

Neuromodulation of the peripheral nervous system

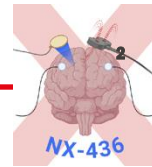
Nx-436

‘Advanced methods for human neuromodulation’

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Provide (brief) information about the physiology of sensory systems

Description of neurotechnologies/approaches to modulate somatosensory processing

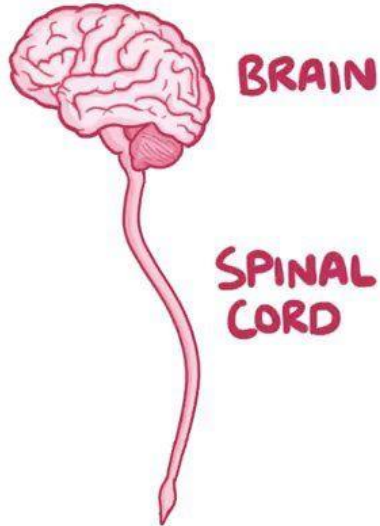
- Peripheral nerve stimulation
- Paired associative stimulation
- Functional electrical stimulation

Description of neurotechnologies/approaches to restore sensory information

- Tactile/proproprioceptive/temperature feedback for amputees

NERVOUS SYSTEM

CENTRAL NERVOUS SYSTEM



PERIPHERAL NERVOUS SYSTEM



SOMATIC

Voluntary
movement
of skeletal
muscle

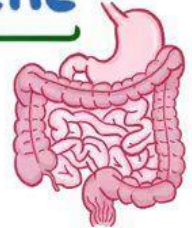


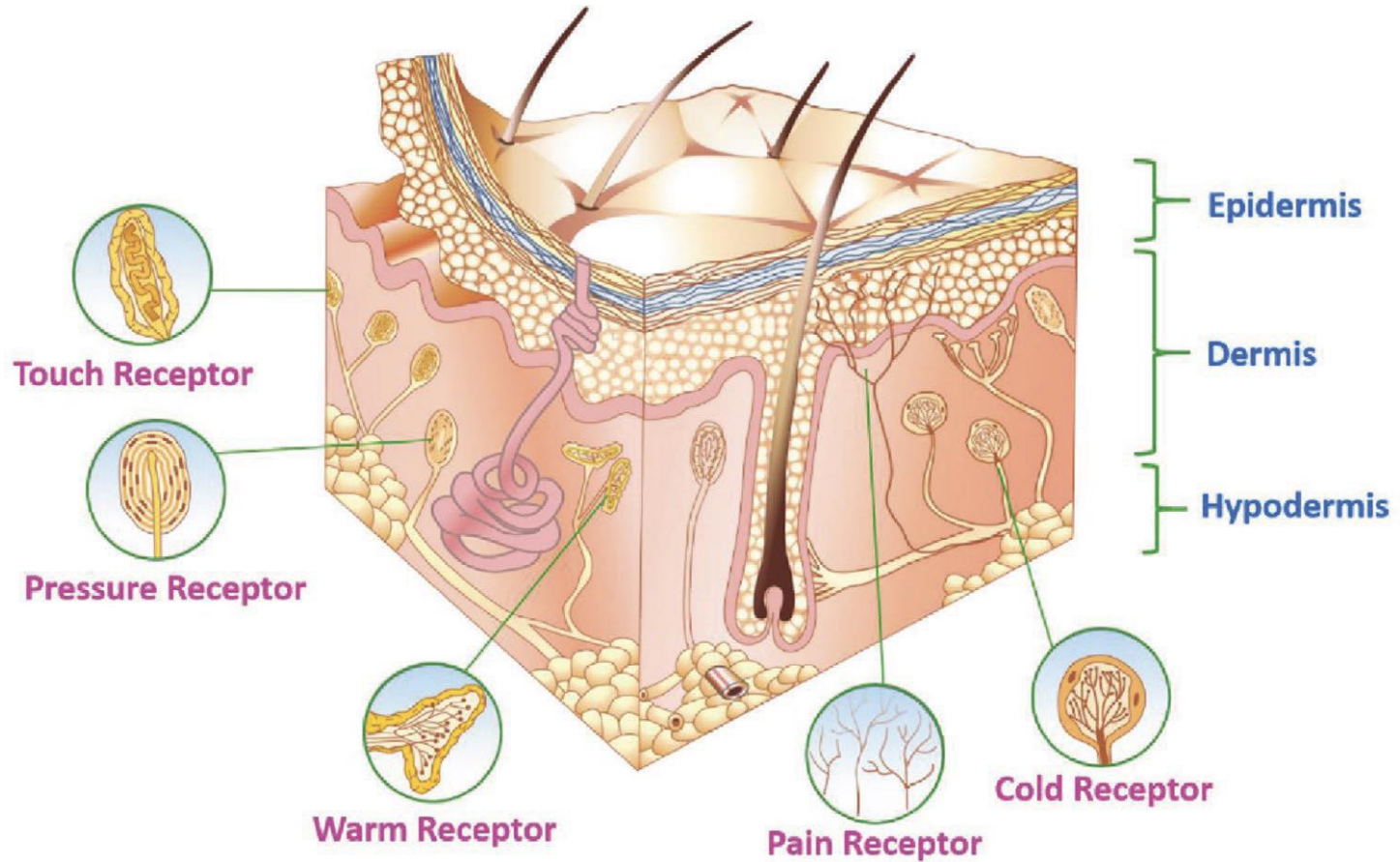
AUTONOMIC

SYMPATHETIC PARASYMPATHETIC

Involuntary movement of

- * Smooth muscles
- * Glands of organs





1. Mechanoreceptors:

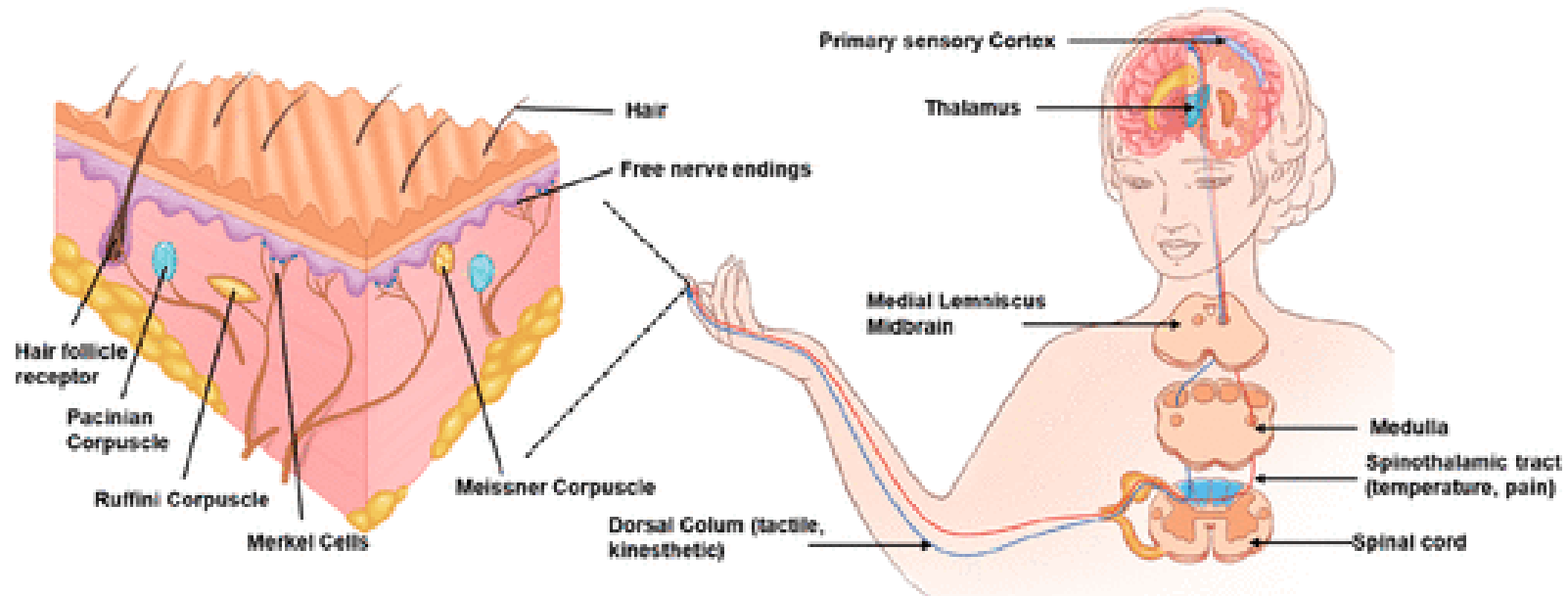
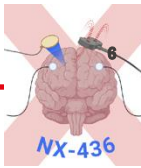
- **Meissner's corpuscles:** Found in the upper dermis, they are responsible for detecting light touch and changes in texture.
- **Merkel cells:** Located in the basal layer of the epidermis, these receptors detect sustained pressure and texture.
- **Pacinian corpuscles:** Situated deeper in the dermis, they are sensitive to deep pressure and vibration.
- **Ruffini endings:** Found in the dermis, these receptors detect skin stretch and contribute to the perception of sustained pressure.

2. Thermoreceptors:

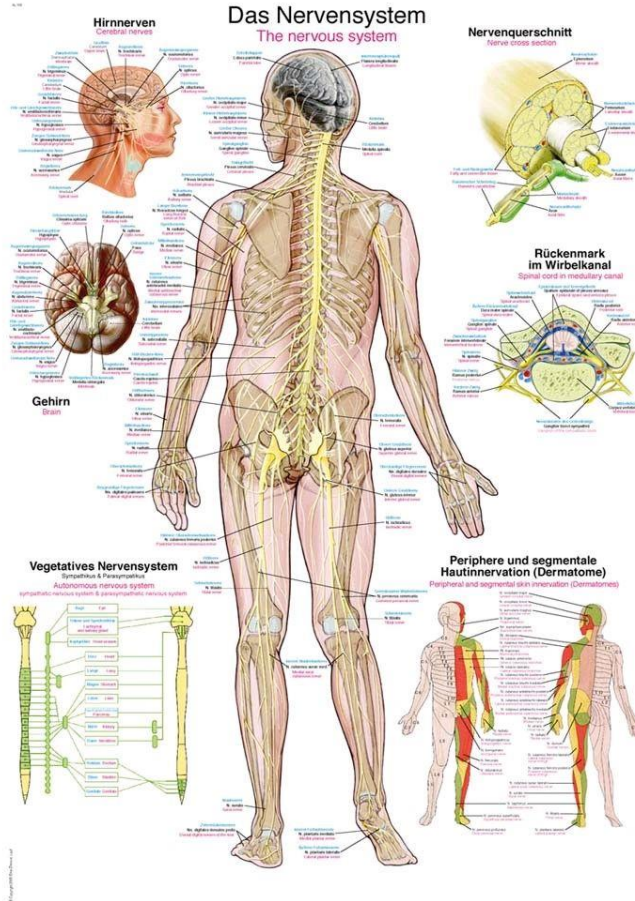
- **Cold receptors (Aδ fibers):** Activated by cooler temperatures, typically below 25°C (77°F), and can be found closer to the skin surface.
- **Warm receptors (C fibers):** Detect temperatures above 30°C (86°F), with maximum sensitivity around 40-45°C (104-113°F).

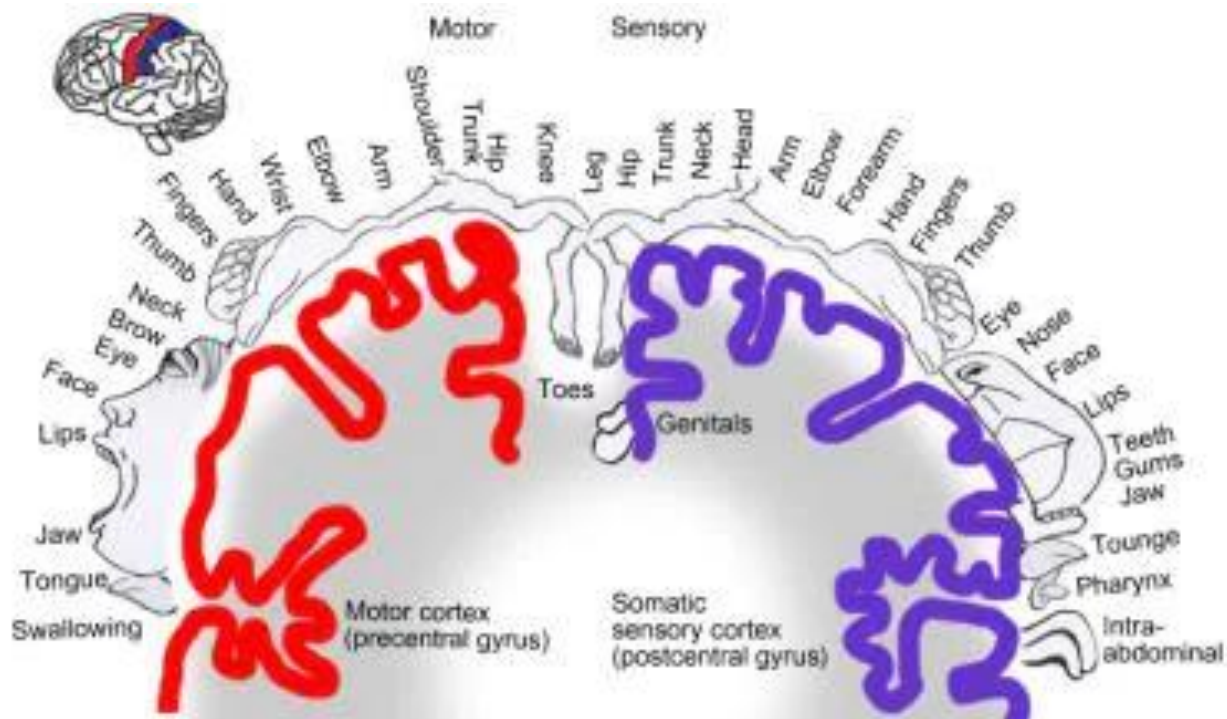
3. Nociceptors (Pain receptors):

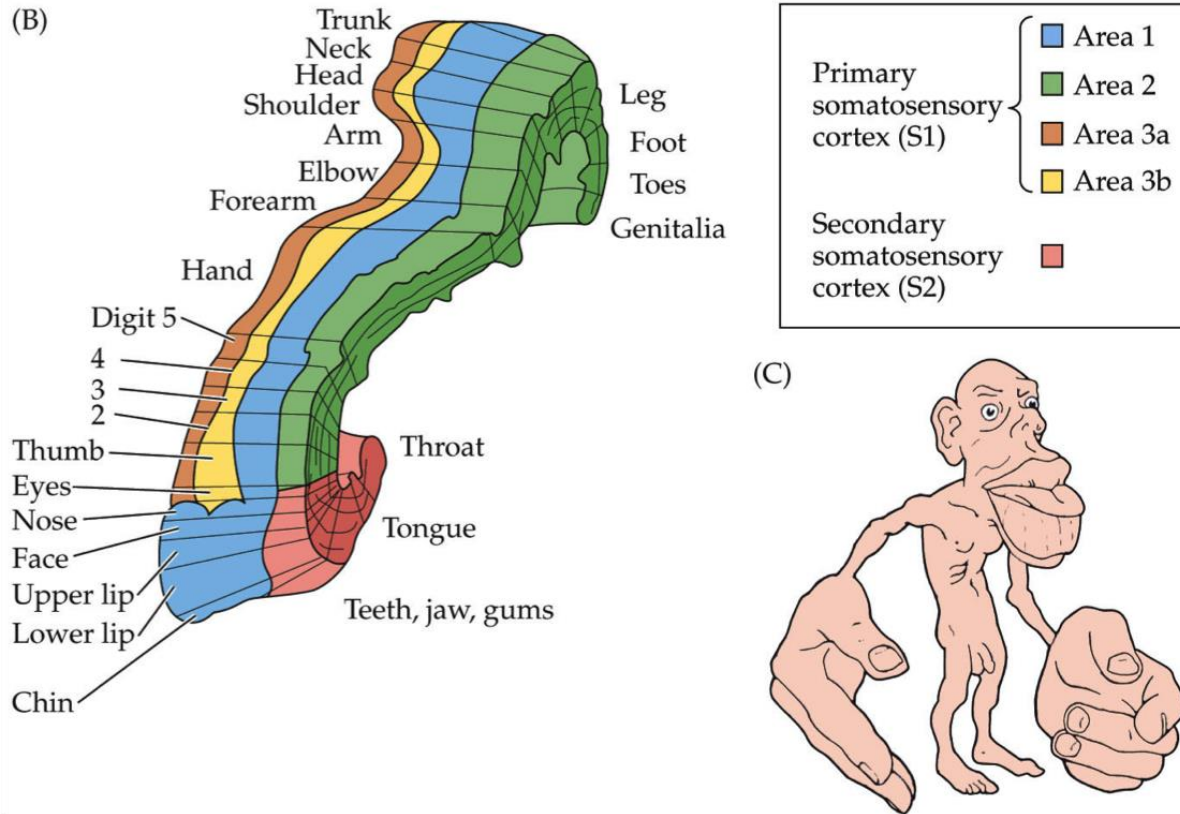
- These free nerve endings respond to potentially harmful stimuli, such as extreme temperatures, mechanical damage, or chemical irritants. There are different types, including thermal nociceptors for extreme heat or cold and mechanical nociceptors for physical damage.

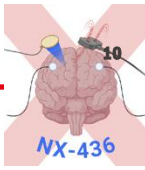


pressure (**touch**), pain (**nociception**), **vibration**, **temperature**, position sense (**proprioception**), and body movement (**kinesthesia**)

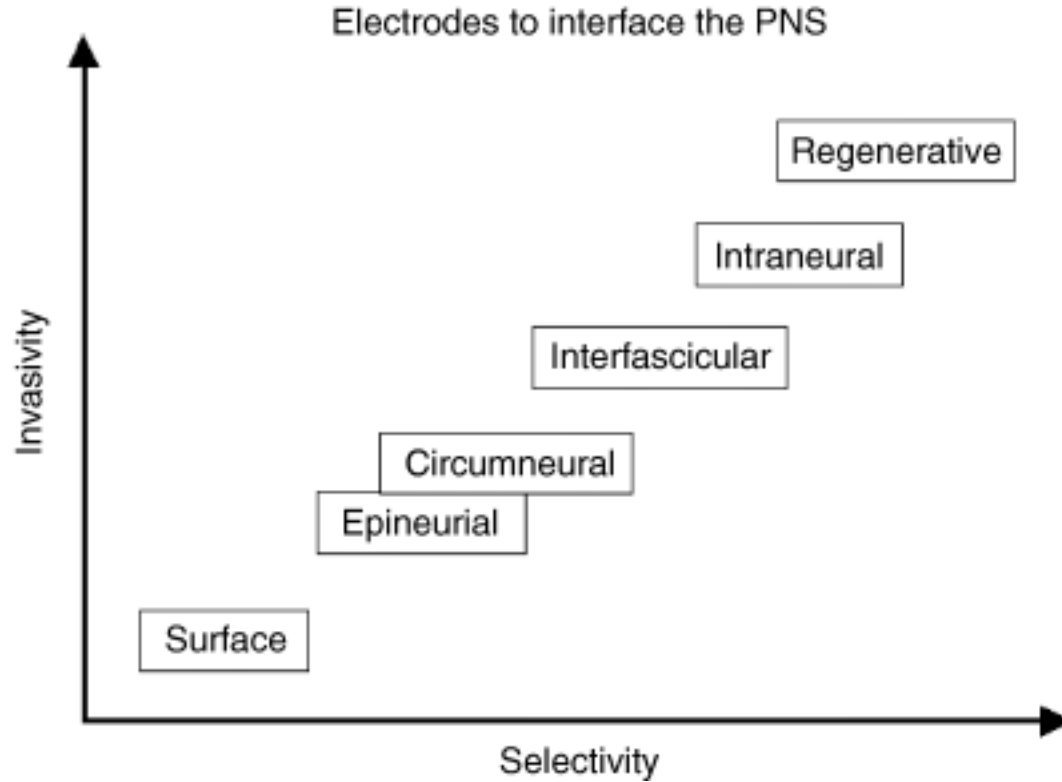




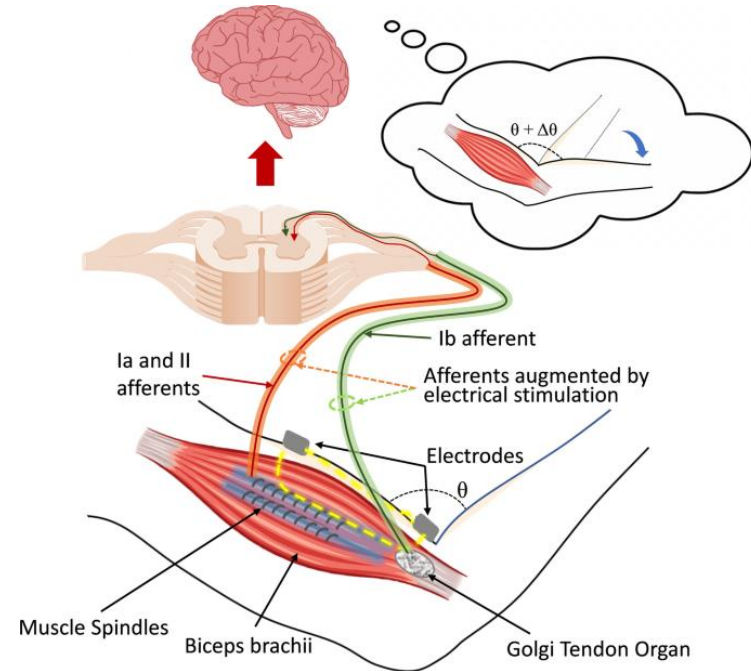
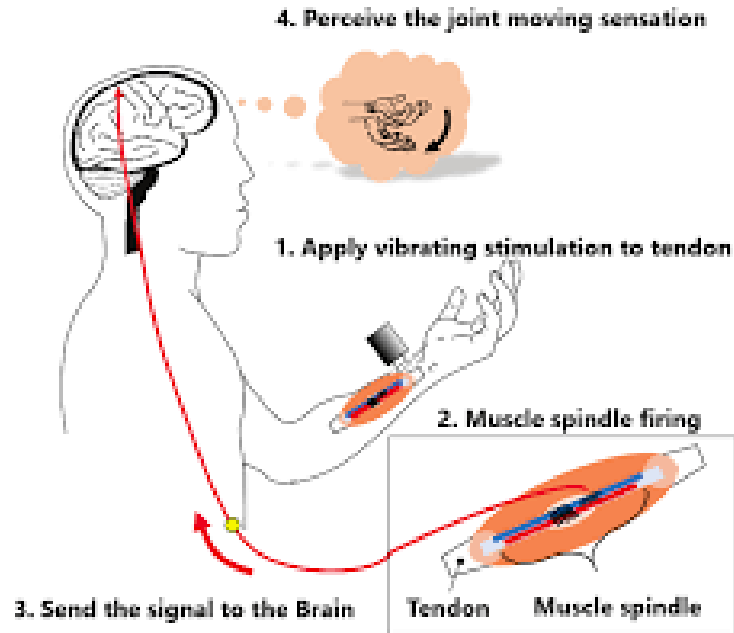


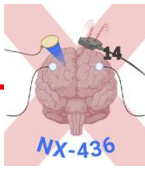


Neuromodulation?

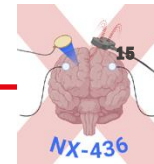


Mechanical Stimulation

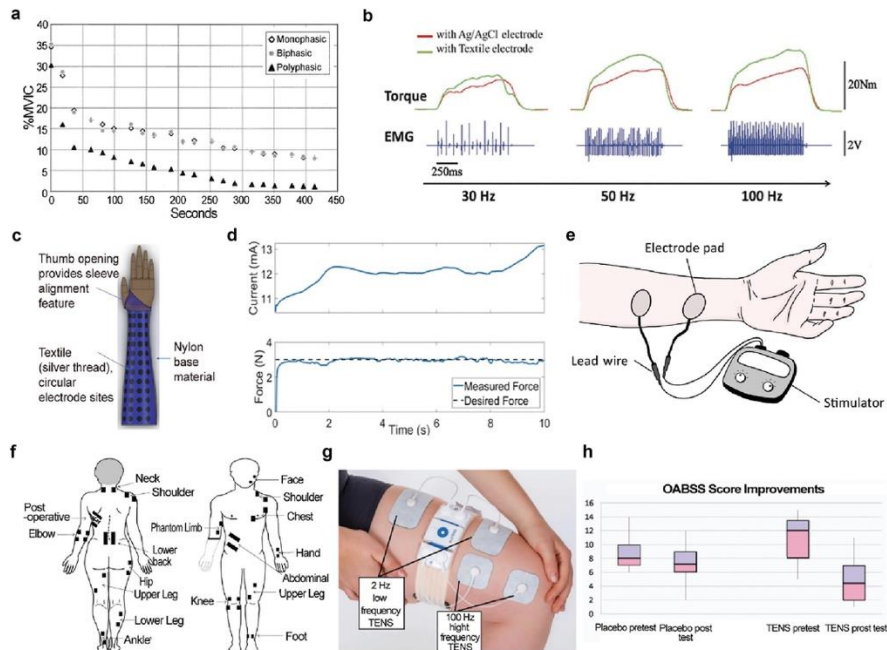




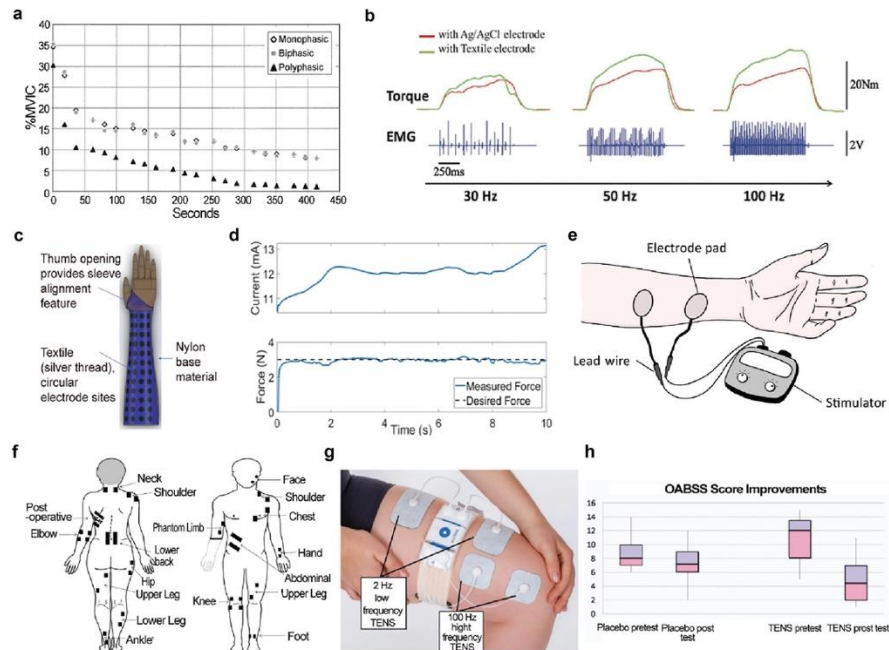
Peripheral nerve stimulation (PNS)



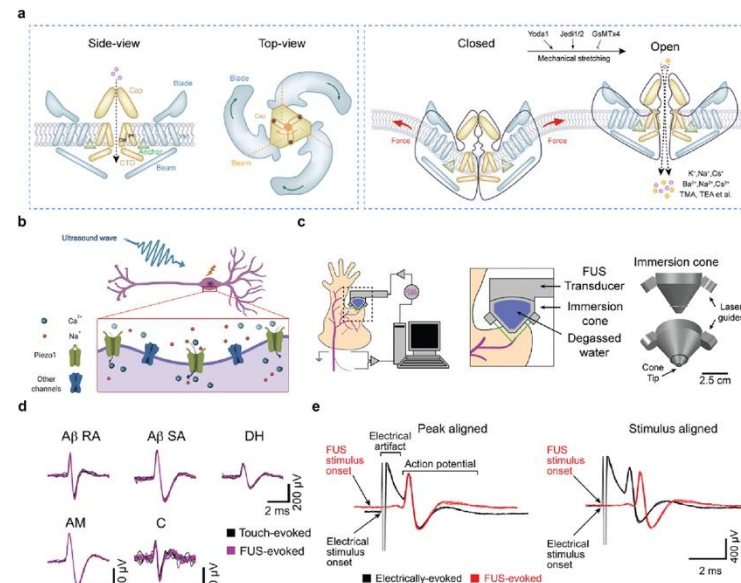
Electrical non-invasive Neuromodulation



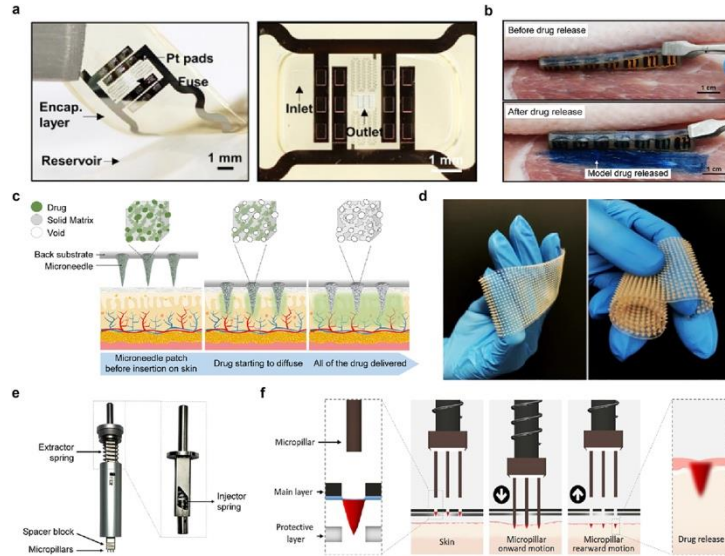
Electrical non-invasive Neuromodulation



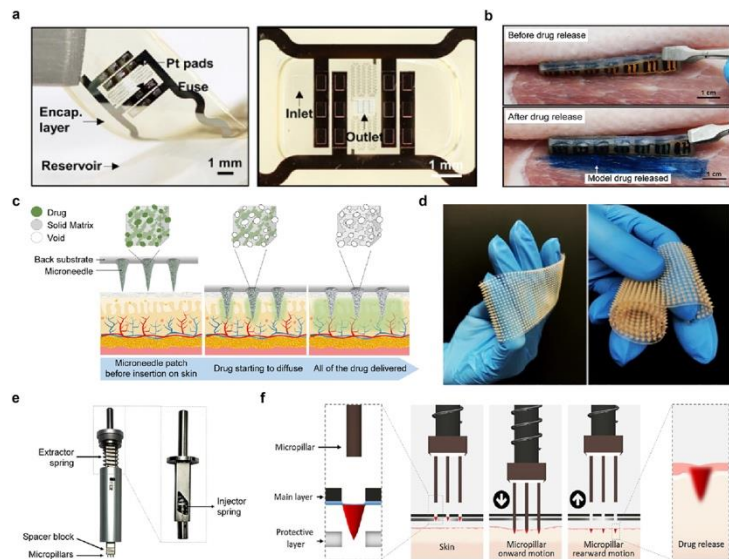
Mechanical Neuromodulation



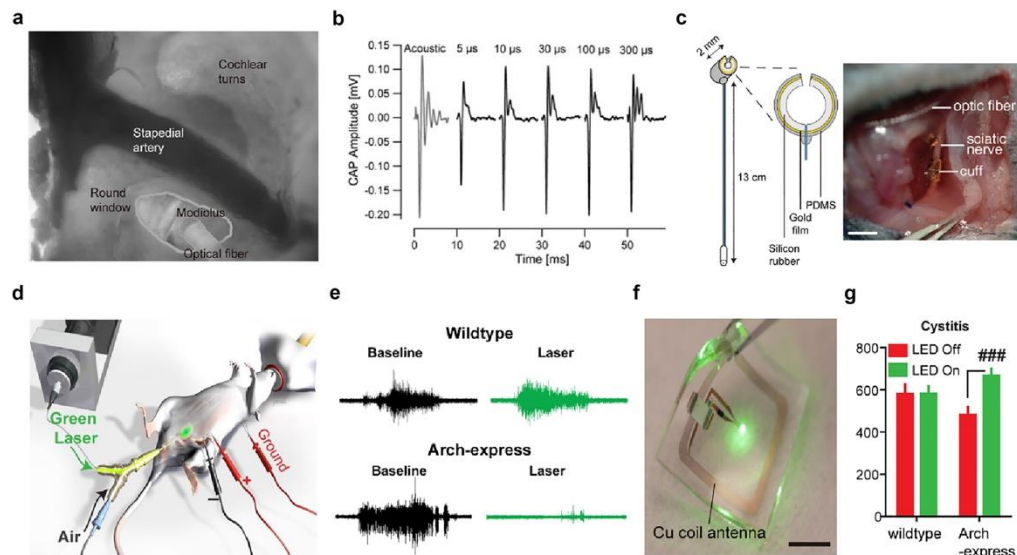
Chemical Neuromodulation

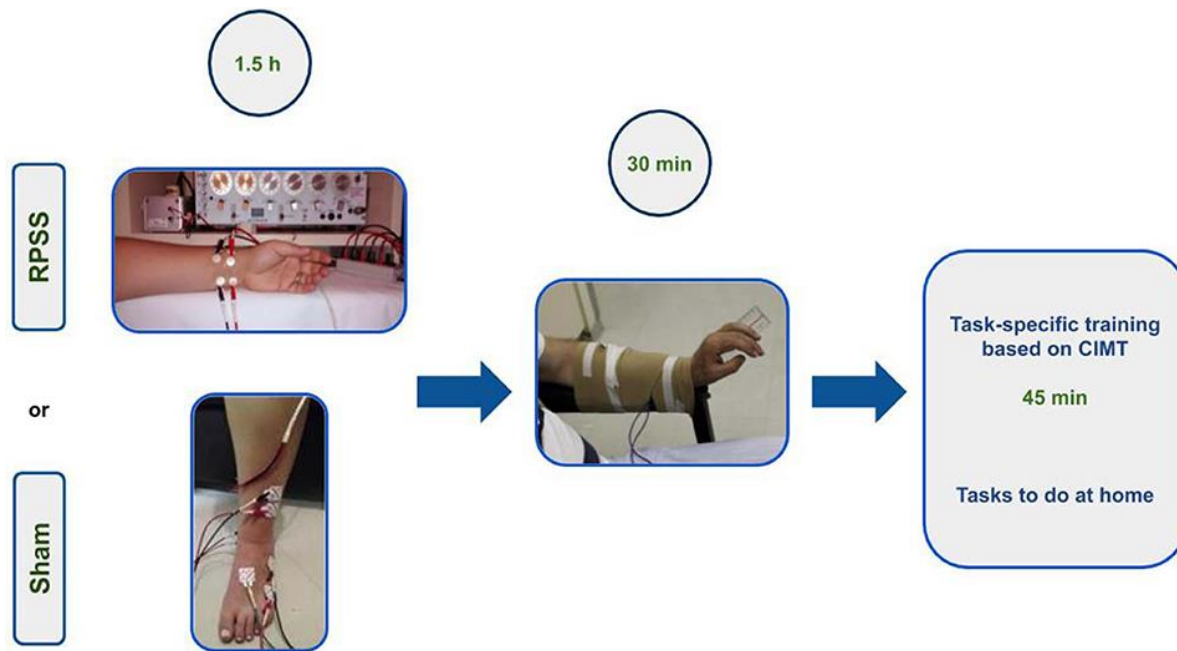
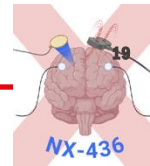


Chemical Neuromodulation

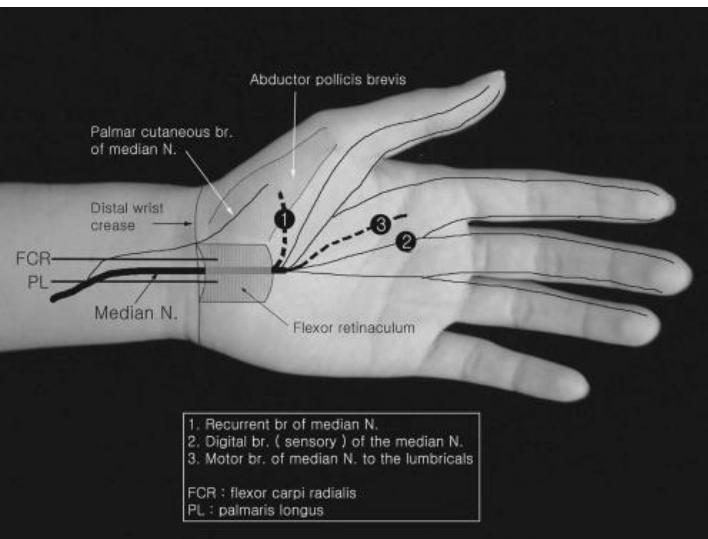
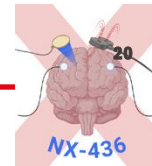
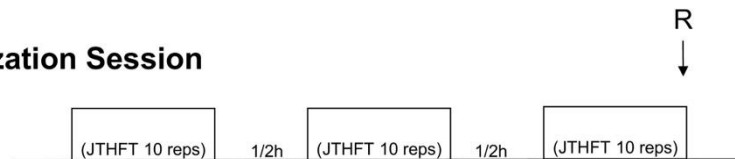
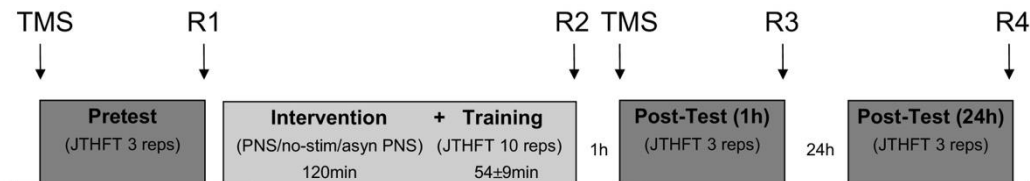


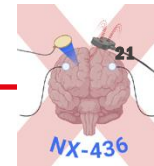
Optical Neuromodulation



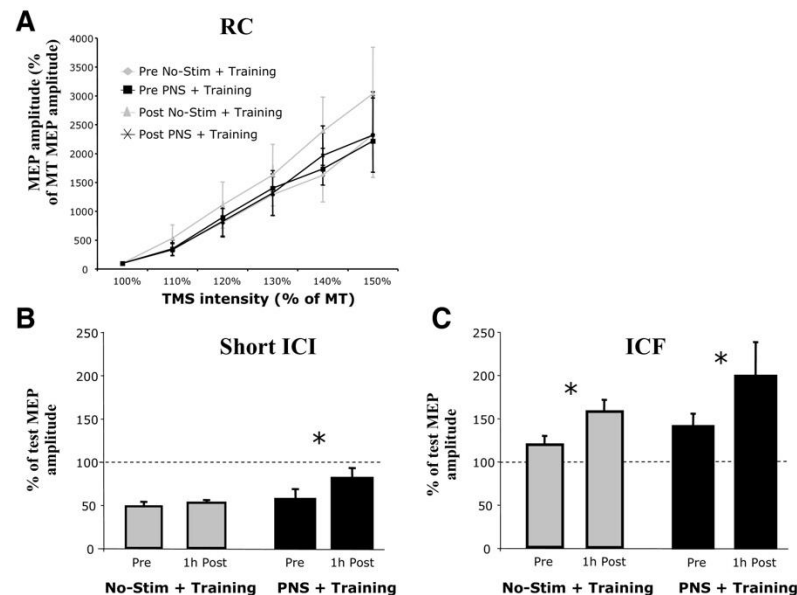
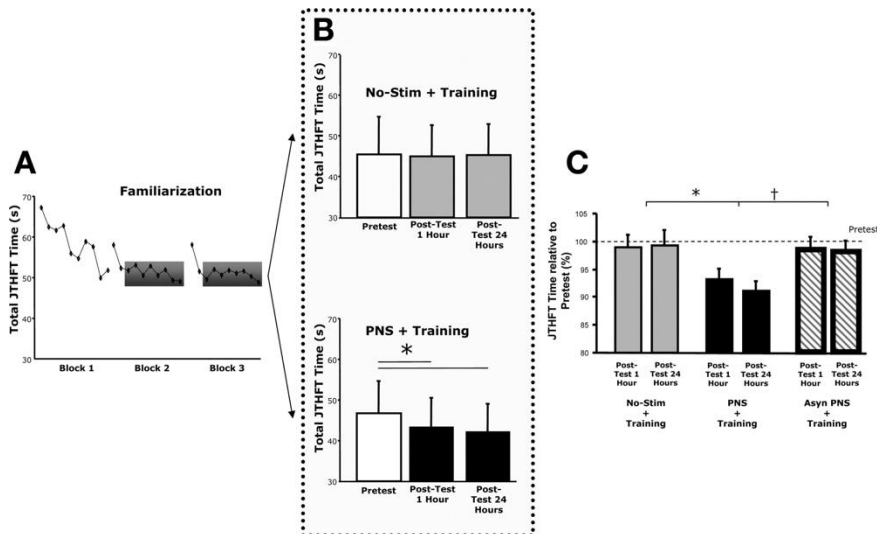


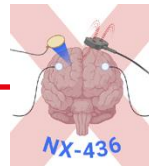
3 times per week for 6 weeks

**A****Familiarization Session****B****Sessions 2-3-4**



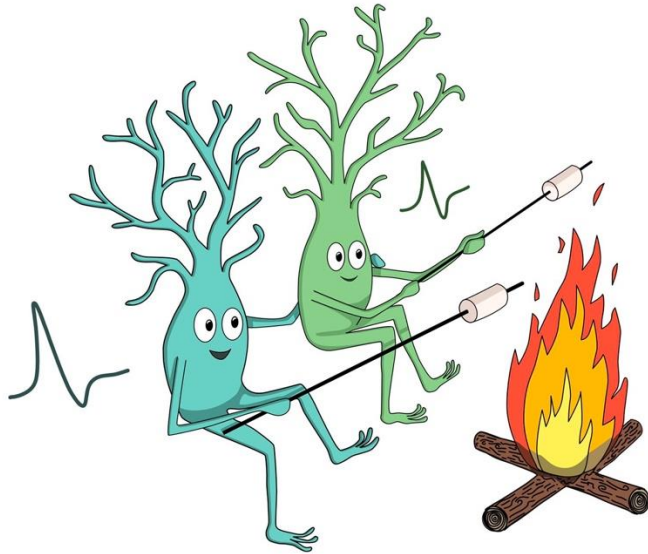
Combination of PNS with motor training leads to an improvement in residual motor functions in stroke patients
This is associated with changes in motor-cortical excitability





- Peripheral nerve stimulation (PNS) allows to modulate cortical activity
- If combined with motor training it leads to an improvement of the effects of training, e.g. in stroke patients

Paired associative stimulation (PAS)

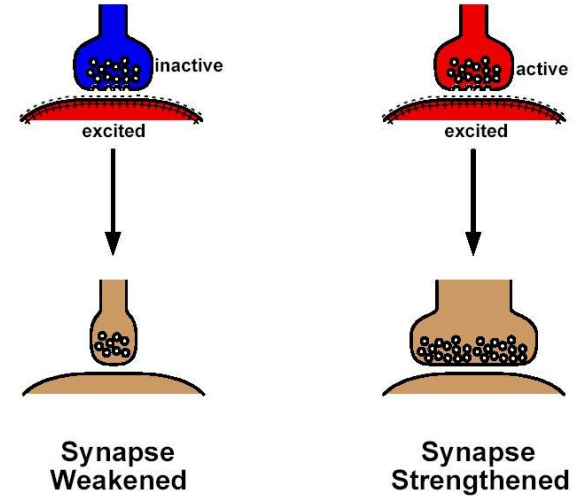


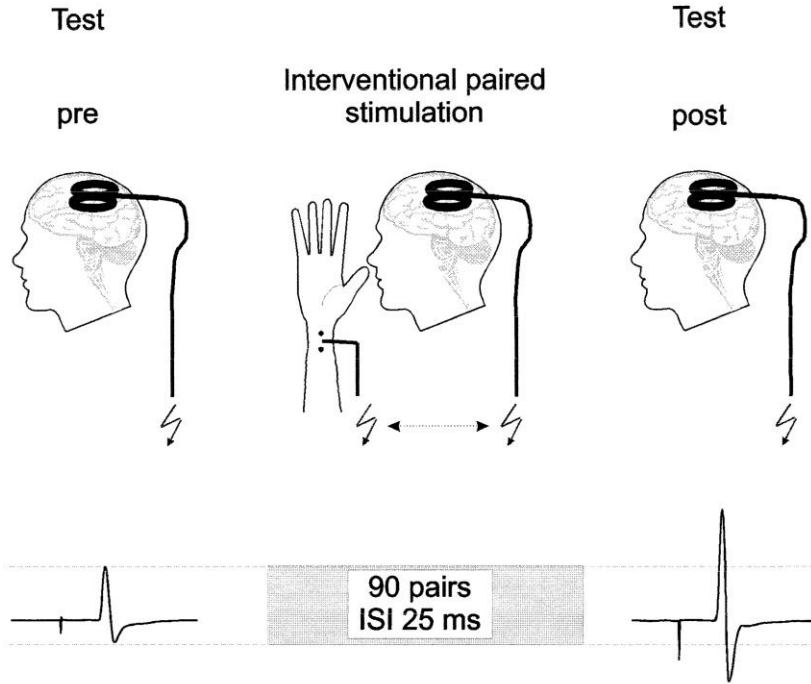
**"Neurons that
FIRE together,
WIRE together"**
- Donald Hebb



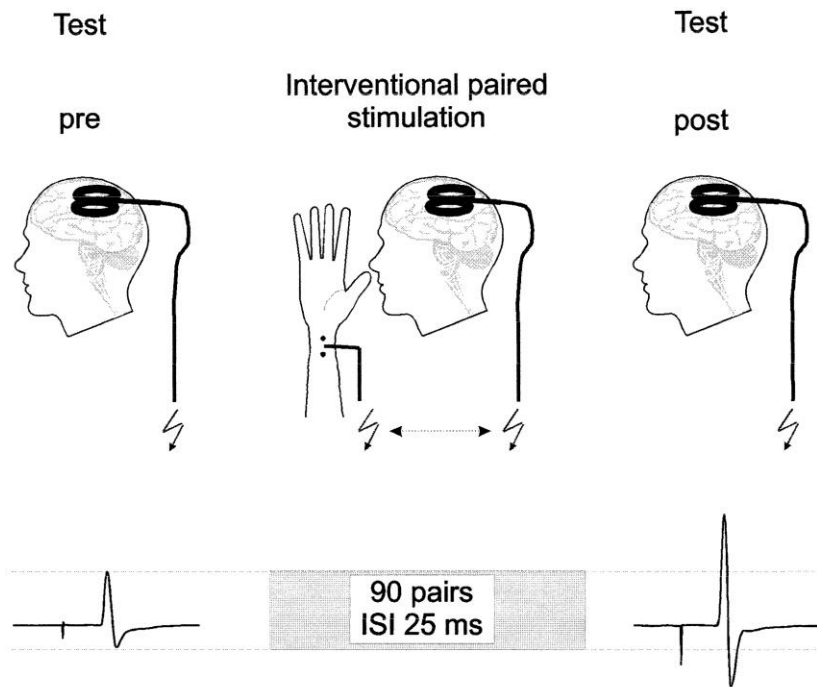
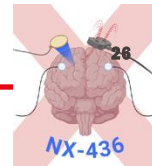
<https://twitter.com/theNeuronFamily/>

A property of Hebbian synapse



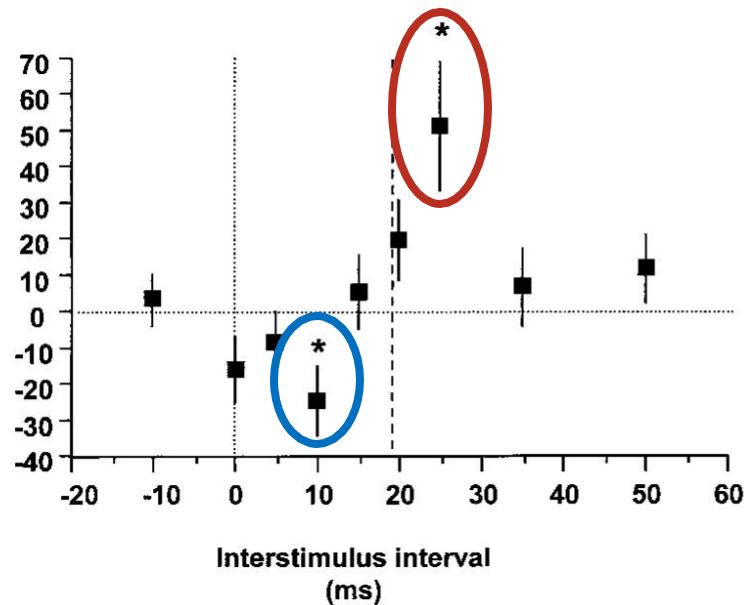


Standard protocol: 90 pairs at 10 or 25 ms ISI and at 0.05 Hz inter-pair interval with 1mV-MEP TMS intensity and 300% sensory threshold for median nerve stimulation



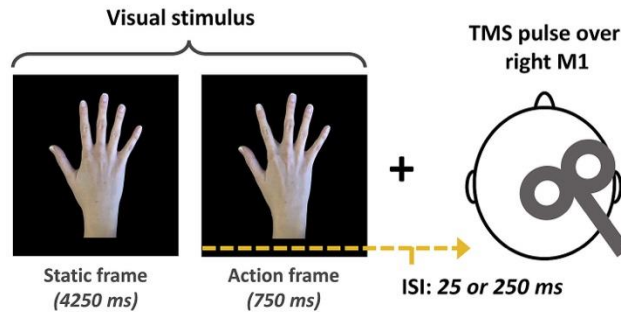
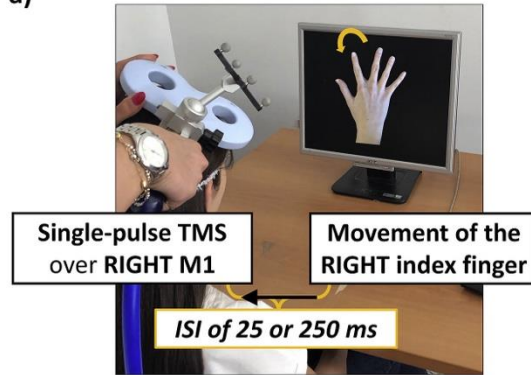
C

Amplitude change
(percent of baseline)



Standard protocol: 90 pairs at 10 or 25 ms ISI and at 0.05 Hz inter-pair interval with 1mV-MEP TMS intensity and 300% sensory threshold for median nerve stimulation

a)



b)

Left Hand
(contralateral
to TMS side)

Right Hand
(ipsilateral to
TMS side)



Static hand
trials



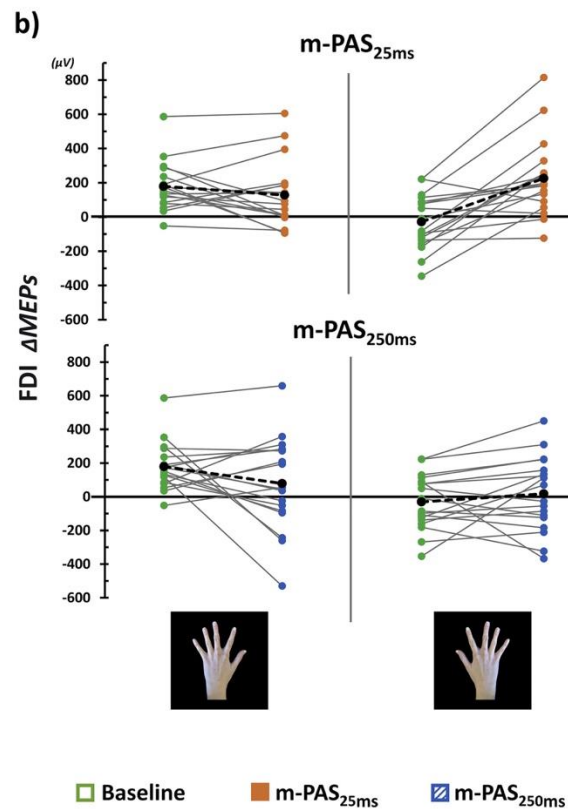
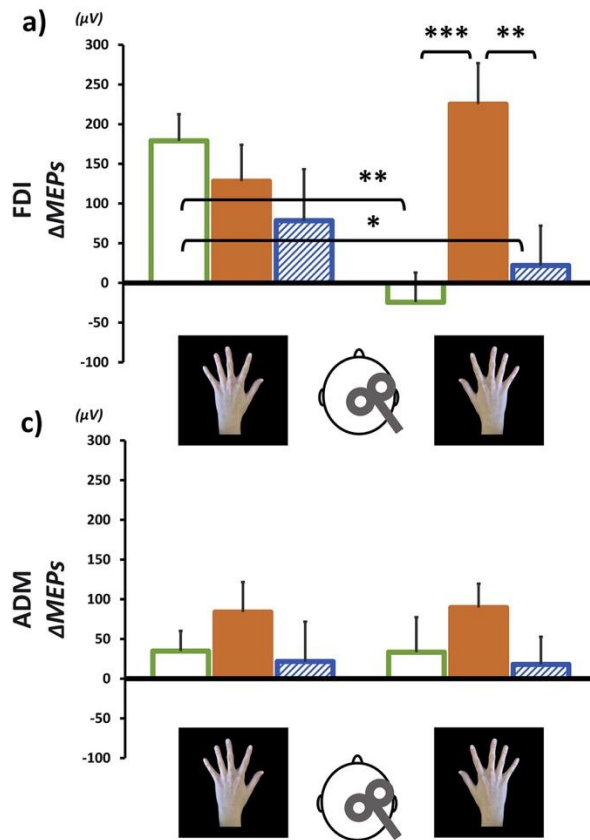
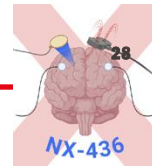
Movement
trials



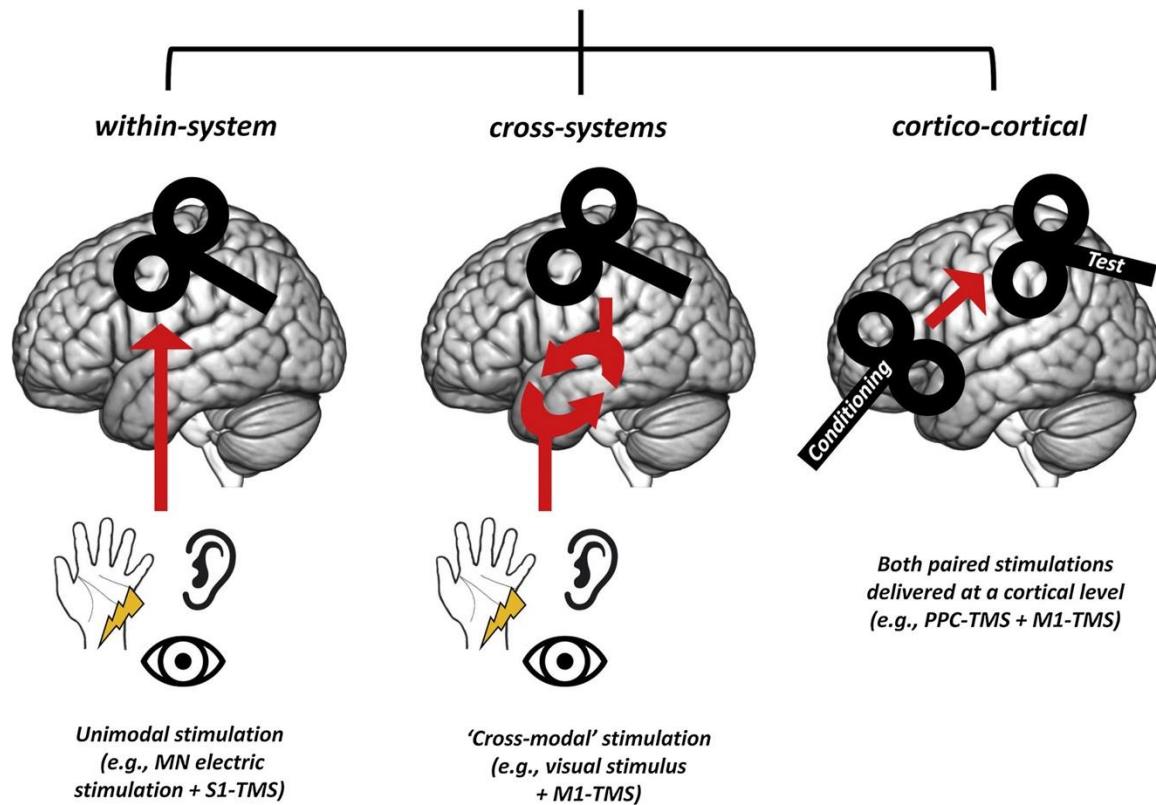
TMS pulse over
right M1

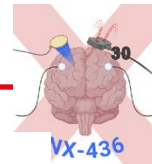


MEPs recorded
from the left hand

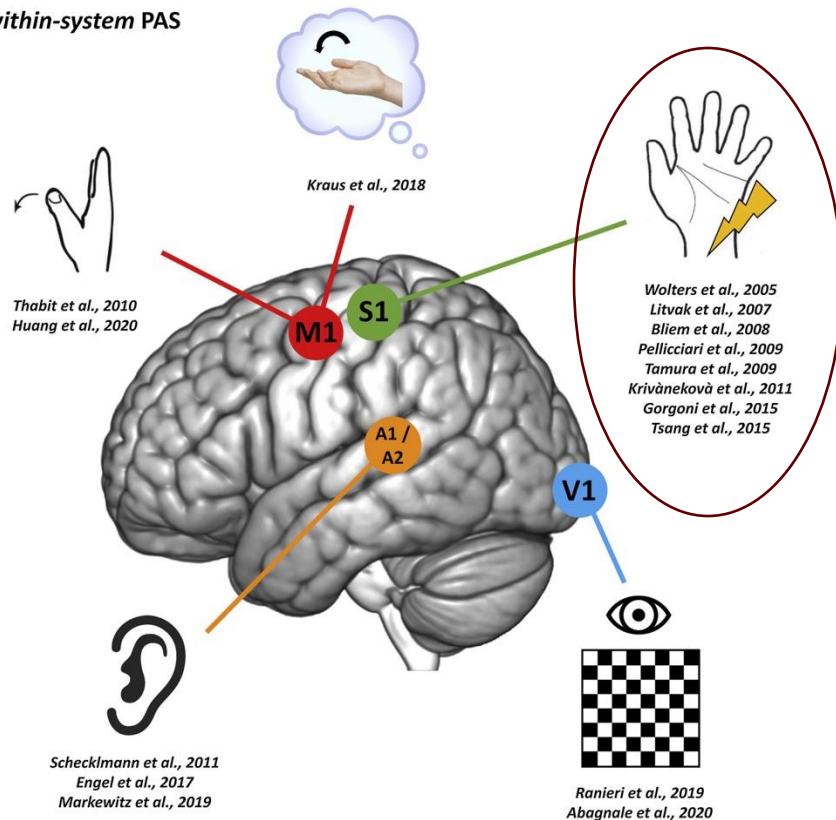


Paired Associative Stimulation - PAS

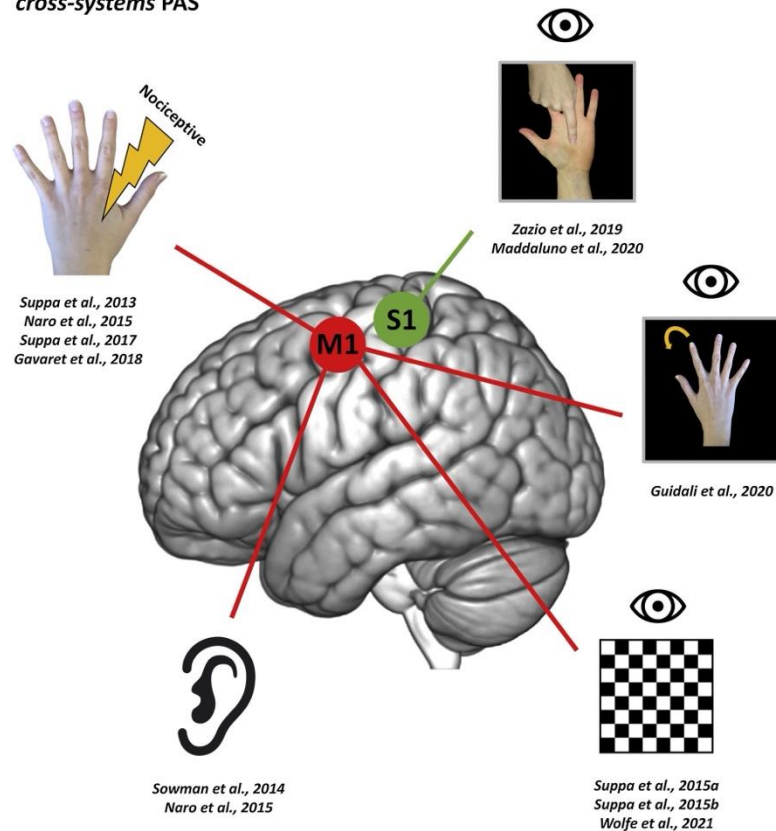


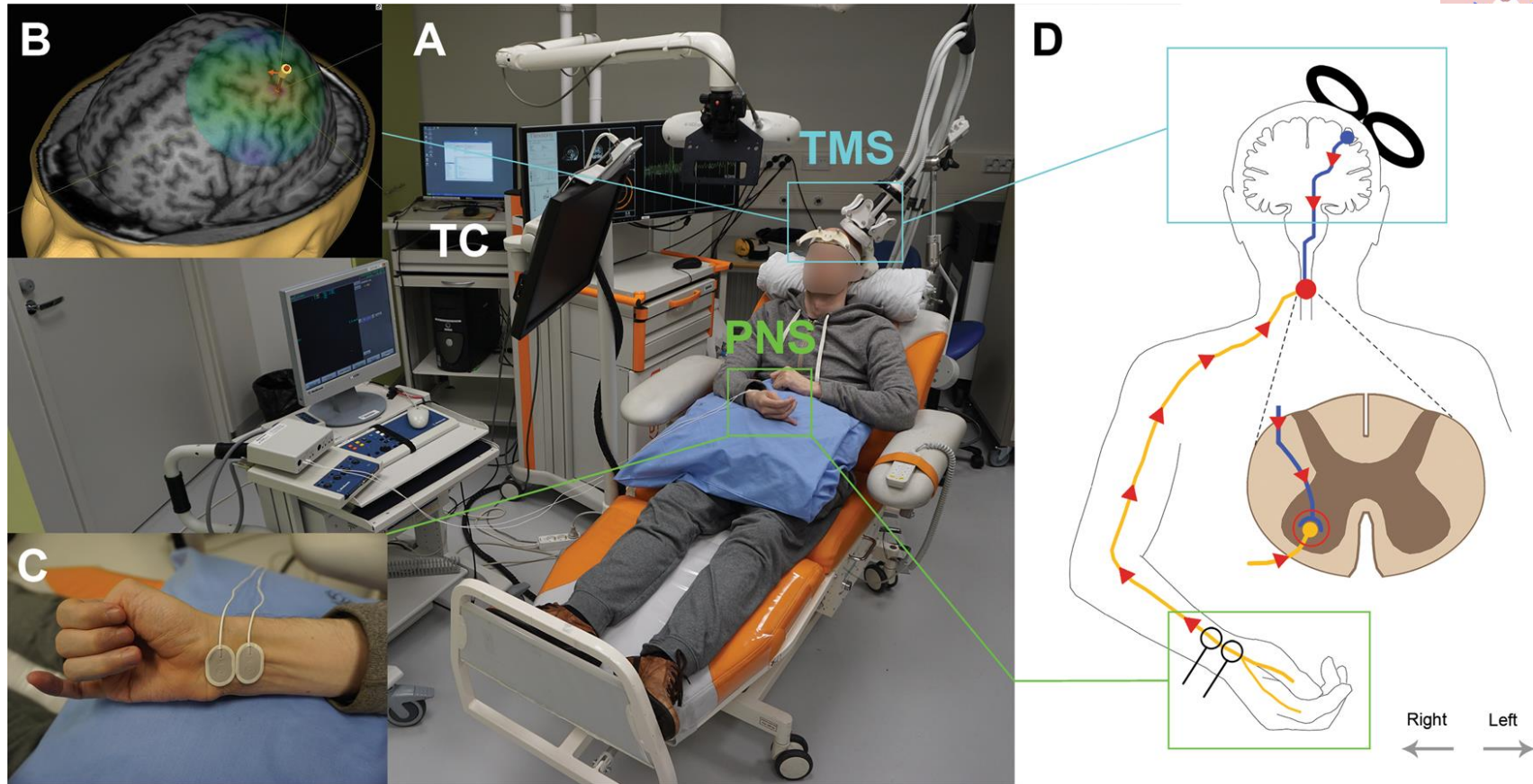
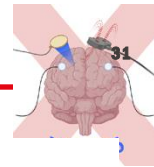


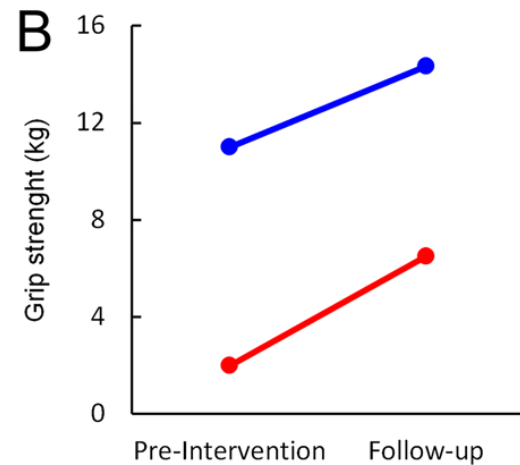
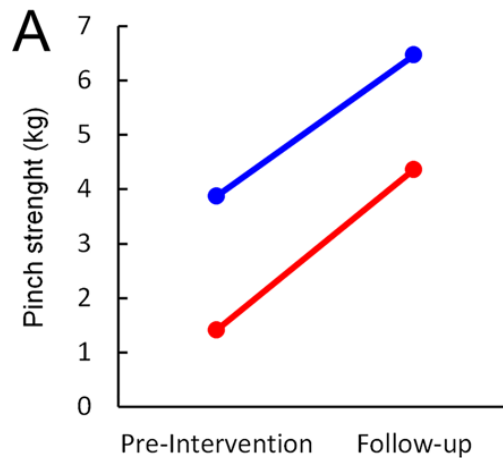
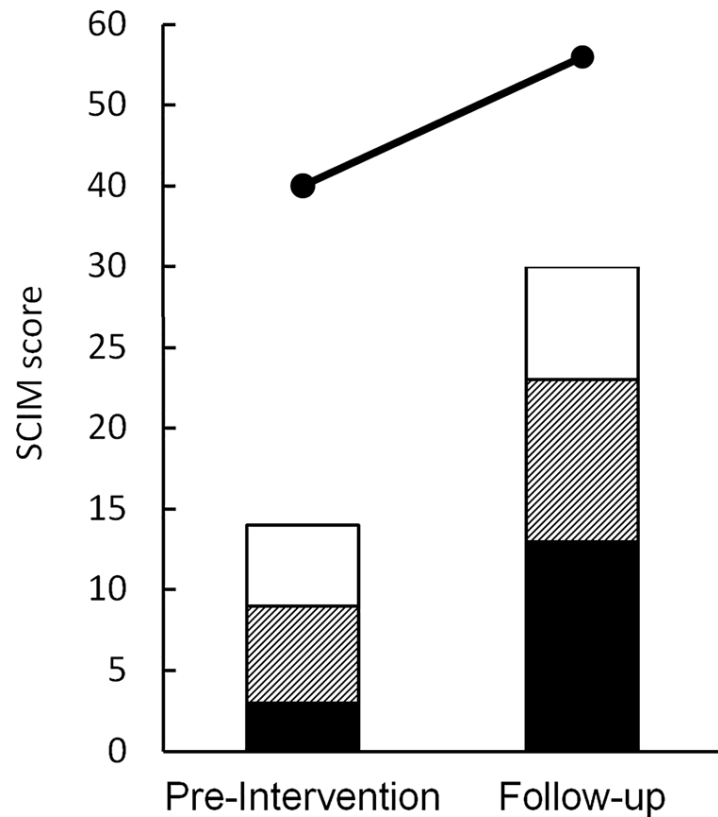
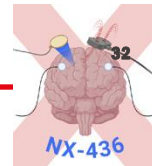
within-system PAS

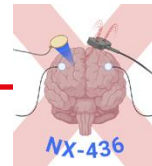


cross-systems PAS

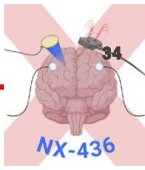




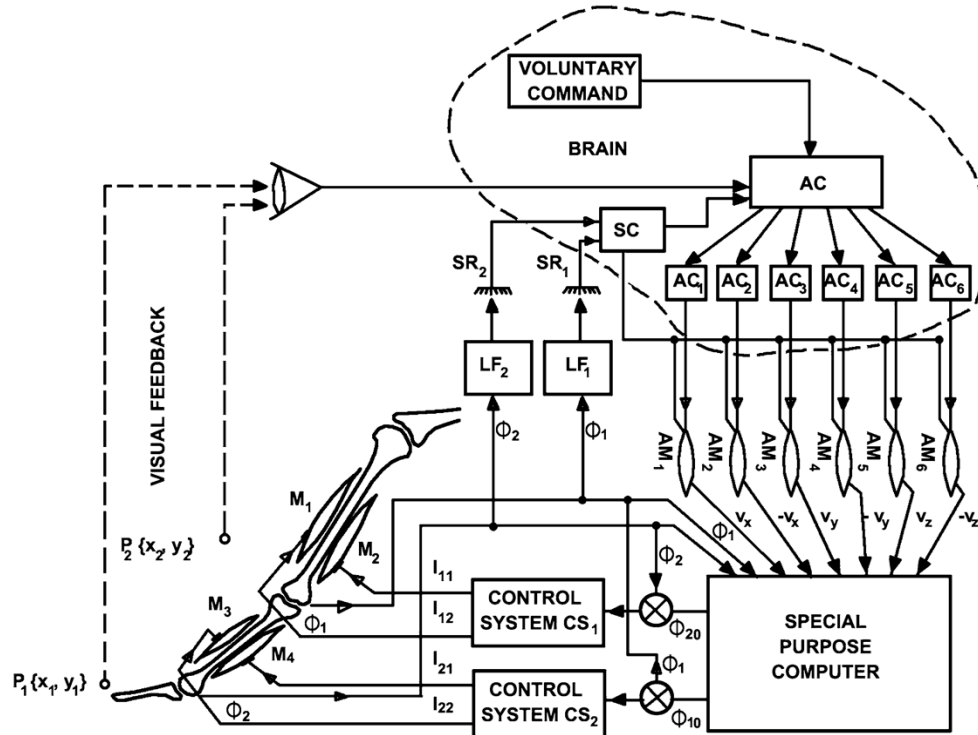


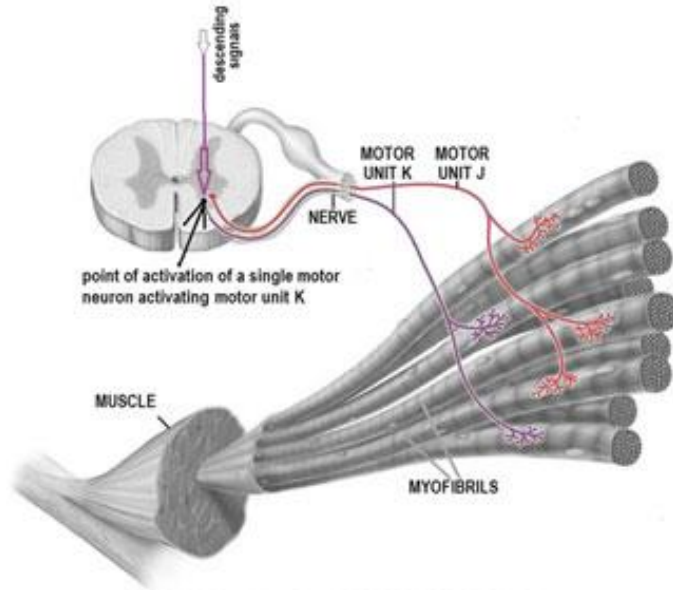


- Based on principles of Hebbian plasticity paired associative stimulation (PAS) allows to modulate cortical processing, plasticity and activity by peripheral stimulation
- Possible within and between domains

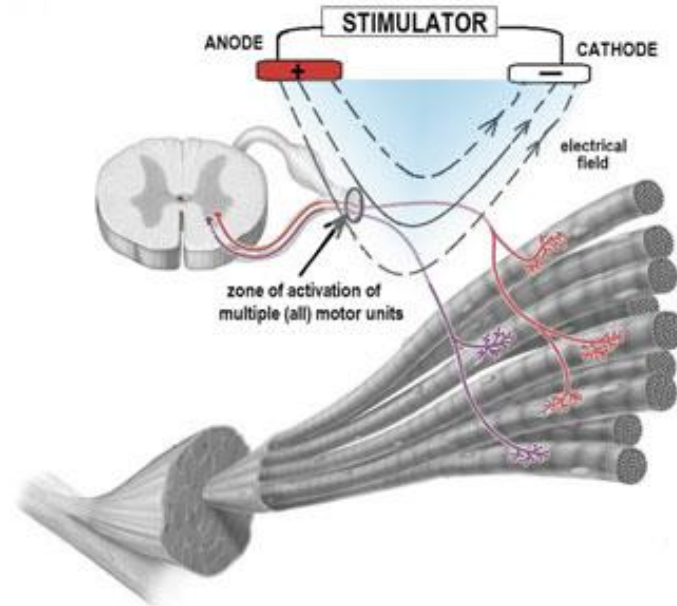


Functional Electrical Stimulation (FES)

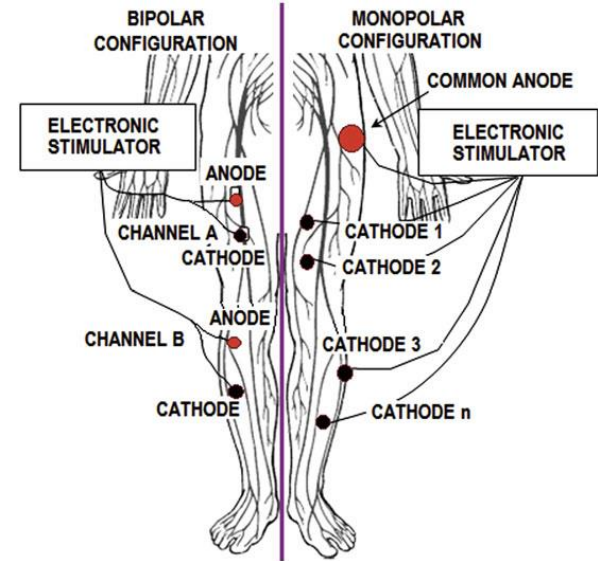
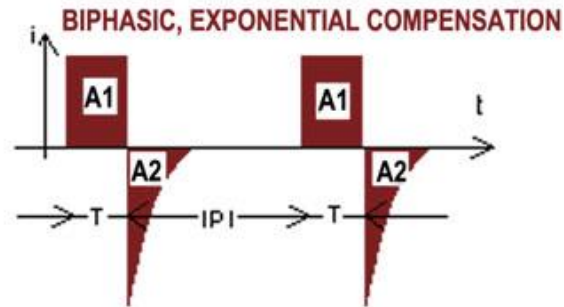
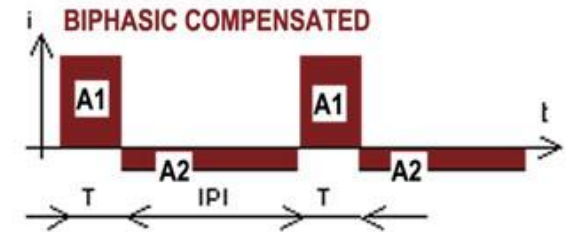
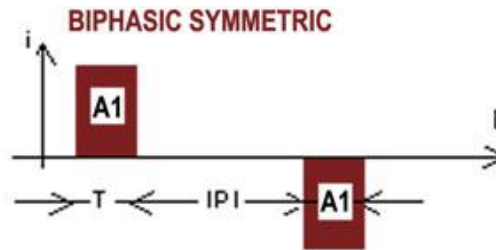
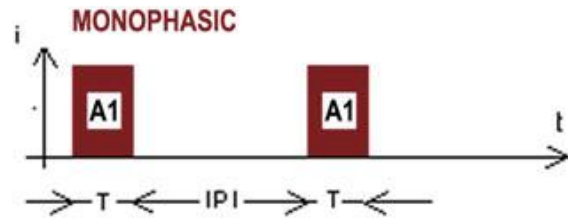


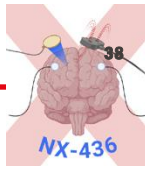


NATURAL ACTIVATION OF A MUSCLE

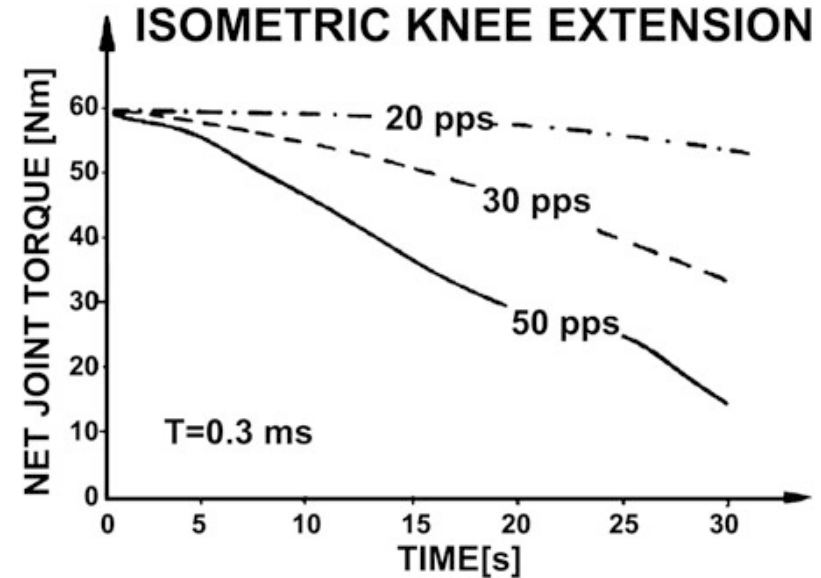
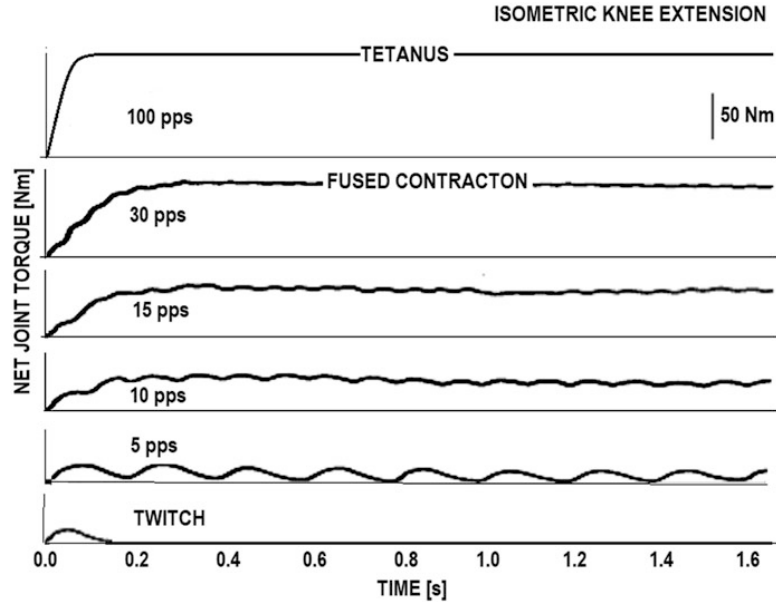


FES ACTIVATION OF A MUSCLE

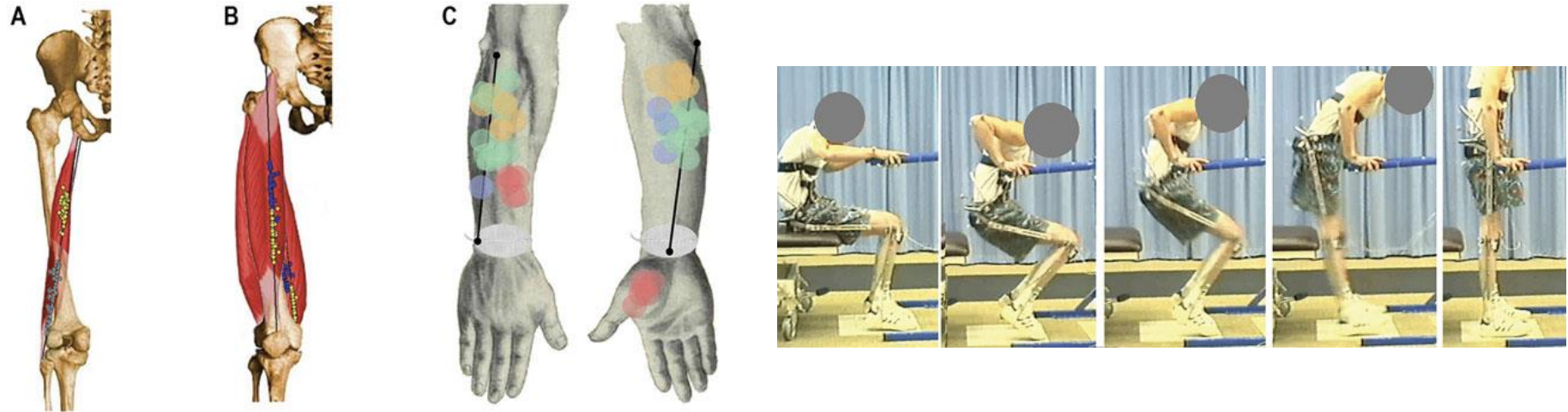


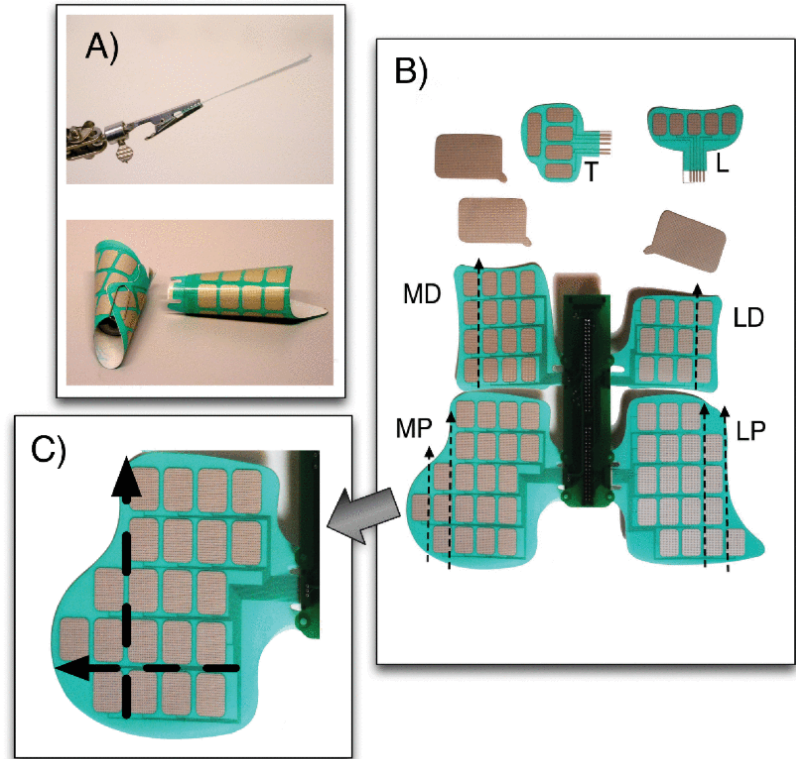
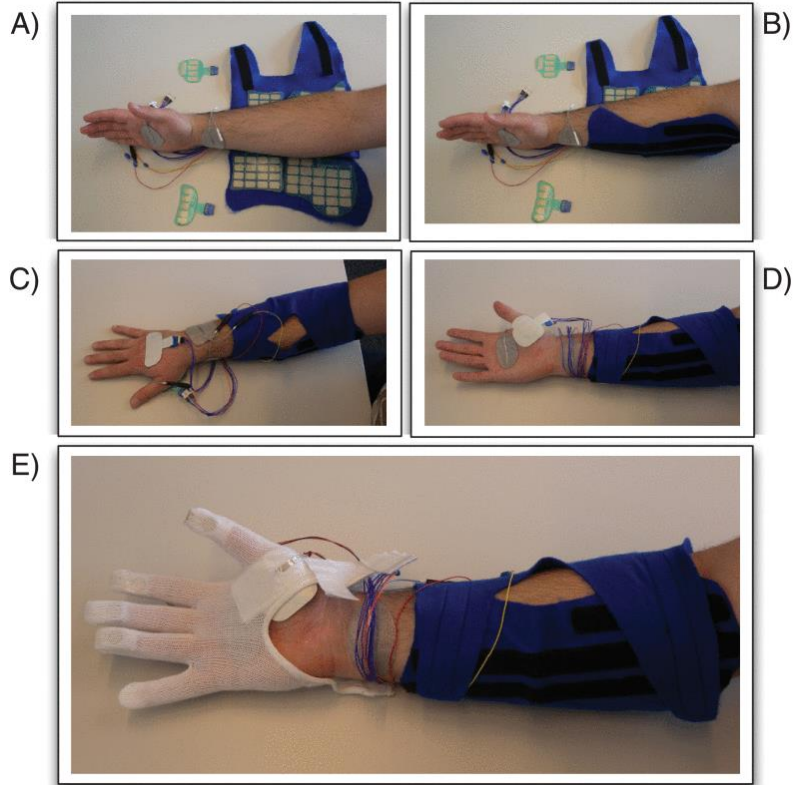
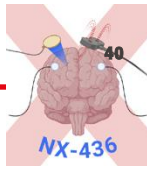


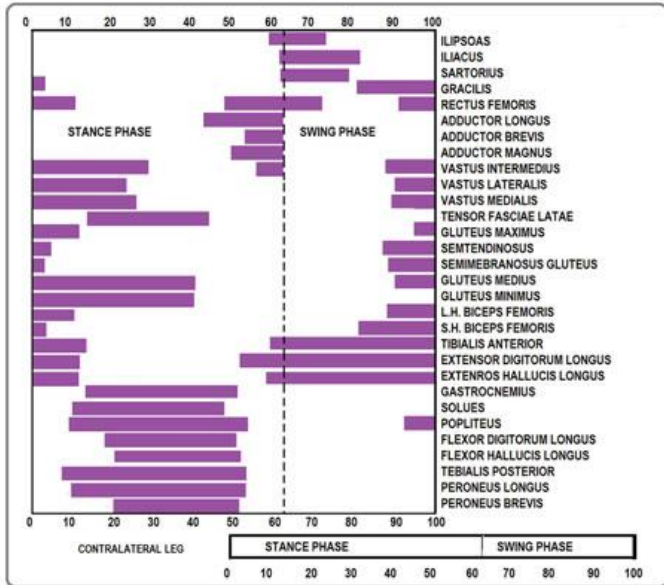
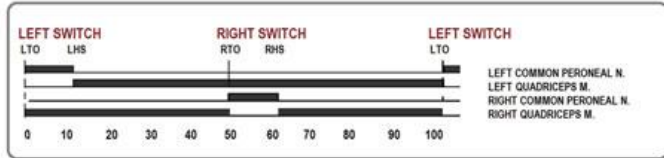
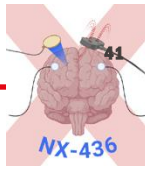
The normalized force to the maximum isometric force at various FES frequencies



The normalized force to the maximum isometric force at various FES frequencies



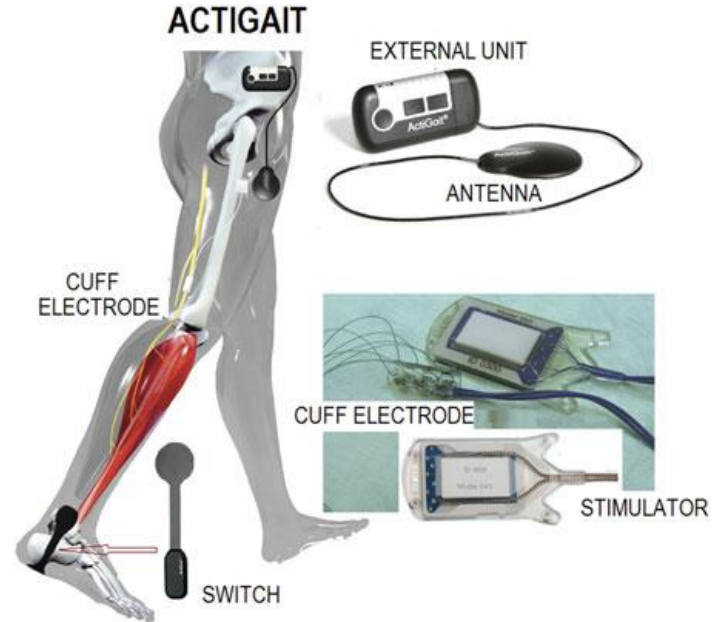


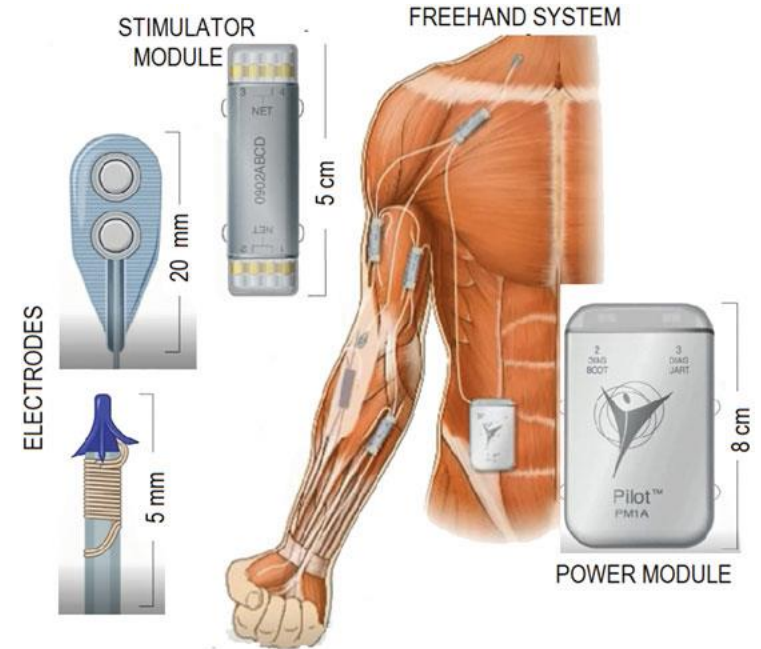
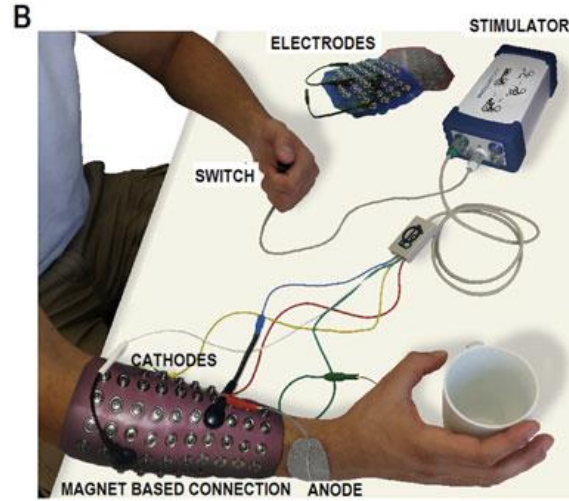


FOUR-CHANNEL FES (SURFACE ELECTRODES)
ASSISTING THE STANCE AND THE SWING

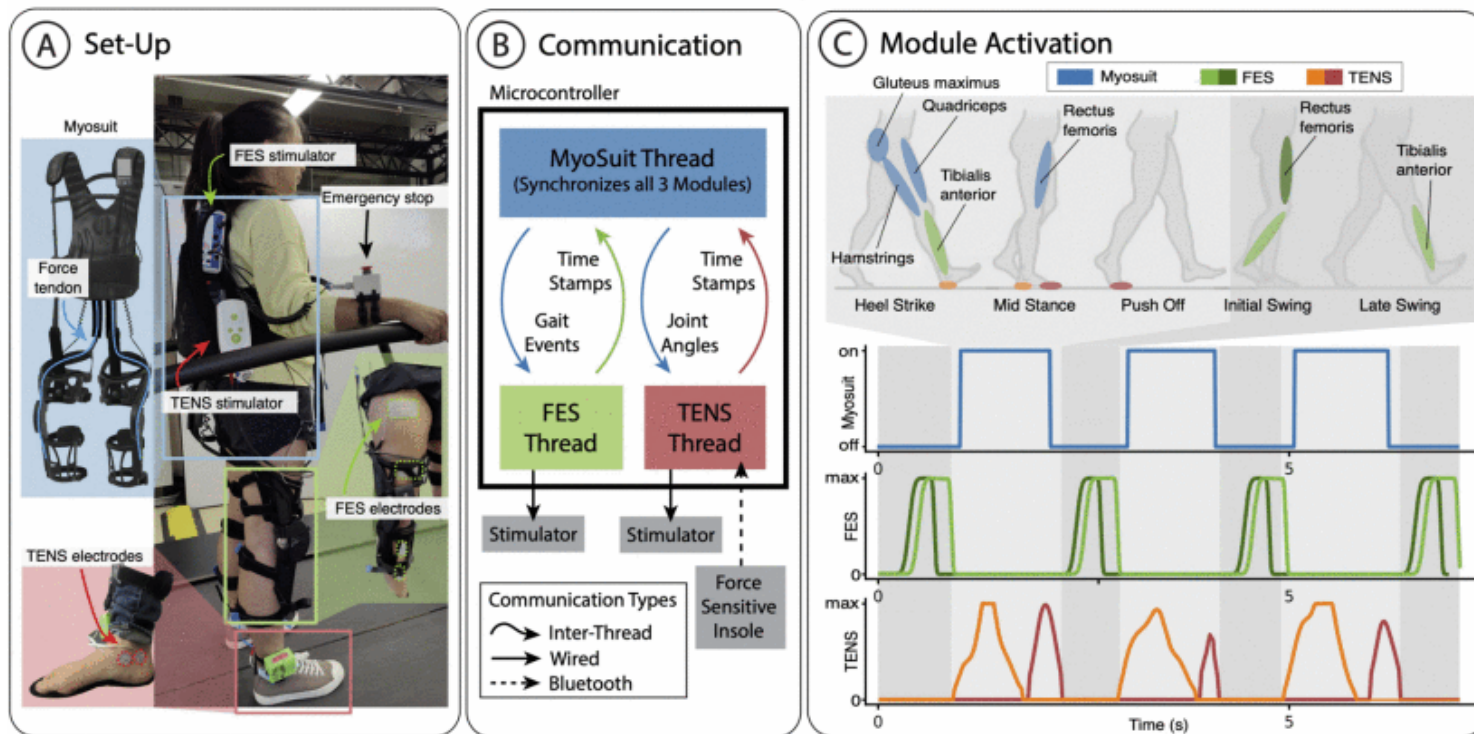


16-CHANNEL FES WITH 64 IMPLANTED
ELECTRODES ASSISTING THE GAIT

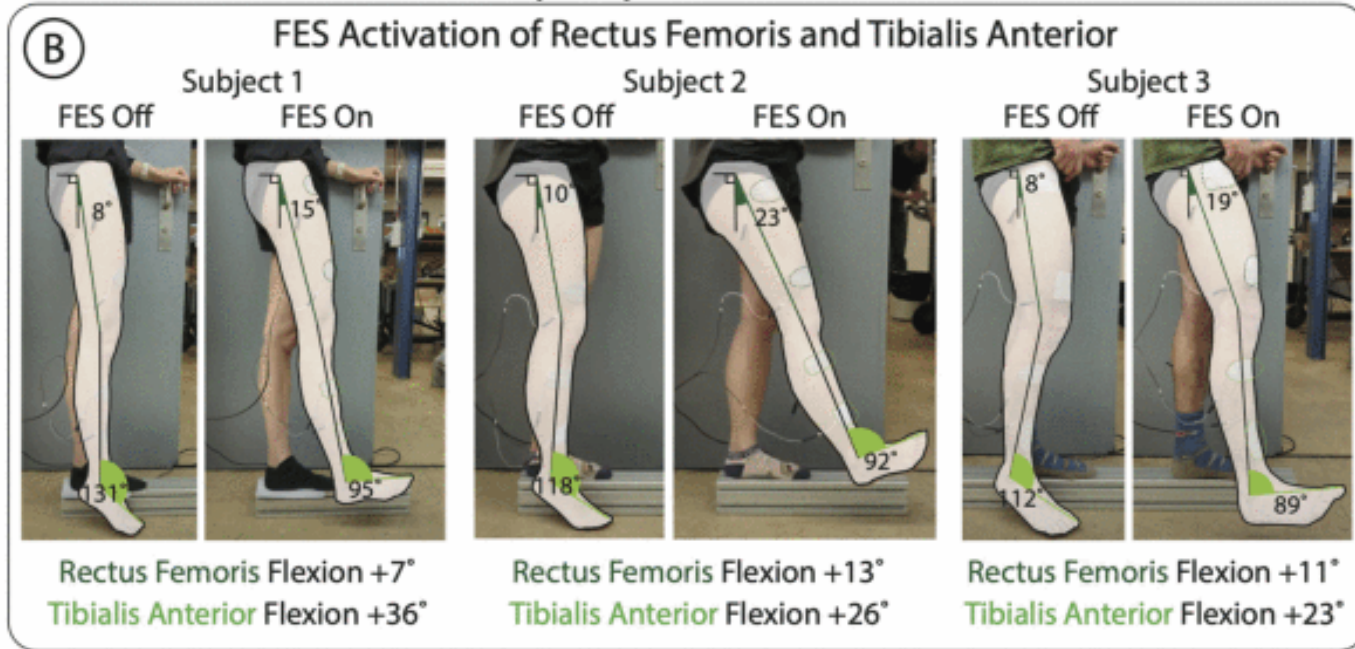
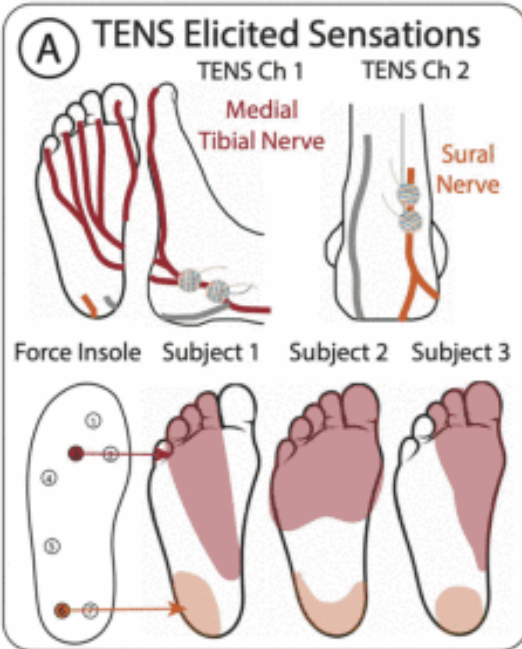


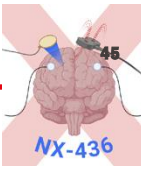


REINFORCE System

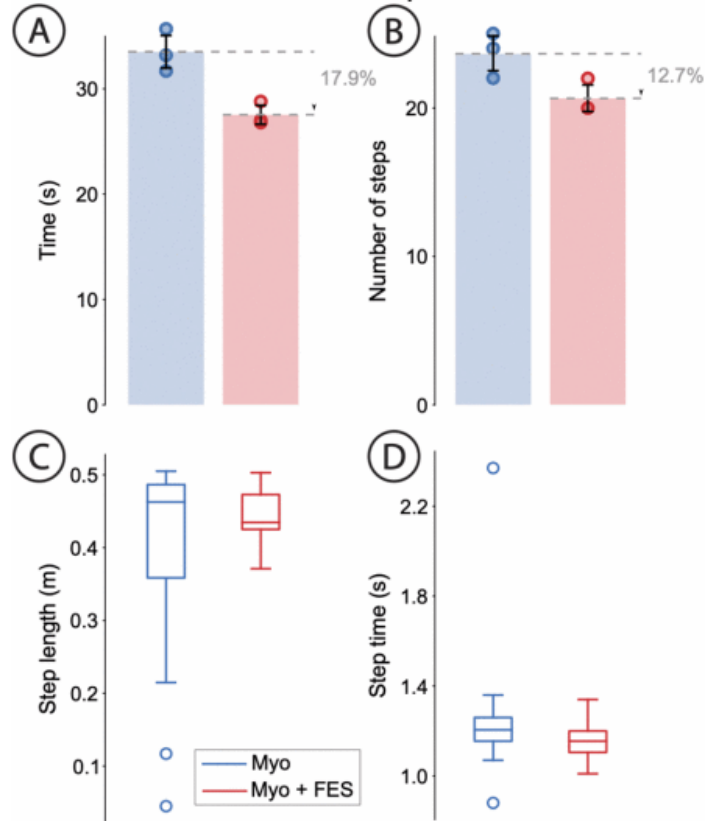


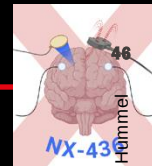
Module Tests in Healthy Subjects



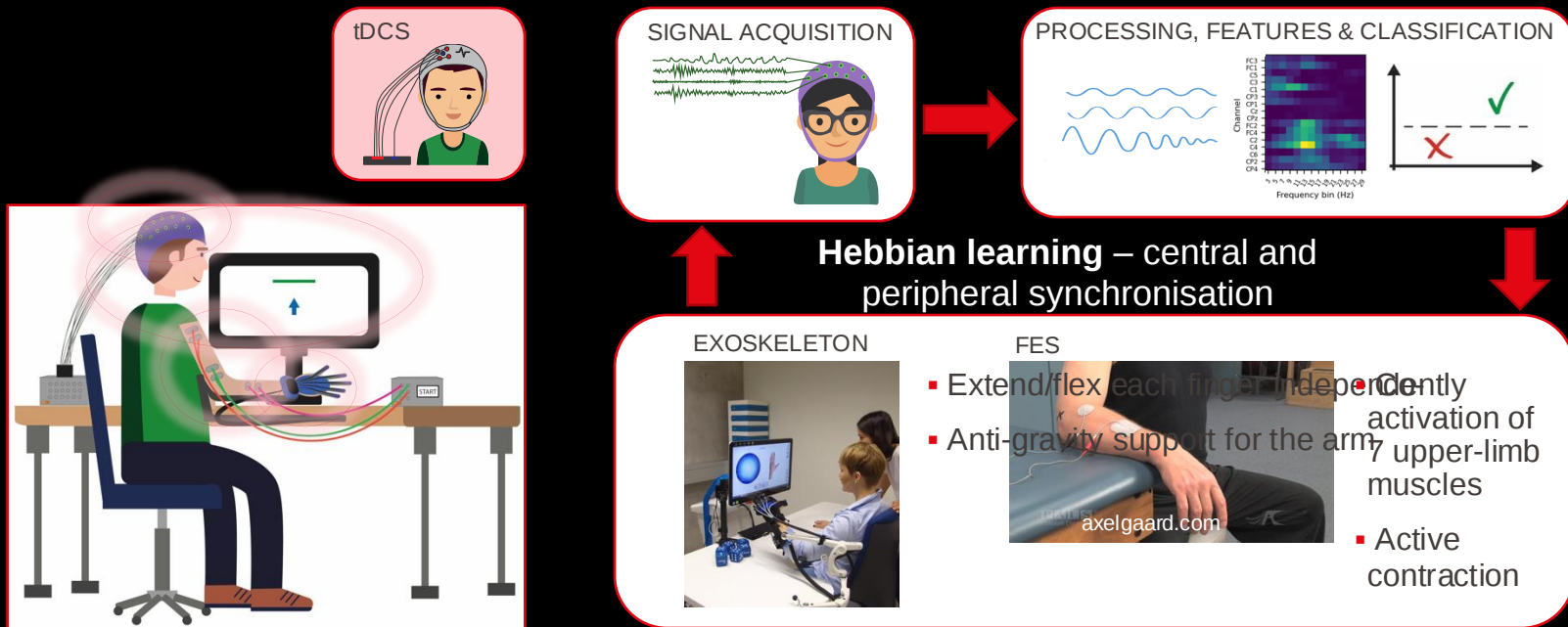


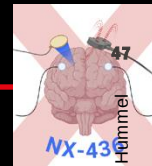
10MWT with MS patient



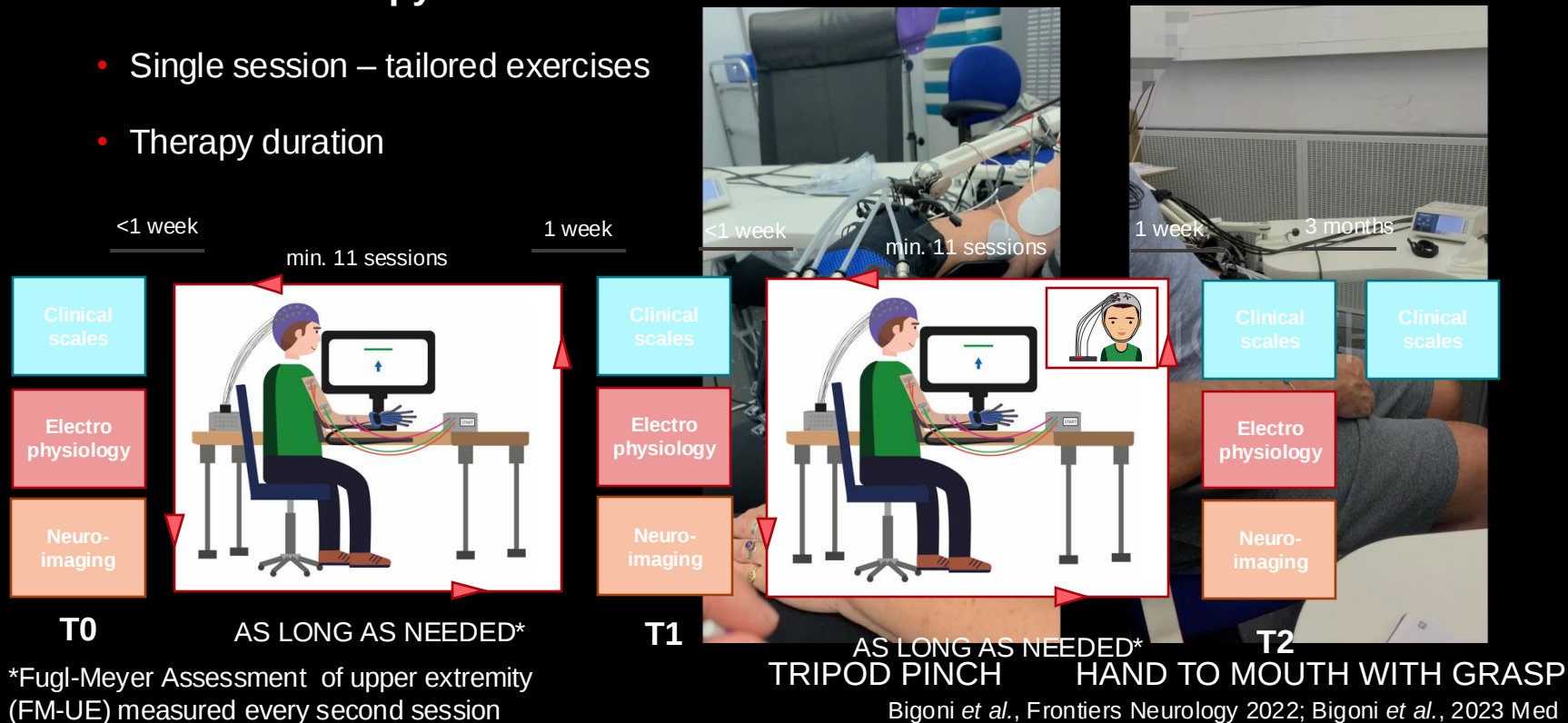


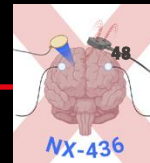
- Combination of neurotechnologies given in hierarchical manner:
 - hand exoskeleton, functional electrical stimulation (FES), brain-computer interface (BCI)
 - Anodal transcranial direct current stimulation (tDCS) to motor cortex lesioned hemisphere



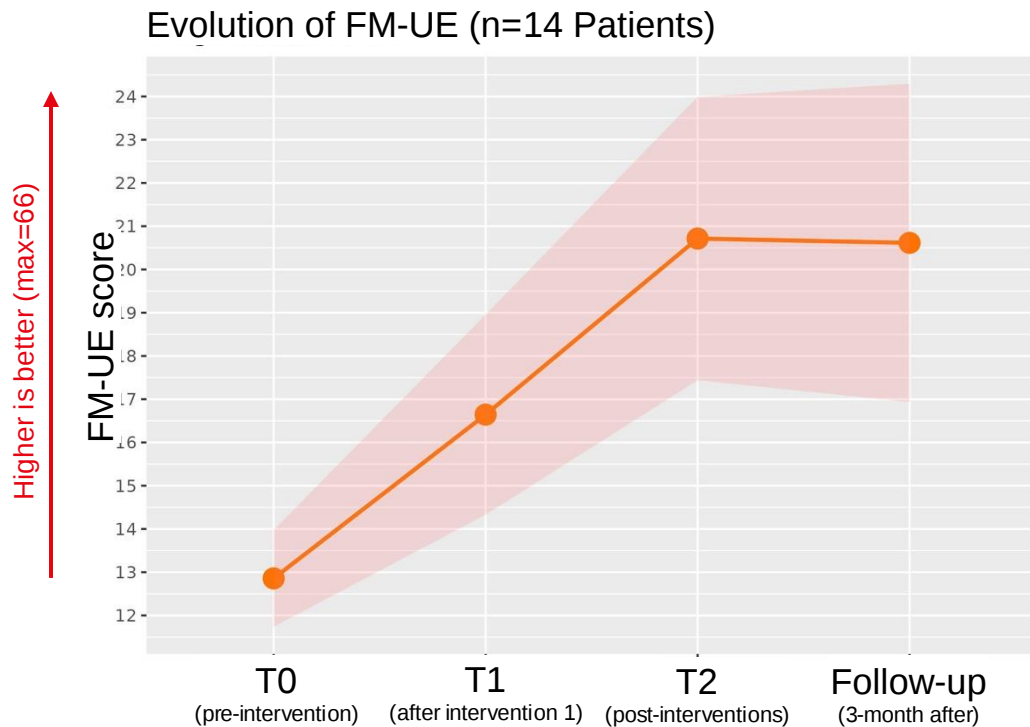


- Combination of neurotechnologies given in hierarchical manner
- Personalized-therapy:
 - Single session – tailored exercises
 - Therapy duration

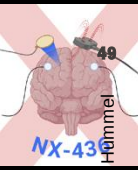




Primary outcome – reduction of motor impairment

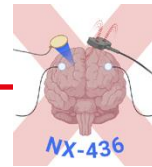


- Primary outcome met
- Average increase of **7.8 points**
- Max increase = **30 points**
- $FM-UE_{T2} > FM-UE_{T0}$
- $FM-UE_{Follow-up} \sim FM-UE_{T2}$
→ **improvement retained**

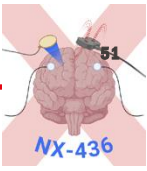


Primary outcome – reduction of motor impairment

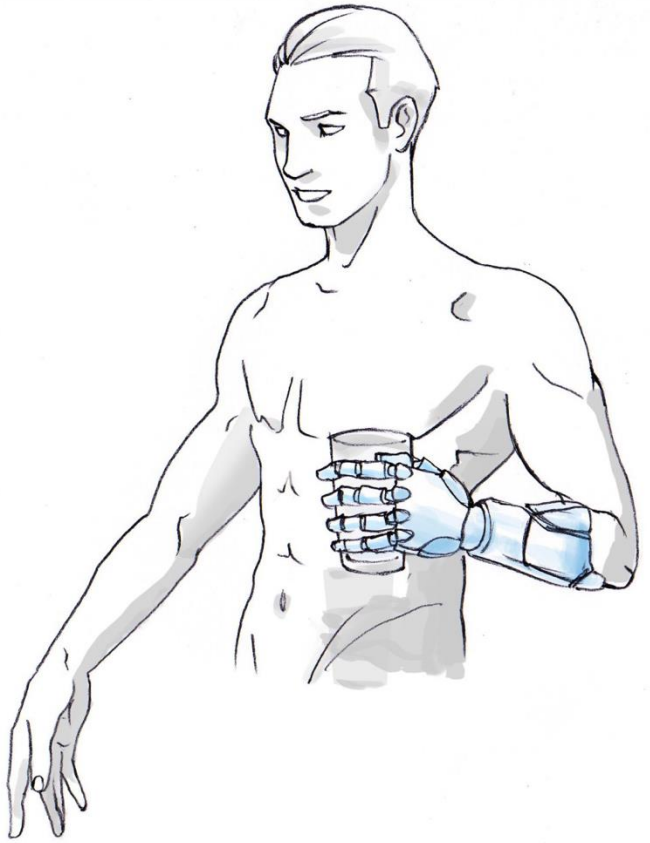




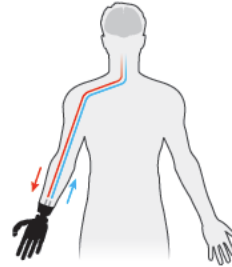
- FES allows to stimulate peripheral muscles to induce functional movements
- Applications range from single to multiple electrode arrays
- Applications in clinical conditions, e.g., to enhance stroke recovery
- Well-suited to be combined to other neurotechnologies, e.g. BCI



Restoration of homologous somatosensory sensations in upper limb amputees

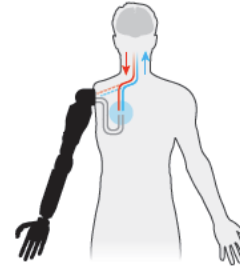


Real-time, and **natural** feedback from the **hand prosthesis** to the user is essential in order to enhance the control and functional impact of prosthetic hands in daily activities, prompting their full acceptance by the users



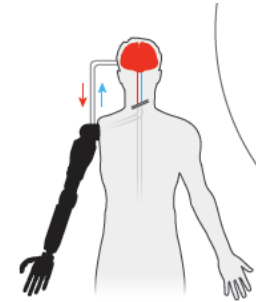
Use the remaining nerves

Electrical leads from the prosthetic's sensors stimulate nerves in the person's stump that once served the real limb.



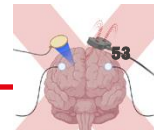
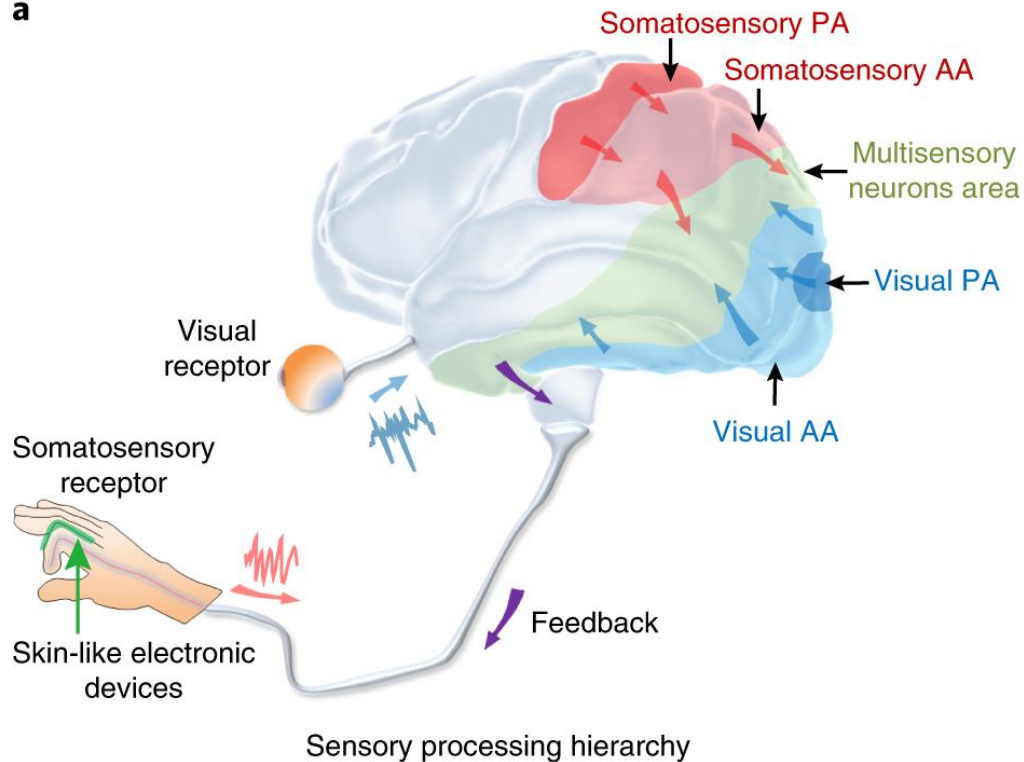
Move the nerves

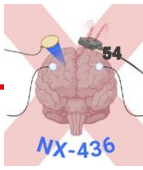
Re-routed nerves grow new endings into muscle and skin, where external devices translate signals going to and from the prosthesis.



Stimulate the brain

Sensory signals are routed around a severed spinal cord and into the brain, where they produce sensations by direct stimulation of the cortex.

**a**



Restoration of sensory feedback

Amputee Feels with Bionic Hand

A prosthetic arm enhanced with sensors making it possible to feel by relaying information directly into the nervous system. The sensory feedback technology was tested on a patient in Rome.

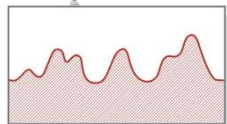
Visual and auditory devices worn for undivided attention on touch sensations.

Sensors

Prosthetic hand enhanced with sensors that detect information about touch.

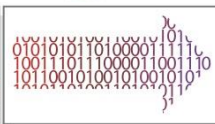
Electrodes

Electrodes implanted directly into nerves in the upper arm.



Electrical signal from sensors

This electrical signal is too coarse to be understood by the nervous system.



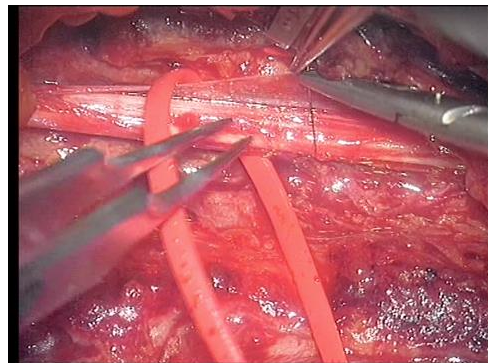
Signal Processing

Translation into a neurophysiological signal.

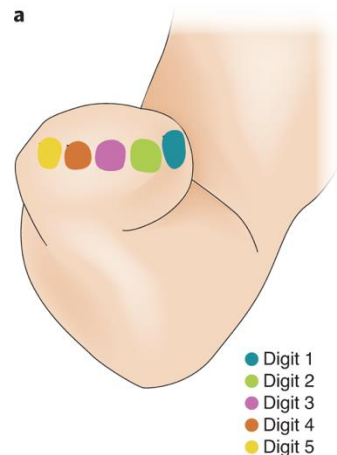


Nerve impulses

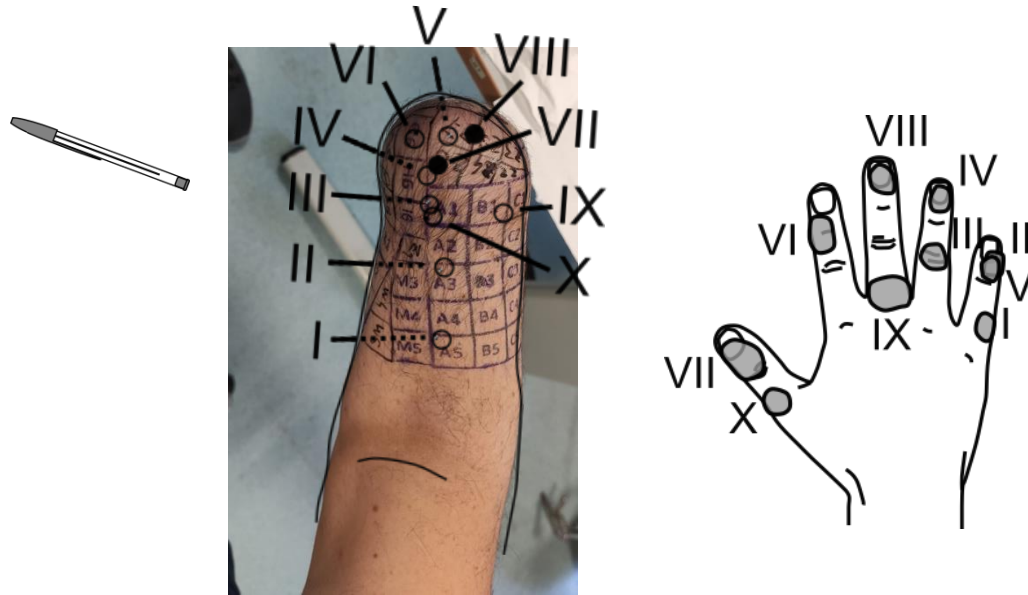
This digitally refined new signal is transmitted through electrodes directly into the nervous system.



Can we provide
phantom thermal
sensations
non-invasively?

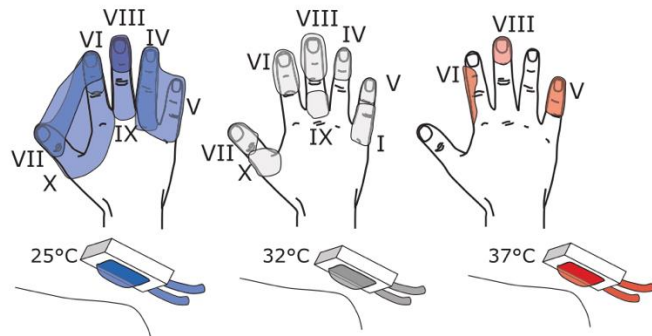


EPFL Presence of tactile phantom sensations in upper limb amputees

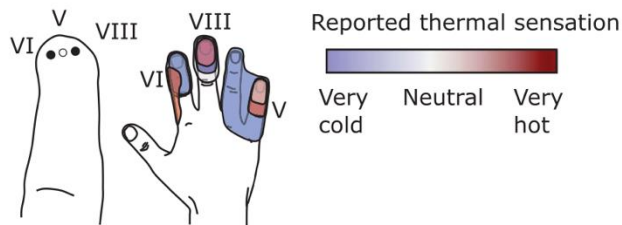


Presence of phantom thermal sensations in upper limb amputees

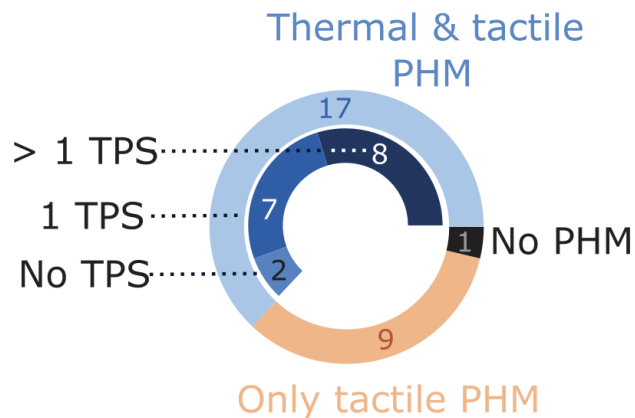
C Example of thermal phantom hand map



D Example of thermal phantom spots



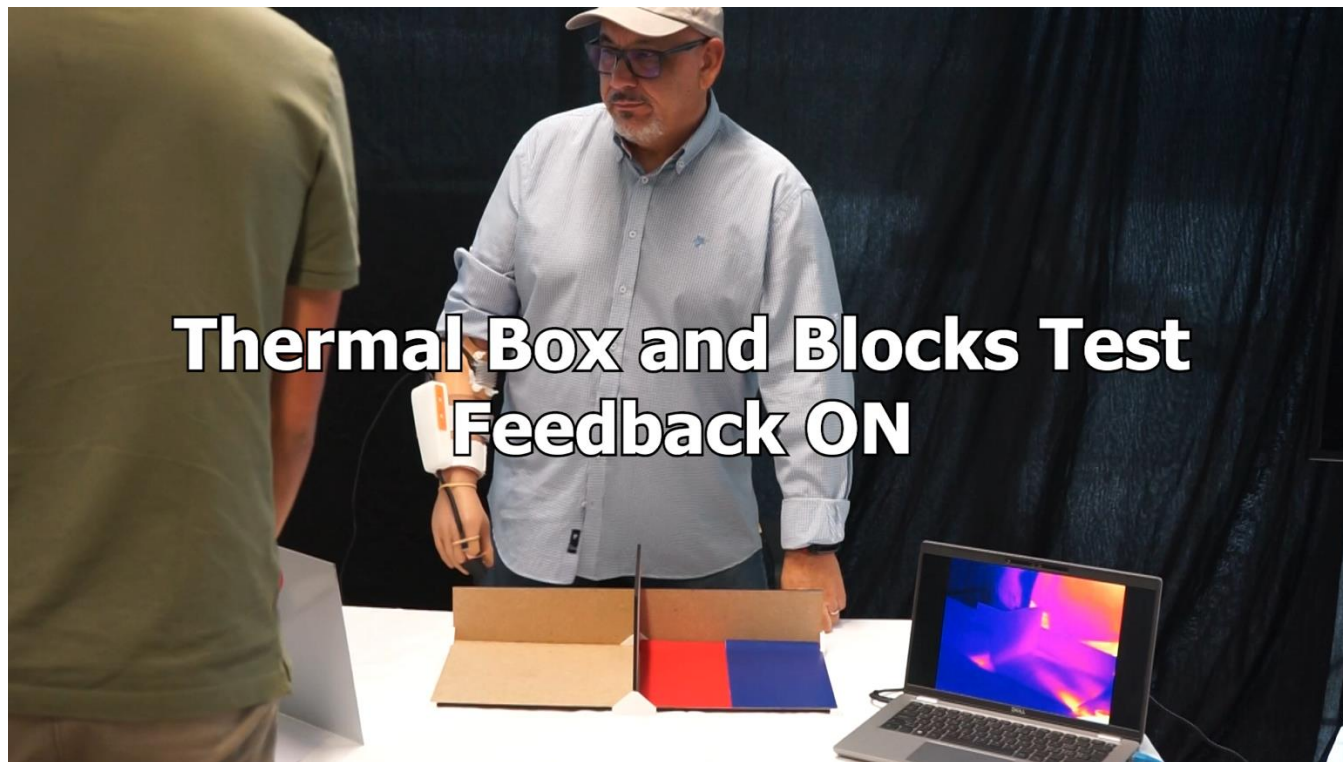
Group statistics

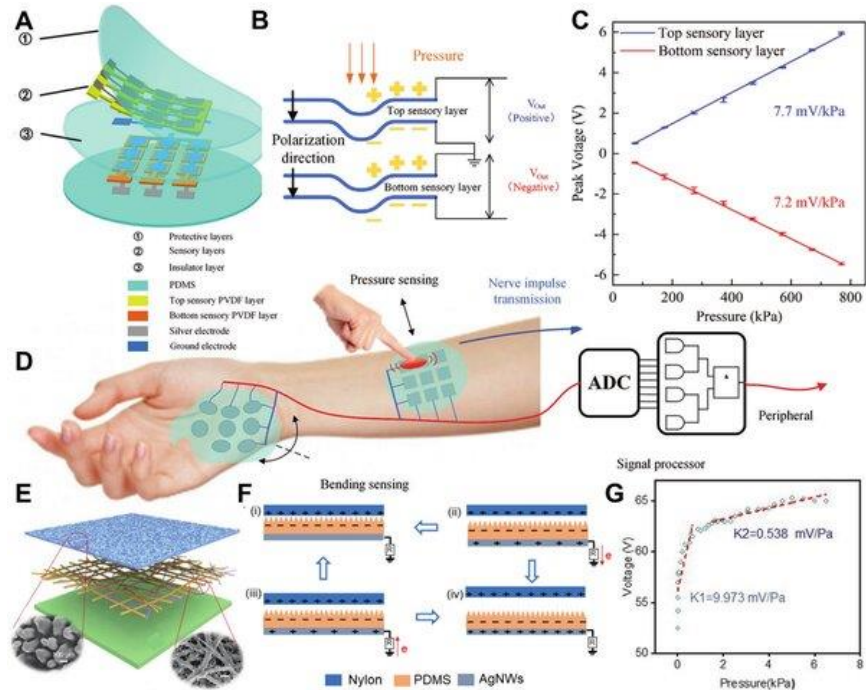


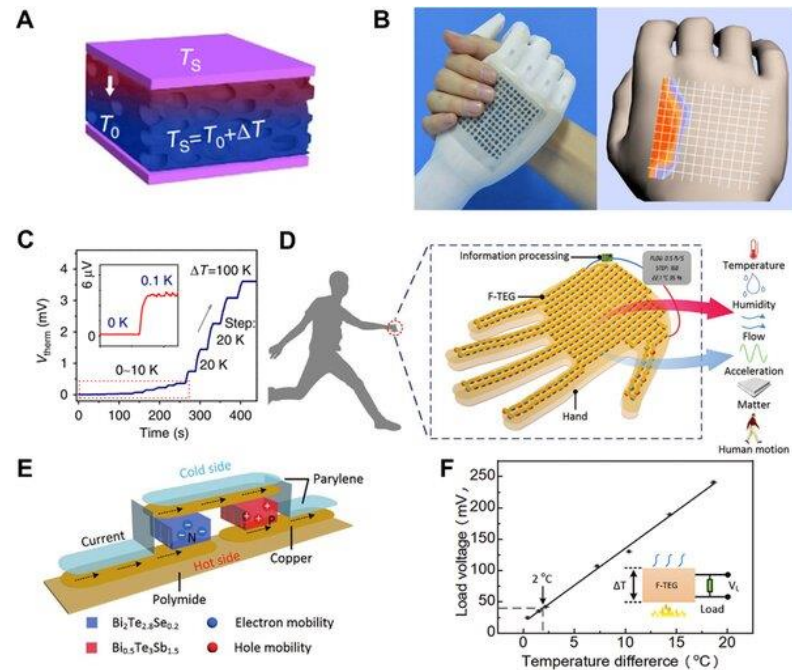
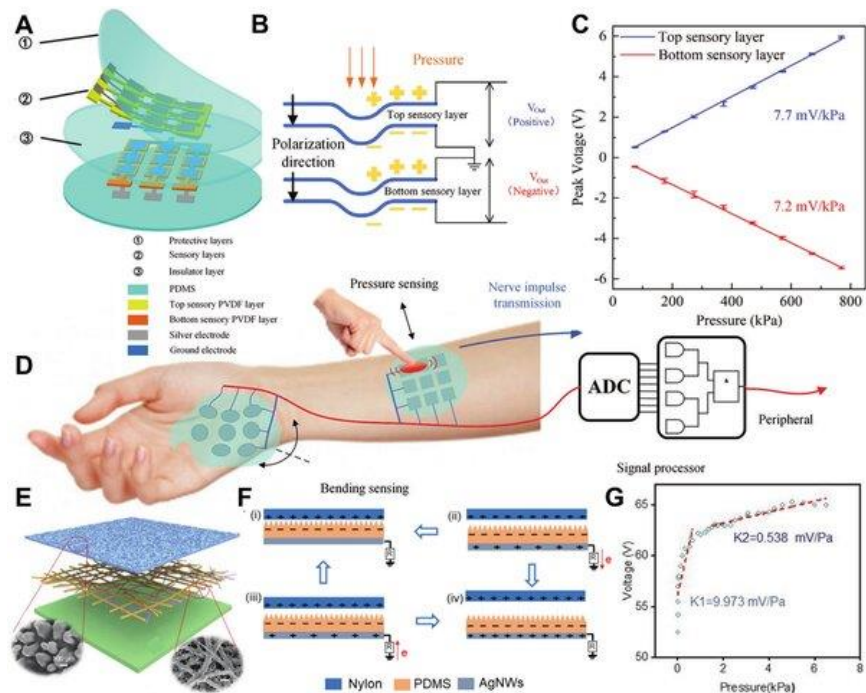
TPS: Thermal phantom spot

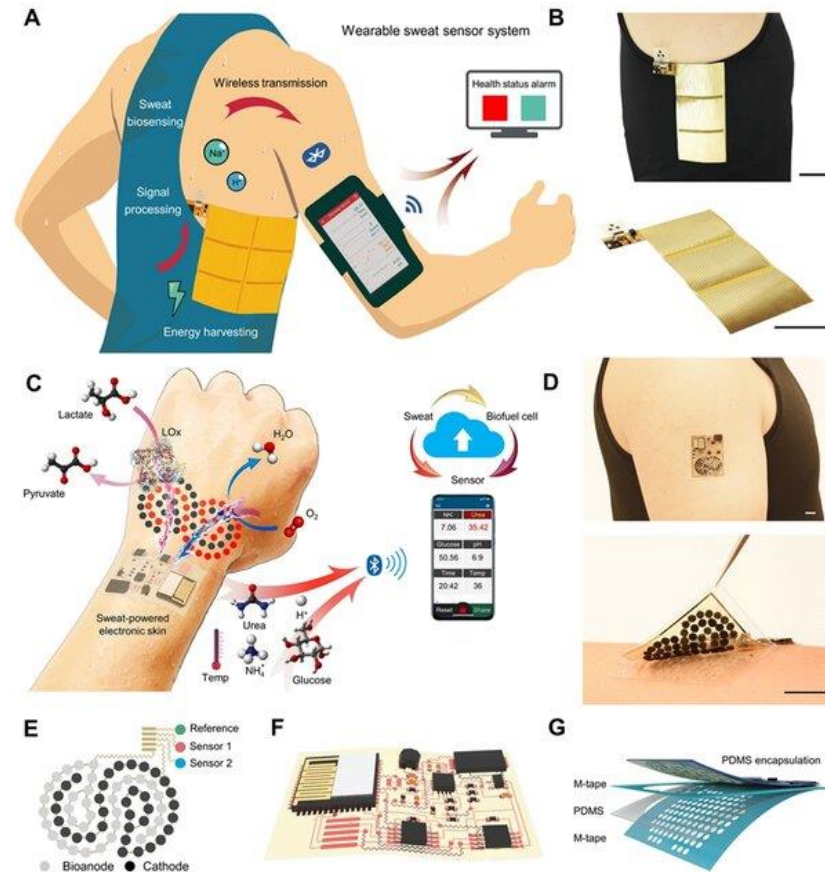
PHM: Phantom hand map

Sensory motor tasks with real-time feedback









- Peripheral nervous system represents important motor and somatosensory aspects that can be neuromodulated
 - PNS
 - PAS
 - FES
- These neurotechnologies can be applied in clinical conditions
 - e.g., to support functional recovery
 - To restore peripheral functions such as e.g. thermal sensations



Questions?