Lecture 1 Glial cells

Nervous system - CNS + PNS

Number of neurons 10^11 or 100 Bn

Synapses: 5x10^12 or 50 Tn

Brain is made up of neurons + glials, around 50% glial cells, intermixed.

Glial numbers and complexities correlated to higher computational power

Key difference between neurons and glials: Electrical excitability

Glial cell functions:

- Homeostasis of ECM
- metabolic need of neurons (bloodflow) active neurons lead to greater bloodflow
- myelination
- Synapse formation, maintenance , and elimination.
- Glials are multipotent, give rise to neuron, glia, and fibroblasts

Glial cell types in the CNS:

- Oligodendrocytes
- Microglial
- Astrocytes: Processes end on blood vessels and synapses (tripartite)

  Process wrap around the synapse, contain NT receptors - Ca2+ signalling, release of gliotransmittors, modulating synapse

Gliotransmittor: glutamate d-serine, ATP, TNFa

Cannabinoid type 1 receptors (CB1R), GPCR:

Cannabinoid bind to CB1R on astrocyte - Ca2+ elevation - glutamate release from astrocyte, lateral NMDA receptors on neurone bind Glu, internalise AMPA receptor, reduced depol.

Astrocyte and memory: Transplantation of human glial cells into neonatal mice lead to greater long term potentiation (memory)(Han et al, 2013)

Astrocyte and mental disease: Mice with schizophrenic astrocyte from humans show symptoms

Glial and homeostasis: oligodendrocytes and glial cells have K+ channels and NT transporters to clear up ECM for discrete signals

Lecture 2: Glial cells: microglia, neurotrophic theory

Astrocyte action sequences: detection of synaptic activity, release of GT (pre/post) Influence synaptic activity(up/down), +ve/-ve feedback

Astrocyte action on blood vessels: NT from synapse bind to astrocyte, Ca signal release vasoactive molecules e.g. prostaglandin, increase bloodflow to active neurons

Microglia: Immune cells in the CNS, migrate into CNS during development, mature in CNS. Cell body stationary, processes moving, surveillance mode.

can become phagocytic once activated. Release cytokines

Migrate towards injury sites. HIV reservoir. Elimination of neurons

- Formation of synapses during development: Mixed culture vs pure neuron culture: neuronal growth observed, astrocyte signals promote synapse formation. (TGF, cholesterol, BDNF, thrombospondin)
- Pruning of synapses at adolescence (activated most frequently are maintained), by microglia
- During aging and disease, abnormal synapse numbers are observed.

• In summary, glial cells control the formation and elimination of brain circuits.

General Neurotrophic theory: Maintenance of neurons

- Larger limbs - greater neuron numbers, less neuron death. Vice versa.
- Target organs release Neurotrophic Growth Factor (NGF) and Epidermal Growth Factor (EGF)
- Kinesin (anterograde), Dynein (retrograde) on microtubule transmit signal between axon terminal and cell bodies. Allow cellular products between positions.
- Neuronal survival signals retrograde transported to suppress default apoptosis, competitive pruning.
- Different mechanism in adults, based on external death signals or intrinsic apoptosis, no death by default.

Lecture 3: The Brain

General brain plan in all species: Forebrain, midbrain, hindbrain(&cerebellum)

- Forebrain: Telencephalon + Diencephalon (Prosencephalon)
- Midbrain: Mesencephalon
- Pons and cerebellum: Metencephalon
- Medulla Oblongata: Myelencephalon (Hindbrain: Rhombencephalon)

Anatomical axises: Rostral-Caudal horizontal in forebrain, dorsal-ventral vertical, reversed in the brainstem and spinal cord.

Axis created by brain flexures: Cervical, cephalic and potine flexures

Planes of sections:

- Horizontal
- Sagittal: Anterior-Posterior along the midline
- Transverse: Dorsal-Ventral (vertical in forebrain, horizontal in brainstem)

Brain anatomy

- Grey and White matters: Cerebral cortex (peripheral grey matter cell body), Axons myelinated are white matters. Deep thalamus area are grey matter.
- Meninges:
  - Dura mater: Fibrous material, Falx cerebri lines longitudinal fissure, tentorium cerebelli wrap around the cerebellum.
  - Arachnoid mater: contain CSF, extend into sulci,

- Pia mater: One cell thick lines the undulations of the brain, perivascular space contribute to CSF formation.

- Ventricles: Derived from the hollow neural tube, contain cerebrospinal fluid
  - Two lateral ventricles in the telencephalon - interventricular foramen into 3rd
  - Third ventricle in the mesencephalon - cerebral aqueduct into 4th
  - Fourth ventricle in the brainstem.
- Diencephalon (part of the forebrain):
  - Consist of epithalamus, thalamus, hypothalamus and optic nerve (CNII)
  - Pineal gland (Epiphysis) associated with epithalamus, pituitary gland (hypophysis) with hypothalamus.
  - Pineal - Production of melatonin
  - Hypothalamus contain many nucleus , CNII, pituitary (Anterior and Posterior) Posterior/Neurohypophysis: paraventricular and supraoptic nucleus extend into pituitary. Anterior/adenohypophysis: neurosecretory neurone into pituitary.
- Midbrain, pons and medulla
  - Peduncles are connections between brain structures, 4 brainstem-cerebellum
  - Midbrain dorsal to the pons and medulla: consist of superior and inferior tectum or colliculi, red nucleus and substantia nigra
- Brainstem cranial nerves
  - All cranial nerves except I and II originate in the brainstem.
  - Sensory/motor/mixed functions.

Lecture 4: The brain (again)

Cerebral cortex: 4 lobes each side, 8 lobes total

Frontal, Parietal, Temporal, Occipital lobes

Fissure/Sulcus - depression, Gyrus - ridges

Longitudinal cerebral fissure between hemisphere.

Lateral sulcus top of temporal lobe

Central sulcus between frontal and parietal lobe

- Cortex neuronal structure
  - Cortical neurones input via dendritic spines, output via axons
  - Arrangement: Either
  - Layered (cortex, cerebellum, hippocampus) separation of input/output layers
  - nuclear (spinal cord, hypothalamus), allow more interdendritic interactions
- Cerebral cortex contain 6 layers, except the hippocampus
  - Cerebral cortex contain pyramidal neurones. With spiny dendrites
  - No cell bodies in the first layer (molecular layer)
- Special functional areas on the cerebral cortex:
  - Broca’s area: Speech generation (Left hemisphere only)
  - Wernicke’s area: Speech understanding (left hemisphere only), lateralisation of function
  - Handedness, more dexterity with one side, also related to lateralisation

- Cortex white matter key tracts:
    - Corpus callosum: tract between cerebral cortexes connect two hemisphere
    - Optic radiations, thalamus to the visual cortex
    - Internal capsule: Cerebral cortex to spinal cord via motor areas

- Hippocampus: medial to lateral ventricle’s inferior horns
    - 6 layer cerebral cortex transition to 3 layered archicortex
    - CA1-4 areas, and parahippocampal areas of subiculum and entorhinal cortex
    - UCL John O’Keefe discovered place cells, responsible for spatial navigation

- Basal ganglia: Deep within the cerebral cortex, lateral to superior horn of lateral ventricles.
    - Consist of caudate, putamen, globus pallidus, subthalamic nucleus

- Thalamus: Relay centre to the cortex, processing

Lecture 5: Membrane potential

Neurotransmitters at the synapse - graded response - after integration AP.

Across the membrane: High Na and Cl outside, high K inside.

More K leak channels than Na leak channels, negative protein inside, positive Na outside

Electrostatic gradient and concentration determines the reversal potential at which there will be no net current

In nernst equation for positive ions, conc outside/conc inside

For negative ions such as chloride, conc inside/conc outside

Setting up and maintaining the membrane potential : NaK ATPase. KinSout.

Also from differential permeability.

Excitatory Post Synaptic Potential are graded if under the threshold

All or nothing AP dependent on voltage gated sodium channels

Hyperpolarisation independent from voltage gated Na channel, voltage gated and leak K channels

Voltage gated Na channel

- Selectivity pore: recognise only Na ions
- Voltage sensitive domain series of +ve charged amino acid residues detect voltage

change

- Activation gate: activate and open at threshold voltages
- Inactivation gate: ball and chain mechanism closes the channel after act gate opens

Lecture 6: Spinal cord structure

Cerebellum

- Folds in the cerebellum called folia instead of sulcus
- Three layers: Molecular(few cell bodies), Piriform(cell bodies of purkinje cells), Granular(cell bodies, granule cells)
- Output from Purkinje cells, input onto dendritic tree of purkinje cells
- Purkinje cells have elaborate dendritic fibres but only in one plane
- Input: climbing fibres up into the purkinje tree, parallel fibres perpendicular to purkinje plane, both granule cells.

Spinal cord:

- Entire cord + brain wrapped by dura sheath
- 8 cervical nerves, 12 Thoracic, 5 Lumbar, 5 Sacral, 1 Coccyx.
    - White matter on the outside, grey matter inside. As descend down SC, white decrease.
    - Greater grey matter in cervical and lumbosacral, due to greater sensitivity
    - Dorsal side has sulcus, ventral side has fissure, funiculus beside the lateral invagination
    - Commissure regions dorsal + ventral, axon cross over.
- Dorsal root: sensory, cell body within dorsal root ganglion outside SC.
- Ventral root: Cell body within the horn

Dermatomes: each sensory areas of the skin correspond to specific spinal nerve, derived from different somites, referred pain from viscera to dermatomes.

Within the grey matter it is also split into layers called Rexed's laminae, numbered with roman numerals (dorsal to ventral)

Circuits:

- Local circuit: monosynaptic simple reflex & antagonist inhibition with one additional synapse
- Ascending tract: Dorsal column(sensory input), spinocerebellar tract(lateral, to cerebellum), spinothalamic(lateral to ventral horn, to thalamus)
- Descending tract: lateral corticospinal tract (lateral to lateral horn), anterior corticospinal (lateral to ventral fissure)

Ascending tract decussation(crossing) at SC: Dorsal column does not, spinalcerebellar partially cross, spinothalamic cross at SC.

Descending tract decussation at SC: lateral corticospinal tract crossed at caudal medulla, not anterior corticospinal tract.

Lecture 7: Synaptic transmission

Larger dendritic spine - more EPSP receptors, (AMPA), stronger synaptic transmission

At post synaptic terminal contains: AMPA, NMDA, SNAREs (vesicle and target)

V-SNARE (e.g. synaptobrevin, VAMP), t-SNARE (e.g. syntaxin, SNAP25), does not cause fusion

chaperones proteins pull vesicle and membrane, change shape allow fusion.

Each vesicle is 35-50nm, synaptic cleft 20nm. 100mM in vesicle, 1mM in synapse.

Ionotropic receptors (post synaptic) (fast<1ms)

- Glutamate receptors (AMPA & NMDA)
    - AMPA(monovalent): open upon glutamate binding, Na+ influx, inward current, EPSC (-ve) (antagonist: CNQX and DNQX)
    - NMDA(divalent): open upon glutamate binding, Mg2+ ion blocks, if large enough depol, Mg2+ moves out, Na+, Ca2+ influx, K+ efflux. Antagonist: AP5 and MK801(only if open)are antagonists
- GABA/glycine
    - GABA: open to chloride ions, reversal potential lower than resting(~70mV), influx, hyperpol.
    - Inhibitory post synaptic potential (reverse potential at -85mV)

Currents:

- Reflect the flow of positive ions, EPSC(inward flow of positive ions)represented as a downward line.
- IPSC represented as upward curve, more likely caused by GABA release.

Current-Voltage curve:

- voltage on X-axis, current on y-axis
- AMPA: total reversal potential at AMPA at 0mV (permeable to both K+ and Na+)

  at resting potential -70mV, far from reverse potential of Na+, inward flow of Na.
- GABA: Reverse potential at -85mV, chloride influx at resting -75mV, positive current.
- NMDA: Permeable to Na, K, Ca. Reversal potential at 0mV, extracellular magnesium block, if depolarise beyond threshold, open channel

Slope of the IV curve is determined by the channel conductance (greater current at every potential)

Lecture 8: Motor control

- Reflex: stereotyped response without signal integration

Motor neurone arrangement in the ventral horn in spinal cord:

- a-motor neurones for proximal muscles - more medial, distal muscle - more lateral
- a-motor neurones for flexor - close to central canal, extensor - distal

Each muscle tissue is innervated by group of neurones - motor neuron pool

Each neuron innervate several muscle fibres - motor unit

Motor neuron recruitment: Size principle

- As signal increase, smaller motor units recruited first before larger ones
- Smaller motor neurons with smaller diameter, greater resistance, easier to depol.

Proprioception:

- 1a afferent neurones and 1b afferent neurones are intrafusal, within spindles.
- 1a afferent neurone detect presence of velocity of change(tonicphasic), 1b afferent detect presence of change. (Phasic)

Extrafusal fibres are force generating, innervated by a-motor neurons,

Intrafusal fibres are detection, innervated by gamma-motor neurones to change length accordingly.

Stretch reflex:

- Stretch applied on muscle fibre, 1a afferent detect, send signal to SC
- a-gamma co-activation, a-MN shorten muscle, gamma-MN shorten spindle, maintain sensitivity
- 1a inhibitory interneuron reciprocal signalling - inhibition of antagonist muscle

Co-contraction of agonist & antagonist when expecting load, inhibition modulated by descending signal from the brain.

Artificial stimulation:

- External stimulation - stimulate 1a afferent with largest diameter (most ion channel)
- Trigger stretch reflex (Hoffman H reflex)
- Larger stimulus - Motor neuron stimulation (M-wave), before H reflex
- Larger stimulus - M wave only, antidromic cancel H reflex.

Golgi tendon organ:

- Tension sensing 1b afferent, detect presence of stretch.
- Clasp knife reflex, inhibit agonist if tension too great.
- 1b interneuron integrate signal from αδ-pain receptor, brain, highly modulated.

Cross-extension reflex: Withdrawl of limb lead to extension of the other limb via interneurones in the SC

Lecture 9

Ohms Law: Relationship between synaptic current, membrane resistance and potential

- Inhibitory channels decrease resistance (e.g. GABA channels increase Cl permeability)
- Greater synaptic drive - more NT released, greater current.

Metabotropic receptors (slow >50ms), (GPCR)

E.g. mGluR, GABAb

Types of GPCRs:

- Gs: activate adenylyl cyclase - increase cAMP - activate PKA
- Gi: inhibit adenylyl cyclase - decrease cAMP - less PKA
- Gq: activate phospholipase C(PLC), convert PIP2 into DAG and IP3, activate PKC and calmodulin

GDP replaced by GTP when ligand binds

E.g. GABAb binding - Gi, inhibit calcium channels (less NT) and activate K channels (less resistance, hyperpol)

Two types of integration: spatial(space) and temporal(time)

dendritic filtering result in decrease in amplitude and increase in delay of signal

Capacitance: ability to store charge and release, larger SA, greater C

Synaptic plasticity: Frequent and strong signals lead to greater efficacy.

Lecture 10: Voluntary Control ☠️

Structures responsible for voluntary motor control in the cerebral cortex: (Ant-post)

- Prefrontal cortex
- Premotor cortex: premotor area(PM), supplementary motor area(SMA)
- Primary motor cortex (M1), followed by central sulci
- Somatosensory Cortex (S1)
- Broadmann area 5 then 7

Thalamus - cortical pathways (Thalamocortical pathways):

Thalamus supply the cortex with signals,

- Ventral anterior nucleus - premotor area
- Ventral lateral nucleus - supplementary motor area.

Corticospinal tract

- Neurons in the primary motor cortex (M1) project motor signal
- Signal via internal capsule to brainstem, lower limb more medial
- Decussation at lower medulla into lateral corticospinal tract, some to anterior CS tract

Convergence: Many motor neurones can innervate one muscle tissue

Divergence: Motor neurone from the cortex innervate many interneuron pools and MNs

Some neurones codes for dynamic muscles, while others code for static force.

Movement control: The hierarchy:

- Primary Motor Cortex receive signal from PM(external cue) & SMA(intrinsic learnt),S1
- PM receive signal from prefrontal cortex, visual area 5(position), 7(property), and cerebellum(via thalamus VLN)
- SMA receive signal from prefrontal cortex, basal ganglia(via thalamus VAN)

Cerebellum

Input: Mossy fibres into the cerebral cortex, climbing fibre from medulla olives

- Spinal cord: proprioception, pain, temperature etc
- Vestibular system: balance, head movement
- Pontine nucleus: Efferent copy from corticospinal pathway

Output: Different areas of cortex - different internal nucleus - different spinal tracts

- Lateral cortex - dentate nucleus - PMC and M1 via thalamus
    - Corticospinal pathway, influence voluntary movements
- Medial cortex - Globulous & Enboliform nucleus - Red nucleus (midbrain) - Spinal cord
    - Rubrospinal pathway, influence ongoing motor movements
- Medial cortex - fastigial nucleus - Vestibular nuclei - Spinal cord / Optic nerve
    - Vestibulospinal pathway, influence posture and eye movements

Cerebellum adjustment of movement:

- Imaginative model within the cerebellum
- Efferent copy from mossy fibre and climbing fibre - cortex, outcome predicted
- Action adjusted according to imaginative model, sent via rubrospinal tract
- If actual outcome different from prediction, adjust model

Basal Ganglia: Group of nucleus in Diencephalon & midbrain: determine action

- Direct pathway: Cortex -> Striatum -| Globus pallidus ext -| thalamus -> SMA
  - Two GABA-ergic synapse: overall excitatory effect
- Indirect pathway: Cortex -> Striatum -|Globus pallidus int -|subthalamic nucleus -> Globus pallidus ext -| thalamus ->SMA
  - Three GABA-ergic synapse: overall inhibitory effect
- Dopamine effect: D1 excitatory receptor on direct pathway, D2 inhibitory receptor on indirect pathway
- Action selection: Lateral inhibition by cortical inputs, strongest input expressed and inhibit all other actions.

Lecture 11: Visual input

Two eyes create stereopsis: 3D vision, depth perception

Majority of retina contain rod cells that detect light, blind spot at optic nerve, cones at fovea, medial to optic disc

Cells in the eye convert light into electrical signal: phototransduction

Three types of eye movements: Smooth eye persuit, vergence movement & saccade movement

Parallel processing: different properties of an image captured and simultaneous transmission by different neurones

Properties include: wavelength(colour), spatial frequency, contrast, orientation, direction

Rod cells contain discs of rhodopsins, cone cells lave lamellae of L/M/S opsins

Phototransduction mechanism:

- Opsin and rhodopsin are GPCRs that contain specific photopigment molecules
- At certain wavelength it undergoes photoisomerisation, changes shape and causes GPCR activation, activate phosphodiesterase PDE
- PDE hydrolyse cGMP into GMP, ligand gated Na+ channel closes, hyperpol.
- Less glutamate release to bipolar cells.
- Graded response produced: Higher intensity, greater GPCR activation, less glutamate.
    - Bipolar cells downstream of photoreceptor cells also have graded responses
- When returning to dark condition, arrestin hydrolyse phosphorylated G-protein

Retina synaptic pathways: ON and OFF pathways in rod and cone cells

- Cone cells have many different bipolar cells for colour and ON/OFF,
  - ON bipolar cell have mGluR inhibitory receptors: light - less Glu - more depol
  - OFF bipolar cell have AMPA excitatory receptors: light - more Glu - less depol
- Rod cells uses amacrine cells to integrate ON/OFF pathways to cone cells, mGluR on AC
  - ON amacrine cells have gap junction with cone BP, light - less Glu - more depol passed to cone BP
  - OFF amacrine cells release inhibitory glycine, light - less Glu - more depol then glycine, less depol on cone BP

Cone bipolar cells form synapse with root ganglion cells, amount of glutamate release determines RATE of action potential, not a graded response.

- Visual defects:
  - Red L cone defect: protan, causes protanopia, insensitivity to red green and yellow
  - Green M cone defect: Deutan, cause deutanopia, insensitivity to red green yellow
  - Blue S cone defect: Tritan, causes Tritanopia, insensitivity to Blue and green
  - Myopia: shortsightedness
  - Hyperopia: far sightedness

Lecture 12: Sensory systems and hearing

- Receptor transduction: external stimulus to action potentials
  - Strength of the stimulus determines the amplitude of receptor potential
  - Amplitude of receptor potential determines frequency of action potential (frequency coding) after exceeding threshold potential.
  - Tonic & phasic: rate of change of stimulus / presence of stimulus
  - Spontaneous firing rate allow on off signals

Vestibular systems: sensory rotation of head

- Three semi-circular canal organs, one utricle, one saccule
  - Utricle in the horizontal direction(back/forward), saccule in vertical direction(up/down), linear sensory
  - Three semi-circular canal for rotation sensory
- within the canals
  - Sensory receptor cells connected to nerves, have hairs on luminal surface
  - Gelatinous cupula top of the hair, orient to the same direction
  - Movement occur, one increase firing rate, one decrease

- Sensory receptor in vestibular semicircular canal
  - Hair cells actin rich stereocilia in a stair case manner, tallest contain microtubule
  - Cadherin 23/15 between hair, pulling open channel, K influx, Ca entry, NT release.

    - Pushing from other direction closes the cation channels, hyperpol.

- adaptations
    - Adaptation (phasictonic) current decrease overtime, decrease in AP frequency
    - Cadherin links resets when held, desensitisation, similar to gamma motor neurone

Lecture 13: Hearing

Human hearing range: 20-20000 Hz, most sensitive at 1000-4000Hz, having lowest auditory threshold, lowest loudness needed.

Decibels: sound pressure levels: 20log(Pt/Pr), Pt is the testing sound, Pr is reference/ threshold, 10 times increase when increase by 20dB.

- Outer ear: connected to midear by tympanic membrane(eardrum)
  - Pinna around the outside, concha outside semi-covering the canal, meatus next to the canal.
  - The outer ear structures amplifies sound by 10-15 dB, unique structure provide localisation of sound.

- Midear: air filled compartment behind eardrum, eustachian tube to nasal canal
  - Three bones: malleus, incus, stapes, connected to oval window
  - Tensor tympani is a muscle provide reflex, adapt to loud sounds
  - Impedance matching by the ossicles:
    - large tympanic drum-small oval window: amplification of pressure (20dB gain)
    - Larger pressure compensate impedance from air to fluid filled cochlea.
  - midear dysfunction: conduction deafness, inner ear: nerve deafness

- Inner ear:
  - Cochlea: fluid filled compartment, 2.5 coils in human. Three compartments, from top down: Scala tympani, Scala media, Scala vestibuli
  - Sensory epithelium on basilar membrane on scala media.
  - Tonotopy: Basilar membrane at different locations of cochlea tuned to be sensitive towards specific frequency, due to increasing diameter (wider membrane, less stiff)
  - Three rows of outer hair cells, one row of inner hair cell connect to most nerve cells. Basilar membrane move, hair rub against tectorial membrane, receptor potential.
- Auditory nerve fibres
  - Type I auditory fibres connect to specific inner hair cells - tonotopic map in the brain, type II connect to outer hair cells
  - Phase locking occur, maximum AP curve at around 3000Hz

Lecture 14: Visual processing

From the retinal ganglion cells into the visual cortex

- Receptive field: each ganglion has a space in which presence of stimulus lead to electrical response
  - size measured by angle of which to fovea.
  - Centre and surround areas of receptive field have opposite response to light. Depending on ON/OFF ganglion type. Higher sensitivity to contrast.
- Horizontal cells
  - connected photoreceptor cells allow lateral inhibition.
  - HCs have excitatory glutamate receptor, and release GABA to central photoreceptors. Create opposite effect.
  - ON ganglion: light increase, central Glu decrease, peripheral Glu decrease, GABA decrease, central Glu increase.

- Two types of ganglion cell populations
  - midget: small receptor field, mostly in fovea, sustained tonic response to light
  - Parasol: large cell large field, around the retina, phasic response to light
  - Specific type of parvocellular ganglion: colour opponency: R-G, G-R, (RG)-B
  - No colour opponency in magnocellular ganglions
  - Each population of ganglion cells arranged in their own mosaic pattern within the same retinal surface area. Allow parallel processing of info received by the area.

- Visual processing: retina to the cortex
    - superior colliculus(visual tectum in the midbrain)
    - Lateral geniculate nucleus: route to the visual cortex from the thalamus
    - Retinal ganglion cells bifurcate at the optic chiasm, nasal half of neurons crosses.
    - Lateral geniculate nucleus relay info to cortex, based on layer(parvo/magno, L/R)
    - Then into primary visual cortex V1
- Within the visual cortex
    - Ascending info arrive at layer 4
    - Info to other layer(radial), to other cortex horizontal connection
    - Info (L/R) not separated in layer 4, monocular neuron only receive from one eye.

- Functional mapping
    - The image is mapped onto different region of cortex
    - Elongated ON/OFF region in visual cortex, small width, different angle, detect angle of edges. Same angled cells arranged in orientation columns vertically.
    - Cortical receptive field types
        - Simple cells: have preference to orientation, but require exact location of line
        - Complex cells: preference to orientation, does not require exact location
    - Direction selectivity: cortical receptor regions cell also show preference to directions

In summary: each area of cortex correspond to certain area on retina, retinal

topographically. With different columnar receptor areas to detect different features.

Lecture 15: Nerve regeneration

Neuronal damage in the axon: Repair possible in the PNS not the CNS

May be intrinsic reasons / environmental cues.

- Neuronal growth: from the growth cone
  - Growth mode: end of axon is actin rich growth cone, microtubule provide axonal transport, (anterograde kinesin retrograde dynein), actin myosin interaction extend process
  - Transmission mode: release of NT

Determining factor: location of injury, not cell body.

- Difference in the glial cells, Schwann in PNS, oligodendrocyte in CNS
- In PNS, schwann cell(myelinating) and remak cell(non-myelinating) provide poor regeneration
- However during injury, transform to repair schwann cells, strong regen support
- Changes in schwann cells:
  - Trophic support: GDNF, BDNF, NGF
  - Break down of myelin, macrophage and autophage of myelin
  - Elongation of cells produce regen tract

In humans long distance, slow growth of axon, chronic denervation, dysfunctional

Regeneration molecules concentration decrease over time. Target tissue also degenerate

- CNS regeneration: less ability to regenerate, inhibitory environment
    - Astrocyte enlarge
    - Oligodendrocyte do not break down myelin, prevented by myelin asso. molecules
    - Microglia accumulate at injury site - glial scar, no growth beyond this
    - stat3 prevent glial scar formation, but increase in neuronal death
    - also less activation of regenerative associated genes

Both CNS and PNS are regenerative in natal stage

Regen attempts: stabilising microtubule, graft, transplant of embryonic neuron

Lecture 16-19: HD, PD, SC, AD, ASD

Huntington's, Parkinson's, Schizophrenia, Alzheimer's, Autism

Striatal Medium spiny neurons(MSN) have dendritic spines that form many synapses

Grey type I: excitatory, thicker post synaptic membrane.

Grey type II: inhibitory, symmetrical synapse

Dopaminergic neurones form many synapses within the striatum

- Huntington's
  - Hyperkinesia
  - Characteristic: enlarged lateral ventricle, degeneration of marginal caudate and putamen nucleus
  - Autosomal dominant on chromosome 4, Huntingtin protein code by huntington gene, with glutamine CAG repeats on exon 1 or N-terminus, length of repeat more than 34 lead to higher risk and earlier onset
  - Affect direct pathway first, then indirect pathway in the BG, decrease messenger
  - Neuron death in striatum, less inhibition on thalamus, hyperkinesia

- Parkinson’s disease
  - Akinesia, shaking palsy, scooped posture
  - Characteristic: cell death in the substantia nigra, Presence of Lewy body, filamentous protein within of α-synuclein
  - α-synuclein proteins coded by synuclein gene, contain 7 N-terminal repeats, missense mutation and gene duplication lead to PD
  - Ventralateral cell death in substantia nigra compacta, which cells contain Lewy bodies.
  - Less stimulation on direct pathway, less inhibition on indirect pathway - akinesia
  - Rescued by dopamine agonist (restore), electrical inhibition of subthalamic nucleus (inhibit indirect pathway)

- Schizophrenia
  - Positive symptoms: hallucination, delusion, disorganised thought
  - Negative symptoms: Reduced speech, Lack of motivation
  - Cognitive:poor memory, poor learning ability, verbal fluency
  - Characteristic: Enlarged lateral ventricles, reduced cortical size and grey matter, occur before onset. NO CELL DEATH, abnormal white matter/ neuronal migration
  - Dopamine increase lead to loss of singular focus - delusions
    - Treated using Thorazine/chlorpromazine (antipsychotic), reduce positive symptom via blocking D2 dopamine receptor in indirect pathway
  - NMDA hypo function also lead to psychosis symptom
    - treated using NMDA agonist D-serine, glycine.
  - Decrease in synapse number (may correlate to decrease in cortical volume)
  - Genetic factors: Glutamate receptor variants, microdeletions, no single deterministic gene

- Alzheimer’s
  - Dementia, loss of memory, spatial memory, eventual visual problem
  - Begin in the medial temporal lobe (hippocampus, entorhinal cortex, amygdala
  - Characteristic: enlarged lateral ventricles, decrease cortical volume, extracellular β-amyloid plaque, Tau neurofilament tangles
  - Genetic factors: Autosomal dominant on Chromosome 21
    - Mutation of Amyloid precursor protein (APP)
    - Plaque contain C-terminus fragment of APP-mutation in cleavage protein presenilin 1 and 2, miscleavage
    - Trisomy 21 down’s syndrome - overexpression of APP
    - Apolipoprotein ε4 allele
  - Tau lead to neuronal deaths
    - single gene for tau, alt spliced, 3 repeat/4 repeats, bind to microtubule
    - Hyperphosphorylated tau
  - Apolipoprotein E
    - Patients with apoE2/E2 genotype less likely to develop AD
    - High β-amyloid plaque but no tau

- Autism
  - Social ability deficit, restricted repetitive movement
  - Hyperexpansion of brain surface area, overgrowth of brain volume.
  - Caused by polygenic risk facter
    - GWAS reveals low risk from common polymorphism mutation
    - Higher risk from rare gene number variance mutation
    - monogenetic mutation: fragile X, Rett syndrome, Tuberous sclerosis
    - Disruption in synaptic formation: neurexin, neuroligin and shank3

Practicals

H-reflex practical

- Co-contraction allow smooth movements, motor command override agonist-antagonist inhibition. 1a inhibitory interneuron integration.
- Co-contraction allow stability, anticipate loads, allow learning of movement.
- Tendon tap reflex triggers muscle spindle receptors.

• Electrical stimulation:

- Large diameter 1a afferent stimulated first, then α-efferent motor neuron

Vision

• Accomodation: change focus to different distances. Power: 1/near(m) - 1/far(m)

- Cornea fixed, 70% accomodative power
- Lens change shape, 20D when relaxed, 40D when contract.

• Refractive errors

- Myopia: shortsightedness, focus on front of retina, biconcave lens required with perscription of -1/far point(m)
- Hyperopia: farsightedness, focus behind the retina, biconvex lens.
- Presbyopia: stiff lens due to old age. Ciliary muscle cant contract, lens remain relaxed, far sightedness, require biconvex positive lens

• Acuity

- Snellen chart viewed at 6m, Acuity = distance(6m) / lowest row.

- Astigmatism: different curvature on different axis of cornea/retina, treated with cylindrical lens.
- Blind spot: optic disc, nasal to the fovea
- Perimetry: 170 degrees horizontally, 60 degrees stereoptic.
- Retinofugal pathway:
    - Nasal side of optic nerve cross at optic chiasm, before entering lateral graniculate nucleus of thalamus, and onto visual cortex.
    - Crossed over optic nerve carry signal from opposite visual field.
    - Right visual cortex process left visual field, left v1 cortex process right field
- Colour blindess: Protanopia(R/L), Deutanopia(G/M), Tritanopia(B/S)

Neuroanatomy and histology

Distinguish between astrocyte and oligodendrocyte processes:

Astrocyte processes near synapses, no microtubule.

Oligodendrocytes have darker appearances.

CNS&PNS differences,

- myelinated axons in PNS associated with cells, in CNS oligodendrocyte processes myelinate axons, not within cells.
- More loosely arranged in PNS compared to CNS.
- Schwann cells form myelin sheath for one internode.
- Astrocyte in white matter - fibroastrocyte, grey matter protoplasm astrocytes
- CNS contain separate unmyelinated axons, in PNS unmyelinated axon around remak cells.

• Brain structures:

- Cerebellum-brainstem connection: Superior peduncles(midbrain), mideum peduncles(pons), inferior peduncles(medulla)

Hearing

- Primary cues of sound localisation: Interaurral time difference, level difference, spectual cues(pinna)
    - ILD and ITD determine left right, and direction on horizontal plane
    - Spectral cues determine elevation and front/back, pinna create spectual notch, lower amplitude at specific frequency.
    - Low frequency - Interaural time difference, diffraction so no level difference
    - High frequency - Interaural level difference, head blocks sound, phase locking fails at high frequency.
- ITD threshold: 75% correct time difference - 50% correct time difference, from complete random guess to detection, smallest change in delay.
- Spatial threshold: Different angles correspond to different ITD, smallest angle change that can be reliably detected.
- Maximum ITD: time for sound to travel around the head: 2πr/2c, c=sound speed

Cockroach

- Biphasic recording derive from sodium, recording electrode more negative than reference: negative overall signal
- Difference in size of signal due to diameter of axon and distance from axon.
- Conduction time is distance of two peaks of biphasic.