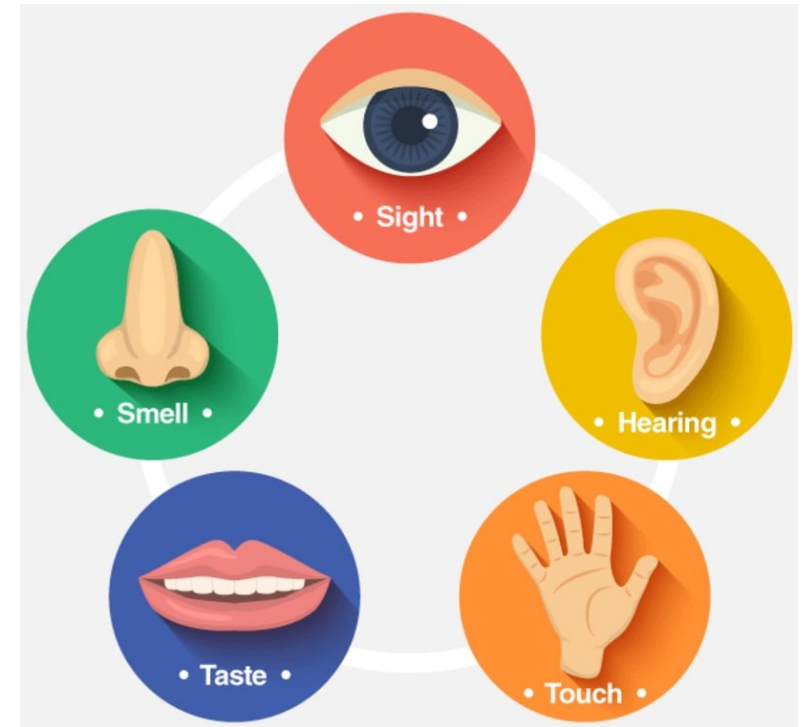
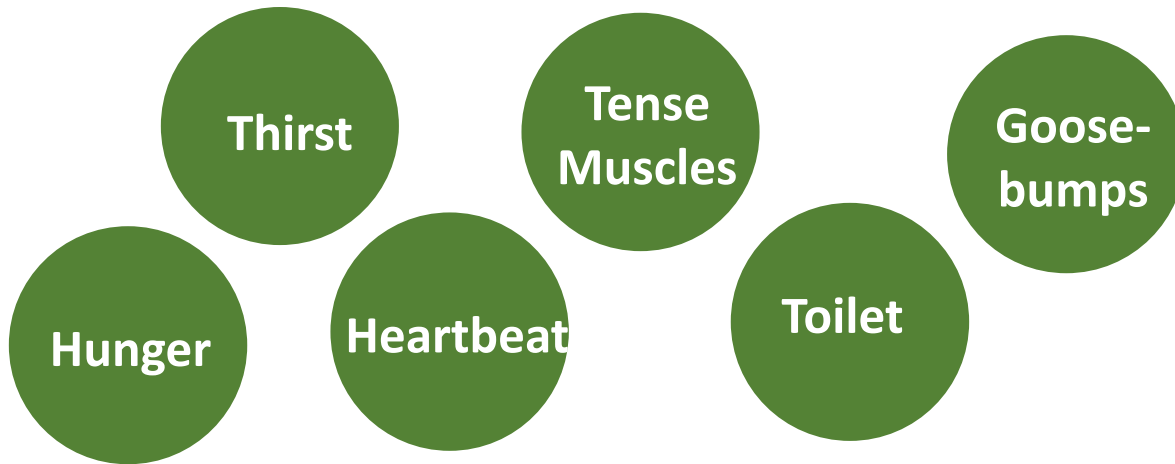
The **body's awareness of position and movements.**

It tells us where our body parts are without having to look for them.

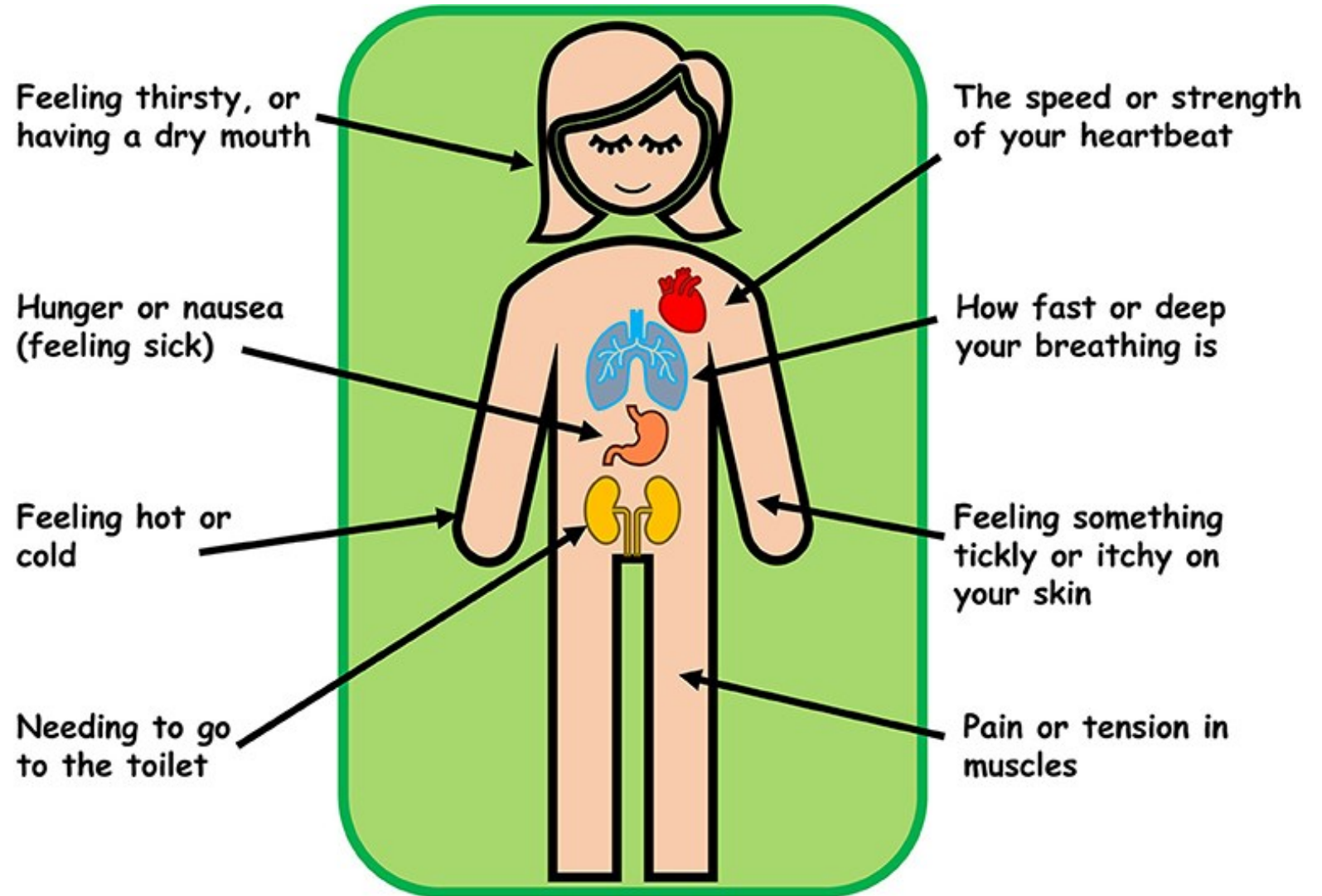
This helps to know where body parts are relative to each other, which strengthens our coordination skills. It also tells us how much force to use when we're holding, pushing, pulling, or lifting objects.

Interoception

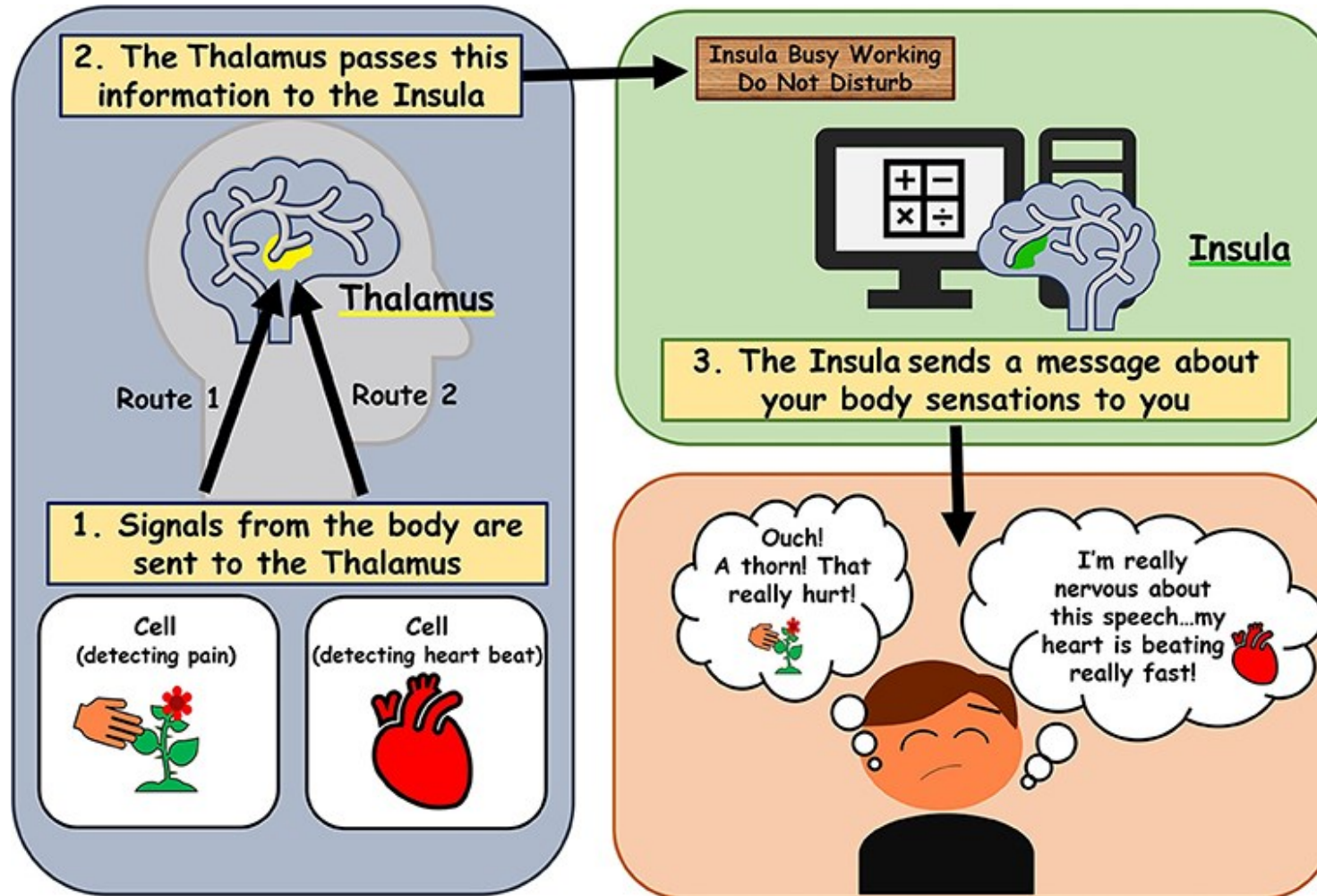
the sense of signals that come from inside the body.



Interoception



Interoception



Somatosensory Disorders

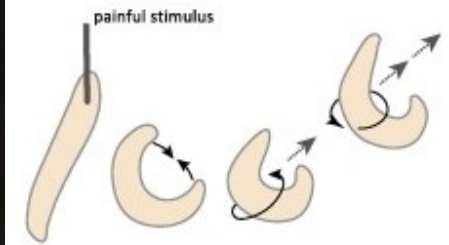
Peripheral Neuropathy: Damage to the peripheral nerves that can cause numbness, tingling, and pain.

Fibromyalgia: A chronic disorder characterized by widespread musculoskeletal pain, fatigue, and tenderness.

Complex Regional Pain Syndrome (CRPS): A chronic pain condition that typically affects an arm or a leg and is usually triggered by an injury or trauma.



Typical escape behavior in response to a painful stimulus

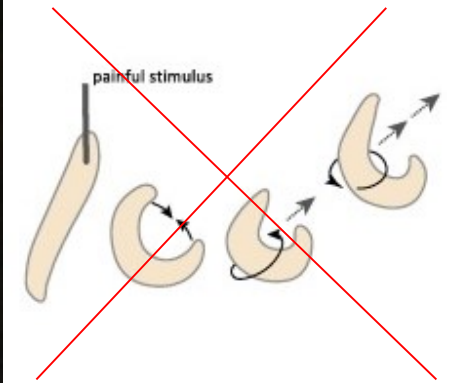


Beqja et al., Transgenic Tarantula Toxin: A novel tool to study mechanosensitive ion channels in *Drosophila*, 2020

Dr. Luna Jammal Salameh



GsMTx-4 blocks piezo mechanoreceptors and abolishes escape behavior in response to a painful stimulus



Beqja et al., Transgenic Tarantula Toxin: A novel tool to study mechanosensitive ion channels in *Drosophila*, 2020

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Proprioception disorders

A

Walking

Difficulty
maintaining
balance and
coordination



Proprioception disorders

A

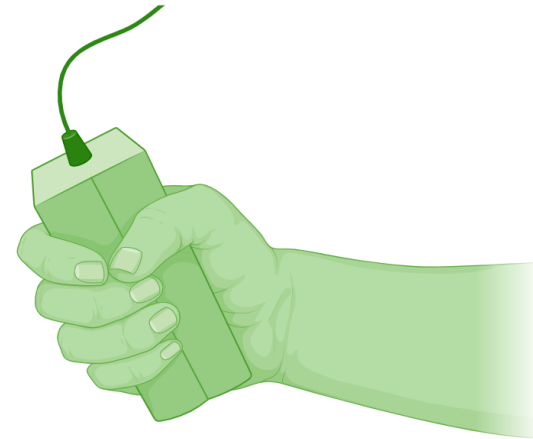
Walking

Difficulty
maintaining
balance and
coordination

B

**Gripping
objects**

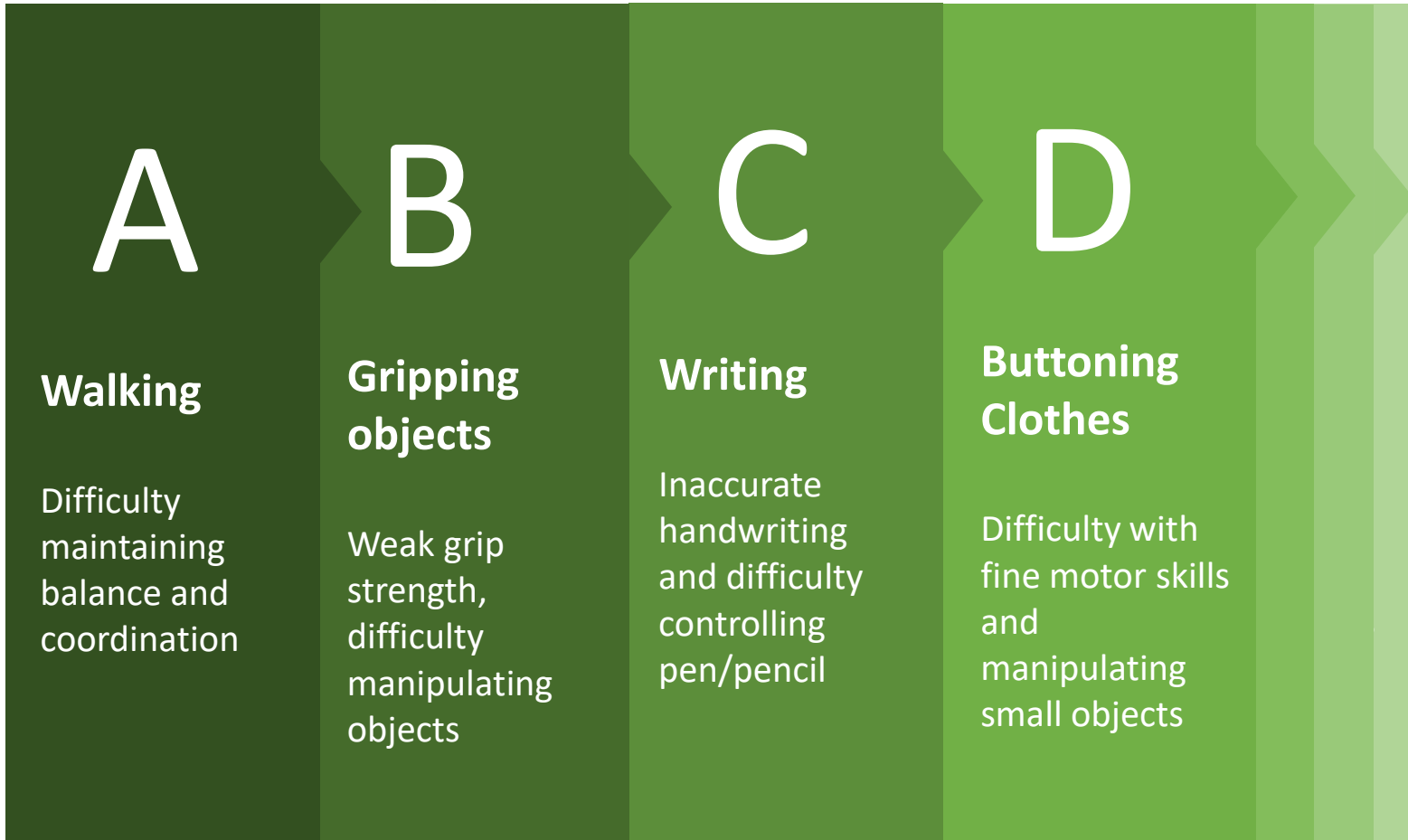
Weak grip
strength,
difficulty
manipulating
objects



Proprioception disorders



Proprioception disorders



Proprioception disorders

A

Walking

Difficulty maintaining balance and coordination

B

Gripping objects

Weak grip strength, difficulty manipulating objects

C

Writing

Inaccurate handwriting and difficulty controlling pen/pencil

D

Buttoning Clothes

Difficulty with fine motor skills and manipulating small objects

E

Eating

Difficulty using utensils and coordinating hand-to-mouth movements



Proprioception disorders

A

Walking

Difficulty maintaining balance and coordination

B

Gripping objects

Weak grip strength, difficulty manipulating objects

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Writing

Inaccurate handwriting and difficulty controlling pen/pencil

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Eating

Difficulty using utensils and coordinating hand-to-mouth movements

F

Playing Sports

Impaired coordination, balance, and reaction time



Proprioception disorders

A

Walking

Difficulty maintaining balance and coordination

B

Gripping objects

Weak grip strength, difficulty manipulating objects

C

Writing

Inaccurate handwriting and difficulty controlling pen/pencil

D

Buttoning Clothes

Difficulty with fine motor skills and manipulating small objects

E

Eating

Difficulty using utensils and coordinating hand-to-mouth movements

F

Playing Sports

Impaired coordination, balance, and reaction time

G

Driving

Decreased ability to accurately judge distances and control vehicle



Conditions resulting in proprioception disorders

Brain injuries

Autism spectrum disorders (ASD)

Multiple sclerosis (MS)

Amyotrophic lateral sclerosis (ALS) or Lou Gehrig's disease

Joint injuries

Joint replacement surgery, especially hip replacement surgery

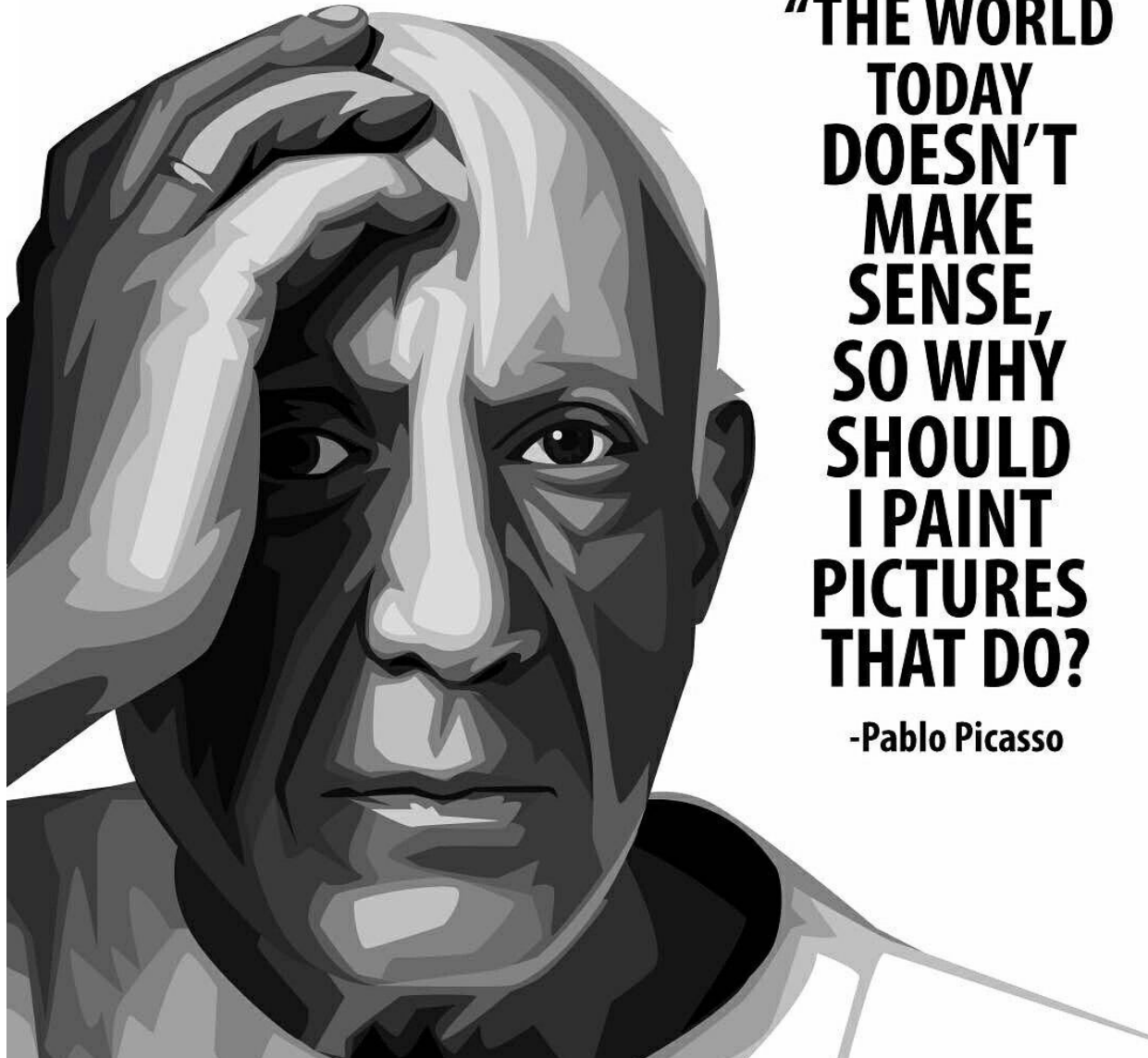
Parkinson's disease

Huntington disease

Stroke

Herniated disc

Peripheral neuropathy



**“THE WORLD
TODAY
DOESN'T
MAKE
SENSE,
SO WHY
SHOULD
I PAINT
PICTURES
THAT DO?”**

-Pablo Picasso

- <https://pubmed.ncbi.nlm.nih.gov/36285142/>
- Supper cool paper for more slides on somatosensation



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