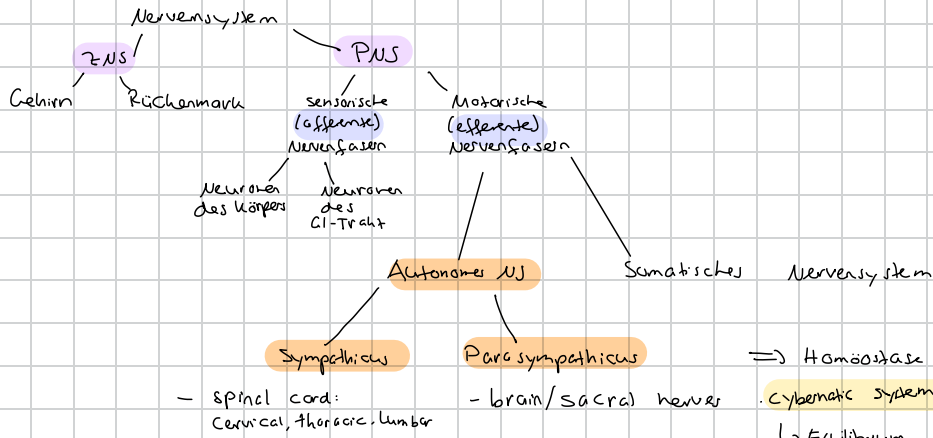


Neuroanatomie



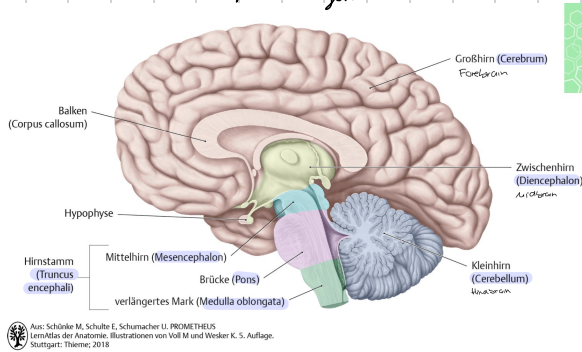
⇒ Homeostase

cybernetic system: body, thermometer, sensor

↳ Equilibrium

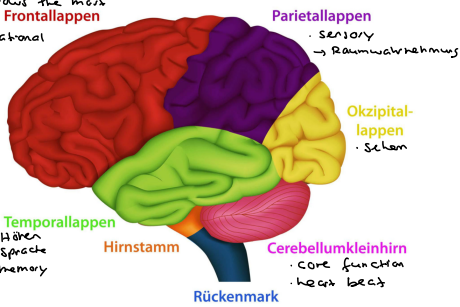
Diseases: Traumatic disorders, ADHS, Depression
↳ alarm mode
↳ sympathicus

CNS: brain + spinal cord
less likely to regenerate



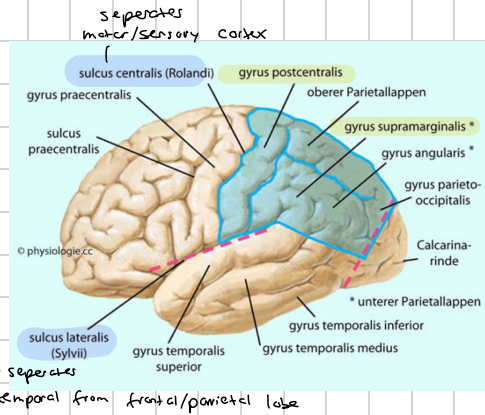
Orientation in the cortex

- OP für Elektroden
- Motorik, Persönlichkeit
- ↳ makes human: cognition
- ↳ grows the most
- Frontallappen**
- = rational

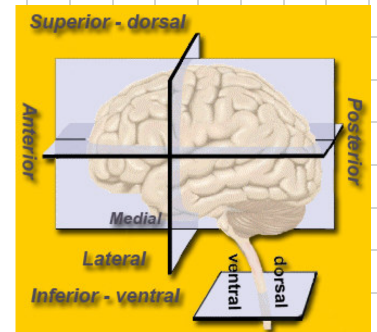


Spektrum der Wissenschaft

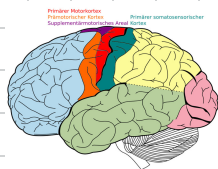
higher cognitive functions
primary motor cortex



= separates
temporal from frontal/parietal lobe



Sensorimotor cortex



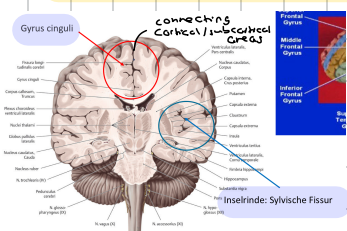
Somato-sensory functions:

- Pain perception

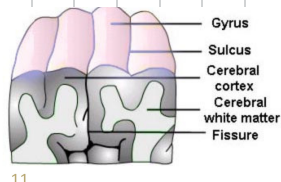
Somato-motor function

- voluntary motor function of the musculature

Structure of the cortex



Structure of the cerebral cortex



Grey matter: cell body (neuron)

White matter: Fibre connections (axon)

I. Molecular layer

II. External granular layer

III. External pyramidal layer

IV. Internal granular layer

V. Internal pyramidal layer

VI. Multiform layer

Gyrus cinguli: limbic system, psychomotoric function

Subcortical structure

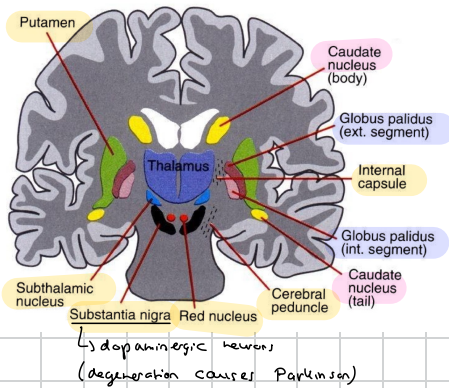
Basal ganglia: Areas of grey matter in the white matter below the cerebral hemisphere

Function: - coordination of movements

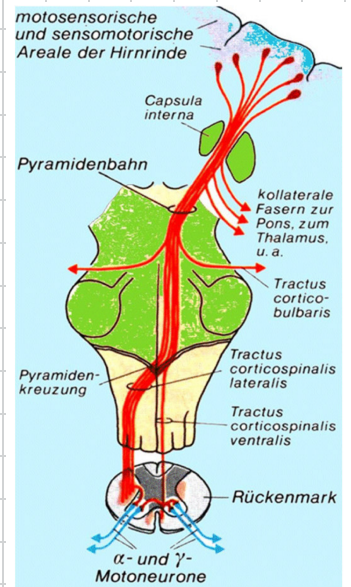
- synchronization of movement sequences with sensory information

⇒ Basal ganglia are affected in various neurological diseases

⇒ important target areas for DBS (Deep Brain Stimulation)



Thalamus: afferent filter function



Pyramid tract

main function: - activation of motor neurons for the execution of voluntary motor movements

- fine motor skills

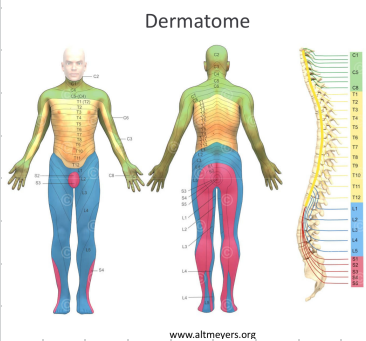
- muscle tone

Peripheral nervous system

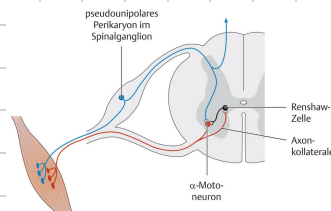
Body area split into dermatomes, distinctive of the innervating spinal nerve

Specific dermatomal problem

↳ indicate injury in the associated vertebral region



Interface central

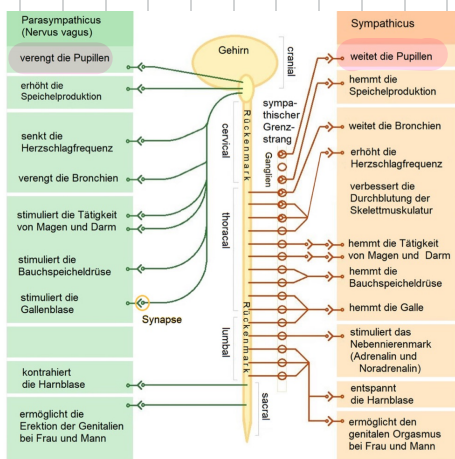


↳ influence the spinal reflex with thoughts

Autonomic nervous system

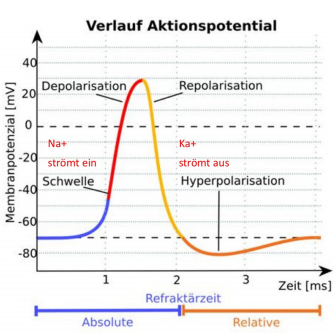
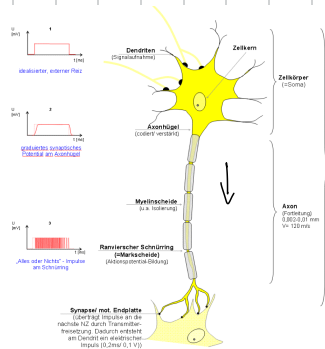
Function: - maintain vital functions (heart beat, respiration, digestion, metabolism)

- Organs are innervated (sexual organs, endocrine/exocrine glands, vascular system (BP), pupil reaction)



Neurophysiologie

Nerve cell/Neuron



Sodium-potassium pump is the most important mechanism for the transport of ions across the cell membrane

Synapses

Chemical: Communication via neurotransmitters

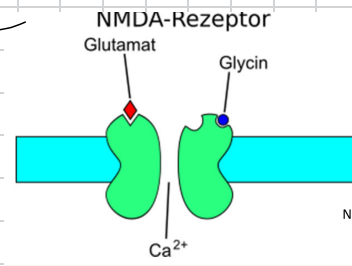
Electrical: Direct electrical communication (less common)

Neurotransmitters + receptors

- 1. PNS: Acetylcholine
- 2. CNS: - Glutamate (excitatory)
- GABA (inhibitory)
- Glycine (inhibitory)
- dopamine, noradrenaline, serotonin

Inotropic receptor:

receptor = ion channel (closed/opened by transmitters)



Metabotropic receptor:

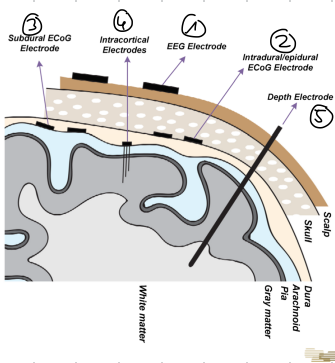
receptor activates signaling cascade in the cell on contact with a neurotransmitter (e.g. dopamine receptor D1)

Elektrophysiologie

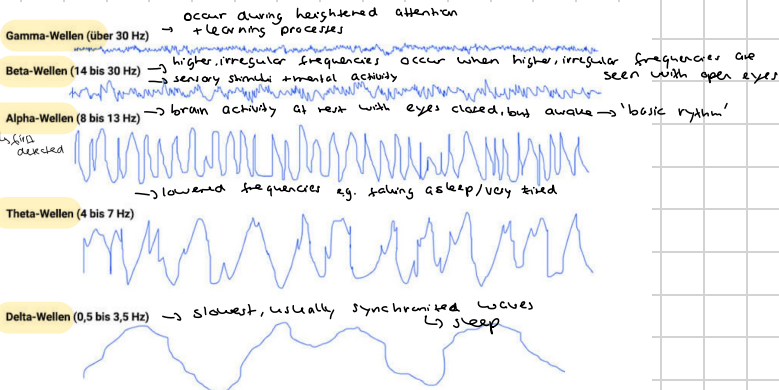
Electroencephalography EEG

- records synchronised activity of many nerve cells

Sources of the EEG signal



Waveforms in EEG



Intracranial EEG

1. detailed focus search
2. Epi or subdural
3. grid + strip electrode
4. Recording + stimulation possible
5. Mapping of relevant regions
6. Can remain for about 2 weeks

Stereotactical EEG (SEEG)

1. several deep electrodes
2. individual implantation
3. Anatomical - Clinical - electrophysiological correlation
4. frameless, frame-based or robot assisted feasible

↳ Robot-Controlled

1. Enable planning of multiple trajectories with CCT + MRI
2. shorter implantation time

Introduction to Electrophysiology

= studies electrical properties of cell and tissue in biological systems

• measures changes in voltage / current flow

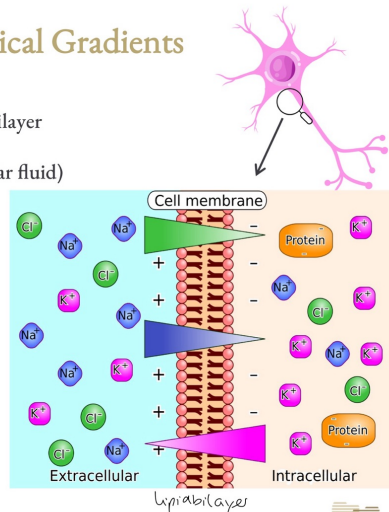
Measures of neural communication:

- Action potential
- Postsynaptic potentials
- Ion channel activity
- Neuromuscular communication:
 - Electrooculography (EOG)
 - Electromyography (EMG)
 - Electrocardiography (ECG)

Bioelectrical Principles of Neurons: Chemical Gradients

- Ions are enveloped by water and cannot easily pass the lipid bilayer plasma membrane
- Ions are unevenly distributed between the cytosol (intracellular fluid) and the extracellular fluid
- The uneven distribution of ions is actively maintained by the $\text{Na}^+\text{K}^+\text{ATPase}$ (Sodium-Potassium Pump)

Ion Type	More Abundant
Protein-Anions	Intracellular
K^+	Intracellular
Cl^-	Extracellular
Na^+	Extracellular

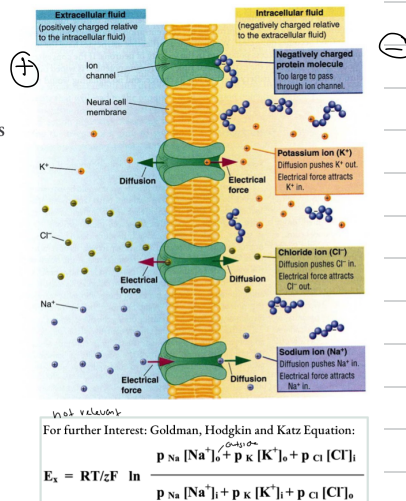


8 Neuron image adapted from <https://en.wikipedia.org/wiki/Neuron>
Image from https://en.wikipedia.org/wiki/Electrochemical_gradient

The Resting Membrane Potential

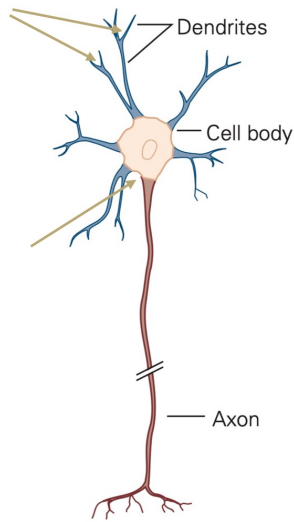
- Selective ion channels cause ion specific membrane permeabilities
- At the equilibrium potential ($\sim -70\text{mV}$) electrical and chemical gradients balance out, this means equally many ions are pushed out as are attracted in (zero net movement)
- The Resting Membrane Potential is driven by the concentration differences of the ions and the ion-specific permeability

Ion Type	Membrane Permeability for Ions*	More Abundant
Protein-Anions	No permeability	Intracellular
K^+	High permeability	Intracellular
Cl^-	High permeability	Extracellular
Na^+	Low Permeability	Extracellular



9 Image from Freberg, L. A. (2010). Discovering biological psychology. (p. 75, Fig 3.14)

input area
Postsynaptic Potentials



Action Potentials

Postsynaptic Potential (PSPs)

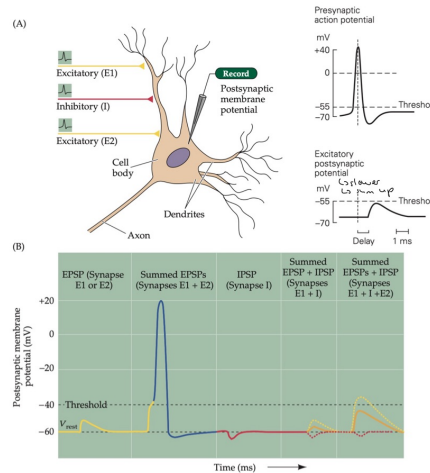
- mediated by ligand gated ion channels
- cation influx: depolarization (EPSP) $\oplus \rightarrow$ Anode
- anion influx: hyperpolarization (IPSP) $\ominus \rightarrow$ Cathode

Summation properties

- ! $\rightarrow$ 1 at a time (don't sum)
- Action potentials and Postsynaptic potentials have different temporal dynamics and therefore different summation properties

Why is this so relevant?

- Direct measure of the processes that enable interneuronal communication



14 Image from Kandel et al., (2012) Principles of Neural Science (Fifth Edition, p.185, Figure 8-8)
Bigger image from Purves et al., (2004). Neuroscience (3rd Edition, p.123, Figure 5.20)

Field Potential

= Extracellular measures of the signaling of multiple nearby neurons

- Local field potential $\Rightarrow$ well understood
- Multi unit activity

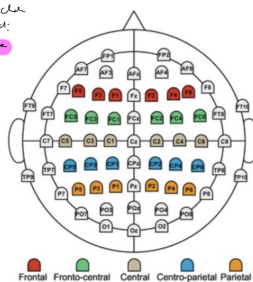
Whole brain recording

- ECOG = Electrocorticography $\rightarrow$ Electrodes are placed under the skull $\rightarrow$ Better spatial resolution due to lower volume conduction
- EEG = Electroencephalographic
- MEG = Magnetoencephalography $\rightarrow$ primarily measures tangentially oriented pyramidal neurons

EEG: What do we measure?

- EEG measures voltage differences on the scalp
 - Reference measure: between two electrodes
 - (Most often an additional ground electrode is added)

$\Rightarrow$ only measure voltage between 2 electrodes
 $\hookrightarrow$ common mode



problem with references
- e.g. Frontal relative to a lot of electrodes
 $\hookrightarrow$ can't see much
 $\hookrightarrow$ adjusted in analysis
 $\Rightarrow$ compute average reference



Dry/Wet EEG
 $\hookrightarrow$ active gel

- Hans Berger 1. human EEG 1924
- neural origin proven 1934 Edgar Adrian, Bryan Matthews

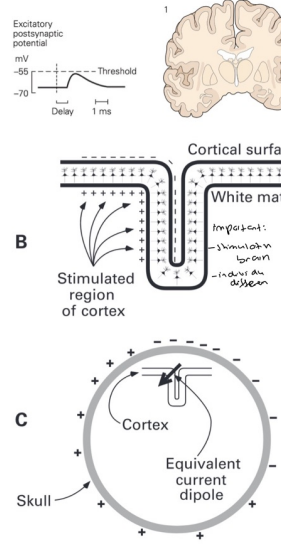
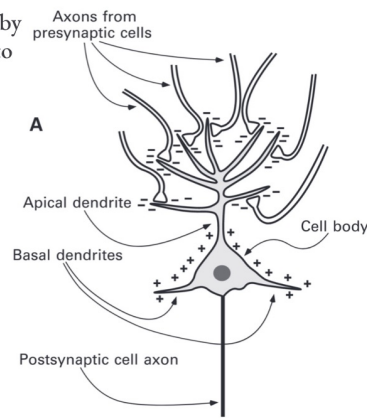
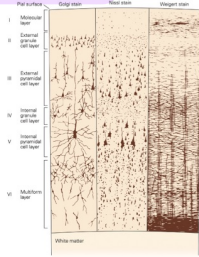
Method	Spatial Resolution	Max. Frequency	Signal Amplitude
EEG $\rightarrow$ local eye no approximation	40 mm	< 100 Hz	5 - 300 μ V
ECOG	4 mm	< 200 Hz	0.01 - 5 mV
LFP $\rightarrow$ directly in tissue local	0.4 mm	< 200 Hz	< 1 mV
Single Unit $\rightarrow$ single cells	< 0.01 mm	< 7000 Hz	~ 500 μ V

$\hookrightarrow$ the closer to the neuron, the higher frequencies can be resolved

Anatomical Origin of EEG Signals

Scalp EEG signals are heavily influenced by
PSPs of cortical pyramidal neurons due to

- Proximity (Nähe)
- Orientation
- Neuron Shape
- Synchronization



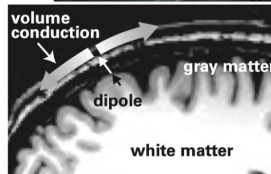
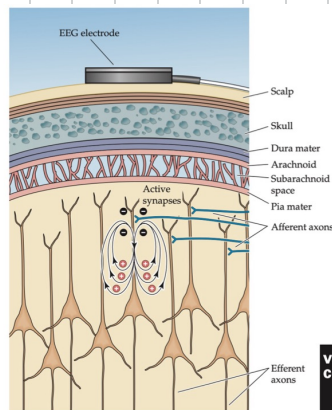
30 Lower right from Luck (2014) An introduction to the event-related potential technique (p. 41, Figure 2.2)
Lower left image adapted from Kandel et al., (2012) Principles of Neural Science (Fifth Edition, p.339, Figure 15-2)

Volume Conduction

= Leitung

- Distance between sources (pyramidal neurons) and sensors
- Voltage spreads through different tissues
- Volume conduction: **tangential voltage spread** when transitioning from skull to scalp
→ neighbouring channels are highly correlated in activity

Reason:
↳ EEG limited spatial resolution



Left image from Purves et al., (2004), Neuroscience (3rd Edition, p.669, Box C)
Right image: https://unsplash.com/de/fotos/mann-mit-stirnlampe-in-der-nacht-8GEdSc-WCg?utm_content=creditShareLink&utm_medium=referral&utm_source=unsplash
Lower right image from Cohen (2014) Analyzing neural time series data (p. 276, Figure 22.1)

Quantifying Neural Response

EEG: The recorded signal

- measure small voltage differences between electrodes
- represent **radially oriented cortical pyramidal neuron** (postsynaptic potential signaling)
- Signal = neural activity + noise:
 - muscles (jaw, teeth)
 - eye (muscle, retina movement)
 - technical sources
 - Sweat

EEG Noise: Artifacts:

- assigned to **true non-neuronal sources** = **artifacts**:
 - Topographic
 - Temporal Pattern

Event-related Potentials (ERPs) → Application: P300-Speakers

- Task relevant activity will be the same for each trial
- Averaging over trials will eliminate noise

Nomenclature

- positive + negative peak
 - ↳ Polarity
 - ↳ latency (ms) or number of occurrence

⊕ Fast, easy + low computational demand

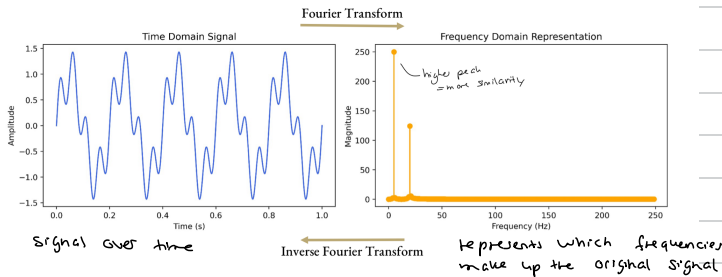
⊕ Very high temporal resolution

⊖ Trial specific information is lost

⊖ Non phase-locked information is lost

Fourier Transform

= Every signal can be decomposed into a sum of sine waves of different frequencies



⇒ 2 representation of the same signal

Neuromodulation I

Modulating the Nervous System

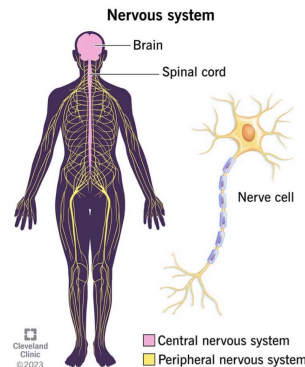
• **Signal Transduction:** How externally applied energy is transformed into a cellular signal

• **Synaptic plasticity** means that the coupling strengths between connected neurons change

• **Plastic changes** extend the duration of the effects of neuromodulation beyond the immediate time of application

3 broad target systems

- specific brain regions
- peripheral nerves + muscles
- spinal cord



Precision in Neuromodulation

! To achieve high precision in neurostimulation, two aspects matter:

1. Target Accuracy (or Sensitivity):

We can effectively activate the desired neural circuits or regions.

1. Selectivity (or Specificity)

We avoid unintended activation of surrounding or unrelated neural structures.

Why does precision matter?

- Optimizing treatment response while minimizing side effects
- Making causal inferences about the role of brain regions in cognitive, sensory or motor processes

Control in Neuromodulation

! Control here refers to our ability to bring our target system, e.g., the brain, into some state that we desire, using a 'controller', in our case, a neuromodulation system.

In general, we distinguish two kinds of control:

1. Open-loop control

e.B. Toaster → uses brain states to trigger stimulation

Our stimulation is independent of the neural effects - whatever is happening in the brain in response to the stimulation doesn't change how we stimulate.

2. Closed-loop control

Our stimulation is modulated by the effects it evokes in the brain - we change the parameters depending on the difference between the current state and the target state.

We use **feedback** from the brain to guide stimulation.

↳ Stimulation is adjusted dynamically + continuously

Most current research is **open-loop**.

Methods of Brain Modulation + Stimulation

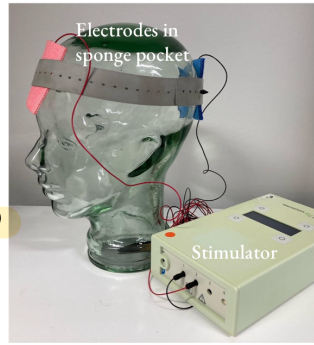
Electrical Modulation of the Cortex

- Plan:** We want to stimulate the cortex from the outside (i.e., 'noninvasively').
- Idea:**
 - Neurons react to electricity
 - We can apply a voltage gradient across a pair of electrodes on the **scalp** to induce currents in the **brain**
 - The currents should be effective, but relatively low (0.5-2mA).
not painful, damaging

This general approach is called **transcranial electrical stimulation (tES)**

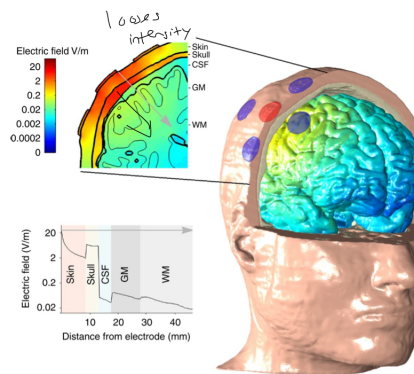
If we use **direct current (Gleichstrom)** we call the method **transcranial direct current stimulation (tDCS)**

If we use **alternating current (Wechselstrom)** we call the method **transcranial alternating current stimulation (tACS)**



The issue with the tissue

- The **conductance of scalp and skull are relatively low**, i.e., their resistances to current high
- This means we need to apply a lot of energy on the outside to get relatively little energy into the brain
- Often the **loss is one or two orders of magnitude**
- This limits the amount of current we can apply to the brain tissue, as we must avoid pain at the scalp. Currently, a maximum of 2mA is recommended.
- Depending on the montage (i.e., arrangement of electrodes), the electric field can be quite broad and unspecific, due to current spread.



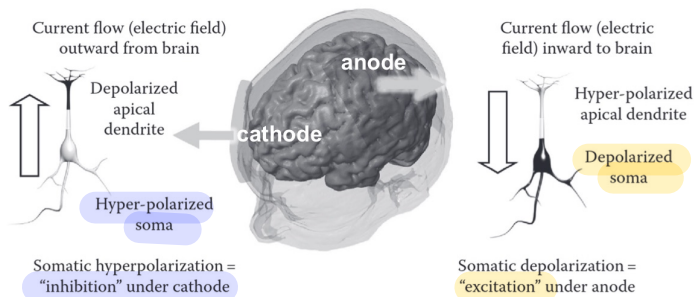
Proposed Mechanisms of tES

- change membrane potential
- Electric fields induced in the brain are sub-threshold for action potential generation (<1 V/m, more often around 0.2 V/m) *(initiator)*
- Fields either **depolarize** or **hyperpolarize** neuron populations **slightly**
- This changes their excitability
- This means we **modulate spontaneous activity**, rather than inducing it directly
- Neurons form intricate interconnected networks, so (we hope) even minor interventions could shift dynamics substantially

Somatic Doctrine of tES

= mechanism for the immediate online effects

The principle of "somatic doctrine" in basic tDCS montage design



Anode (+) depolarization of neuron soma
(and apical dendrite hyperpolarization)

Cathode (-) hyperpolarization of neuron soma
(and apical dendrite depolarization)

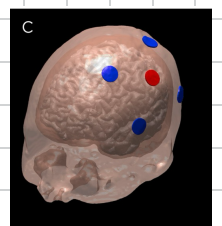
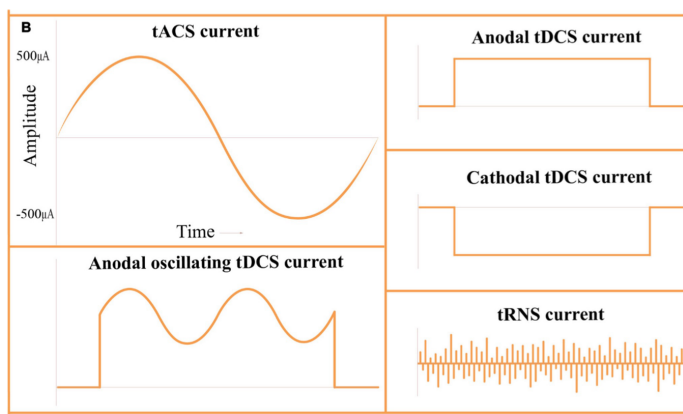


Image from Bikson et al., 2012. Cellular and Network Effects of Transcranial Direct Current Stimulation. Fig 3.3a

Montage HD-tDCS (C) uses a ring configuration to achieve better localized fields

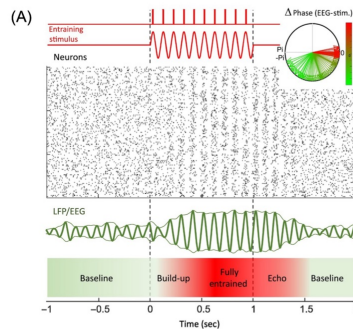
Current waveforms



21

tACS

- tACS is the use of sinusoidal alternating currents in tES
- This means neuron populations go through regular cycles of enhanced and diminished excitability (via somatic de- or hyperpolarization, respectively)
- It is assumed that this can **entrain** (mitnehmen) **frequencies** (via constructive or destructive interference as well as resonance), so that internal oscillators follow the external oscillation
- Entrainment effects have been shown in single neurons in macaques, and are stronger with higher currents (Johnson et al., 2020)



Simulated data from Handmar et al., 2019. Modulating Human Memory via Entrainment of Brain Oscillations

Role of Neural Oscillation

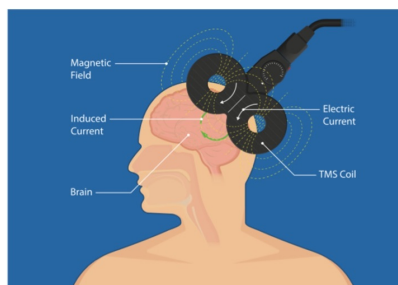
- Oscillations are implicated in a variety of functions
 - Synaptic plasticity changes at specific phases of theta oscillations in hippocampus
 - LFP oscillations modulate individual neuron firing
 - Interregional synchronization between brain areas

Current issues:

- tDCS mediated increases in cortical excitability are substantially weaker under topical anesthesia of the scalp
- Effects of tDCS could partially be mediated by peripheral nerves which are subject to much higher field strength than cortical neurons

TMS

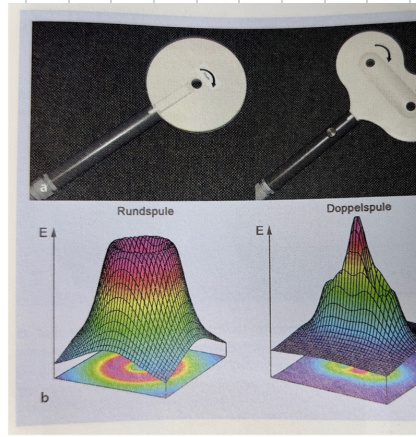
- Idea:** We want to induce action potentials in a spatially limited region of the brain.
- Problem:** Via scalp electrodes, it is not feasible to inject enough current to induce localized suprathreshold depolarizations (If we'd do that, we would have electroconvulsive treatment)
- Solution:** One can circumvent that by inducing a current via a magnetic field. Magnetic fields are barely affected by the skin or the skull. This magnetic field in turn can be generated via a charged coil.
- This allows us to induce currents strong enough to make neurons fire in a well-circumscribed part of the brain, depending on the position and geometry of the magnetic field



TMS Coils

↳ induced electrical field effects on target tissue

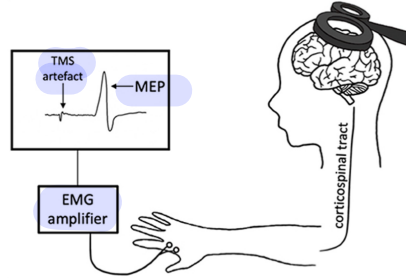
- There are round coils and figure-eight coils that produce different electrical fields:
 - The round coil produces an electrical field that is strongest in a ring shape concentric to the coil center, in the center, the field is zero
 - The figure-eight coil produces electrical fields that overlap only in a small area directly under the center of the coil
 - When using the figure-eight coil with low intensity, only the small part of the overlap between the electrical fields will be strong enough to alter neural activity allowing for **high spatial precision** neuromodulation



Measure of TMS response

In the motor domain, it is easy to see a direct measure of the effect of our stimulation, so called **motor evoked potentials (MEPs)**.

- MEPs measure the **excitability and connectivity** of the motor pathways during TMS.
- They are recorded using electromyography (EMG) after TMS pulses activate motor neurons.
- MEP size reflects cortical and spinal cord responsiveness to TMS stimulation.



MEPs can be used to individualize stimulation strength, e.g. by defining the resting motor threshold (e.g., the intensity needed to achieve a MEP above $50\mu V$ in 50% of trials)

MEPs can also be used as readout of cortical excitability

Repetitive TMS (rTMS)

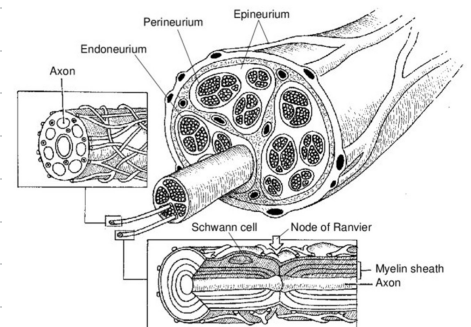
- Low frequency rTMS ($< 1 \text{ Hz}$) → **inhibitory**
- higher frequency rTMS ($> 5 \text{ Hz}$) → **excitatory**

Stimulating:

- brain neuron (cell body)
- peripheral neurons
- Assozyten
- Microglia
- Endothelial cells
- Axon terminals

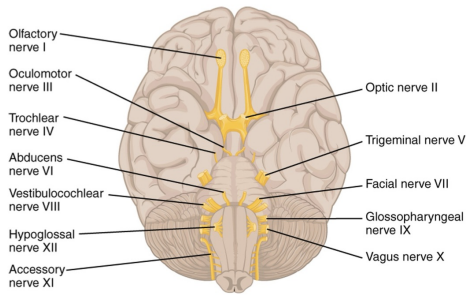
Peripheral Nerves

- Nerve = bundles of parallel axons embedded in connective tissues
- Cranial nerves**: originate directly in the brain
- Spinal nerves**: originate from the spinal cord
- efferent (motor / secretory)
- afferent (sensory)
- depending on info: sensory, motor, mixed



Peripheral Nerves

↳ cranial



1. Olfactory
2. Optic
3. Oculomotor
4. Trochlear
5. Trigeminal nerve
6. Abducens
7. Facial
8. Vestibulocochlear
9. Glossopharyngeal
10. Vagus
11. Accessory
12. Hypoglossal

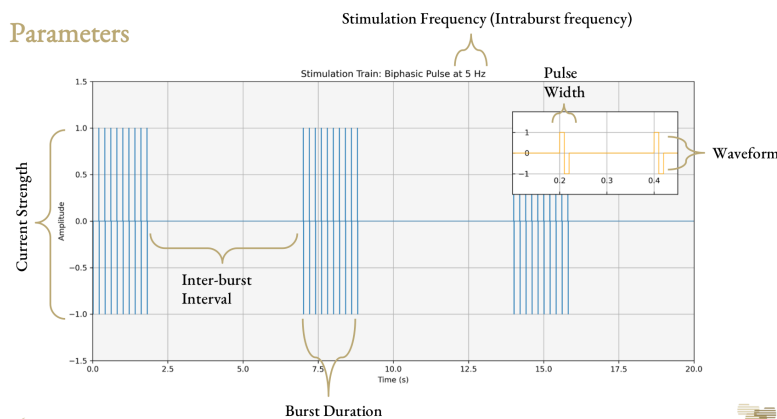
<https://www.google.com/url?sa=i&url=h>

Peripheral Nerves

- easy to stimulate for nerves directly under the skin surface
- high field strength
- induced action potential travels along axon in two directions:
 - Antidromic (back to its own cell body)
 - Orthodromic (to its effector organ or sensory endings)

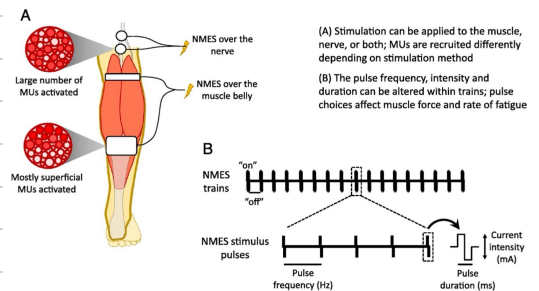
<https://www.google.com/url?sa=i&url=https%3A%3A>

Parameters



Neuromuscular or Functional Electrical Stimulation

- biphasic stimulation over the nerve directly above the muscle / over the muscle belly (sticky electrode)
- 20-50 Hz
- individual current strength (maximal tolerated intensity)
- recruitment of motor units not in physiological order → easier muscle fatigue
- NMES Neuromuscular stimulation (NMES) = basic application
- FES = Coordinated use of NMES → recapitulate whole, functional movements
- used in rehabilitation + sports



(A) Stimulation can be applied to the muscle, nerve, or both; MUs are recruited differently depending on stimulation method

(B) The pulse frequency, intensity and duration can be altered within trains; pulse choices affect muscle force and rate of fatigue

Application of NMES with Neurostimulation

- modulate the motor pathway function between: brain + specific muscle
- signals converge in the spinal cord
- Hebbian principle: What fires together, wires together
- paired associative stimulation:
 - Pairing stimulation of the motor cortex / inducing motor imagery with a following muscle stimulation
 - (25 ms after the cortical stimulation)
 - ↳ enhance motor control in patients

Trigeminal nerve (V)

mixed nerve

- sensation to the skin of the face, scalp, mucous membrane of mouth/nose

Ophthalmic (V1)

Sensation from forehead, scalp, upper eyelid, nose

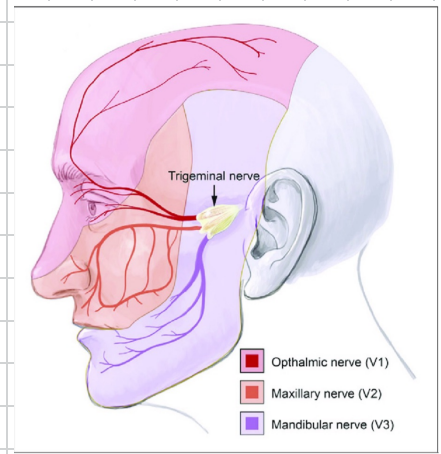
Maxillary (V2)

Sensation from cheeks, lower eyelid, upper teeth, palate

Mandibular (V3)

Sensation from jaw, lower teeth, chin, part of tongue (anterior 2/3)

↳ chewing, swallowing



Trigeminal stimulation

tES device

biphasic pulse → action potential

often ophthalmic branch stimulated, jaw

parameters vary → 60-120 Hz
→ 5-20 mA

Use cases & effects

headaches, migraine, epilepsy, ADHD, major depression

modulation of sympathetic + parasympathetic system via brainstem circuits

Reported Effects of TNS (in humans or in animals):

- Increase in Cerebral Blood Flow
- Decrease of Neuroinflammatory Responses
- Increase of noradrenaline signalling
- Increase in attention
- Decrease in depressive symptoms
- Modulation of cortical excitability and aberrant synchronization
- Peripheral vasoconstriction

projection to:

- nucleus of the solitary tract (NTS)
- Locus coeruleus (LC)
- raphe nuclei
- reticular activation system

Pupil response to TNS

Pupil dilation → indirect read out of locus coeruleus (LC) activity

↳ Noradrenaline important for attention, arousal, threat response

Seminick have shown a large pupil response to TNS ↔ median nerve, no stimulation

Vagus Nerve: Efferent Control

Efferent control of target organs

Afferent Relay

both parasympathetic control + sensory functions

Majority of nerve fibres are afferent (80%)

CNS-brain axis

Four Vagal Nuclei in Brainstem

- Nucleus of the solitary tract (NTS)** ! → cVNS
 - Visceral sensory information
- Nucleus spinalis nervi trigemini (Sp5 N)** ! → taVNS
 - Somatic sensory information
- Dorsal Motor Nucleus of the Vagus (DMNV/DNV)**
 - Parasympathetic motor output
- Nucleus Ambiguus (NA)**
 - Motor control for swallowing and speech

How to stimulate?

Invasive VNS

↳ Cervical VNS (cVNS)

Transcutaneous VNS (non-invasive)

↳ cervical VNS (cVNS)

↳ auricular VNS (taVNS)

- treat epilepsy
- implantation surgery
- electrode left cervical vagus branch
- electrical pulses activate afferent fibres

Neuroanatomical Pathway

- Signals travel preferentially to the **Nucleus Tractus Solitarius (NTS)** in the brainstem
- NTS sends projections to
 - Locus Coeruleus (LC) → Noradrenaline release
 - Substantia Nigra (SN) → Dopamine release
 - (Other areas like the hypothalamus and cortex)

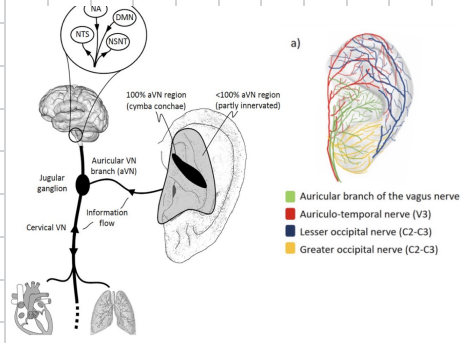


in clinical application:

- FDA approval for treatment of**
 - treatment-refractory epilepsy (TRE)
 - chronic treatment-resistant depression (TRD)
- Also used to **treat Heart Failures**
 - Implanted on the **right cervical branch of the VN**
- Allows for **closed-loop applications**
- VNS efficacy for many clinical indications is **probed**
- Implantation is **costly** and has (small) risks
- Overstimulation might damage the nerve

taVNS - Anatomy

- Transcutaneous = through the skin
- Stimulating through small sensory branch in earlobe → A RVN
- Part of outer ear is mostly innervated by the A RVN (nearby: Occipital, Auriculotemporal nerve)
- A RVN joins other Vagus Fibers at the Jugular Ganglion
- ↳ signals relayed upstream to brain



→ stimulation electrode in cymba conchae of the outer ear

- ⊕ non-invasive
- ⊕ inexpensive
- ⊕ minimal side effects
- ⊕ self application possible

⇒ strongly ↑ in popularity over the last decade
 ⇒ broad range of effects:

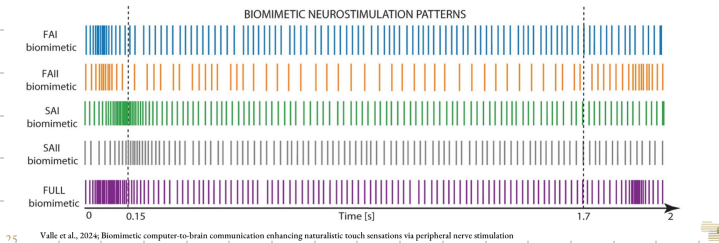
- extinction learning
- associative learning of novel later-sound correspondences
- motivation

cVNS	taVNS
Most fibers project to the NTS	Most fibers project to Sp5 N
Cell bodies reside in the inferior ganglion	Cell bodies reside in the superior ganglion
Highly specific activation of VN fibers	Co-activation of neighboring nerves?

Ant
Post

Biomimetic Stimulation

- Tries to find stimulation patterns and protocols that can mimic the physiological recruitment order of nerves and muscles
- This can help with better use for instance in neuroprosthetics (i.e., by mimicking natural stimulation patterns)
- Or less fatigue for neuromuscular stimulation



Clinical Cases

Conditions that can be treated with neuromodulation:

Neurological:

- Parkinson
- Stroke
- Dystonia
- Trauma
- Epilepsy
- Pain

Psychiatric

- Depression
- Alzheimer
- Tinnitus
- ADHD
- Autism
- Schizophrenia

Non-invasive Neuromodulation

- Transcranial magnetic stimulation (TMS)

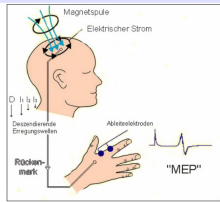


Abb. 1.1: Transcranische Magnetstimulation (TMS) des primärmotorischen Kortex (M1) zur Auslösung einer magnetisch evocierten motorischen Potentials (MEP)

- Transcranial direct current stimulation (tDCS):

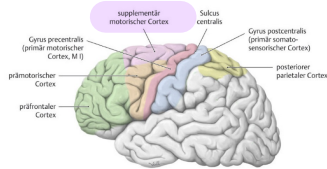
- Low-amplitude direct current (1-2 mA) → surface electrode on the scalp
- Changes brain function → altering neuronal resting membrane potential
- depolarisation (Anode) → activating → tDCS über Motor Cortex verringert hyperpolarisation (Kathode) → inactivating
- 'Freezing of Gait' - Episoden durch anodale tDCS stimulation

Targets: MN (motor symptoms)

- DLPFC (cognition and mood)
- Combined MN + DLPFC (motor symptoms)

Forms of stimulation

repetitive



Excitation (exzitatorisch)	Inhibition (inhibitorisch)
high frequency rTMS: > 5Hz Anodale tDCS	low frequency rTMS: ≤ 1Hz Kathodale tDCS

- ↳ most approaches TMS level
- ↳ broad distribution of approaches → different frequencies, duration, places

Ansatz nicht invasiver Stimulation bei Parkinson:

1. Exzitatorische Stimulation MN ⇒ Aktivierung Motor Cortex
2. Hemmende Stimulation SMA

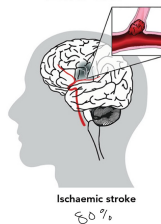
Stroke

Differentiation: - ischaemic (occlusion)
- haemorrhagic (bleeding)

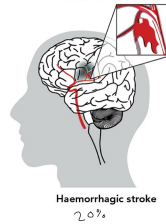
Causes: - Embolism (cardiac origin)
- Thrombus
- Aneurysm

Consequences: - speech / language disorder
- visual disorder
- attention disorder
- memory disorder
- personality change

Block



Bleed



Neuromodulation Approaches After stroke

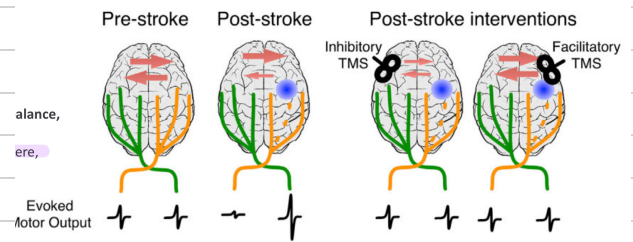
After stroke:

Hemisphere not in balance: · Strong inhibition

healthy → affected hemisphere ⇒ **Overactivity healthy hemisphere**

Approach: Restore balance

- Strengthening the affected hemisphere $> 1 \text{ Hz TMS}$
- Inhibition of healthy hemisphere 1 Hz TMS



Perspectives

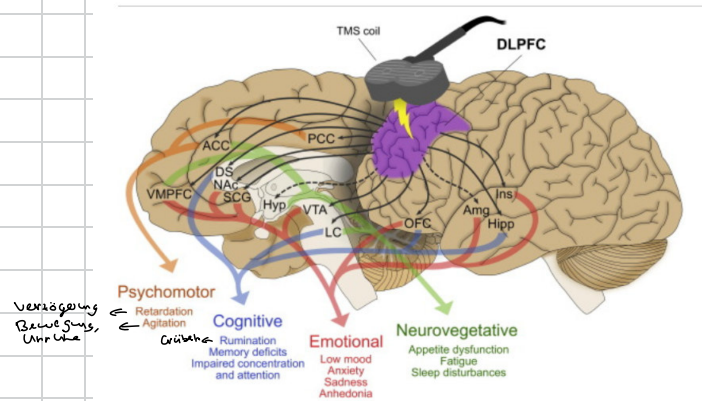
- Current approaches not effective for stroke patients with severe motor impairments

Alternative:

- Strengthening healthy hemisphere and ipsilateral pathways

Depression

Approach: stimulation of the dorsolateral prefrontal cortex (DLPFC), e.g. with rTMS



DLPFC stimulation with TMS for the treatment of depression

- since 2008 FDA approved
- Precondition: patients don't respond to drug treatment
- Therapy: daily for 4-6 weeks
- ↳ study on effectiveness (2012)
- ↳ improved quality of life (2014)

DLPFC stimulation with tDCS

- tested with distractor working memory task
- ↳ performance improves after tDCS

Perspectives

- Brain state-dependent stimulation
- Phase-dependent stimulation