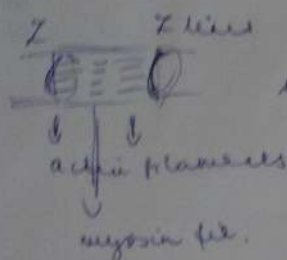


Karl's base Control of movement

- movement:
 - involuntary
 - rhythmic involuntary
 - voluntary
- Locomotion
 - Sea squirt
 - a. muscles, dorsal nervous system
they attach to the sea surface
 - a. they form a non-moving structure
- more complex movements → more complex NS is needed
by learning → increasing efficiency
strategy to survive → planned movement, action
- chimpanzees are predators (strategists)
sophisticated planning
hierarchy
- development of NS
 - phylogenetically among species
 - ontogenetically toddler → adult
- skeletal-muscular system → that / long distance runner
- no neuronal network has developed already in toddlers
that controls movement
despite the gap, they can see, walk etc. immediately after birth.
normal posture → vestibular system, cerebellum has to be developed.
- Summary
 - involuntary NS
 - contractile elements + control system (muscle, bone angle changing)
 - 206 bones → connected by joints (joints)
 - muscles conn. to bones by tendons
→ collagenous fibers
 - ↓
 - protected with connective tissue
epithelium → cell membrane
 - muscle fibres
→ highly organized structure
 - sensory organs
neurogenesis
planning



sarcomere → primary unit

troponin
tropomyosin

Ca^{2+} required for contraction

① slow 2.

Sarcoplasmic reticulum

motor unit: motor neuron + all innervating muscle fibers
MUSCLE FIBERS → determine speed and force of contraction

① slow

slow → oxidation of glucose

contraction force is low

no fatigue red muscle fibers

② FAST FATIGUE (→ glycolysis → ATP production)

glycolysis → ATP production

white m. f.

③ FAST FATIGUE RESISTANT (→ new glycolysis)

MUSCLE TENSION AND FIRING RATE

tension → individually ~~not~~ cannot be operated

sum → gradually increasing ~~rate~~

Ca^{2+} concentration increases continuously

generate longer contraction

Setting muscle tension:

Golgi tendon organ ④

Muscle spindle → nuclear bag
nuclear chain

- single muscle twitch (5 Hz)
- contractile force maintained by summation (20 Hz)
- incomplete tetanus (80 Hz)
- tetanus (100 Hz)

increasing motor neuron firing rate

Summary: - physical parameters of contraction is determined by the sarcomere

- adjustable effectors: motor units and muscles

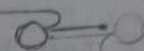
INHIBITORY REBOUND

slow depol. → hyperp. → back to rest

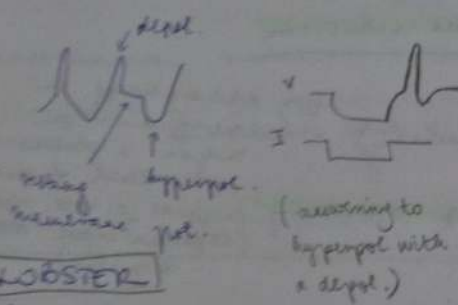
leads to AP.

Half-center oscillator:
reciprocally connecting neurons
generate rhythms
→ alternating muscular contraction
and relaxation

to motor neurons



to motor neurons



LOOSTER

digestive circuit

(reacting to hyperp. with a depol.)

POSTINHIBITORY REBOUND:

- voltage-dependent Ca^{2+} channels or T-type Ca^{2+} channels partially inactivated at resting potential.
- transient hyperp. releases the channels from inactivated state
- threshold of AP is lower
- leads to generation of AP

neural inhibitory system, innervated by interneurons

AD: conditional burst cell → Control
it generates burst activity

replace AD with dopamine/serotonin
examining the effect on interneurons in the network

LEET (pudca)

segmental animal

short activation of trigger neuron

generates long lasting depol.

input from sensory neurons

initiates rhythmic activity of MPBs

AMPET (ortholacta)

Sd. stretch receptors

higher order: excitatory input

long lasting depol.

DRIVER POTENTIAL

21. dia
due to conditional burst activity, when A cell is active, a short depol induces driver (plateau) potential in B neuron

→ AP burst generation

determine duration of MPBs activity



leads to long lasting burst activation of CPBs and motor neurons

→ innervates muscle

house spinal cord → rhythmic burst activity by ventral roots: (motor)

upper extremities → upper limbs

lower → lower

stimulating dorsal root for a longer period

sensory

to decide → stimulation from here (dorsal root)

↓

L: lower

leg of cat: carrier - lifting leg up

depending on the side of the stimulus

BASAL GANGLIA

inhibitory output (when not moving)



globus pallidus has to be dis-inhibition

striatum
putamen → globus pallidus

Substantia nigra (dopaminergic nucleus)

↓
activation of striatum

⇒ akinesia, rigidity, as
certain microscopic
injury to globus
pallidus leads to
inhibition of basal ganglia
(dopamine input substantia
nigra)

posterior parietal area → visual cortex

cortical neurons are also involved when filling more water
inside the bucket (increased force), not only spinal and neurons
function.

floor ↔ anterior (only one of them works at a time)

internal cues animal has to remember → SMA activated
external cues responding immediately → premotor area

Stroop 719?

not all topics

schizophrenia
sensory cells
motor function
olfactory

Motor system continue ...

motor endplate

axons of somatic motoneurons innervate skeletal muscles
→ neuromuscular junction / motor endplate
ACh neurotransmitter → release → contraction of muscle

sarcolemma: membrane of the muscle fiber

sarcomer: functional unit of a myofibril

muscle fiber → myofibrils: protein filaments
↑
actin myosin

- ① release of ACh → electrical impulse
- ② release of Ca^{2+} from sarcoplasmic reticulum
- ③ actin filament + tropomyosin strand + troponin (✓)

Human gait (✓)

- phasic component: rhythmic alternating contractions of distal limb muscles
• produced mainly by central pattern generators (CPG)
• functional at birth → located in spinal cord

- tonic component: associated with postural muscles
• emerges at birth
becomes functional by the maturation of

- musculoskeletal system
- sensorimotor network
- higher brain centers
- descending motor pathways
- ascending sensory

network of spinal neurons (interneurons, motoneurons) generate rhythmic motor pattern

CPG: neuronal network which is capable of maintaining a rhythmic output without sensory or external input

HPG

- by network activity of non-oscillating neurons
- by endogenous rhythmic neurons

- posture and balance

continuous processing of sensory input (+ proprioceptive input)

- vestibular
- visual

- **Proprioception**: unconscious sense of self-position and movement

Stretch reflexes → compensatory actions

↳ phasic and tonic components

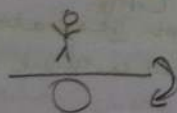
- **Noiceptive reflex** → posture maintained even if rapid changes occur in body support

1) **ANKLE STRATEGY** → feedback mechanism



moving platform triggers this
forward movement of platform - backward sway

2) **HIP STRATEGY** → feedback mechanism



tilting platform triggers it
forward tilting - forward sway

- **feedback correction**: unexpected postural disturbance
feedforward → expected

- **vestibulocervical + vestibulocolic reflexes** stabilize head and body posture → stretch in neck + stimuli to vestibular organ → efferent pathways that contract neck and limb muscles to oppose

- **ROMBERG TEST**: removal of visual input
only proprioceptive and vestibular sensors are used

→ Medial postural system (4h.)

- vestibular nuclei in connection with cerebellum
to receive sensory info

- superior vestib. nucleus → medial longitudinal fasciculus → motor nuclei of the eye

- lateral → spinal cord → activate extensor muscles of ipsilateral limbs

lateral voluntary system (16) (6")

{ corticospinal pathway
subcortical - "

primary motor cortex → predominantly pyramidal cells
agranular! → layer 6 is reduced/absent
no lateral granular layer

Plasticity of motor cortex

- muscles are used intensively for prolonged periods
- motor-evoked potential amplitudes are much larger

Summary

- neurons in primary motor cortex encode the direction of the force during movement
- premotor + supplementary cortical areas prepare the motor system for movement
- ^{lateral} posterior parietal lobe provides the visual info for the targeted movement

17. dia

CNS lesion ^{scb} → impairment of movements

- spinal cord: protective reflexes
walking 1.) SPINAL CORD INJURY

- brain stem: chewing, swallowing
breath taking
walking
eye movements

- cerebellum: coordination of movements
effort
association of stimuli 2.) DECEREBRATION

- ^{brain stem} diencephalon: eating, drinking

- basal ganglia: initiation of movement
behavior

3.) DECORTICATION

- cerebral cortex: speech
hand-finger movement

- locomotion can be initiated by neurons from several brain regions, the principal role is brain stem, but some inhibition from basal ganglia prevents locomotion.

discharge of neurons is correlated with the direction of movement
and the force exerted.

↓
ensemble activity of large population
of cortical neurons for a
particular direction of movement

Somatosensory organisation → motor cortex

premotor, supplementary cortical areas → prepare motor system
for the movement

Posterior parietal lobe provides the visual info for
targeted movements

Hippocampus

2017.
07.14.

- I. entorhinal, perirhinal cortex
 - II. perirhinal cortex
 - III. perirhinal cortex
- input to/output from hippocampus (Muller, 1990, 1991, 1992)
 - memory structure
 - epilepsy is connected to hippocampus
 - epileptic seizure (benzodiazepine)
 - h.c. essential in storing memory, but old memory is not stored here
 - ~~cooperative~~ HMP
 - ~~swath~~ rat in cage → different regions of the cage
→ diff. neurons are firing
 - h.c. builds cognitive map of the environment
place where neurons fire → placefields

GRID CELLS

- entorhinal neurons where firing in spots when the animal was running around
- grid cells
- get the knowledge of the whole space → mapping, orientation, distances

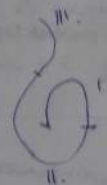
EEG: BEHAVIOR PATTERNS

- walking → 4-8 Hz oscillation (theta)
- field potentials are measured (field recording)
- accumulating info
- stopping → big spikes, hippocampal sharp waves
- consolidation (burning in info)
- states characterizing different behaviors

Wiring of h.c.

network developing into coding space.

- 3 subunits:
 - dentate gyrus (entorhinal)
 - cornu ammonis (CA3)
 - subicular entorhinal cortex (CA1)



⊗

- I. granule cells are principal cells
dendrites form molecular layer above
axons travel to II. CA3, CA1
→ innervate pyr. cells.
- II. pyramidal cells
axons to CA1 (many fibers)
→ axons of granule cells
- III. incoming axons from entorhinal cortex → perforant path
they innervate granule cells
- projection from CA2 → CA1: Schaffer collateral

major collaterals go back to entorhinal cortex → output
(answers are in wrong direction)

→ h.c. does sg. to with information → memory

Local connections

- entorhinal c. → granule cells → CA1 → CA3 → back to e.c.

recording / associating different type of synapses are used
triynaptic / disinp. / monosyn. loops

- m.c.: mossy cells → assoc. neurons

com: commissural

- granule cells never innervate each other.

90% of neurons in h.c.
→ local collaterals to m.c.s
relating info not responsible in epilepsy
- CA3 pyr. cells are connected to each other → firing together
→ generating sharp waves
burning in info.
synchronous activity

h.c.

↓
epilepsy
epileptic spikes,
synchronization

- inhibitory interneurons (10%)
GABA

huge convergence and divergence in network

orange (inhibitory) → axons to further layer
selectively control entorhinal input

green: avoiding pyr cell body layer

yellow: pyr cell sends collaterals only to pyr cell body layer

red (basket cells) inhibitory → controlling AP generation of pyr cells

1 → 100 pyr cell
basket cell

- **chandelier cells** (inhibitory)
 axo-axonic

vertical axon boutons are innervating **pyr cell axon**
initiation segments

↓
 highest density of voltage-gated ion channels
 lowest threshold of AP generation

↓
 best place for inhibition

c.c. major type of perisomatic inhibitory cells

yellow: axon in segments

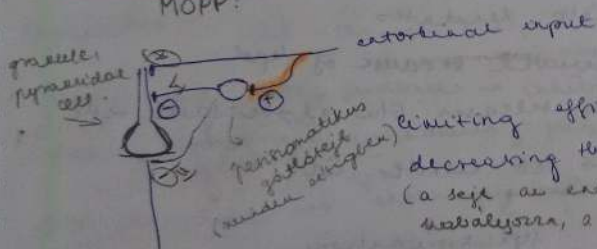
green: **chandelier cells** specifically innervating **axon in segments**

lower green: **basket cells** innervating **cell bodies**

- direct entorhinal input to ^{outermost} dendrites of ^{molecular layer} of c. layer
 → red inhibition, cell body and ^{some} ^{feedback} inhibition

- **feed forward inhibition**

MOPP:



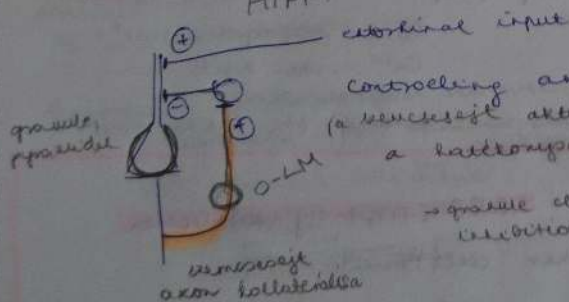
limiting efficacy of incoming excitation
 decreasing the strength of exc.

(a sept. an. entorhinalis palya kottongyolga
 szabalyozza, a bevezetel is innen kapja)

→ granule cell: dendrite & axon is str.
 inhibition molecular kott. 2/3. axon
 about on E.C. input kott. cells

- **feed back inhibition**

HIPP:



controlling amount of excitation
 (a bevezetel aktivizaciokat fogynak szabalyozza
 a kottongyolgot)

→ granule cell: ax. axon a str. molecular kott. 2/3. axon, dendrite a kottongyolga

mossy cell → excitatory

OLM → oriens - lac. n. interneuron

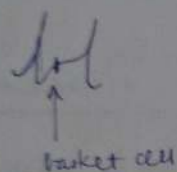
dendrite
 soma

axon

②

1. cell $\rightarrow$ AP (excitatory neuron)
2. cell $\rightarrow$ EPSP (inhibitory)

a single basket cell is enough to inhibit py cells firing

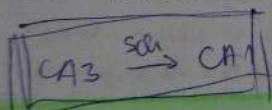


aim of inhibition $\rightarrow$ to synchronize pyr cells $\rightarrow$ strengthen synapses between them
 long term potentiation (LTP) $\rightarrow$ main cause of synaptic change requires coincident EPSPs & synaptic activation
 prep. and postsyn. cells fire together $\rightarrow$ all kinds of mechanisms of memory

AMPA $\rightarrow$ Glu $\rightarrow$ Na⁺ influx $\rightarrow$ depolarization
 NMDA $\rightarrow$ Mg²⁺ blocks, NMDA: ligand and voltage-gated
 back propagating AP into dendrites

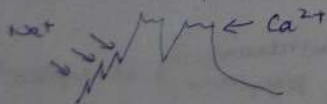
NMDA Mg²⁺ blockade is removed because of depol. of prep. cell $\rightarrow$ release releases Glu at the base

$\rightarrow$ NMDA binds Glu $\rightarrow$ let influx Ca²⁺



synchronization (graded depol. as equilibrium shifted)

Ca²⁺ spikes potentiate synapses



back-propagation $\rightarrow$ Ca²⁺ - rich appt $\rightarrow$ to depol. down $\rightarrow$ + so for Glu release EPSP + membrane

subcortical region, septum $\rightarrow$ GABA-GABAergic inhibition

GABAergic inhibitory pacemaker cells
 send axons to local inhibitory interneurons

$\rightarrow$ synchr. inhibitory cells $\leftarrow$ this type septal pacemaker cells

$\rightarrow$ synchr. neuronal activity in principal cells

(CA1, CA3 pyr cells and dentate gyrus granule cells)

dentate gyrus granule cells is particularly selective

field pot. polarity changes

↳ because of local propagation

population spike



S: septal neurons → reduce inhibition
rhythmic oscillation

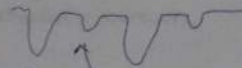
★: glutamergic

✿: GABAergic

b₁: GABAergic axon terminal

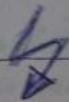
S: cell body

septal axons form synapses only on GABAergic interneuron dendrites



↑ less inhibition

↑ more inhibition



Optogenetics

ChR2 → channelrhodopsin

hippocampal septal feedback → inhibit pacemaker neurons

rat → moving → synchronizing pacemakers
(na)

EPW: sharp wave → cholinergic tone blocks SPWS

↳ firing of CA3 cells

HS: hippocampal septal cells

HS: medial septum cells

separating encoding from retrieval

↓
coherent cells active
basket cell down

plasticity

↳ coherent cells active
no plasticity

Laurel Barrow @ fear condition

amygdala will remember (fear memory)

raphe nuclei → serotonergic axons

attenuating inhib-source

↳ because of perisomatic inhibition
BC
basket cell, chandelier cell

delay in ^{PC} Pyr cell firing and BC firing in CA5
monosynaptic

CA5 responses for SWs

pyr. cells have extensive local collaterals
excitatory each other

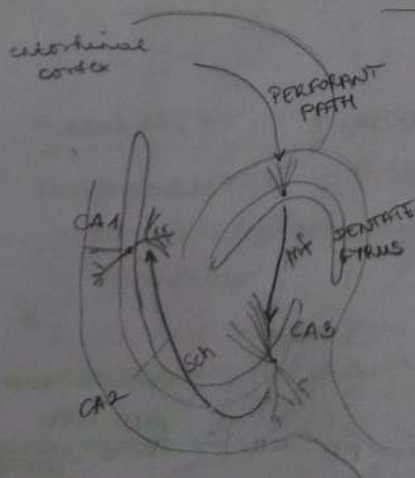
synchron. population burst.

LTP: long term potentiation

epilepsy: hypersynchronous bursts of pyr. cells.

↳ evoked new circuit states

- parahippocampal cortex
perirhinal cortex
entorhinal cortex
↓
hippocampus
- becsődés
tanítás az érzékelési információkhoz
de! memória segít nem itt tárolódik el
- COGNITIVE MAP (segít maga a agyban térképezni fel)
 - térzárkany sejtek (place cells) belül kognitív térképet építenek fel
az adott környező környezetből
 - térzárkany - selektivitás (place field), az idegsejtek az adott helyen 'kódolt'
területen aktiválódnak, tízezeri frekvenciájuk többszöröse más
időpontjában történő kódoláshoz → potenciális
- GRID CELLS (fx)
 - generated in medial entorhinal cortex
 - animal moving around, neurons fire in different spots → grid cells
↓
grid pattern generated
 - no visual input required
 - aim is mapping, knowledge of distances, orientation (position in space)
- BEHAVIOR - DEPENDENT ACTIVITY PATTERNS
 - walking: 4-8 Hz theta oscillation
= accumulation of information
hippocampal sharp waves, big spikes
= burning in information (konsolidáció)
 - stopping (resting, eating, SWS):



- 3 subunits:
- dentate gyrus
 - CA3
 - CA1

1. entorhinal cortex
perforant path
2. dentate gyrus → granule cell dendrites
3. granule cell axons = mossy fibers →
CA3 pyramidal cell dendrites
4. CA3 pyr. cell axons = Schaffer collaterals →
CA1 pyr cells → back to EC.

Local recurrent connections (14. slide)

- I. - granule cell axons, mossy fibers have local collaterals
they innervate mossy cells and interneurons
 - granule cells DON'T innervate each other
 - II. - mossy cells innervate granule cell dendrites
 - III. CA3 pyramidal cells INNERVATE each other with extensive recurrent collaterals
 - IV. CA1 pyr. cells DON'T innervate each other
their axons end on feed-back interneurons (to entorhinal cortex) (inhibitory)
- granule cells, mossy cells and pyr. cells are the principal cells (80%)
inhibitory interneurons, GABA NT (10%)



- granule cell, pyr. cell:

NT: Glutamate

input: 15-20K synapses

pyr. output: 10-60K other pyr. cells, large divergence and cons.

- CA1 pyr cells don't have many collaterals, they end on mainly inhibitory cells.

PYR. CELL LAYER (18. slide)

ALVEUS

AXON

STR. ORIENTS

STR. PYRAMIDALE → soma

STR. RADIANUM

DENDRITE

STR. LACUNOSUM - MOLECULAR

INHIBITION (19.)

perisomatic inhibitory neurons

str. pyramidale

Synapse on the proximal dendrites
on axon initial segment
on pyr. soma

synapse onto:

pyr. cell

body, proximal dendrite

- BASKET CELLS (can innervate up to 1000 pyr. cells) → pyr. cell
- CHANDLER CELLS (axo-axonic connection with pyr. cells) → pyr. axon init. segment

FEEDBACK INHIBITION

FEED FORWARD INHIBITION (lapozas vintás)

egyes gátoló szinaptikus áramok
(16 félé)

x neuro-peptidek
x Ca²⁺-kötő proteinek a dendritben

(PV) parvalbumin (perisomaticus gátoló szinaptikus)
→ csak a str. piramidale-ekben

GABA-erg axon terminálisok minden szinapszisban

cholecystokinin (CKK) főleg perisomaticus gátoló szinaptikusban

DENTATE GRANULE LAYERS

MOLECULAR LAYER → dendrit

GRANULE CELL LAYER → soma

HILUS → axon

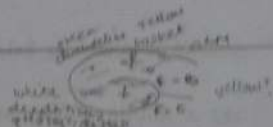
LTP: LONG-TERM POTENTIATION !!! (lapozas vintás)

→ synchronization of pyramidal cells.

→ increasing EPSP

dendritikus gátoló szinapszisok (16-félé)

(30. dia!)



→ inhibíció a distalis dendritben (piramiszi) (str. lacunosum - moleculare)

→ 0.5-2mV-os IPSP, 5-18 szinaptikus

→ szinapszisok nemcsak piramisziak és az axonkomplexusok közelében

→ megakadályozza az NMDA-receptorok aktiválódását → LTP-t

PIRAMISZI

perisomaticus gátoló szinapszisok

- basket (2-3mV IPSP; 2-axonos szinapszisok)
- chandelier

dendritikus gátoló szinapszisok (24. slide)
(distalis dendritekben)

GRANULE CELL

dendritikus gátolás

feed-forward

feed-back inhibition

(25.-26. slide)

mechanizmus a fontos!

granule cell and

pyramidal cell as well.

most: dendritikus gátolás

④ SINKRONIZÁCIÓ (lapos vörö)

Mért kell 2 közepet típus az onkoreceptorok?

PV közepet
(pancreatin)

- rövid, nem plasztikus
műve

CCK közepet
(cholecystokinin)

- főn hangolás, érzelm és
motivációs információ-tartalmú
kéreg alatti pályák hatásának
közvetítője

mediat magke nuclei
↳ agytörzs

serotoninszerű

?

SEPTALIS ÉS SINKRONIZÁCIÓ

HIPPOCAMPUS
archicortex

CORTEX
neocortex

→ septohippocampalis axonok type 1/type 2

type 1 (vastag) GABA-erg → selektíven beágyaz

a hippocampus GABA-erg interneuronokat

ilyen interneuron lehet pl.

calbindin - tartalmú

somatostatin - tartalmú dendritikus gátlósejt

parvalbumin - tartalmú korábbi

(perisomaticus, dendritikus gátlósejt is!)

GABA - GABA-erg disinhibíció

septalis, GABAerg input

↓
perisomaticus, dendritikus gátlósejtekre (GABA-erg) ?

↓
hippoc. principális sejteknek sinkronizációja
dentate gyrus, granule cell

CA3 pyramidal cell

CA1 —

1. septalis ingerlés → gátló interneuronok elhárításnak →
parasomatossejtek (monosinaptikus IPSP)

↓
parasomatossejtekre szintén depolarizáció
(spontán IPSP-k elhárítás)

62. dia → septalis mfx!

2. 1/2 septalis ingerlés → aktív gátló interneuronok →

↓
parasomatossejtek néhány esetben okai elhárítás

(X, ✓, X...)

(64. dia)

Hiba működés: retroaktív a magnét a zajbe

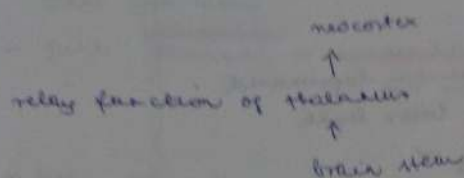
↓
vagyis - paris
magnétikus
retroaktív
gátlás

↓
csúcs - paris

THALAMUS

Louis Acedo

2017.
03-21.



continuous reiteration, information moving in circle
(over thalamus → corpus callosum)
medial thalamus → higher cognitive functions

HEMINEGLECT

ignoring half of the world, unilateral damage of medial thalamus
right thalamus damage → left part of the world ignored
contralateral to the affected side

coronal section

thalamus-cortical
cortico-thalamic fibers

- main: conscious state → regain some consciousness
- major damage in white matter (not in thalamus)
- brain stimulation (used in Parkinson's disease)
100 Basal ganglia
- stimulating electrodes into medial thalamus
100 Hz
- 6 parameters (x axis)
on: arousal of entire neocortex
turning off: functions remain, but reduced in efficacy
prolonged effect!
- Hans Berger: α -waves
low amplitude, desynchronous activity while eyes opened
high amplitude, synchr. highly organized while eyes closed
↑
↑ sync. activity between Pyr. cells.
↑ sync on and off period
- Cajal
more cell types in brain, than in whole body
is heterogeneous severely → complexity
spanning different types

- what if silencing or deactivating red cells

→ optogenetics:

light sensitive ion channels
illumination → pore opens up → neuron depolarized
selectively controlling by simple laser light
→ activating single type of neurons ✓

- how to control med. thal.?

midline excitation (red)

inhibitory input to intralaminar neurons (green)

inhibitory fibers (rodent - human)

black: fibers → remounting

brown: thalamic cell bodies

animal moving → behavioural arrest
↳ importance in behavioural response

* activating midline part
- animal sleeping $\xrightarrow[\text{light}]{\text{laser}}$ waking up moving around

cannot go back to sleep immediately → to more active awake state

- lighting for only 1 mp → tiny movements only
microarousal
short, briefest muscle arousal

→ importance in mediating arousal

Thalamus is different

multiplication of unit modules

↓

neocortex: cortical canonical microcircuits, modular organization

but, not in the case of thalamus!

→ NO microcircuits

1. all cort. areas receive thalamic input
2. no cortical region without thalamic input block (ip)

on the right: cerebellar micro. for

multiplication of modules

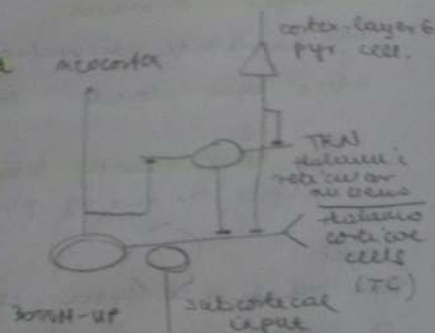
subcortical input for. retina

↳ important inputs:

- info transfer from cortex layer 6

- **TRN: thalamic reticular nucleus** →

part of the ventral thalamus that forms a capsule around the thalamus laterally, innervated by external auditory thalamus



- feedback from TC to THN
- fast forward inhibition from cell C to THN
- loop → oscillation
- THN inhibitory
- points: subcortical terminal → surrounding dendrite of TC
 - up to 16 synapses (arrows)
 - multisynaptic → faithful relay
- left: connection again
- right: increasing freq. stimulation (from subcort input to TC)
 - EPSP
 - lower amplitude evoked response
 - strong short term depression

faithful transmission (at any freq, same amplitude response)

Francis Crick: **SELECTIVE ATTENTION**

Searchlight → point where attention is directed
 THN
 suppression → reticular thalamic nucleus is responsible (inhibitory decrease)

conditions:

- brown noise: visual, no audio → activity in THN goes down → depol of TC → good transmission of visual signal
- blue n: auditory ignore light

faithful transfer

THN activates
 → hyperpolarize TC
 → inhibit visual signal
 ↓
 short term depression

LOW PASS FILTER
 (THN always activates & inhibits a visual input)

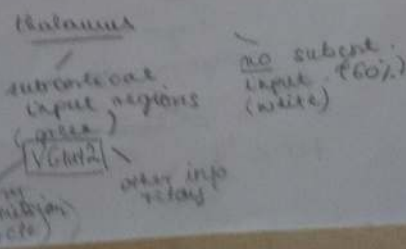
neurochemical marker: **VGlut2**
 (vesicular Glu transporter)
 ↓
 present in all **subcortical neurons**

How big part of the thalamus deals with the transfer of subcortical info?

large excitatory terminals (subcortical inputs)
 → to proximal dendrites

VGlut1: only in cortical neurons
 small terminals from layer 6 pyr cells

- (11 slide)
- 1. white regions: no subcort input (60%)
 other type of relay @
- green regions: only 30%
 sensory transmission (red)
 V. po. cerebellar input



→ sensory relay is not the primary mode of info transfer in the thalamus

II. Pulvinar

↳ no direct inputs at all (VGlut2)

↳ glutamate (VGlut1)

from cortical region

→ 2 types of cort. inputs

major input from layer 5

and input from L-6

↳ different function!

25% of thalamus is dedicated to this type of info transfer

→ large parts of the thalamus are dedicated entirely to process cortical inputs each to the cortex.

Cortex → Thalamus

III. Labelling layer 5

→ green: we can see glute terminals similar to glute subcort. input

freq. increase → response amp. decrease

avoiding TH cells! (big red dots)

no collaterals from L-5 cells to TH

- inactivation of pulvinar (thalamus) → no response

loop is necessary for proper functioning of sensory cortex

- awake: inactivation of subcort. input low → bigger activation

sleeping: high → low activation

SENSORY AND FRONTAL NEURAL CODES DURING DECISION MAKING

- monkey: freq. separating task

↓
low/high

decision making

needs to memory to compare

S: sensory cortex → during stimulation high

PFC: primary frontal cortex → info of 1st signal is maintained

HPC: motor → movement executed

needs to maintain persistent activity



fMRI

Ivan Vodyanov

fMRI - functional MRI

- simultaneously search brain activity
- high spatial resolution

BOLD

Can't decide whether excitatory or inhibitory the activity was
correlates with LFP $\rightarrow$ depending on frequency
examining bigger regions of the brain

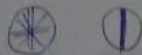
+ optogenetics

Analysis of fMRI

Seed regions: e.g. visual cortex
default mode (resting) $\rightarrow$ information processing

Visual Cortex:

- Orientation based firing of neurons $\rightarrow$ coding: an area has a specific pattern of responses to different stimulation
- motion selective regions
- visual cortex is coding more frequencies of the visual area (21 slide)
 - * ventral stream
 - that object recognition
 - * dorsal stream
 - where object moving in visual field, spatial perception
- object agnosia: ventral visual system damage
 - object copy, car memory
 - perform visual guided movement



- topographical = retinotopic mapping of visual field: topographical representation of visual field. (10)

- object categorization < 150 ms
- object discrimination < 200 ms
- } efficient and fast when viewing conditions are good (11)

- model of the environment $\rightarrow$ try to predict the next image
- predictive coding theory: neural cycle, constant perception

- combined fMRI and EEG

$\rightarrow$ image and $\rightarrow$ waveform comparison

resting state fMRI (rs fMRI)

rPPA: face recognition
rLOC: processing of moving faces } wired and connected together

Active process of vision

vision + memory $\Rightarrow$ interpretation of incomplete data, based on previous experiences

(average, main face $\rightarrow$ turns out to be the nicest)

functions: exploration of world

- acquire info about visual environment
- visual cues guide our actions

- eye movement
- attention
- learning

3 components of attentional network:

- alerting
- orientation

executive function $\rightarrow$ behavior most complex

attention is faster than eye movement

FOV: foveal eye field

'top-down'

myelination of corpus callosum

translational research

translational research $\rightarrow$ drug development

Biomarkers

$\rightarrow$ how drug affects personal activity

Pain is a state.

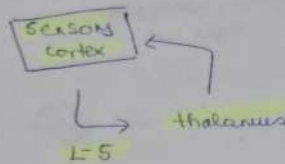
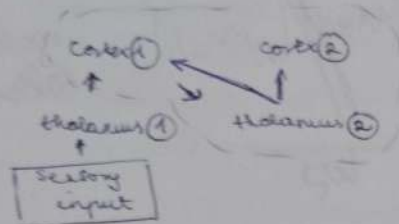
pain is stronger if it is unexpected

many brain regions are involved in processing

Thalamus

Cortex

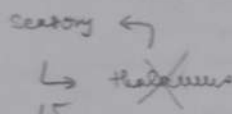
Sensory Cortex - thalamo-cortical circuit



- e.g. there is no visual response in V1 after blocking pulvinar
- L5 down thalamic loop is required for primary cortical visual responses

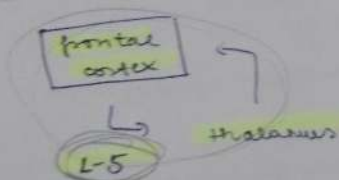
→ top-down cortical sensory maps to thalamus lacking sensory inputs.

Cortex receives a thalamocortical loop sensory input.



large bottom-up or top-down excitatory terminals

- activity linked to the presence of stimulus
- extract salient features of transient signals?
- both bottom-up AND top-down large terminals are necessary for sensory functions



- decision making
- working memory
- planning
- movement organization
- motor execution

this loop combines highly diverse inputs

! maintain persistent activity in the absence of sensory stimulus (monkey experiment!)

Sensory cortex and frontal cortex → completely different circuit logic

- feed forward excitation via T1
- small unitary synaptic terminals
- postsyn. target is the spine
- innervation of distal dendrites

(29. slide)

- heterogeneous thalamic units

fMRI

BOLD: Blood Oxygenation Level Dependent method

Bold signal:

- measured on T_2^* weighted images and its strength depends on the local magnetic field homogeneity
- determined by the balance of desoxygenated = paramagnetic $\leftrightarrow$ oxygenated = diamagnetic. haemoglobin in blood within a voxel

$\downarrow O \rightarrow$ paramagn. DECREASE local homogeneity
 $\uparrow O \rightarrow$ diamagn. INCREASE local hom.

- only an indirect measure of neural activity
- magnitude affected by:
 - oxygen consumption
 - blood flow volume
 - local microvascular architecture

$\Rightarrow$ megnyitott aktivitás
 $\downarrow$
megnö. aszisztolizáció
 $\downarrow$
vörösvérsejt oxidatív reakciók

- Bold signal correlates with LFP $\rightarrow$ frequency-dependence
- Bold signal also affected by spiking activity of local, excitatory neurons
- anticipatory = endogenous / stimulus evoked haemodynamic response components
- there is one component related linearly to local spiking which cannot be explained by neuronal spiking or stimulus attributes.
- Bold is more sensitive to neuromodulatory than to driving activity
 - $\downarrow$
 - like attentional, predictive, anticipatory processes
 - $\downarrow$
 - induce larger changes
- $\downarrow$
- sensory processes

Resting state fMRI (H. slide)

Functional connectivity $\rightarrow$ interdependence between distinct brain regions (különbséges agyi részek közötti függőség)

RS-fMRI FC $\rightarrow$ studying of FC during wakeful rest $\rightarrow$
by measurement of spontaneous slow fluctuations in BOLD (below 0.1 Hz)
across various brain regions
(FC vizsgálata BOLD jelekkel)

① WHAT / WHERE

PERCEPTION

vs.

ACTION

inferotemporal cortex

object-based

conscious

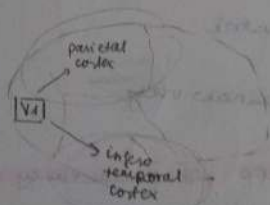
object identification

posterior parietal cortex

viewer-based

attentional

movements



② Protocol for retinotopy $\rightarrow$ V1

aim is to probe the entire visual field

- rotating wedge $\rightarrow$ info about visual field quadrants

- expanding/contracting ring $\rightarrow$ info about eccentricity

eccentricity map

(left visual field $\rightarrow$ right hemisphere visual cortex)

③ low visibility $\rightarrow$ object recogn. becomes slower, more effortful
visual system must recruit additional processes

using FFA: fusiform face area

LCC: lateral occipital cortex

Memory

Academy Level

I.)

Engram : while learning, new physical structure is built in the brain. → engram = memory trace
→ persistent alteration in the brain as a result of specific event

II.) info can be recalled only if info was perceived during encoding

III.) **ECPOHORY** : ability of engram to change behavior, when reactivated with the appropriate key.

IV.) in dormant state between encoding and retrieval

(invariable substrate = brain)

Track where memory traces can be seen :

- LTP : longer effect of presyn. cell to the postsyn. cell
- nuclear events
- structural changes (size, shape, longevity)
- neural networks

memory capacity is low if too many neurons participate

- brain regions, memory systems

life cycle of engram :
encoding 2. (KODOLAS)

1. (BEVÉSÖDÉS)

consolidation : allows the system to store memory traces

spontaneous activity of the brain

↓
dormant state 3. (ALVÓ ÁLLAPOT)

reconsolidation { significant stimuli
network reactivates again
retrieval 4. (VÍSSZAKERESÉS)
↓
we need new consolidation again
5. (ÚJ BEVÉSÖDÉS KELL)

Place cells, hippocampus

→ place cells are the engram of this specific environment

- animal starts moving → sequence of place cell activity
memory trace of linear track
0 → 5 mp

- during sleep these neurons fire in the same sequence
→ consolidating memory trace
(0,15 mp)

only firing in
small time window $\rightarrow$ LTP
increase in syn strength

$\rightarrow$ while sleeping firing within a short time

- the order is specific to the given environment
- sleep replay can be recorded only for 24 hours
the memory trace is there, but cannot record their
activity any longer

Summary:

1. After encoding, the cyprian reactivates spontaneously during sleep
as cyprian reactivates memory (solid traces) $\rightarrow$ solid traces reactivated, connect
2. The degree of reactivation is correlated with the degree of memory retention
($\rightarrow$ even reactivation of solid LTP $\rightarrow$ robust reactivation, a memory trace is still there, even reactivation, and suggests reactivation)
3. no learning will take place when reactivating reactivation, the memory trace will improve, knowledge, knowledge, mapping (of the animal) suggests reactivation
4. sensory stimuli during sleep again $\rightarrow$ reactivation of sensory stimuli

- human brain?

cyprian neurons active first
 $\rightarrow$ pronounce symptoms

Study of dormant cyprian (1)

$\rightarrow$ labeling memory trace

Tag Tag method

1) tetrazolium

2) tTA

- Optogenetics $\rightarrow$ activation and deactivation of labeled neurons and (neurotransmitter activation)
yellow light

1) white cyprian neurons $\rightarrow$ less fear
bad condition less freezing

2) blue light
activate cyprian neurons $\rightarrow$ more fear
good condition more freezing
 $\rightarrow$ changing behavior of animal

Study of dormant program

Demonstrating the existence of the dormant program (sleep relay only for 24h)

→ labeling (dormant) program cells.

activity dependent neuronal labeling

immediate early genes : c-fos
(IEG)

Arc

Zinc finger 268

linked to markers which are expressed permanently

GFP

lacZ

Channel Rhodopsin

Labeling specific cell population which participates in coding

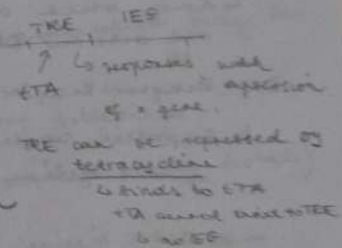
Tag Tag method

1) TRE: tetracycline response element : IEG
regulates the transcription of an immediate early gene
X no tetracycline → TRE control → IEG

2) tTA: tetracycline transactivator protein : binds and activates to TRE

3) ↑ if there is no tetracycline

* Tetracycline controlled transcriptional activation
tetracycline : antibiotic use



Condition A : ✓ tetracycline → X IEG transcription

Condition B : X tetracycline → IEG (linked to markers) will be expressed in a FIVEP time window

→ subject the animal to learning situation

specific markers are expressed in the cell population which was activated during learning situation

key:

dimin tetracycline (near time IEG), markers

all cells transcribe tetracycline

but tetracycline → IEG expression (markers) (markers) (markers)

→ also tetracycline controls (tetracycline only 24 days)

→ 24 days when is a marker of the activation of program (dormant state - like is tetracycline)

Allocation

↳ select given neurons to the engram

- 1) neurons which are spontaneously more depolarized than the average during the learning situation → more likely to participate in generating the engram

⇒ If we are able to slightly depolarize a given cell population → we can promote their participation in the engram

⇒ we can do this by: → step-function optics
(super-sensitive channel rhodopsin
opened by blue light pulse
closed by green or yellow light pulse)

→ DREADDs

↳ Designer Receptors Exclusively Activated by Designer Drugs

DD: Designer Drug

↳ drug, which can be injected systematically, crosses the BBB and acts on DRs at nanomolar concentration

DR: Designer Receptor

↳ G-protein coupled receptor which has no ligand in the mammalian nervous system (excitatory / inhibitory
M2 / M4)

→ genetic basis

Chemogenetic activation

Experiment:

- 1) Express DR in a well-defined cell population
- 2) Inject DD
- 4) subject the animals to a learning situation

↳ labeled cells will more/less likely to participate in the engram

DREADD
induced
excitation

DREADD
reduced
excitation

Types of memory:

MOTOR memory

- requires training, practice
 - rigid: can be recalled in situation identical to learning situation
 - display ^{mutual} plasticity in case of brain damage
 - can be destructed by learning similar things
- e.g. sport, dancing

EVENT MEMORY ^{explicit} (declarative explicit)

- requires single event
- recalled in various situations
- no recovery after damage
- more difficult to destruct

e.g. personal events, spatial navigation, words

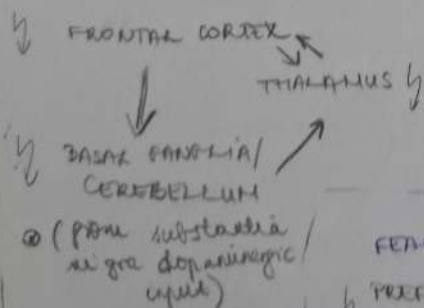
FEAR MEMORY

- in case ^{element} of significant events → ~~significant~~ ^{single} association may be sufficient
- recalled in situation identical to learning situation
- highly pronounced vegetative responses (heart, breathing, blood)

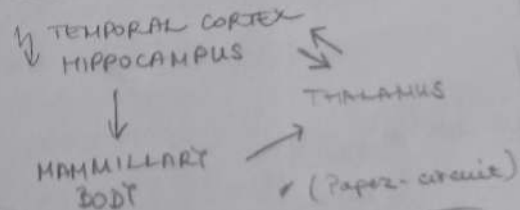
e.g. foot shock, snake

↓ plastic synapse

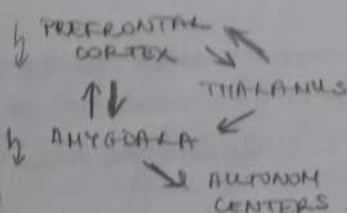
MOTOR MEMORY CIRCUIT



EVENT MEMORY CIRCUIT



FEAR MEMORY



! 0

Midterm Test 2014-15

- 1)
 - voltage-dependent ion-channels
 - Na-K pump
 - insulator lipid bilayer
 - resistor component of RC $\rightarrow$ phospholipid bilayer / ion channel [Ⓟ]
 - linear sum of postsyn potentials in dendrites due to $\rightarrow$ spatial and temporal propagation of potentials / IPSP and EPSP summation
 - analogue component of info process: $\rightarrow$ below threshold membrane potential
 - signal propagation in axon facilitated by: $\rightarrow$ voltage-gated ion channels
 - declining part of AP: $\rightarrow$ K⁺ ion, outflow into extracellular space.
 - amplitude of backpropagating AP depends on: $\rightarrow$ distance from the soma
 - Ca²⁺ ion
 - concentration change tracked by $\rightarrow$ two-photon microscopy.
 - main NT in CNS: $\rightarrow$ Glutamate
 - desensitization leads to: $\rightarrow$ STD: short term depression
 - retrograde signaling molecules: $\rightarrow$ NO, CO; lipid; NT (GABA), neuropeptide (dynorphin)
 - electrical synapse: $\rightarrow$ gap junction

2) a) different transcription factors function $\rightarrow$ different parts of the same DNA will be copied resulting in different proteins

b) Notch-Delta system: determines whether between cell division or cell differentiation. Notch = receptor, Delta = ligand $\rightarrow$ binding $\rightarrow$ NICD migrates to nucleus $\rightarrow$ Hes gene expression $\rightarrow$ bHLH transcription factors are activated $\rightarrow$ differentiation

Notch Intracellular Domain

c) e.g. AVE Anterior Visceral Endoderm

↳ decides head - not head region

Shh sonic hedgehog morphogene

↳ important in the creation (folding) of the neural tube.

d) IPSC

↳ advantage: - improvement in drug testing

↳ disadvantage: - high probability of non-controlled proliferation (tumor formation)

- unknown routes of cell development

e) two properties for info transmission to great distances:

? - AP doesn't have any loss when propagating (everything / nothing)

- AP prop ^{axons with} in myelin sheath is $\approx 120 \text{ m/s}$

f) cell types lacking axons:

? - olfactory bulb, granule cells

→ horizontal cell in retina

g) adult brain neurogenic zones:

- SVZ

- olfactory bulb

- hippocampus (granule cells)

LFP: spatio-temporal summation of synaptic and voltage-gated conductances, it reflects the population activity in the brain.

Brain oscillation: generated by the periodic and synchronous activity of a population of neurons.
e.g. theta oscillation in hippocampus

Disinhibition ^{STRATUM} → when initiating movement the globus pallidus (striatum) needs to be disinhibited by dopaminergic input from substantia nigra.

Hippocampus

GABA-GABAergic disinhibition: $\uparrow$ excit. parameter cell activation inhibits perisomatic inhibitory cells $\rightarrow$ which leads to the synchronisation of principal cells in the hippocampus.

@ disinhibition: $\uparrow$ the inhibition of an inhibitory cell, which leads to the activation of the excitatory cell.

[4] Potentiation rebound: $\uparrow$ ^{transient} hyperpolarisation leads to depolarisation of a cell by pulling Na^+ -channels into active state $\rightarrow$ $\uparrow$ threshold is lower.

[5] Half-center oscillator: reciprocally inhibited cells, which inhibit each other generate rhythmic $\rightarrow$ leads to alternating muscle contraction and relaxation.



[6] Theta phase precession: $\uparrow$ ^{if time remaining} neural inhibit potentiated excitatory synapses, and inhibit excitatory neurons, a result a precise report $\rightarrow$ and process as info, while obs will be. (prefactory info)

[7] Identity code: $\uparrow$ ^(#) participating cells in information coding is important.
~~the other coded activity pattern is~~
 (each has 'population', 'identity' and 'temporal' code)

[8] Sensory coding: @ seeing different contours

1) a) adaptation of olfactory system.

The electrical responses of OSNs show adaptation $\rightarrow$

increase in concentration of odors $\rightarrow$ decrease in the amplitude of odor evoked olfactory receptor - evoked current.

b) Apical dendrites of mitral cells which project to the same glomerulus are connected with electric synapse $\rightarrow$ synchronization



c) specific effect of a given odor molecule

1 OSN $\rightarrow$ 1 OR gene expression $\rightarrow$ high specificity

1 OR $\rightarrow$ activated by many different odor molecules $\downarrow$
low specificity

d) synchronous and periodic firing

$\hookrightarrow$ LFP oscillation

e) dendro-dendritic connection:

- periglomerular cell - mitral/tufted cell
- granule cell -

5. a) postsynaptic triad: photoreceptor (rods and cones) are connected with 3 partners: 1 bipolar + 2 horizontal cells

b) hyperpolarization of photoreceptors:

light $\rightarrow$ cGMP $\Rightarrow$ GMP transformation $\rightarrow$ Na⁺ channels which gated by cGMP become closed

c) photopic vision: in good visual conditions photopic vision allows color perception mediated by cone cells.

d) OFF bipolar cell:

in darkness ^{cone} photoreceptor releases glutamate, OFF bipolar cell is depolarized in darkness (AMPA-receptor on the surface)

e) how does bipolar cell transmit signal?

bipolar cells transmit signals from the photoreceptors or horizontal cells to ganglion cells directly or indirectly (via amacrine cells). They communicate with graded potentials (not AP)

6) center - surround organization

on-center cell: fires when light is on the center only of the receptive field

off-center cell: fires when light is on the surround of the ~~center~~ receptive field only.

are excited differently to light stimulus depending on their receptive field.

6) a) ACh

b) intermingled

c) ~~multiple~~ Botanic (electrical contraction when the muscle shortens)

d) single

e) Golgi tendon organ

f) spinal cord and brainstem are detached

g) medial posterior system → cerebellum

h) layer 4 is highly sensitized in primary motor cortex

i) plasticity in the motor cortex

j) extensive activity

7) 1) spinal cord → CPG for gait control

2) brain stem → vestibular reflexes

3) basal ganglia → locomotion initiation

4) cerebellum → posture and balance

5) cerebral cortex → somatotopic

8) A)

cortex layer 6 → small terminal

thalamocortical nuclei → small terminal

subcortical input → multisynaptic, giant terminal

cortex layer 5 (where is subcortical input) → giant terminal

8) ???

C) 1) cortical

2) internal

3) Hb

oscillation ?



nerve
to dia

5) A) HH condition and symptoms:

hippocampus of HH was removed from both sides,
he wasn't able to ~~maximize~~ new information, but
any ~~some~~ memory remained

B) consolidation: encoding $\rightarrow$ dormant state
reconsolidation: retrieval $\rightarrow$ new consolidation
is needed

C) 1. E

2. E, H, T

3. E

4. E

5. M

6. E

7. E

8. T

D) A) F: dentate gyrus is organized in 3 layers:
1. molecular layer
2. granule cell layer
3. hilus

(CA3, CA1)
but pyramidal cell layer consists of 5 layers:

5. alveus

4. str. oriens

3. str. pyramidale

2. str. radiatum

1. str. lacunosum-moleculare

2) F: major part of CA1 pyramidal cells project back to
entorhinal cortex, forming the output of the hippocampus.

3) T

4) F: basket cell is not equal to chandelier cell, but there
two types of cells are both inhibitory perisomatic cells.

5) T

6) feed-back?

T

7) T

8) F $\rightarrow$ hippocampus septum $\rightarrow$ hippocampus

E) a) Structure:

A: CA1

B: CA2

C: CA3

D: Dentate gyrus

Pathway:

1. perforant path
2. mossy fibers (= granule cell axons)
3. Schaffer collaterals (= CA3 pyramidal cell axons)

b) CA3 pyramidal cells have recurrent collateral network (CA3 region)
pyramidal cell LTP ensures learning

c) Hippocampal oscillation types:
theta (4-7 Hz): noise filtering, learning
gamma (40 Hz): binding problem → creating conscious perception
sharp wave and ripple oscillation: consolidation

EXPERIMENTAL, DIAGNOSTIC APPROACHES:

- a) intracellular recording
- b) patch-clamp technique → cell-attached (examining one ion-channel)
- c) by high frequency stimulation (electric)
- d) neurochemical identification and electron microscopy
- e) EEG recording
- f) giving high frequency stimulus to the muscle (electric)
- g) neurochemical marker
- h) fMRI
- i) Romberg test
- j) electric brain stimuli

2.2.16
OH, OH

VISUAL SYSTEM

↳ α and β ganglion cells

seeing details / dynamics

Pawo cells $\rightarrow$ small cells

Magno cells $\rightarrow$ large cells

Brodmann - area

visual field $\rightarrow$ divided into 'quadrants'

left field terminates in right visual cortex
right left

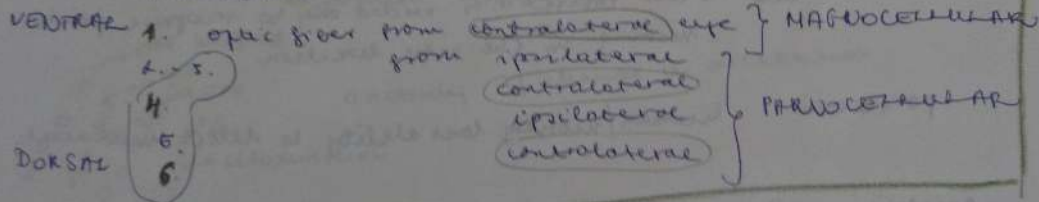
optic tract:

50% will ~~have~~ decussate

50% will remain on the same side

visual thalamus = lateral geniculate body

↓
classical



Defects of

visual cortex is laminar

80-85% pyramidal cells ^{suppl}

running almost vertically ~~to the~~ in the cortex

layer 4 termination

lighter / darker region $\rightarrow$ ocular dominance

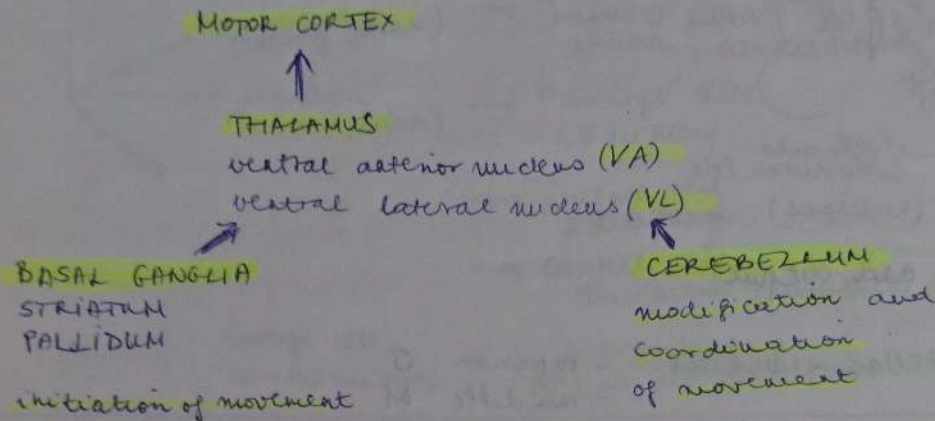
masking input from right/left eye
strip pattern

Bless $\rightarrow$ cytochrome oxidase blobs
mitochondrial enzymes

↳ color sensitive cells
function unknown

Movement control. Imre Kaelo

Movement execution:

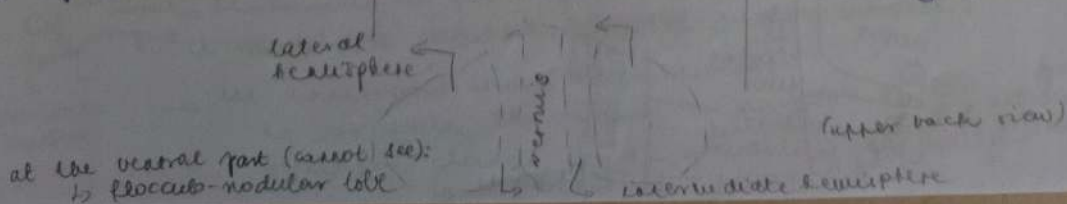


→ Cerebellum → record and playback device
learns movement pattern → then make the movements automatic
e.g. playing the piano

→ Cerebellum → 10% of all brain volume
but 50% of all neurons are here!
these cerebellar neurons are monitoring the other half of neurons!

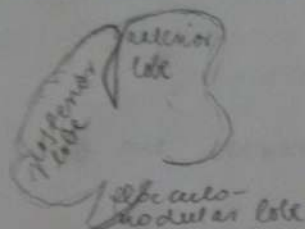
Subdivisions of mammalian cerebellum

Archicerebellum	Paleocerebellum	Neocerebellum
FlocculoNodular part	Medial part (Vermis) + Intermediate Cortex	Lateral cortex
= Vestibulocerebellum	= Spinocerebellum	= Cerebrocerebellum
TASKS		
- posture - balance - eye movements	- involuntary movements - muscle tone regulation	planning and controlling voluntary movements



Macroscopic and microscopic structure

Medio-lateral section:



Input and output

Cerebellar peduncles:

- superior S
- middle M
- inferior I

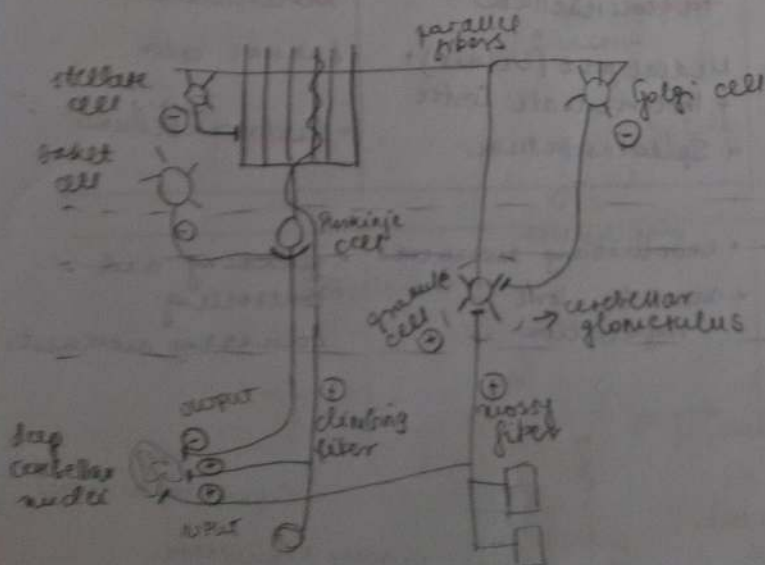
Deep cerebellar nuclei:

- dentate nucleus → S (output)
- interposed nuclei → M (input)
- emboliform nucleus
- globose nucleus
- fastigial nucleus → I (input)

Cerebellar gray matter = Archicortex has 3 layers:

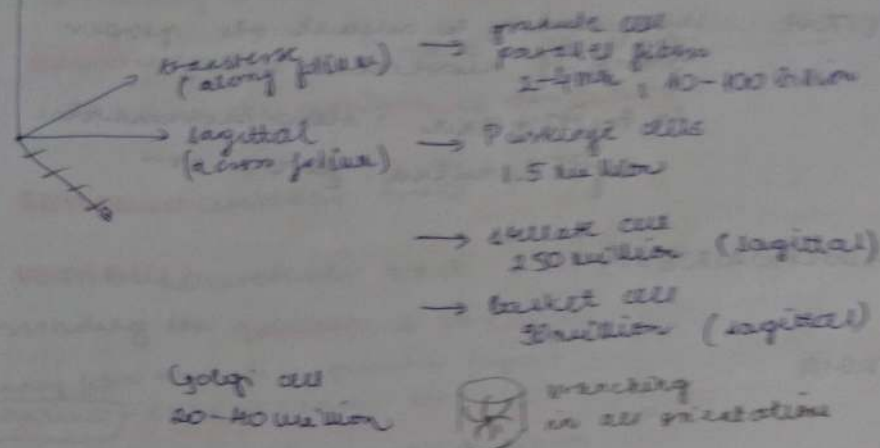
- molecular layer (outermost)
- Purkinje cell layer
- granular layer (innermost)

11. dia: str.



3D orientation of basic neuron types

dorsal
(to cortical surface)



- Synapses: P.C. and parallel fibers → cross over synapse
- G.C. + M.F. - Golgi cell → glomerular synapse
- P.C. and B.C. → basket like synapse
- P.C. and climbing fibers → parallel synapse

basket cell innervates P.C. body and axon hillocks

input of cerebellum: climbing fiber (inferior olive)
nerve fiber (pontine nucleus and spinocerebellar tract)
 (entering through inferior and middle cerebellar peduncles)

Operation of the cerebellum!

1. - generates neuronal activity pattern for most movements (conscious and unconscious as well)
- learning of cerebral activity pattern, which are related to neuromuscular system

storing of the corresponding motor output patterns

2. 1. fine pattern cerebellum recognizes a cerebral activity pattern
 2. output → thalamus → primary M1 motor cortex → it sends the related motor output

3. overwrite → M1 innervates lower motor neurons
 is overwrite the output on purpose or by sudden change in the prevailing conditions
 ↳ CEREBELLUM = AUTOPHLOT

MOTOR SYMPTOMS OF CEREBELLAR DYSFUNCTIONS

ATAXIA : absence of coordination of body parts

DYSMETRIA : incapability to adjust the proper extent of movement

→ **hypometria** : slow movement
→ **hypermetria** : fast

DYSIDIOCHOKINESIS

ASYNERGIA

HYPOTONIA

NYSTAGMUS

ACTION TREMOR
(INTENTION TREMOR)

Basic inputs (input)

Pathways terminating in mossy fibers

- I. **PONTO** cerebellar tract
↳ reaching what we willing to do
- II. **SPINO** cerebellar tract
↳ reaching the position of our limbs
- III. **RETICULO** cerebellar tract
- IV. **VESTIBULO** cerebellar tract
↳ reaching the position of our body

(mossy fibers terminate in granular layer)

① **GRANULO** - CEREBELLAR MODULE

↳ P.C. innervated by parallel fibers

2-4 mm distance P.C. is innervated by PF

1 P.C. → ~200,000 synapse from P.F.
⇒ not efficient

Pathways terminating as climbing fibers

→ **OHVA INFERIOR**

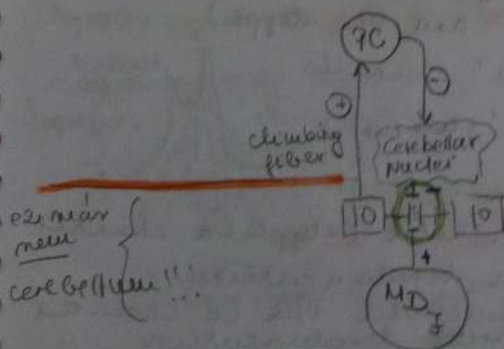
- has a role in learning
- major input from parvocellular nucleus
- function: read the output of motor cortex
- normal adaptation in healthy control
- abnormal (climbing fibers are from inferior olive) in IO lesion

② **OHVO** - CEREBELLAR MODULE

↳ P.C. innervated by climbing fibers

1 C.F. → 10 P.C.

1 P.C. has ~300 - 1000 parallel contact-type synapses
⇒ highly efficient!



→ **Glomeruli** is formed where inhibitory cerebellar nuclei terminal interact with excitatory terminal from brain stem, MDJ.

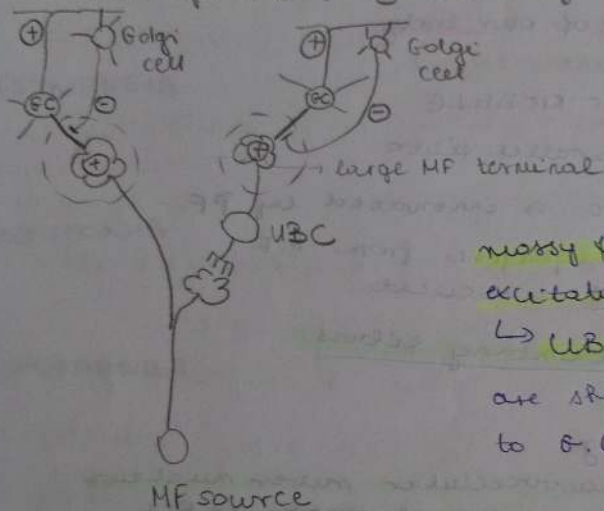
• inferior olive cells inside the glomeruli are coupled to gap junctions

Brain Stem: Meso-Diencephalic function

→ molecular layer interneuron: basket cell } inhibit P.C.
stellate cell }

→ inhibit granule cells
 and Golgi cells stay within the boundaries of the P.C zones.

These inhibitory cells are innervated
 directly by parallel fibers
 ('disorderly')
 via spillover by climbing fibers



mossy fiber axons of local
 excitatory interneurons
 → UBC: Unipolar Brush Cells
 are short and forward signal
 to P.C.

→ Granule cell axons span multiple olivo-cerebellar modules

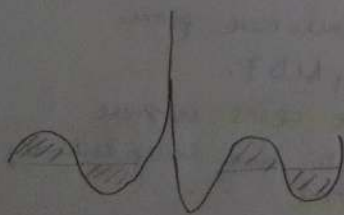
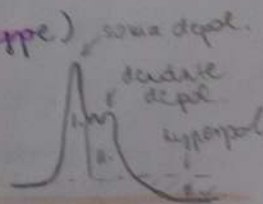
Activity pattern in the olivo-cerebellar module

Intrinsic olive neurons have:

- oscillatory membrane potential
- occasional spiking

→ spikes are mediated by:

1. Ca^{2+} channels (T and P/Q-type)
2. voltage-gated Na^{+} channels
3. Ca-dependent K^{+} channels



Oscillation:

1. low threshold T-type Ca channel
 → soma depolarization
2. high threshold P/Q Ca channels
 → dendrite depolarization
3. K^{+} channels
 → hyperpolarization

Activity of PC

Purkinje cells have:

- single spikes

- complex spikes

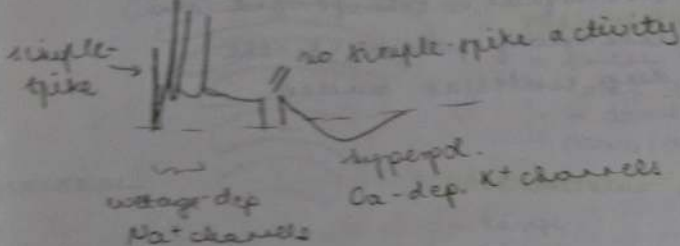
↳ after complex spike → pause of simple-spike activity

↳ mediated by:

1. voltage-gated Na^+ channels

2. but the subsequent ^{slowly} afterhyperpolarization;

Ca-dependent K^+ channels



Synchronization of complex spikes by 10 glomeruli

influenced by

1. level of gap junction coupling

2. excitation

3. inhibition in the olive

(zones - microzones) (?)

* Spike-time dependent plasticity (STDP) → turn page back

② between which cells

Activity pattern of cerebellar nuclei (CN)

electrical stimulus to CN neuron

⇒ burst of rebound action potentials

- mediated by

1. Na^+ channels

- T-type

- low

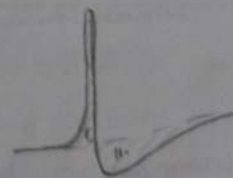
- high

- N-type

voltage activated Ca channels

2. Ca-dep. K^+ channels

- membrane potential of CN neurons is continuously depolarized by Ca-channel activation!



Summary

1. Cerebellum produce neuronal activity patterns via
 - complex learning processes
 - stereotyp developmental l.p.
 - dynamic l.p.

l.p are activated by afferent info and transferred to spec. target areas.

2. afferent signal $\rightarrow$ P.C. excitation



this signal is transformed into inhibitory pattern in the deep cerebellar nuclei.

Visual processing Zoltan Kivárdy

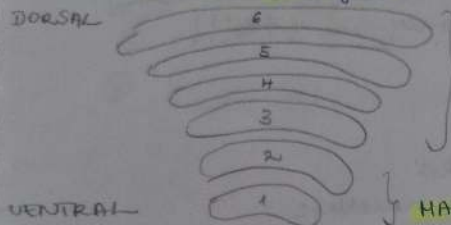
1. Visual pathway and processing movement, color and contour info.

visual field → lateral geniculate body → visual cortex

Thalamus is a relay center

visual-thalamus = lateral geniculate body

→ it has 6 layers



PARVOcellular cells

- small
- tonic activity pattern
- 4 dorsal parvocell. layers
- parvo/midget/X neurons

MAGNOcellular cells

- large
- phasic activity pattern
- 2 ventral magnocell. layers
- magno/parasol/Y neurons
- shape recognition

Tract of visual info

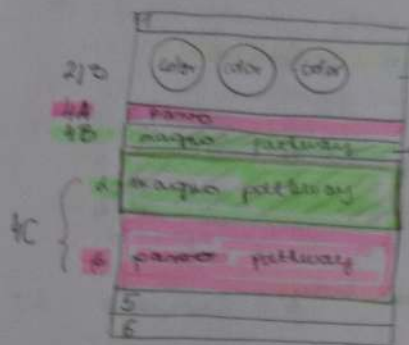
visual field → optic nerves → optic chiasm → optic tract →
(50% of nerve fibers decussate)

→ lateral geniculate body → magnocell. pathway → visual cortex
optic nerve fibers from parvocell. pathway V1
contralateral eye: 1, 4, 6. (Area 17)
ipsilateral eye: 2, 3, 5. Broadmann
terminate in these layers
this projection is retinotopic

- Defects of the visual field is dependent on the characteristics of the site and extent of injury
↳ H. dia + kavalyröl vizsgál!

- Significant portion of cerebral cortex is involved in info processing
↓
column-like units (RETINOTOPY)
retina-hor → okémoskóp
↑
columns of eye dominance
(1-2 altatja ill 6 megvan, melyik szemről info.)
(mitochondrial enzyme) cytochrome-oxidase + columns in visual cortex = 'BLOBS'
↳ it marks a group of color-sensitive cells (in 2 layers)
function is unknown (of the enzyme)

Cortical connections of magno- and parvo pathways V1 visual cortex layers



'blobs' color-sensitive cells

depth and motion

← only the pathways inside here

← magno- and parvocell cells are only in LGB!!!

V0 cortex layers

depth
form
color
form
depth

1 block

→ 3 blocks

of this structure

These project to V2, V4 and other areas

! Latency
Parvocell - dorsal
Temporal - ventral
Balanced pathway

dynamic

WHERE → action (magnocell)

WHAT → perception (parvocell)

static

object

(V5, MST etc. etc.)

→ action (magnocell)

→ perception (parvocell)

projections

(V4 etc. etc.)

! LGB

Magno pathway

MT: medial temporal cortex

= Motion area (V5)

action- and direction-
sensitive cells

Inferior - medial area
of occipital cortex

color-sensitive cells

Aperture - problem

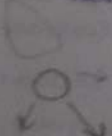
? perpendicular component is seen only

- cells at lower levels of hierarchy carry out 'simple' image processing and transfer the result to cells at higher levels of hierarchy (V1 → V5 → MST ...)

- solved by V5 (MT) cells → if V5 lesion there is disturbance in motion perception



⇒



! V5-MT (MT) a

directional movement

sensitive cells

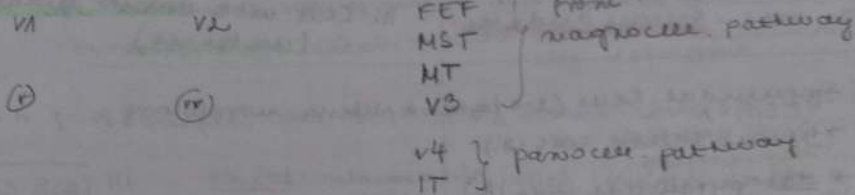
2) Factors determining

Monocular (far-field) depth vision ($> 30m$) (22. dia. right eye)

Binocular (near-field) stereoscopic vision ($< 30m$)

[?] * binocular ^(binocularly) disparity: identical points of 3D objects are projected to different (non-corresponding) points of the retina.

Stereo-recognition appears already in VI.



MT: Motion Area $\rightarrow$ (motion selective) motion-selective cells

|| - MST region $\rightarrow$ depth- (disparity) sensitive cells

Medial Superior Temporal cortex 'near-far' cells

also sublateral occipital cortex
|| - IT: Inferior Temporal Area $\rightarrow$ detect shape and colour differences

$\rightarrow$ IT cells are selective for complex shapes e.g. faces

$\rightarrow$ bilateral IT lesion results in prosopagnosia

[?] $\rightarrow$ large receptive fields (+ central area) frequent binocular representation

Binding problem

$\rightarrow$ depending on our attention $\rightarrow$ seeing different contours

- oscillation and synchronous firing pattern is different during attention
e.g. (2 faces or vase contour)

- perception is represented by the activity of different neuronal assemblies

MT
MST
IT

II. Structure and function of visual cortex

basic cell type: pyramidal cell.

→ Subdivision of visual cortical areas:

According to Brodmann:

Area 17/18/19.

Nowadays:

V1, V2, V3 etc.

MT, IT etc.

→ Classification of cell types:

(6 layers of visual cortex)

I. Cells with spinous dendrites

II. Cells with smooth dendrites
(no spines)

main excitatory {
→ pyramidal cells (2-6 layer)
(L3, 5, 6)
→ spinous stellate cells (4.)
→ star-pyramidal cells (4.)

+ diverse morphology

Features:

70% **EXCITATORY**

- asym. (Gray 1) synapse
- sand vesicles
- Glutamate

Features:

20% **INHIBITORY**

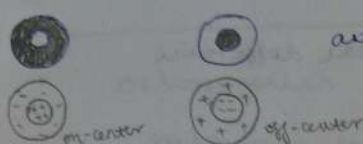
- sym. (Gray 2) synapse
→ tabblele dabbau 10000
- pleomorphic vesicles
- GABA
Gamma Amino Butyric Acid

→ Neurotransmitter-specific labelling by autoradiography or immunostaining

② 48-49. slide: electrophysiological characteristics of cortical neurons

III. The receptive field. Orientation selectivity

Receptive field is Gabor function: it models the structure of the receptive field in the visual cortex
 on- and off-center ganglion cells (2)



antagonist 'center-surround' structure

Simple-type receptive field (Simple cells: ON-OFF regions segregated)

(primary visual cortex)

→ r.f. of concentric cells of retina and lateral geniculate body
 on-center / off-center → retina, thalamus (stimulation) → 1st synapse

→ r.f. of simple cells of primary visual cortex

[53. dia] !!!

Handout: thalamocortical receptive fields
 p. 3 on 'receptive fields' (concentric cells) → on-center, off-center
 receptive fields overlap

Complex-type receptive field (complex cells: no ON-OFF segregation, place-invariant (helfgott))

Grating patterns when stimulating
 Simple cell receptive field [56. dia] !!!

Spatial frequency: simple cell with receptive field

↳ low spatial freq. → good for SC with big RF
 not good for SC with small RF
 high spatial freq. → good for SC with small RF
 not good for SC with big RF

Phase

difference in the phase of the two gratings



RF excited



RF inhibited

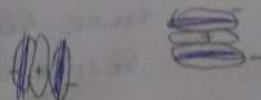
Contrast

clearest grating → will be most excited

blurred grating → less excited

Orientation

↳ spatial orientation of grating also matters



58. - 71.

2

Orientation selectivity

Orientation selectivity = "receptive field aspect ratio"

the stronger the OS $\rightarrow$ the greater the difference between responses evoked by optimal and null orientation

the greater the "aspect ratio" the more orientation-selective the cell

létező orientáció selectív:

különböző sejték különböző dőlésszögű válaszokhoz reagálnak jobban (egy sejt egy adott szögű irányban tűz, de az elterjedés közelebb van a tűzhez) $\rightarrow$ populációs aktivitás, vektorképp

Contrast invariance

$\rightarrow$ firing intensity of thalamic cell changes parallel with the extent of contrast

Gyakorlat

- * lateral inhibition $\leftarrow$
- * antagonistic ON-OFF cell (?)
- * postsynaptic rebound (közvetlen elpusztítás után?)

ON-OFF segregation

- * komplex kézműködés $\rightarrow$ motor control 1.
 - bilateral (mindkét oldal)
 - contralateral (ellenoldal)
- * neuronal assembly
 - orientation coding
 - sejt-összetétel különböző irányokban
 - türelmes nagy frekvenciákkal

- ✓ premotor cortex - külső
- supplementary cortex - belső
- ✓ minor neurons

✓ oligodendrocytes

külső és belső fajok → sorrendben és időrendben fejlődése alapján

- * központi mintagenerátor
- ↳ mi is hogy működik?

pl. váz nem tud járni → de a lába is
egy kis mozgás, járás, azaz mozgás
miniat. general.

✓ Cion mozgás [???

- ✓ mikor van feed-back correction?
- ✓ proprioceptive reflex
- ✓ medial postural system function

✓ hippocampus, theta oscillation

Sharp Wave → how it generated? → CA3 region

✓ FMRi biomarkers

- Eignung:

1. persistent

- Retina

1. kóba: T

az optik. axonjai az inner plexiform layerben
leltek vannak

2. kóba: amacrine cell-eket keresztül érintkeznek

- Scheme:

1. higher brain centers: perifériális és gyűjtés
2. reticulospinal neuron: nagy mozgás
3. LIPG: basic alteration
4. stretch receptor: érzékelés és feedback
5. motor neuron: vezérlés és irányítás

OPTOGENETICS

- observation & manipulation
 - electrical ^{but fast, reliable}
 - pharmacological ^{without noise and non-specificity as with dr.} → low temp resolution

selectively manipulating with high ^{temporal} resolution

↳ optogenetics
light related genetic modification

- artificial photosensing protein → rhodopsin
photosensitive ↓ sensing photons
- 7 transmembrane channel → G-protein coupled receptor
2. modulates other ion channels to metabolic signalling pathway
↳ modulate release of ACh or other NT.
23. dia → Chimeric GPCR: as opsin's light sensitive domain + GPCR intracellular protein binding domain
- microbial opsin for manipulation
↓
Bacteriorhodopsin

photon will cause ion pump activation

→ ~~getting~~ photon gated current (photopump, photocurrent)

- focus the light to specific brain areas

4 - electr. stim → activation of brain only
(indirect)

opt. gen. → directly deactivating as well (hyperpolar of neuron that expresses the given protein)
not always depolarisation

① deliver the gene of the opsin with viral gene array

affect the virus into the brain area
opsin + promoter region

↳ these neurons will express the artificial protein
not a good transduction

artificial
virus → neuron → express genetic compound

↳ this rate of transduction is not so high

② force neuron to express protein

use specific recombinases

enzymes can modify DNA/RNA

Cre
recombinase

• flip some segments of DNA

• delete stop seq. from DNA region

↳ cell can express the protein

⑦

LoxP

→ remove or flip

EF-1α open stop

seq.

Flp
miffordites!

• ubiquitous (minden sejben kifejeződik első promotor)

③ without viral vectors

cross two mouse strains

driver line

reporter line

contain
recombinase

contain opkn

(LoxP x2 kútdőzős Δ stop

Charrel Rhodopsin 2

- cation channel

Na^+ , Ca^{2+} currents

- making spec. channels

need spec. sensitivity → green/red/blue/yellow

ionpumps:

HR modification (Halorhodopsin)

- chloride channel → inhibition

pump chloride inside the cell. → change pH but

pumping protons from inside to outside

can kill the cell

BR/PR protonpump

↳ Bacteriorhodopsin

Miniaturization

- depending to the size of mouse
- weight and size of light source and recording systems
- (neurons containing Somatostatin, PV)
- Bursting activity, electrophysiological properties differ in pyramidal and interneurons. (?)

[?] optical - / or phototagging
could make individual responses ... ?

→ Kim et al. 2017 Nature Reviews

2-photon imaging

small illuminated spot is not enough to

activate ChR2

→ increasing the spatial resolution of light stimulation

As need temporal precision of the beam by increasing spot size

not only light for activation, but eg. wireless energy flow

using high freq. radio waves to activate

spec. receptors → TRPV1 cation channel

translating heat (genetically encoded temperature sensor)

Success rate is worse than in the case of optogenetics

but approach method is good

Pharmacogenetics

As receptor seeking only spec. ligands

(editing: neurons filled with light sensing proteins)

As deliver the artificial receptor as well to a spec. cell population

- 2 different recombine systems are used → combinatorial (6)

e.g. FLP and Cre

selectively influence 2 diff. cell types simultaneously (7)

virus can also be injected by patch-clamp
only into 1 cell.

Parkinson's, epileptic activity

↳ inhibition of principal cells

! we cannot use optogenetics in treatments

↳ invasive

↳ can't influence the brain by viruses genetically

+

(sequit)

24. dia → light relieves inhibition

Lox: light sensitive domain

Rac1 & effector

25. dia → light-induced gene transcription

TALE + Cryptochrome-2 + UBI

26. dia → Advantages

36. dia → problems to be solved

- membránpotenciál változások vezet:
- koncentrációváltozás
 - konduktanciaváltozás (akciós pot. fontos)

$$E_m = \frac{RT}{2F} \cdot \ln \frac{P_K [K^+]_{kült} + P_{Na} [Na^+]_{kült}}{P_K [K^+]_{belső} + P_{Na} [Na^+]_{belső}} = 61,54 \text{ mV} \cdot \log_{10} \dots$$

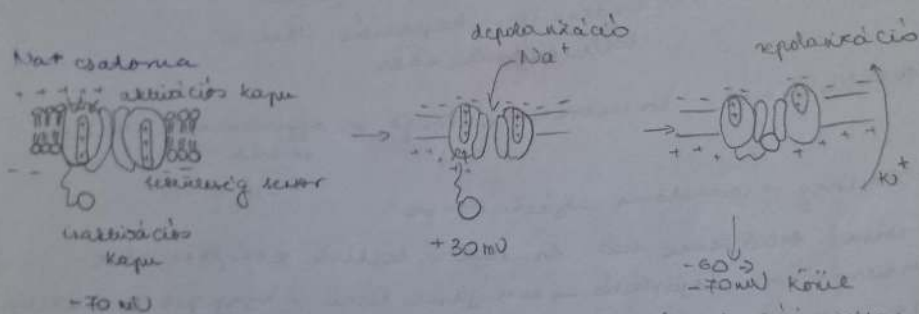
K^+ 10-szer nagyobb permeabilitással nyugalmi állapotban, mint Na^+

$$E_m = 61,54 \text{ mV} \cdot \log \frac{40(5) + 1 \cdot (150)}{40(100) + 1 \cdot (15)} = 61,54 \cdot \log \frac{350}{4015} = -65 \text{ mV}$$

ingerek elvezetése (ideg- és izomsövet)

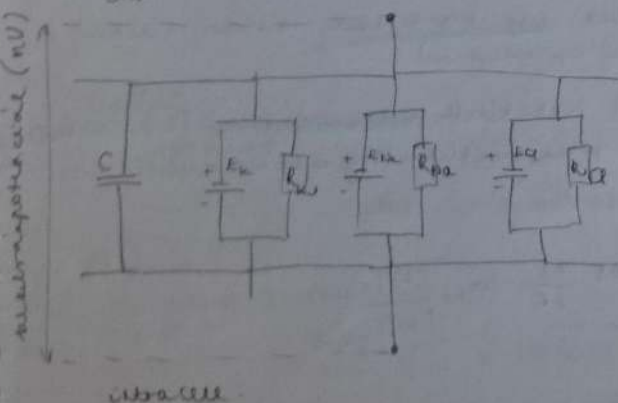
membránpotenciál érzékelő függő ioncsatornák
h-on két nagy vezetőképességűket

akciós potenciál:
→ feszültségfüggő ioncsatornák



- 60 to -70 mV körül
- kapusok zárnak vissza a belső membrán felé
- csatorna zárnak

RC helyettesítő kép
extracell.



- C kapacitás → lipid kettős réteg szigetelő tulajdonsága, feltöltődés
- R ellenállás → ioncsatornák ($G = \frac{1}{R}$ konduktancia és ezekkel számolunk → vezetőképesség)
- E feszültségforrás → K^+, Na^+, Cl^- koncentrációkülönbsége a két oldalon

Képzelt membránpotenciál
minden egyse írás

hipermembrán képzés a belső felére közt

elektronos polarizáció (feszültség) = membránpotenciál

membr. - 70 mV (negatív előjelet a belső felé negatív töltéssel)

plazmát hipermembrán → depolarizáció
→ csekély polarizáció
→ csekély membránpotenciál
→ csekély polarizációt jelen
→ hiperpolarizáció
is

Elektronos megkötés

hipermembrán = elektronos költő

- ellenállás
- kondenzátor
- töltésgyűjtő

lipid képzés → kettős szelvény megkötés

→ kondenzátor, kapacitív ellen is
töltésközlés

diffúziós ionok koncentrációkülönbsége → egyenlőtlenség
forrás
 E_K, E_{Na}, E_{Cl}

membrán → ionok áteresztő

Ca^{2+} ionok, belső felére Na^+ negatív töltésű jónak neve
a membrán nem áteresztő → nem jöhet be a nyug. pot. kialakítá-
sában → de a Na^+, K^+, Cl^- ionok jöhetnek.

Membrán-egyenlet:

egyenlőség: potenciál meghat. egy ionra nézve, amikor minden
ion átlagos (termodinamikai egyenlőség)

1. koncentrációkülönbség által kialakított elektronos erő (kapcsolatosság)
= két oldal közötti potenciálkülönbség = membránpotenciál

2. az elektronos erő a diffúzió ellen hat

pl. $E_K = \frac{RT}{zF} \ln \frac{[K]_{belső}}{[K]_{külső}} = 2.303 \cdot \frac{RT}{zF} \cdot \log_{10} \frac{[K]_{belső}}{[K]_{külső}}$

R : gázállandó
 F : Faraday konstans

$0.0111V \times -1.3 = -0.0144V$

Goldschmidt-egyenlet

- több diffúziós ion is jelen van a rendszerben → csekély feszültséget adja meg
- kevés függ. van a membránok az egyes ionokra erre relatív permea-
bilitás (vezetőképesség) → nyugalmi K^+ magas, Na^+ alacsony nagyon
- E_m nyugalmi membránpotenciál adja meg

Basal Ganglia

Basal Ganglia

Basal ganglia → major neuronal system, affects behavior through cortex

- voluntary movement

(neurodegenerative diseases: Huntington's chorea, Parkinson's)

- ③ - subtle components of voluntary mov.
e.g. action selection, memory, motivational and emotional aspects
- learning, habits, addiction

4 main regions of basal ganglia:

① **Striatum**

- caudate nucleus

- putamen nucleus

- globus pallidus (GPe)

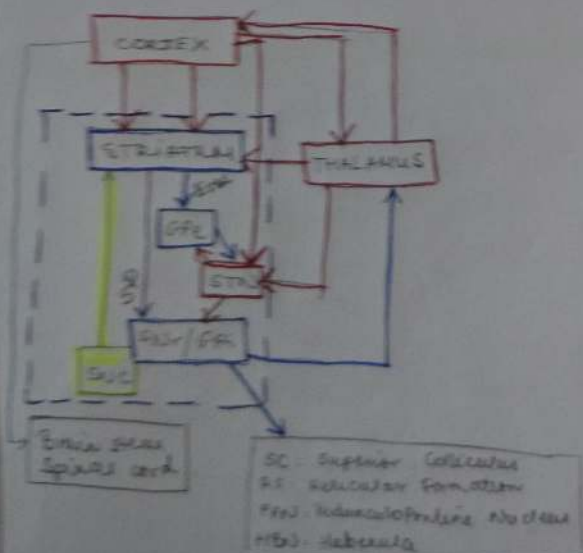
- putamen (SNr)

② **Striatum**: caudate nucleus, putamen

③ **Globus pallidus** GPe, GPi

④ **Substantia nigra**: pars compacta SNc, pars reticulata SNr

⑤ **Subthalamic nucleus** STN (thalamic nucleus, striatum, SNr, SNc)



3 main neurotransmitters:

GABA

Glutamate

Dopamine

Co-transmitters:

ACh

Somatostatin

Enkephalin (GPe)

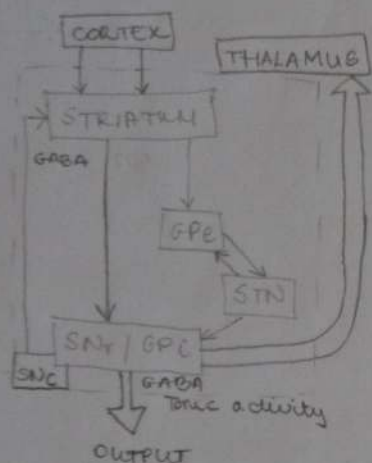
Substance P (SNr)

Dynorphin

(neuropeptides in the projection neurons of striatum)
(cortex-dependent)

- SNc: major modulatory control of striatum
- Cortex: most important input of striatum
- Thalamus: most important output of basal ganglia

Direct pathway:



Resting conditions:

Striatum: quiescent

SNr/GPe: tonically active

tonical inhibition of targets:

- thalamus
- other outputs

Activated direct pathway:

Striatum: active, GABA release

Inhibition of SNr/GPe

DISINHIBITION of targets

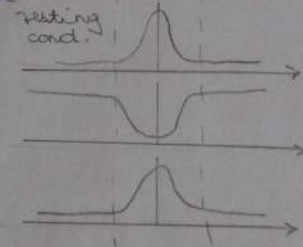
↳ important in movement initiation

eg. Saccadic eye movement:

Striatum

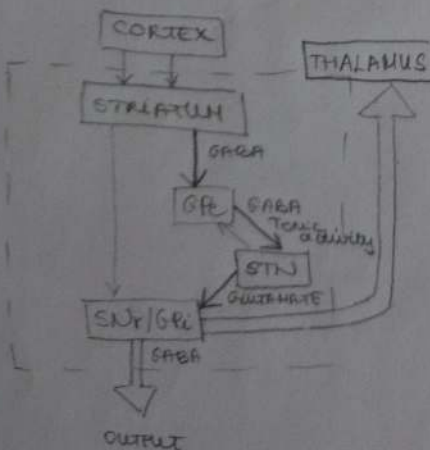
SNr

Superior Colliculus



! for movement initiation → the disinhibition of basal ganglia is needed!

Indirect pathway:



Resting conditions:

Striatum: quiescent

GPe: tonically active

STN: tonically inhibited

SNr/GPe: tonically active

tonic inhibition of targets

Activated indirect pathway:

Striatum: active, GABA release

GPe: inhibited, no GABA

STN: activate GABA release from tonic to enhanced activity

SNr/GPe: active, GABA release from tonic to enhanced activity

INHIBITION of targets

[*] Synchronous activity → focusing

[?]

Sequential activity → sequencing

preparation

execution

SNr ✓

⇒

SNr ✗

SC ✗

⇒

SC ✓

Striatum → 30% GABA-ergic projection neurons with **spiny dendrites**

↳ **MSN**: medium-size neurons

(not)
Neurons projecting to

Direct pathway

Indirect pathway

→ **Neuropeptide**: (neurochemical difference)
(co-transmitter)

• Substance P, dynorphin

• Enkephalin

→ **Receptor binding dopamine**

• **D1** receptors

• **D2** receptors

Inputs to MSN in striatum

I. **Cortex**

II. **Thalamus**

III. **Substantia nigra**

→ **Neurotransmitter** released to striatum:

• Glutamate

• Glutamate

• Dopamine

→ **Terminals** containing:

• vGLUT1

• vGLUT2

• TH [?]

↳ vesicular Glu Transporter

→ **Synapse** locations:

• dendritic spine

• dendritic spine and shaft

• dendritic mainly shaft and less spine

→ **Immunostaining**:

• immunogold

• immunogold

• immunoperoxidase

→ **Name of input pathway**:

• corticostriatal pw. (25% of the projections)
↑

• thalamostriatal pw. (25% of the projections)
↑

• nigrostriatal pw.
↓

modulation of excitation effectiveness
(if dopamine receptors are insensitive → more effective excitation)

- Imbalance between the activity of the two pw-1
 - ↳ lead to Parkinson's and Huntington's disease
 - ↳ direct pw: down-regulated
 - ↳ indirect pw: up-regulated

→ Attempts to restore balance → surgical intervention (PD)

- ↳ pallidotomy (damaged GPe is removed)
It destroys the output of basal ganglia

- ↳ subthalamotomy (damaged STN)

- ↳ deep-brain stimulation
stim. electrodes are targeting STN

- ↳ L-Dopa treatment
L-Dopa is precursor of dopamine
long time treatment causes depression


rotate right
amphetamine

- ↳ cause more dopamine release from remaining neurons of SN


rotate left
apomorphine

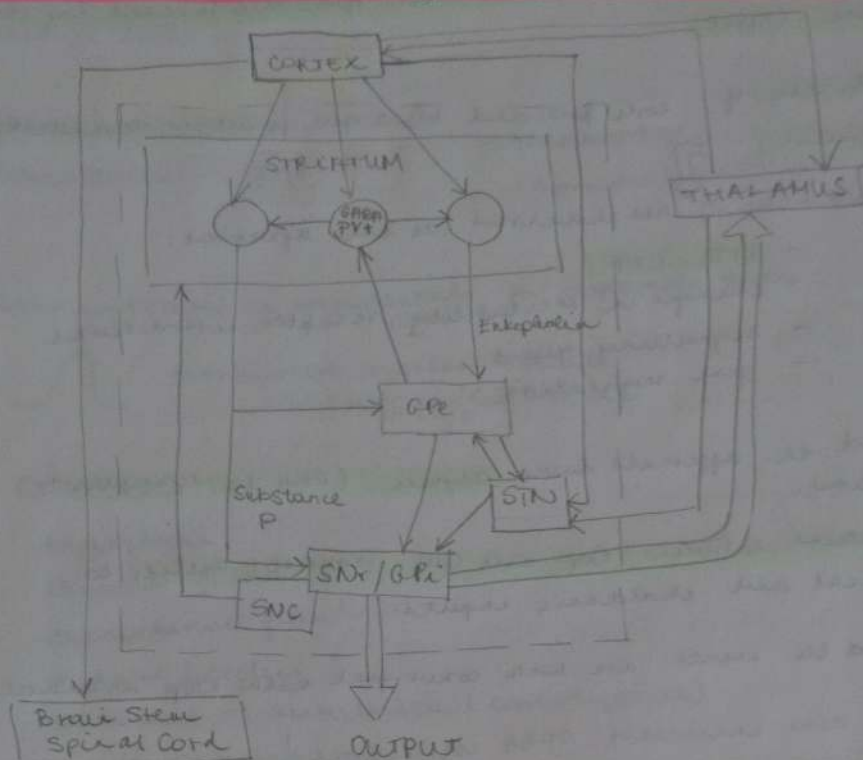
- ↳ D₁ receptor agonist
increased sensitivity of D₁ receptors,
less dopamine from SN

- Convergence of direct and indirect pathways
 - ↳ axon terminals of both pw. end on the dendrite of basal ganglia target

→ Neurons of GP and their interaction with GABA interneurons in striatum

- GP neurons innervate all caudal parts of striatum via collaterals
- ~1/3 GP neurons innervate the striatum
- ~3.25 pallidal boutons / striatal neuron

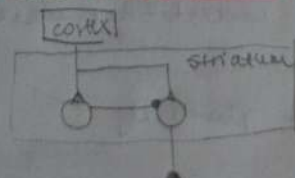
Detailed model of basal ganglia and its circuit



- striatum : ~ 30% MSN gaba-erg (spiny dendrite) neurons
 ~ 10% GABA interneurons with smooth dendrites.
GPe neurons inactivate PARACRYSTALLIN-positive GABA interneurons.
 ↳ PV + GABA intern. also receive input from cortex
 ↳ these interneurons inactivate large number of spiny neurons.

Role of GABA interneurons:

- feed-forward inhibition of striatal MSNs.



- synchronising the activity of different MSN groups.

[?] → spatio-temporal selection of spiny neurons

[?] only PV + GABA interneurons?

Corticothalamic PW and thalamocortical PW modulated by the dopamine input

↳ plasticity of C.S. PW and th. S. PW is shared by the dopamine



big variety of mechanisms are involved:

- LTD, LTP
- changes in excitability, receptor interactions
- signalling PWs
- gene regulation

↳ C. and th. afferents have different (but 1) synaptic striatum

↳ interaction between Dop and Gln equally applies to cortical and thalamic inputs

↳ C. and th. inputs are both convergent with Dop terminals

↳ cortex also innervates thal. interneurons!
thalamus doesn't inn. —!

CORTEX: motor and cognitive signals

THALAMUS: sensory and 'attentional' signals
(subcortical structures)

SUBSTANTIA NIGRA: motivation
salient stimuli
reward expectation error

STRIATUM $\left\{ \begin{array}{l} \text{direct PW} \\ \text{indirect PW} \end{array} \right.$ context-dependent behaviour

↳ short and long term plasticity

(note: glutamate is key neural modulator in striatum
examples (C, T, SN) → cortical propagated activity)