Spinal cord injuries- clinical assessment. New pharmacological approach in brain and spinal cord neuroprotection and neurorecovery treatment

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The topic of this teaching course is not covering current physiatric endeavors in SCI treatment like: low-level laser therapy (LLLT), functional electrical stimulation (FES), oscillating field stimulator (OFS), magnetic stimulation (MS), stimulation of the spinal central pattern generator (CPG), etc.

Also, cell and tissue transplantation is beyond the scope of this teaching course.

Learning objectives

- CLASSIFICATION OF SCI
- HOW TO ESTABLISH THE NEUROLOGIC

LEVEL OF INJURY?

- PHYSICAL EVALUATION

- TREATMENT – BASIC ASPECTS

Ø INTRODUCTION

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Spinal cord injury (SCI) is an insult to the spinal cord resulting in a change, either temporary or permanent, in its normal motor, sensory, or autonomic function.

- EU: 330 000 people are living with SCI sequels (11000 new cases every year).

- USA: between 227,080 and 300,938 people are living with SCI sequels (2007) (annual incidence of approximately 12 000 new cases).

Mechanism and pathophysiology

Primary injury – the mechanisms are not yet completely elucidated

- Destruction from direct contusion and axonal strech
- Compression by bone fragments, hematoma, or disk material
- Ischemia from damage or impingement on the spinal arteries

The secondary injury process leads to disastrous consequences: neuronal necrosis, neuronal apoptosis like, scar and cyst formation, demyelination, disruption of neural pathways (disconnection).

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Classification and terminology

The International Standards for Neurological and Functional Classification of Spinal Cord Injury is a widely accepted system describing the level and extent of injury based on a systematic motor and sensory examination of neurologic function.

The following terminology has developed around SCI:

- Tetraplegia (replaces the term quadriplegia) - Injury to the spinal cord in the cervical region, with associated loss of muscle strength in all 4 extremities

- Paraplegia - Injury in the spinal cord in the thoracic, lumbar, or sacral segments, including the cauda equina and conus medullaris

Spinal shock

- Spinal shock is a state of transient physiologic (rather than anatomic) reflex depression of cord function below the level of injury, with associated loss of all sensorimotor functions. An initial increase in blood pressure due to the release of catecholamines, followed by hypotension, is noted.

Flaccid paralysis, including of the bowel and bladder, is observed, and sometimes sustained priapism develops.

These symptoms tend to last several hours to days until the reflex arcs below the level of the injury begin to function again (e.g. bulbocavernosus reflex, muscle stretch reflex [MSR]).

Neurogenic shock

- Neurogenic shock is manifested by the triad of hypotension, bradycardia, and hypothermia. Shock tends to occur more commonly in injuries above T6, secondary to the disruption of the sympathetic outflow from T1-L2 and to unopposed vagal tone, leading to a decrease in vascular resistance, with associated vascular dilatation.

Neurogenic shock needs to be differentiated from spinal and hypovolemic shock. Hypovolemic shock tends to be associated with tachycardia.

- Autonomic dysreflexia is an autonomic dysfunction, including orthostatic hypotension and impaired cardiovascular control following SCI. It is recommended that an assessment of autonomic function be routinely used.

American Spinal Injury Association (ASIA) classifications and assessment

Extent of injury is defined by the ASIA Impairment Scale (modified from the Frankel classification), using the following categories:

- A - Complete: No sensory or motor function is preserved in sacral segments S4-S5
- B - Incomplete: Sensory, but not motor, function is preserved below the neurologic level and extends through sacral segments S4-S5.

- C - Incomplete: Motor function is preserved below the neurologic level, and most key muscles below the neurologic level have muscle grade less than 3.

- D - Incomplete: Motor function is preserved below the neurologic level, and most key muscles below the neurologic level have muscle grade higher than or equal to 3.

- E - Normal: Sensory and motor functions are normal.

Perform a rectal examination to check motor function or sensation at the anal mucocutaneous junction. The presence of either is considered sacral-sparing.

Definitions of complete and incomplete SCI are based on the above ASIA definition with sacral-sparing.

- Complete - Absence of sensory and motor functions in the lowest sacral segments
- Incomplete - Preservation of sensory or motor function below the level of injury, including the lowest sacral segments

Other classifications of SCI include the following:

•Central cord syndrome often is associated with a cervical region injury and leads to greater weakness in the upper limbs than in the lower limbs, with sacral sensory sparing.

•Brown-Séquard syndrome, which often is associated with a hemisection lesion of the cord, causes a relatively greater ipsilateral proprioceptive and motor loss, with contralateral loss of sensitivity to pain and temperature.

•Anterior cord syndrome often is associated with a lesion causing variable loss of motor function and sensitivity to pain and temperature; proprioception is preserved.

•Conus medullaris syndrome is associated with injury to the sacral cord and lumbar nerve roots leading to areflexic bladder, bowel, and lower limbs, while the sacral segments occasionally may show preserved reflexes (eg, bulbocavernosus and micturition reflexes).

•Cauda equina syndrome is due to injury to the lumbosacral nerve roots in the spinal canal, leading to areflexic bladder, bowel, and lower limbs.

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How to establish the neurologic level of injury?

Motor strengths and sensory testing

Muscle strength is graded using the following Medical Research Council (MRC) scale of 0-5:

- (5) - Normal power
- (4+) - Submaximal movement against resistance
- (4) - Moderate movement against resistance
- (4-) - Slight movement against resistance
- (3) - Movement against gravity but not against resistance
- (2) - Movement with gravity eliminated
- (1) - Flicker of movement
- (0) - No movement

You have to keep in mind that there are 8 grades of muscle strength.

Muscle strength always should be graded according to the maximum strength attained, no matter how briefly that strength is maintained during the examination. The muscles are tested with the patient supine.

The following key muscles are tested in patients with SCI, and the corresponding level of injury is indicated:

Upper limb – 5 items

- C5 - Elbow flexors (biceps, brachialis)
- C6 - Wrist extensors (extensor carpi radialis longus and brevis)
- C7 - Elbow extensors (triceps)
- C8 - Finger flexors (flexor digitorum profundus) to the middle finger
- T1 - Small finger abductors (abductor digiti minimi)

Lower limb – 5 items

- L2 - Hip flexors (iliopsoas)
- L3 - Knee extensors (quadriceps)
- L4 - Ankle dorsiflexors (tibialis anterior)
- L5 - Long toe extensors (extensors hallucis longus)
- S1 - Ankle plantar flexors (gastrocnemius, soleus)

Sensory testing is performed at the following levels:

- C2 - Occipital protuberance
- C3 - Supraclavicular fossa
- C4 - Top of the acromioclavicular joint
- C5 - Lateral side of antecubital fossa
- C6 - Thumb
- C7 - Middle finger
- C8 - Little finger

- T1 - Medial side of antecubital fossa
- T2 - Apex of axilla
- T3 - Third intercostal space (IS)
- T4 - Fourth IS at nipple line
- T5 - Fifth IS (midway between T4 and T6)
- T6 - Sixth IS at the level of the xiphisternum
- T7 - Seventh IS (midway between T6 and T8)
- T8 - Eighth IS (midway between T6 and T10)

- T9 - Ninth IS (midway between T8 and T10)
- T10 - 10th IS or umbilicus
- T11 - 11th IS (midway between T10 and T12)
- T12 - Midpoint of inguinal ligament
- L1 - Half the distance between T12 and L2
- L2 - Midanterior thigh
- L3 - Medial femoral condyle

- L4 - Medial malleolus
- L5 - Dorsum of the foot at third metatarsophalangeal joint
- S1 - Lateral heel
- S2 - Popliteal fossa in the midline
- S3 - Ischial tuberosity
- S4-5 - Perianal area (taken as 1 level)

You have to keep in mind that there are 28 levels to be evaluated.

Sensory scoring is for light touch and pinprick, as follows:

- 0 - Absent
- 1 - Impaired or hyperesthesia
- 2 – Intact

A score of zero is given if the patient cannot differentiate between the

point of a sharp pin and the dull edge.

Motor level - Determined by the most caudal key muscles that have muscle strength of 3 or above, while the segment above is normal (= 5)

Motor index scoring - Using the 0-5 scoring of each key muscle, with total points being 25 per extremity (per limb) and with the total possible score being 25 x 4 limbs (=100).

Sensory level - Most caudal dermatome with a normal score of 2/2 for pinprick and light touch

Sensory index scoring - Total score from adding each dermatomal score with possible total score = 112 [28 items x 2 sides x 2 maximum (pinprick and light touch)]

Neurologic level of injury - Most caudal level at which motor and sensory levels are intact, with motor level as defined above and sensory level defined by a sensory score of 2

Zone of partial preservation - All segments below the neurologic level of injury with preservation of motor or sensory findings (This index is used only when the injury is complete)

Skeletal level of injury - Level of the greatest vertebral damage on radiograph

Lower extremities motor score (LEMS) - Uses the ASIA key muscles in both lower extremities, with a total possible score of 50 (ie, maximum score of 5 for each key muscle [L2, L3, L4, L5, and S1] per extremity). A LEMS of 20 or less indicates that the patient is likely to be a limited ambulator.

A LEMS of 30 or more suggests that the individual is likely to be a community ambulator.

Differentiating a nerve root injury from SCI can be difficult. The presence of neurologic deficits that indicate multilevel involvement suggests SCI rather than a nerve root injury.

In the absence of spinal shock, motor weakness with intact reflexes indicates SCI, while motor weakness with absent reflexes indicates a nerve root lesion.

With the ASIA classification system, the terms paraparesis and quadriparesis now have become obsolete.

The ASIA classification using the description of the neurologic level of injury is employed in defining the type of SCI (e.g. C8 ASIA A with zone of partial preservation of pinprick to T2).

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Physical evaluation in SCI

The primary survey focuses on life-threatening conditions. Assessment of airway, breathing, and circulation takes precedence (A-B-C).

The degree of respiratory dysfunction is dependent on:

- preexisting pulmonary comorbidity
- the level of SCI
- associated chest wall or lung injury.

Any or all of the following determinants of pulmonary function may be impaired in the setting of SCI:

- Loss of ventilatory muscle function from denervation and/or associated chest wall injury
- Lung injury, such as pneumothorax, hemothorax, or pulmonary contusion
- Decreased central ventilatory drive that is associated with head injury or exogenous effects of alcohol and drugs

A direct relationship exists between the level of cord injury and the degree of respiratory dysfunction.

- With high lesions (ie, C1 or C2), vital capacity is only 5-10% of normal, and cough is absent.
- With lesions at C3 through C6, vital capacity is 20% of normal and cough is weak and ineffective.

- With high thoracic cord injuries (ie, T2 through T4), vital capacity is 30-50% of normal, and cough is weak.

- With lower cord injuries, respiratory function improves.

- With injuries at T11, respiratory dysfunction is minimal. Vital capacity is essentially normal, and cough is strong.

Other findings of respiratory dysfunction include the following:

- Agitation, anxiety, or restlessness
- Poor chest wall expansion
- Decreased air entry
- Rales, rhonchi
- Pallor, cyanosis
- Increased heart rate
- Paradoxic movement of the chest wall
- Increased accessory muscle use
- Moist cough

In all patients, assessment of deep tendon reflexes and perineal evaluation is critical. The presence or absence of sacral sparing is a key prognostic indicator.

The sacral roots may be evaluated by documenting the following:

- Perineal sensation to light touch and pinprick
- Bulbocavernous reflex (S3 or S4)
- Anal wink (S5)
- Rectal tone
- Urine retention or incontinence
- Priapism

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- Ø Emergency Department Care
- Ø Consultations
- Ø Further Inpatient Care
- Ø Steroid therapy in SCI
- Ø New therapies

Treatment

Pre-hospital care

- We need to stabilize and immobilize the spine according to standard protocols
- Patients are usually transported to the ED with a cervical hard collar on a hard backboard.
- The patient should be secured so that in the event of emesis, the backboard may be rapidly rotated 90 degrees while the patient remains fully immobilized in neutral position.

Emergency Department Care

Assessment and treatment of airway, respiration, and circulation takes precedence.

Airway management in the setting of SCI, is complex and difficult.

- The cervical spine must be maintained in neutral alignment at all times.
- Clearing of oral secretions and/or debris is essential to maintain airway patency and to prevent aspiration.
- Intubation may be required in others. Failure to intubate emergently when indicated because of concerns regarding the instability of the patient's cervical spine is a potential pitfall.

Hypotension may be hemorrhagic and/or neurogenic

A diligent search for occult sources of hemorrhage must be made.

The most common causes of occult hemorrhage are:

- Chest injuries
- Intra-abdominal, or retroperitoneal injuries
- Pelvic or long bone fractures.

Appropriate investigations include radiography or CT scanning. FAST (focused abdominal sonography for trauma) ultrasonographic study may be required to detect intra-abdominal hemorrhage.

- Once occult sources of hemorrhage have been excluded, we have to initiate the treatment of neurogenic shock, if it's the case, focused on fluid replacement (isotonic crystalloid solution, maximum 2 liters, in the first step). Overzealous crystalloid administration may cause pulmonary edema.

- Systolic blood pressure (BP) should be 90-100 mm Hg.
- Heart rate should be 60-100 beats per minute in normal sinus rhythm.
- Hemodynamically significant bradycardia may be treated with atropine.
- Urine output should be more than 30 mL/h. Placement of a Foley catheter to monitor urine output is essential (low doses of dopamine in the 2- to 5-mcg/kg/min range are sufficient if it's the case)
- Prevent hypothermia.

- Associated head injury occurs in about 25% of SCI patients. A careful neurologic assessment is mandatory. Noncontrast head CT scanning should be performed.

- Ileus is common. Placement of a nasogastric tube is essential. Antiemetics should be used aggressively.

- The patient is best treated initially in the supine position. Use analgesics appropriately and aggressively to maintain the patient's comfort.

- Prevent pressure sores. Denervated skin is particularly prone to pressure necrosis. Turn the patient every 1-2 hours. Remove the spine board as soon as possible.

Consultations

- Neurosurgeon and/or orthopedist is required
- General surgeon or trauma specialist
- Other consultations may be required.

Further Inpatient Care

- Admit all patients with an acute SCI, depending on the level of neurologic deficit and associated injuries, the patient may require admission to the ICU, neurosurgical observation unit, or general ward.

Studies from the 1960s and 1970s showed that the patients experienced no improvement with emergent surgical decompression.

In the only recent (1997) prospective, randomized, controlled study to determine whether functional outcome is improved in patients with SCI, Vaccaro reported no significant difference between early (<3 d, mean 1.8 d) or late (>5 d, mean 16.8 d).

Emergent decompression of the spinal cord is recommended in those

select patients with extradural lesions (e.g. epidural hematomas or abcesses).

The role of immediate surgical intervention is limited to:

- impingement of spinal nerves
- facet dislocation
- bilateral locked facets
- cauda equina syndrome.

- Treatment of pulmonary complications and/or injury in patients with SCI includes supplementary oxygen for all patients and chest tube thoracostomy for those with pneumothorax and/or hemothorax.

The ideal technique for emergent intubation in the setting of SCI is fiberoptic intubation with cervical spine control.

Indications for intubation in SCI are :

- acute respiratory failure
- decreased level of consciousness (Glasgow score <9)
- increased respiratory rate with hypoxia
- PCO_2 more than 50
- Vital capacity less than 10 mL/kg.

In the presence of autonomic disruption from cervical or high thoracic SCI, intubation may cause severe bradyarrhythmias from unopposed vagal stimulation.

Preoxygenation with 100% oxygen may be preventive. Atropine may be required as an adjunct. Topical lidocaine spray can minimize or prevent this reaction.

Steroid therapy in SCI

The National Acute Spinal Cord Injury Studies (NASCIS) II and III, a Cochrane review of all randomized clinical trials and other published reports, have verified significant improvement in motor function and sensation in patients with complete or incomplete SCIs who were treated with high doses of methylprednisolone.

Absolutely no evidence from these studies suggests that giving the medication earlier (eg, in the first hour) provides more benefit than giving it later (eg, between hours 7 and 8).

Steroid therapy in SCI

The authors only concluded that there was a benefit if given within 8 hours of injury following the NASCIS trials.

- The use of high-dose methylprednisolone in nonpenetrating acute SCI had become the standard of care in North America. Nesathurai and Shanker revisited these studies and questioned the validity of the results.

Steroid therapy in SCI

- A number of professional organizations have therefore revised their recommendations pertaining to steroid therapy in SCI.
  - The Canadian Association of Emergency Physicians is no longer recommending high-dose methylprednisolone as the standard of care.
  - The Congress of Neurological Surgeons has stated that steroid therapy "should only be undertaken with the knowledge that the evidence suggesting harmful side effects is more consistent than any suggestion of clinical benefit."

Steroid therapy in SCI

The American College of Surgeons has modified their Advanced Trauma Life Support guidelines to state that methylprednisolone is "a recommended treatment" rather than "the recommended treatment.“

- The current recommendation is to treat all SCI patients according to the local/regional protocol. If steroids are recommended, they should be initiated within 8 hours of injury with the following steroid protocol: methylprednisolone 30 mg/kg bolus over 15 minutes and an infusion of methylprednisolone at 5.4 mg/kg/h for 23 hours beginning 45 minutes after the bolus.

New therapies

- For a variety of reasons, very few randomized control clinical trials in neuroprotection and neurorecovery have generated positive results in the last 30 years.

- Although extensive analyses have been performed by different studies, we will only mention the following points:

O'Collins VE, Macleod MR, Donnan GA, et al. 1,026 experimental treatments in acute stroke. Ann Neurol 2006;59(3):467-477.
Labiche LA, Grotta JC. Clinical trials for cytoprotection in stroke. NeuroRx 2004;1(1):46-70.
Maas AI, Roozenbeek B, Manley GT. Clinical trials in traumatic brain injury: past experience and current developments. Neurotherapeutics 2010;7(1):115-126.

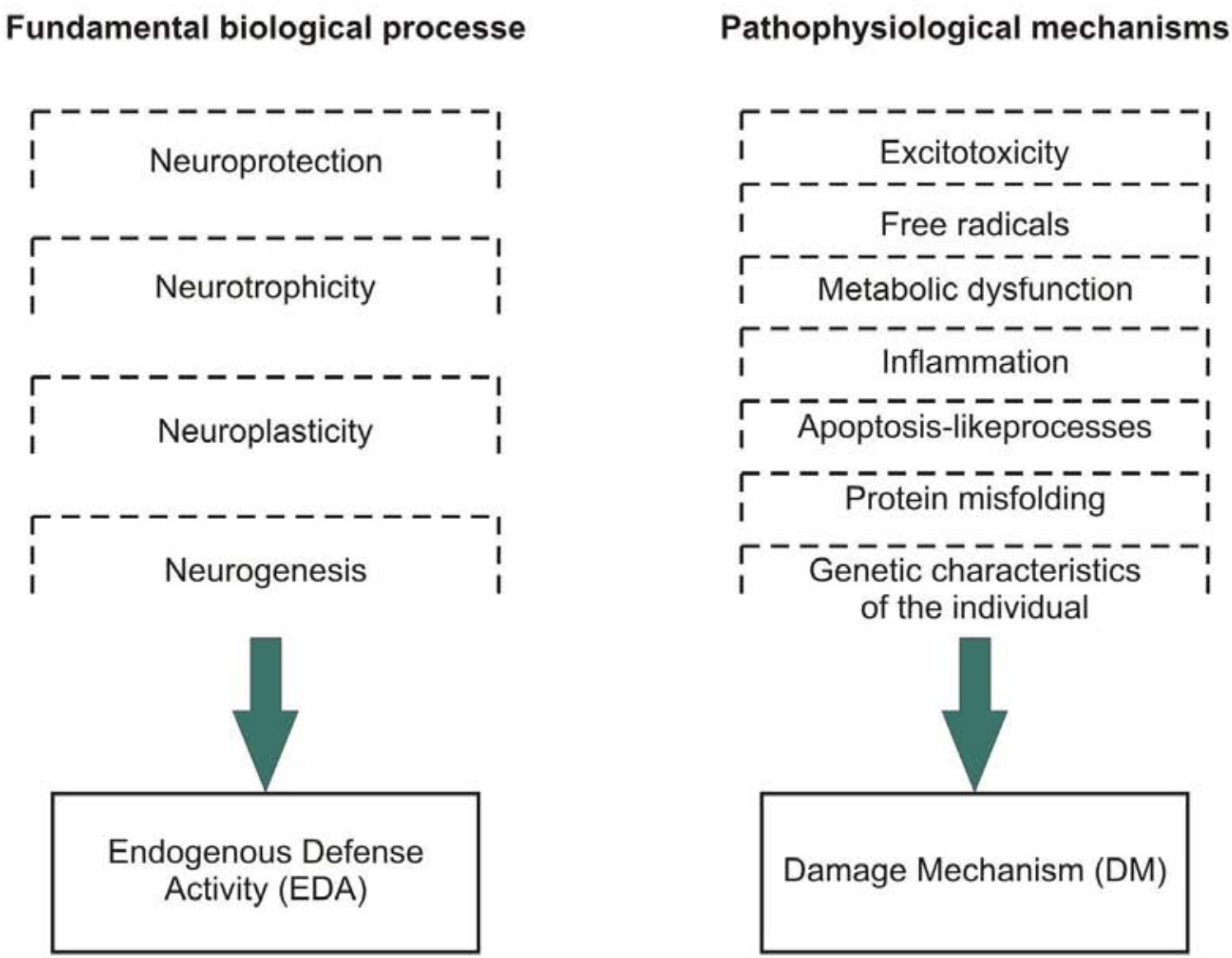
i. Unsustainable neurobiological concepts that generate inadequate strategies (e.g., suppressive strategy) using inappropriate molecules for pharmacological support in brain protection and recovery treatment;

ii. Inconsistencies in basic research neuroprotection studies that generate inflated positive results that have not been confirmed in randomized control trials after translational processes;

Minnerup J, Sutherland BA, Buchan AM, et al. Neuroprotection for stroke: current status and future perspectives. Int J Mol Sci 2012;13(9):11753-11772.
O'Collins VE, Macleod MR, Donnan GA, et al. 1,026 experimental treatments in acute stroke. Ann Neurol 2006;59(3):467-477.
Sahota P, Savitz SI. Investigational therapies for ischemic stroke: neuroprotection and neurorecovery. Neurotherapeutics 2011;8(3):434-451.

iii. Mismatches between randomized controlled trials design in this field and recent advances in our understanding of lesional and reparatory mechanisms in the brain.

Here, we briefly review the concept of damage mechanism (DM) and its interactions and overlap with protection and reparatory neurobiological processes, which has been conceptualized as endogenous defense activity (EDA).



D. F. Muresanu, Management of Acute Stroke: Neuroprotection; Stroke. Basel, Karger, 2009, pp 128–136

D., F. Muresanu, Neuromodulation with Pleiotropic and Multimodal Drugs – Future Approaches to Treatment of Neurological Disorders ; *Brain Edema XIV*, Acta Neurochirurgica Supplementum Vol. 106, DOI 10.1007/978-3-211-98811-4_54, © Springer-Verlag/Wien 2010

- A useful clinical-neuropharmacological classification of potential candidates for pharmacological support in this therapeutic area, will be presented:

Muresanu DF, Buzoianu A, Florian SI, von Wild T. Towards a roadmap in brain protection and recovery. J Cell Mol Med. 2012 Dec;16(12):2861-71.

Muresanu DF. Neuromodulation with pleiotropic and multimodal drugs -- future approaches to treatment of neurological disorders. Acta Neurochir Suppl. 2010;106:291-4

- Monomodal drugs in neuroprotection
  - with a single mechanism of action in neuroprotection; the majority failed to demonstrate clinical relevant effects
  - with a pleiotropic mechanism of action in neuroprotection; these are still under investigation
- Monomodal pleiotropic drugs in neurorehabilitation (modulating only neuroplasticity).
- Multimodal drugs with pleiotropic neuroprotective effect and long-term recovery enhancement.

Muresanu DF. Neuromodulation with pleiotropic and multimodal drugs -- future approaches to treatment of neurological disorders. Acta Neurochir Suppl. 2010;106:291-4.

Muresanu DF, Doppler E, Novak P. Neurotrophic factor treatment of neurological disorders: the benefits of a pleiotropic treatment approach. Commentary. CNS Neurol Disord Drug Targets. 2011 Jun;10(4):415-6.

Disclosure

None