Parkinson’s Disease: 95% of PD cases are idiopathic while only 5% have a genetic origin.

MPTP: Drug that is metabolized. In mice and apes, it leads to human like symptoms of PD: Bradykinesia, postural instability, compromised gait, muscular rigidity (later on: hypokinesia or even akinesia).

Non-motor associated symptoms: depression, hallucinations, bladder dysfunction, no response to dopaminergic treatment, dementia, psychosis.

The PD phenotype can be improved to some extent through visual cues and kinaesthetic feedback.

MPTP is metabolized to MPP+ which ultimately inhibits the respiratory chain in the mitochondria resulting into oxidative stress within. Then, it is transported in vesicles via vesicle monoamine transporter (=: VMAT), where it will bind to negatively charged proteins in the cytoplasm.

In mice, the normal phenotype can be recovered when superoxide dismutase 1 (=: SOD1) is overexpressed in the mitochondrial genome.

The basal ganglia is responsible for the initiation of voluntary movement. Final downstream target of the basal ganglia network is the brainstem. The STN and GPe are target of DBS therapy, which can partially recover the normal phenotype. In the putamen, the D2 and D1 receptors are the main target for optogenetics therapy.

Biomarkers in PD: Loss of olfactory function in 70-100% of all patients and they do not respond to dopaminergic treatment normally later on.

Concordance: 30% vs. 5% (monozygotic vs. dizygotic).

L-DOPA: A precursor of dopamine which is applied in PD to recover the normal phenotype. It acts on the striatum (putamen/caudate) on the D2 and D1 receptors . Permanent use of L-DOPA has dyskinesia as a side effect. Life expectancy is typically reduced by 10 years.

Cell biological and genetic factors in PD: Lewy bodies are observed in the SNpc. They originate from the misfolding of proteins leading to filament formation and aggregation of amyloid bodies finally. Often, alpha-synuclein is involved synucleinopathy. Other proteins are tau, amyloid-beta and TDP-43 (only in ALS though). Bradykinesia will occur only if more than 60% of the neurons are affected by synucleinopathy in the SNpc (synucleinopathy probably leads to cell death in striatal neurons).

Genes: PARKIN, PINK1, ubiquitin C-terminal hydrolase 1, alpha-syn.

Motor systems: Spinal chord injury

Lesion levels and their consequences: Damage on a level affects all levels below.

C1-4: breathing

C2: neck movement

C5: shoulder movement

C6-7: elbow and wrist movement

C7-T1: hand and finger movement

T1-12: sympathicus

T2-T12: trunk stability

T11-L2: parts of sexual function

L2: hip movement

L3: knee extension

L5: knee flexion

L4-S1: ankle movement

S2-3: sexual functions

S2-4: bladder functions

Consequences of SCI: hypokinesia or hyperkinesia, depression, sexual dysfunction, bladder dysfunction, clonus, spasticity.

Spinal disk: left upper side: motor associated functions, left lower: posture and stability, right upper: sensory functions (like touch), right lower: pain and temperature. These things are of course symmetric.

Syndromes: Central cord syndrome: incomplete damage, different things can be targeted.

Brown-Séquard syndrome: one side is damaged: ipsilateral loss of motor functions and proprioception and contralateral loss of pain and temperature sensation.

Anterior cord syndrome: Only dorsal part undamaged (sensory functions) – loss of motor functions, pain, temperature and postural balance.

Posterior cord syndrome: All but dorsal part intact – loss of sensory functions.

Cauda equina syndrome: lower motor neurons affected.

Conus medularis syndrome: lower and upper neurons affected.

Tetraplagia: arms, limbs, upper and lower motoneurons affected. Paraplagia: legs, upper and lower motoneurons affected. Conus medularis: upper and lower motoneurons affected (lowest part of the spinal cord). Cauda equina: lower motoneurons (nerve fibers lying within the spinal cord) affected.

Ration: 3,8 : 1 (male : female) – most injuries occur at C4/C5 level and around T11-L1.

Motor unit: alpha-motoneuron with innervated nerve. There are also gamma-motoneurons that innervate intrafusally (alpha-motoneurons innervate extrafusally) which are needed for proprioception. When alpha-motoneurons activate without gamma-motoneurons, there will be a shortening of the Ia fiber as the muscles contracts and when activation occurs with the activation of a gamma-motoneuron, then there will be no decrease in Ia fiber while contracting.

Ia fiber: type 1 a sensory fiber (primary afferent nerve fiber).

Basal ganglia needed for proper initiation of movement and gait. Cerebellum needed for comparing intended and performed movement and correcting the error so that movement is smooth and nice. Also, the cerebellum is involved in motor skill learning (there are stem cells and ongoing cell proliferation in the granule cell layer).

Local motor circuits are needed for complex movements. There is a central pattern generator that works autonomously when it is stimulated/activated. Cats can be completely decerebrated and put on a treadmill and they will generate normal movement as long as they are on the treadmill. Humans cannot, but experiments have shown that there is a human CPG which can be used for recovery. The CPG also works independently of sensory feedback or supraspinal centres, but they help modulate the CPG.

Flexion: Activation of flexors and inhibition of extensors is ipsilateral. Inhibition of flexors and activation of extensors is contralateral.

Targets of therapy: neuroprotection, rewiring, goal-directed therapy (physiotherapy), reactivation.

A dermatome is a segment of skin that is provided by one spinal nerve (collective representation of skin not discrete representation of every single skin cell).

Corticospinal tract exam: let arm work against gravity and see how well it does.

Dorsal column exam: light touch.

Spinothalamic exam: stinging with safety pin.

Severity of lesion evaluated with the ASIA scale: integrates motor and sensory functions: AIS A is complete loss of function and AIS E is normal function (healthy).

MEP: motor evoked potential to test the pyramidal tract. SSEP: Somatosensory evoked potential to test dorsal column. CHEP: contact heat evoked potential to test spinothalamic tract (pain especially).

Lower motoneuron syndrome: paralysis/paresis, areflexia, loss of muscle tone, denervation signs.

Upper motoneurons syndrome: paresis, minor atrophies due to disuse, spasticity, Babinski’s sign, loss of fine voluntary movements.

Upper motoneurons are found in the brainstem and cerebral cortex.

The visceral nervous system: involved in sympathetic (T1-L2/3) and parasympathetic (S2-4) autonomous functions.

Lesions at T6 and above lead to severe cardiac dysfunctions. Also, tetraplegia patients have a disturbed circadian rhythm (problems falling asleep?).

In the sympathicus, the preganglionic axon (the one descending from the CNS) is short and cholinergic and the postganglionic axon (the one closer to the organs) is long and noradrenergic. In the parasympathicus, the preganglionic axon is long and postganglionic axon is short and both are cholinergic. The hypothalamus is a key structure in the visceral nervous system. (Cholinergic: acetylcholine is the neurotransmitter acting. Noradrenergic: norepinephrine is involved in transmitting the nerve impulses as a neurotransmitter.)

Functions of sympathetic and parasympathetic nervous system:

Sympathetic: increase heart rate, dilate pupils, inhibit salivation, relax airways, inhibit digestion, stimulate release of insulin and glucagon, stimulate gluconeogenesis and release, stimulate secretion of norepinephrine and epinephrine.

Parasympathetic: slow down heart rate, increase salivation, promote digestion, constrict airways, stimulate gall bladder for bile release, dilate blood vessels in intestines and rectum.

Autonomic dysreflexia: life-threatening, noxious (or non-noxious) stimuli below the lesion level (it does not reach the brain, but signalling is still ongoing locally).