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Development of Complex Curricula for Molecular Bionics and Infobionics Programs within a consortial* framework**

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Neuromorph Movement Control

Neuromorf mozgás szabályozás

Movement diseases: symptoms and possible rehabilitation techniques

(Mozgás betegségek: tünetek és lehetséges rehabilitációs
technikák)

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Main points of the lecture

- **Here we present some well known and studied diseases affecting the elementary movements of the limbs**
- **Such movement disorders or disfunctions:**
 - **SCI (spinal cord injury)**
 - **PD (Parkinson's Disease)**
 - **Dystonia**
 - **Stroke**
 - **HD (Huntington's Disease) etc...**
- **Symptoms and possible rehabilitation techniques are also presented**



Neuromorph Movement Control:

Movement diseases: symptoms and possible rehabilitation techniques

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Different types of movement disorders

- **Akathisia**
- **Akinesia**
- **Chorea**
- **Dystonia**
- **Parkinson's Disease**
- **Huntington's Disease**
- **Tic disorders (Tourette's Syndrome)**
- **Spinal Cord Injury (SCI)**
- **Stroke**
- **Spasm**





Neuromorph Movement Control:

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Further types of movement disorders

- **Associated movements**
- **Ballismus**
- **Cerebral palsy**
- **Genoispasm**
- **Restless leg syndrome**
- **Wilson's disease**
- **Stereotypy**
- **Stereotypic movement disorder**
- **Tremor (resting, postural, kinetic, essential, cerebellar)**
- **Ataxia**



Spinal cord injury (SCI) – Symptoms and classification

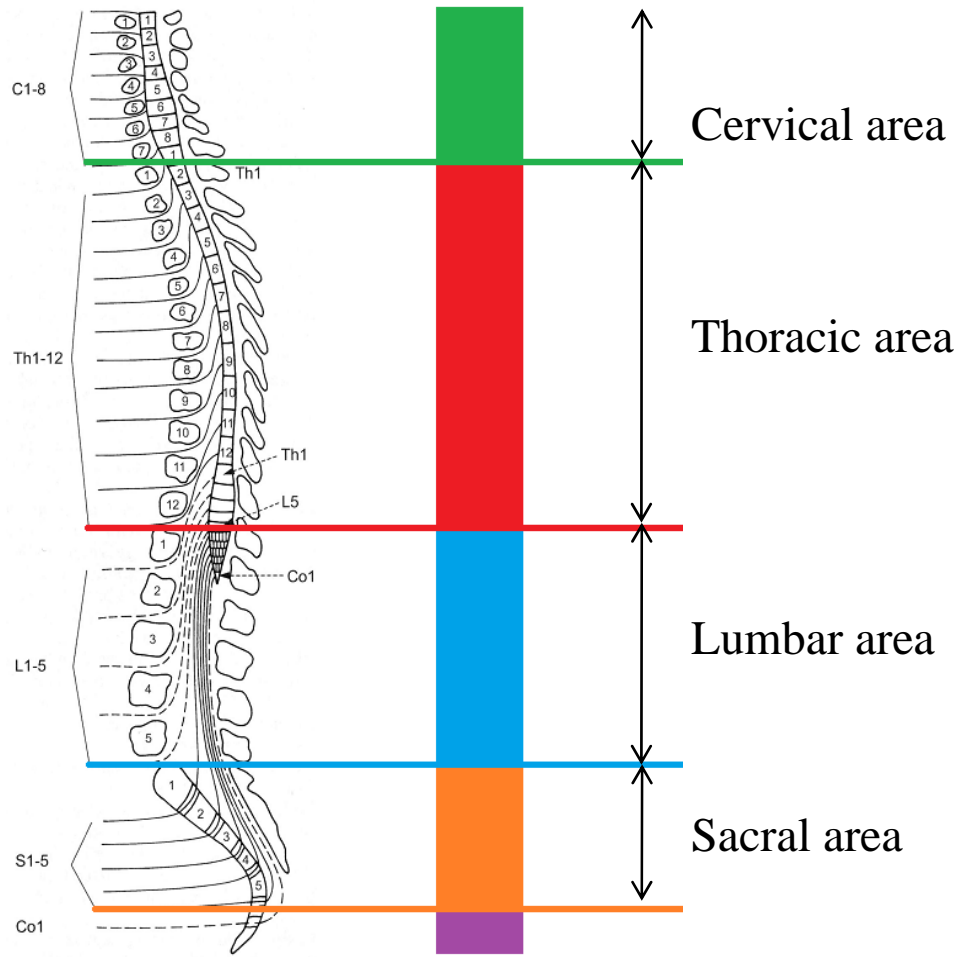
- **As a movement disfunction it means:** an injury to the spinal cord resulted by:
 - Traumatic
 - Other damage of the nerve roots
- **Main causes of SCI:**
 - **Trauma** (accidents, sport activity,)
 - **Ischemia** (resulting from occlusion of spinal blood vessels)
 - **Vascular malformations** (different types of ataxia)
 - **Neurodegenerative diseases**
- **Grey matter in the center of the spinal cord can also be included**



Spinal cord injury (SCI) – Statistics from USA

- **Nearly 250.000 people are involved**
 - 53% paraplegics
 - 47% tetraplegics
- **Astonishing facts**
 - 11.000 new patients/year
 - 56% are between the ages of 16-30
- **Expenses:**
 - 1st year after injury(paraplegics): \$152,000
 - 1st year after injury(tetraplegics): \$417,000
 - Further expenses(paraplegics) (injured when 25): \$428,000
 - Further expenses(tetraplegics) (injured when 25): \$1.35 million

Spinal cord injury (SCI) – Symptoms and classification



- **The spinal cord** is divided into five sections: the cervical, thoracic, lumbar, sacral, and coccygeal regions

- **The level of injury determines the extent of paralysis and/or loss of sensation**

- **Two exactly same injuries: almost impossible**

Spinal cord injury (SCI) – Symptoms and classification

Spinal Cord Level	Function	Spinal Cord Level	Function
C1-C6	Neck flexor	L2,L3,L4	Thigh adduction
C1-T1	Neck extensor	L4,L5,S1	Thigh abduction
C3,C4,C5	Diaphragm supply	L5,S1,S2	Leg extension in the hip joint
C5,C6	Shoulder, elbow flexion-supination	L2,L3,L4	Leg extension at the knee
C6,C7	Elbow, wrist extension, pronation	L4,L5,S1,S2	Leg flexion at the knee
C7,T1	Wrist flexion	L4,L5,S1	Dorsiflexion of the foot
C7,T1	Hand muscle supply	L4,L5,S1	Toes extension at the foot
T1-T6	Intercostals and trunk above the waist	L5,S1,S2	Plantar flexion of the foot
T7-L1	Abdominal muscles	L5,S1,S2	Flexion of toes
L1,L2,L3,L4	Thigh flexion		



Spinal cord injury (SCI) – Symptoms and classification

- **SCI patients (symptoms) were categorized by the American Spinal Injury Association (ASIA)**
 - **This classification is an international standard**
 - **Based on:**
 - Neurological responses
 - Strength of 10 main muscles of the body (on each side)
 - Sensations in all limbs
- **5 main classes are defined by the standard**
 - **A: complete SCI without any motor or sensory function in S4-S5**
 - **B: incomplete where sensory but no motor function below the neurological level and includes S4-S5**

Spinal cord injury (SCI) – Symptoms and classification

- **Further main classes of SCI standard are:**
 - **C: incomplete** where motor function is present below the neurological level; more than half of the muscles below the same level have a muscle grade less than 3.
 - **D: incomplete** where motor function is found below the neurological level and minimum half of the muscles below the level have at least a muscle grade of 3
 - **E: normal** motor and sensory functions are normal. (SCI symptoms might present)

Spinal cord injury (SCI) – Symptoms and classification

- **The main symptoms of SCI**
 - „malfunctioning” of the bladder and bowel sensation
 - Sexual function may also be affected
 - Spasticity (increased reflexes and stiffness of the limbs).
 - Osteoporosis (loss of calcium) and bone degeneration
 - Atrophy of muscle
- **Importance of the accurate localization of the level of the injury**
 - **The determination of the exact level of the injury is really important:**
 - **Making predictions of affected body parts and life functions**
 - **Planning of further rehabilitation methods**

Spinal cord injury (SCI) – Symptoms and classification

- **Types of injuries as a functions of spinal cord level:**
 - **Cervical injuries:** the general result of ‘C’ region is the full or in some cases partial **tetraplegia**
 - a paralysis caused by illness or injury of the spinal cord resulting the loss of use of all their limbs
 - **Thoracic injuries (‘T’ region):** generally causes **paraplegia**. Normal movement functions of the neck, hand and thorax are usually not effected.
 - is a damage in motor or sensory function of the lower limbs
 - **Lumbar and Sacral injuries:** generally decreases the control of the legs and hip, urinary system, and anus.

Spinal cord injury (SCI) – Treatment and Rehabilitation

- **The efficiency of the treatment and especially of the rehabilitation applied highly depends on the time interval elapsed from the injury**
- **Why?**
 - The longer this interval is the more main symptoms of the SCI are present
 - This is true especially for muscles (atrophy) and bones (degeneration of bone shapes)
- **A really efficient method applied in medical rehabilitation is the electrical muscle stimulation (EMS) or functional electrical stimulation (FES)**
 - In lecture number 8 the benefits of EMS and FES are presented

Spasm

- **As a disorder: it is a sudden, involuntary contraction of a muscle or group of muscles.**
 - As an after effect: followed by a burst of pain
- **The most common form of spasm is the: Hypertonic muscle spasm or hypertonus**
 - In this form of spasm the spasm too much muscle tone is produced
 - The main cause of hypertonus: is the malfunctioning of feedback nerves that results in permanent muscle contraction without relaxing time interval
- **The most effective treatment: passive and active training**

Parkinson's Disease (PD) – Symptoms and classification

- **Parkinson's disease (Parkinson's, PD):** a degenerative disorder of the central nervous system (CNS) damaging the patients
 - Cognitive functions
 - Mainly motor functions
- **The movement disorder is represented by:**
high level muscle rigidity and tremor, postural and gait abnormalities, slowing of physical movement (bradykinesia) and a loss of physical movement (akinesia).
 - **Akinesia: is one of the most serious representation of PD**

Parkinson's Disease (PD) – Symptoms and classification

- **Primary symptoms in general:**
 - are the results of decreased stimulation of the motor cortex by the basal ganglia. (It involves insufficient formation and thus action of dopamine produced in the dopaminergic neurons of the midbrain (substantia nigra).
- **Secondary symptoms in general:**
 - include high level cognitive dysfunction and subtle language problems
 - Language problems: mostly difficulties in forming live speech

Parkinson's Disease (PD) – Symptoms and classification

- **The main effects of the PD are** tremor at rest, stiffness, slowing of movement and postural instability
- **According to the area in which PD originates it can be divided into 4 main categories:**
 - **Primary** (idiopathic) - (origin is unknown)
 - [the common form of parkinsonism]
 - **Secondary** (acquired)
 - Hereditary parkinsonism,
 - Multiple system degeneration (Parkinson plus syndromes)
- **The borders between different categories are „thin”**
 - Exact classes are difficult to discern

Parkinson's Disease (PD) – Symptoms and classification

- Independently from the 4 main categories of the symptoms generally PD produces (*with time effects are becoming more serious*)
 - **Motor symptoms**
 - **Rest tremor:** which reaches its maximum intensity when the limb is resting and disappearing with voluntary movement and sleep
 - **Rigidity:** according to joint stiffness and increased muscle tone (sometimes with joint pain)
 - **Non-motor (Neuropsychiatric) symptoms including cognitive-sensory disfunctions and even sleeping difficulties, mood and behavior problems**
 - Cognitive problems: occurring in the early stages of the parkinsonism with poor task execution, oscillating attention, and memory problems

Parkinson's Disease (PD) – The roots

- PD has been considered a non-genetic disorder.
 - However numerous studies have revealed that: nearly 15% of PD patients have a first-degree relative to be involved in PD
- From neurobiological point of view:
 - The basal ganglia is a group of brain structures innervated by the dopaminergic system
 - **In PD patients: the mostly effected** part of the brain is **the basal ganglia** and the **dopaminerg system**
 - **In addition:** symptoms of PD originate from the decreased activity of dopamine cells due to cell death in the substantia nigra

Parkinson's Disease (PD) – Treatment and Rehabilitation

- **Unfortunately:** at the present there is still no cure for PD patients
- **It was showed:** in lecture number 7 how important was to make quantitative comparisons of healthy subjects and PD patients so that to be able to apply proper treatment on the patient
- **The applied cure depends on the stage of the disease**
 1. **Widely used:** (L-DOPA method) in which L-DOPA is transformed into the dopaminerg system to recover the number of dead cells
 2. **DBS (deep brain stimulation):** implanting electrodes surgically and stimulating deep areas of the brain (e.g.: thalamus)
 3. An alternate solution could be the FES help when tremor is present at a high level of activity

Parkinson's Disease (PD) – Treatment and Rehabilitation (Deep Brain Stimulation)

- **DBS is a commonly used surgical method involving:**
 1. the implantation of a medical device (brain pacemaker) via electrodes
 2. The implanted pacemaker sends electrical impulses to specific parts of the brain
- **Despite of the long employment of DBS some underlying principals have not been cleared yet**
- **The system itself consists of 3 main components:**
 - **Implanted pulse genertor (iPG)**
 - **Lead and extension**

Parkinson's Disease (PD) – Treatment and Rehabilitation (Deep Brain Stimulation)

- **iPG:** is a battery-powered electrical stimulator placed in a titanium housing below the clavicle or the abdomen.
 - it sends electrical signals to the brain in order to interfere with neural activity
- **Lead:** is a coiled wire insulated in polyurethane with four platinum iridium electrodes placed in the target sites of the brain
- **Extension:** the lead is connected to the IPG through this interface.
 - a wire running from the head, down the side of the neck, behind the ear
- **Targeted brain sites:**
 - subthalamic nucleus
 - globus pallidus interna

Dystonia – Symptoms and classification

Dystonia: is a neurological movement disorder where **oscillating (random) muscle contractions** result in twisting and uncontrolled repetitive movements with abnormal postures.

- **It can be:**
 - Hereditary
 - Caused by some other factors like trauma, infection, poisoning
 - reaction to drugs
- **Types of dystonia**
 - Generalized
 - Focal
 - Segmental
 - Intermediate



Dystonia – Symptoms and classification (Segmental Dystonia)

- **There are 4 different types of dystonic disorders**
 - **Segmental dystonia** is the kind that affects the adjoining segments (mostly the extremities)
- **Types of segmental dystonia:**
 1. **Hemidystonia:** affects an arm and a leg on the same side of the body.
 2. **Multifocal dystonia:** affects many different parts of the body.
 3. **Generalized dystonia:** affects most of the body, frequently involving the legs and back.
- **Treatment is difficult and has been limited to minimizing the symptoms of the disorder, since there is no cure available**
- **The causes have not been known yet**

Stroke – Symptoms and classification

- **It is the rapidly increasing loss of brain function(s) due to disturbance or damage to the blood supply of the brain.**
- **Major causing reasons:**
 - lack of blood flow (**ischemia**) caused by some blockage in the vessels of the brain (thrombosis, arterial embolism)
 - leakage of blood.
- **Result:** the affected area will be unable to function, which leads to the **inability** of limb movements on one side of the body; **inability** to handle (understand; generate) speech; **inability** to see one side of the visual field.

Stroke – Symptoms (subtypes of stroke) and classification

- Different subtypes of stroke are discerned depending on the effected area

Stroke Subtypes (from motor/movement/sensory disorder point of view)

- hemiplegia
- reduction in sensory and/or vibratory sensation
- muscle weakness of the face
- decreased reflexes
- Balance problems

Brainstem is involved

- Problems with movement coordination – **cerebellum is involved**

Stroke – Statistics and Rehabilitation

- **Stroke as a disorder is the leading cause of adult disability in the United States and Europe as well:**
 - It is not a movement disorder but the consequences of stroke can lead to have movement/motor disfunctions
- Here are some interesting statistics:
 1. **NEARLY 700.000 PEOPLE ARE INVOLVED EACH YEAR**
 2. **50% OF PEOPLE INVOLVED MAY HAVE PARALYSIS ON ONE SIDE OF THEIR BODIES AFTER REHABILITATION PROCEDURE**
- **Depending of the stages and the size of the affected areas of the brain rehabilitation of stroke patients can be partly succesful**
 - **Thus:** it is really important to improve rehabilitation methods applied (movement disfunctions could be partly recovered by using FES)

Huntington's Disease (HD) – Symptoms and classification

- HD is a neurodegenerative genetic disorder, which **affects muscle coordination** and leads to cognitive decline.
- **The causes of HD: Originates from genetically programmed degeneration of nerve cells, in certain areas of the brain.**
 - This degeneration causes typically: **uncontrolled movements**, loss of intellectual faculties, emotional disturbance.
 - Effected cell structure: basal ganglia and structures deep in the brain with functions including coordinating the movement of the body.
 - Within the basal ganglia, HD attacks neurons of the striatum.
 - Thinking, perception and memory could be threatened if HD attacks the outer regions (cortex) of the brain

Huntington's Disease (HD) – Symptoms (from motor control/movement point of view) and treatment

- HD may begin with **uncontrolled movements (chorea)** in the:
 - Fingers; feet
 - Face; trunk
- **If the patient is anxious** the intensity of the uncontrolled movements may increase
- In some cases HD begins with problems in balancing the body.
- If the disease is **in latter stages**: the patient can produce **problems in walking** and the **likelihood of falling is at an increased level**
- **Unfortunately**: there is still no cure for HD but:
 - there are treatments available to reduce the intensity of some of its symptoms

Tourette's Syndrome (TS) – Symptoms and classification

- **Tourette Syndrome (TS):** is an inherited neurological disorder, discovered by Georges-Albert-Edouard-Brutus-Gilles-de la-Tourette)
 - Nearly 100,000-200,000 are affected only in the U.S.
 - The chance of inheriting TS is 50%. (Males seem to be getting it more than females.)
- **It is an autosomal dominant disorder that causes involuntary actions: tics**
- **Tic:** is an involuntary physical action such as like:
 - Sudden waving of arms, vocal actions (obscenity, profanity).
 - Tics are resulted by altering the way the part of the brain that controls all your actions.

Tourette's Syndrome (TS) – Clinical description

- **TS affects how the basal ganglia handles its transmitter chemicals**
- **Anatomical origins:** the basal ganglia part of the brain is responsible for controlling the actions made by a human independently from being physical or verbal.
- **Location of basal ganglia:** it is found in the center of the brain.
- **Main function:** it utilizes the transmitter chemicals such as:
 - dopamine, serotonin, norepinephine.
- **An example of an physical tic** is a body part twitching a lot.
- **An example of a verbal tic** is shouting profanity.

Tourette's Syndrome (TS) – Treatment

- **There is no cure for tourette syndrome.**
- **Most patients do not need medical treatment because the symptoms are mild**
 - They are not prevented in being the member of the society
- **More than one medication to prevent symptoms**
- **Here is a list of some drugs used to treat Tourette syndrome.**
 - Haloperidol (Haldol)
 - Pimozide (Orap)
 - Fluphenazine (Proxlixn)
 - Clonidine (Catapres)

Locked-in-Syndrome

- **Locked-in syndrome:** is a condition in which a patient is aware and awake but cannot **move or communicate verbally** due to complete paralysis of nearly all voluntary muscles in the body except for the eyes.
 - **Total locked-in syndrome is a version of locked-in syndrome where the eyes are paralyzed as well.**

Affected regions

- Neuronal tracts that run in the ventral and medial areas of the medulla, pons, and lower mid-brain
- Medial lemniscus (fine touch, vibration, proprioception)
- Corticospinal and corticobulbar tracts (voluntary movement)
- Eye cranial nerve nuclei

Possible solution for communication to locked-in-syndrome patients (without further details)

- **A possible solution to make contact with patients is the BCI (brain computer interface) based on EEG (*electroencephalogram*)**
- **Electroencephalogram:** is a measure of the brain's voltage fluctuations as detected from scalp electrodes.
 - It is an approximation of the cumulative electrical activity of neurons
- **P300 evoked potential is used as a control signal to BCI**
 - occurs in response to a significant but low-probability event
 - 300 milliseconds after the onset of the target stimulus
 - Focus specific

Locked-in-syndrome communication through P300 evoked potential

- A large display is placed in front of the subject
 - On the display characters of the alphabet are flashed one after each other
- **EEG measurement is in progress while displaying the alphabet**
- The patient thinks on a certain character (e.g.: „C”)
- When „C” appears P300 activity is evoked and it can be measured accurately if the patient is able to handle his/her thoughts in the proper manner
- **If P300 detected:** then the selected character is going to be displayed on a 2nd display



Locked-in-syndrome communication through P300 evoked potential (**Pros and Contras**)

+

The patient is able to communicate with the environment

Hence: the mental state of the patient can be improved

Through communication physical state might be improved as well

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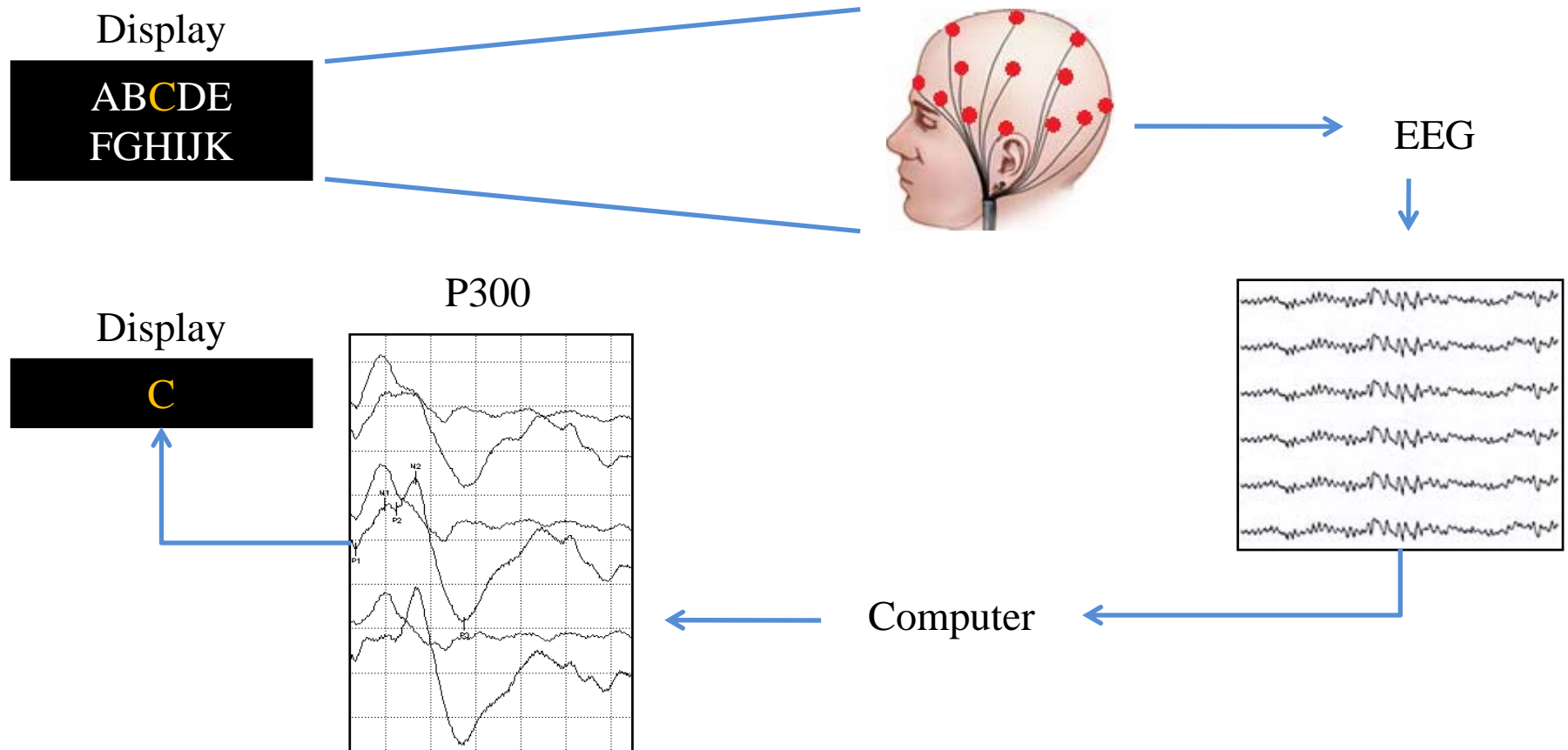
To detect a clear P300 evoked potential the patient must clearly focus on the desired character

To focus on the desirable character the patient has to learn a lot

Long lasting learning period



Locked-in-syndrome communication through P300 evoked potential (system components)



Multiple sclerosis (MS)– In general

- **It is an inflammatory disease**
- **In which:** the fatty myelin around the axons of the brain and the spinal cord are damaged
 - Fatty myelin: is a material surrounding and protecting nerve cells
- It affects the ability of axons to have proper communication with each other
- When the myelin is no longer available axons cannot conduct electrical signals
 - Action potentials are not transferred
- It often causes physical and cognitive disability

Multiple sclerosis – Signs and symptoms

- **MS patient may suffer any neurological symptoms**
- **Symptoms:**
 - Loss of sensitivity
 - Procking
 - Numbness
 - **Muscle weakness**
 - **Muscle spasm**
 - Problems in speech and swallowing
 - Bladder and bowel difficulties
 - Emotional symptoms (depression)

Multiple sclerosis – Classification

- **4 main subtypes of MS – it is important to know in which subtype the patient can be classified for**
 - Accurate prognosis
 - Therapeutic decisions
- **HOWEVER: no known cure is available for MS**
- **Standardized subtype definitions:**
 - Relapsing remitting
 - Secondary progressive
 - Primary progressive
 - Progressive relapsing

Summary

- **In this lecture some known diseases like PD,HD,stroke,SCI etc... were presented.**
 - Symptomes, the origins (**if they have been revealed**), classifications were summerized as well
- **Rehabilitation methods and alternative treatment techniques were collected together and presented**
 - In the cases of some **SCI patients, stroke patients** who are met some requirements concerning to the stages of their diseases we showed the benefits of FES (functional electrical stimulation)

Summary

- In the case of the **PD patients** FES as a possible rehabilitation technique was suggested and **DBS (deep brain stimulation)** as a common treatment was introduced with technical parameters
- A serious neural-movement disease locked-in-syndrome was also presented together with its symptoms
 - As an available technique for building up the communication with these patients a system and its components was presented
 - This system makes the communication based on the detection of P300 evoked potential

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