Differential diagnostic deliberation in neurology/PGS

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Introduction

Diagnostic deliberation in neurology progresses from the detection of disease symptoms to formulation of a **syndromological, topical** and **nosological** diagnosis, ideally to an **etiological** diagnosis.

The basic instruments of the diagnostic procedure are a detailed, structured *anamnesis* (patient history) and a careful, systematic *clinical neurological examination* (Tab. 1) *(For detailed instructions on the neurological examination, see web Neurology clinic 1. LF UK (https://el.lf1.cuni.cz/neuronorma/))*. To verify a clinical suspicion, it is usually necessary to carry out some of the **auxiliary examinations**.

By **syndromological diagnosis** we mean the sum of the individual manifestations of the disease (subjective symptoms and objective symptoms found during a neurological examination), which are grouped in a characteristic combination of a certain syndrome (e.g. a combination of motor deceleration with resting tremor and muscle stiffness forms an extrapyramidal hypokinetic- rigid or parkinson's syndrome).

Topical diagnosis defines the level of impairment within the peripheral or central division of the nervous system (in the case of Parkinson's syndrome mentioned above, it is a structural or functional impairment of basal ganglia).

Nosological diagnosis formulates the name of the clinical unit (disease) characterized by the identified neurological syndrome together with the clinical course of the disease, reaction to treatment, etc. In the example above, it will most likely be Parkinson's disease (parkinsonian syndrome with a positive response to the administration of levodopa), caused by the death of dopaminergic neurons in the substantia nigra, pars compacta).

The **etiological diagnosis** - the cause of the disease - usually cannot be determined with certainty from the medical history and neurological examination alone. Targeted **auxiliary examination methods** (especially morphological imaging, methods of clinical neurophysiology, biochemical and molecular genetic laboratory tests) are of decisive benefit here.

In the following overview, we present the basic characteristics of the impairment of the individual levels (floors) of the peripheral and central parts of the nervous system, which can be distinguished by the findings from the neurological examination.

Tab. 1. Neurological examination procedure

Orientational examination of mental/psychological functions	
Side dominance	Anamnestic findings of right-handed/left-handed/ambidexterity, possibly verification of tests of dominance.
Consciousness, orientation, attention	Glasgow coma scale or another scale for disorders of consciousness (see Acute states in neurology and disorders of consciousness/PGS). Orientation by person, time and place. Repeating numbers, automatic series (months of the year, etc.).
Symbolic functions	Spontaneous speech (fluency, content and grammatical correctness, articulation, errors, paraphasia, neologisms, etc.) Name objects, parts of the body, colors when prompted. Show objects, execute simple commands. Repeat words and sentences. Read the text aloud, check understanding. Signature, writing any sentence and dictation. Numbers. Right-left orientation.
Memory	Memorizing 3 words, immediate and delayed recall. Recent memory capacity (last meal, current news, etc.), long-term memory (past events).
Practice	Execution of simple and complex commands, description of actions, imitation of gestures. Drawing simple shapes, tracing a pattern.
Executive functions	Verbal fluency (number of words per minute from a given category – animals, fruit, etc. or beginning with a given letter). Movement series (alternating fist-palm right and left, etc.).
Logical thinking	Similarities and differences, interpretation of proverbs.
One's own neurologic examination	
Cranial nerves	(I) anamnestic changes in smell, possibly orientational olfactory tests (II) orientational examination of vision and perimeter (III, IV, VI) oculomotor innervation – following object movement, size, symmetry and response of pupils to light (V) configuration and strength of masticators, corneal and masseter reflex (VII) symmetry of the face at rest, when closing the eyes and clenching the teeth, labial phenomena (VIII) orientational examination of hearing (IX, X) speech articulation, position and mobility of the soft palate, gag reflex (XI) sternocleidomastoid muscle strength (shoulder lifting, bilateral chin rotation) (XII) tongue at rest and while crawling (atrophy, deviations, abnormal movements)
Extremities (upper – UE a lower – LE)	Configuration, standing at rest, in a static position (on forearms, wing position with elbows out), during non-targeted and targeted movement (toe-nose, heel-knee) - observe asymmetries and abnormalities of posture, atrophy, the presence of tremors and other abnormal movements . Range of active and passive movement, muscle tone and strength, signs of rigidity or spasticity during passive movements, dexterity and coordination. Tendon-bone reflexes, pyramidal phenomena of extinction (Mingazzini) and irritation (Juster, Babinski), grip reflex.
Standing and gait	Holding the torso and limbs in a standing position, the width of the base lower limbs. Spontaneous walking, step length and regularity, start and stop (hesitation and pulse, deviations from direction), upper limb synkinesis. Standing stability including standing with legs close together and standing on 1 leg, with eyes closed (Romberg test) and the test of twisting the trunk behind the shoulders back (pull-test).
Senses	Tactile, algic, thermal, vibration (tune) stimuli across the area of the roots and nerves of extremities and nerve roots of the torso. Proprioception of upper and lower extremities.

Peripheral and central disability

The basic task is to recognize whether the individual has peripheral (Tab. 2.) or central (Tab. 3.) damage and further to specify the location of the damage. In a particular patient, the situation may be difficult due to incomplete diability expression or several symptoms make combine from peripheral and central levels. For the requirements of basic decisions, the above mentioned basic characteristics and differences between peripheral and central disabilities are sufficient (Tab. 4.).

Tab. 2. Disability levels of the peripheral nervous system

Muscle
Neuromuscular plate
Peripheral nerve (sensory – motoric – mixed)
Nerve plexus
Roots (dorsal root – ventral root – combined root defect)
Peripheral motoneuron (lower motoneuron, alpha motoneuron, cell of the anterior horns of spinal)

Tab. 3. Disability levels of central nervous system

Spinal cord (nuclei a tracts)

Brain – infratentorial part
▪ brain stem
  ▪ elongated spinal cord
  ▪ pons
  ▪ mesencephalon
▪ cerebellum

Brain – supratentorial part ▪ cortex (frontal – temporal – parietal – occipital) ▪ white matter of the hemispheres (ascending, descending pathways) ▪ thalamus ▪ basal ganglia ▪ other subcortical nuclei

Tab. 4. Basic differences between peripheral and central impairment

Parameter	Peripheral lesion	Central lesion (with dominant involvement of the pyramidal pathways after the acute stage has subsided)
Proprioceptive reflexes	Decreased to absent	Increased
Muscle tone	Decreased (weak paresis)	Increases (spasticity)
Irritating pyramidal phenomena (so-called spastic)	Absent	Present
Disorders of proprioception	If they are present, then in the appropriate distribution *(areae nervinae, radiculares or with an acral maximum)*	If they are present, they are *extensive, whole limb*
Muscle atrophy	Yes, from an early stage in the relevant distribution	Only in later stages
Fasciculation	Yes	No
Muscle weakness	Yes, in the relevant distribution	Yes, in the relevant distribution

Note: The above characteristics of a central involvement correspond to the symptoms of an upper motor neuron lesion. *Pseudo-weak symptoms, pseudo-weak paresis* - a few days to weeks after acute central involvement, there may be muscle weakness, areflexia and hypotonia. Only after this stage of the so-called spinal shock (however, it also affects the brain) does the typical central symptomatology with hyperreflexia and spastic phenomena develop.

Area nervina – area supplied by one nerve

Area radicularis – area supplied by a root

Clinical characteristics of peripheral impairment

Clinical characteristics of peripheral impairment

Within the peripheral system, manifestations may vary depending on which part of periphery is dominantly affected.Their typical or even specific manifestations will be described in a more detailed description of the disabilities of individual levels. Without a doubt the general manifestations of peripheral disability are often present (see Tab. 4.). In the following text and in the diagram in Fig. 1. the basic features of the individual levels of the peripheral lesion are presented.

Muscle impairment

- muscle weakness (localization depends on distribution of involvement)
- atrophy, hypertrophy, pseudohypertrophy (replacement of muscle by non-functional tissue in some types of muscular dystrophy)
- hypotonia
- reduced (but can also be normal) proprioceptive reflexes
- no sensory impairment, but pain (myositis, rhabdomyolysis) may be present

Impairment of neuromuscular junction

- muscle fatigue, weakness depending on previous exertion
- no sensory impairment

- no pain
- normal muscle tone
- normal proprioceptive reflexes
- normal muscle trophism

Peripheral nerve damage

- muscle weakness, hypotonia and hyporeflexia, after prolonged muscle hypotrophy (peripheral, "weak" paresis) in the distribution of the area nervina
- sensory impairment in the distribution of the area nervina or in the "glove, sock" distribution (it may not always be present, it depends on whether a nerve with a sensitive component is affected)
- pain can be present

Impairment of a nerve plexus

- Muscle weakness, hypotonia and other manifestations of weak paresis and sensory disturbances in a distribution not corresponding to the area nervina or radicularis (it is more extensive, plurisegmental)

Impairment of roots

Impairment of the posterior root

- sensory impairment and possibly pain in the distribution of area radicularis
- reduction of proprioceptive reflexes (unless they are not compensated from neighboring roots supplying the same muscle)
- there is no muscle weakness
- muscle fasciculation are not present

Impairment of the anterior root

- muscle weakness, hypotonia and other manifestations of poor paresis in area radicularis distribution
- muscle fasciculation
- no sensory (sensitivity to temperature, pain, proprioception etc.) impairment
- no pain

Most often root impairment, contains a combination of both anterior and dorsal root damage.

Lower motor neuron impairment

- muscle weakness, hypotonia and other manifestations of poor paresis in the area corresponding to the extent of affected cells of the anterior horns of spinal cord may not correspond to area radicularis
- Otherwise identical findings are present as in anterior root impairment

Clinical characteristics of central impairment

Clinical characteristics of central impairment

Central impairment cannot be characterized by a simple common definition. It includes control, modulation and correction systems, which are all involved in information transmission. Significantly different central syndromes arise when affected at the level of spinal cord vs at level of brain.

Syndromes from spinal cord impairment

When examining a patient suspected to have spinal cord damage, it is necessary to determine the patient's subjective problems, including, for example, impaired micturition disorders, defecation and sexual functions. This is followed by a thorough examination of momentum and sensation with regard to the exact character and distribution of the disorder in terms of horizontal and vertical spinal topography (Fig. 3). Based on such a clinical exmination, it is possible to determine the location of the lesion with high probability, onto which further auxillary examinations focus on.

General manifestations of spinal cord impairment

(not all must be expressed/manifested simultaneously)

- failure to move
  - in the affected segment: peripheral ("poor") paresis

    - below the lesion level: central paresis (in the acute stage "pseudo-weak" - see above, in chronic stage accompanied by muscle hypertonicity and spastic phenomena), usually dominated on the lower limbs while walking
- standing stability and gait disorders
- sensitivity disorders below the level of the lesion
- sphincter disorders (depending on the amount of lesion of retention or incontinence of urine and stool)
- back pain and feelings of constriction in certain segments

Focal manifestations

Centromedullary syndrome Anterolateral syndrome Unilateral syndrome Syndrome of anterior and posterior cords

- **centromedullary syndrome** (central cord syndrome, syringomyelia syndrome) The most common cause is trauma, tumor, syringomyelia or ischemia in the area of the a. spinalis anterior. *Basic characteristic* - a disturbance in the perception of heat and cold pain bilaterally in the affected segments with gradual spread in the caudal direction, usually with sacral sparing, with preservation of tactile and deep sensation (proprioception, inclusing vibrational sensation) - the so-called syringomyelic dissociation of sensation. Later, peripheral paresis develops at the level of the affected segments (damage to lower motor neurons).
- **anterolateral syndrome** Most common cause is ischemia. *Basic characteristic* – peripheral paresis at the level of the affected segments, central paresis caudal to the site of the lesion due to damage of the upper motorneurons (pyramidal pathways). The perception of pain, heat, cold is also affected (tr. spinothalamicus), tactile and deep sensation is preserved.
- **unilateral syndrome** (spinal hemisection syndrome, Brown-Séquard syndrome) The most common cause is trauma or multiple sclerosis. *Basic characteristic* - at the level of the lesion there is peripheral (weak) paresis in the relevant segment, on the ipsilateral (ipsilateral to the lesion) lower limb there is central paresis due to damage to the descending pathways and a disorder of deep and partly tactile sensation due to the involvement of the pathway of the posterior cords, there is no movement disorder on the contralateral lower limb and trunk, but there is a thermal and algic sensation disorder with preservation of tactile and deep sensation (i.e. syringomyelic dissociation of sensation - see above). *The upper limit of contralateral sensory impairment is shifted lower than would correspond to the level of impairment because the spinothalamic tract crosses to the other side of the spinal cord about 2 segments above the entry of the posterior roots.*
- **posterior cord syndrome** The classic cause is neurosyphilis, today rather metabolic disorders (diabetes mellitus), possibly localized trauma, tumor. *Basic characteristic* – below the lesion site, a disorder of deep and partially also tactile sensation (discriminative sensation), ataxia, areflexia. There is no paresis, algic and thermal sensation are preserved (so-called tabic or posterior cord dissociation of sensation), but there are often paresthesias.
- **posterior and lateral cord syndrome** The most common causes are Friedreich's disease and other spinocerebellar degenerations or B12 deficiency. Basic characteristics – disorder of deep and tactile sensation, ataxia (sensitive due to impairment of proprioception and cerebellar due to impairment of spinocerebellar pathways), central (spastic) paresis, characteristic spastic-atactic gait. Algic and thermal sensation is relatively preserved.

Brain impairment syndromes

Manifestations of brain impairment/damage can be divided into general symptoms that can arise from various causes and it is usually not possible to infer the exact nature and localization of the pathological process from them:

- headache, possibly as part of intracranial hypertension syndrome or meningeal syndrome
- disorders of consciousness
- generalized epileptic paroxysms

and **focal** symptoms, which on the other hand have a considerable localizational value:

- focal neurologic deficit manifesting as impaired movement or sensation on contralateral limbs
- focal epileptic paroxysms
- cranial nerve impairment
- disorders of speech and cortical functions.

From a practical point of view, it is also important to divide brain symptoms and syndromes into those that arise when either infratentorial or supratentorial structures are affected.

Infratentorial impairment

The main brain structures located beneath the cerebellar tentorium are the brainstem and the cerebellum. Very often, they are affected simultaneously, due to their location in a relatively small, enclosed space and as a result of their common blood supply and close functional connection. Tab. 5 shows the most common clinical manifestations of the involvement of these structures.

Tab. 5. Postižení infratentoriální oblasti – klinické projevy

- Nausea, vomitus, vertigo
- Nystagmus
- Impairment of stability while standing and walking
- Ataxia
- Cranial nerve impairment
- Alternating trunk syndromes (peripheral involvement of the cranial nerves on the opposite side to the hemiparesis and hemihypesthesia)
- Tremor (especially kinetic)
- Hemi- or quadriparesis, disorders of sensitivity
- Disorders of consciousness (with extensive involvement of the trunk or with the craniocaudal progression of the pathological process)

Supratentorial impairment

Impairment of the various supratenotrially located areas in the brain do not show uniform symptomatology. The main manifestations can be divided into cortical involvement and involvement of the white matter of the hemispheres (see tab 6). Some other sub-strucutres of the supratentorially located central nervous system have coordination, modulation and switching functions, and their failure will thus manifest with different symptoms.

E.g. damage to the basal ganglia results in Parkinson's syndrome or dyskinesia, damage to the thalamus leads to complex sensory disturbances, etc.

Tab. 6. Impairment of supratentorial areas – clinical manifestations

Cortex (different manifestations depending on whether the dominant or non-dominant hemisphere is affected)	
disorders of speech	frontal and temporal lobes
disorders of praxis and gnosis	parietal lobes
behavioral disorders	prefrontal areas of the frontal lobes, temporal lobes
cortical disorders of vision	occipital lobes
epileptic paroxysms	the severity of the attack depends on the localization of the focus
paresis and sensory disturbances	frontal and parietal lobes in the vicinity of sulcus centralis
Subcortical nuclei and their connections	
extrapyramidal hypokinetic syndrome	substantia nigra, nigrostriatal connections
chorea	striatumm
dystonia	basal ganglia, thalamus, various levels
autonomic dysfunction, metabolic and endocrine dysregulation	hypothalamus
epileptic paroxysms	amygdala, hippocampus
White matter of the hemispheres (long ascending and descending tracts)	
Central paresis	in the contralateral hemidistribution to the lesion
Sensory disturbances	in the contralateral hemidistribution to the lesion

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