

NEUROMODULATION IN SPINAL CORD INJURY (OVERVIEW OF METHODS)

NEVROMODULACIJA PRI OKVARAH HRBTENJAČE (PREGLED METOD)

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Abstract:

The International Neuromodulation Society describes neuromodulation as "a field of science, medicine, and bioengineering that encompasses implantable and non-implantable technologies, electrical or chemical, for the purpose of improving the quality of life and functioning of humans." The use of various neuromodulation therapies in spinal cord injuries (SCI) promotes neuroplasticity and mainly aims to improve recovery of incomplete lesions and limit disorders in complete or incomplete lesions, such as spasticity, neuropathic pain, autonomic dysreflexia and orthostatic hypotension. The lecture will first give a brief overview of neuromodulation as a physiological process of the central nervous system and as a treatment, then present the different types of neuromodulation in SCI, and conclude with some special considerations.

Key words:

neuromodulation; spinal cord injury; neurotransmitters; neuroplasticity

Povzetek:

Mednarodno združenje za nevromodulacijo definira nevromodulacijo kot "področje znanosti, medicine in bioinženiringa, ki vključuje električne in kemijske tehnologije v obliki vsadkov ali brez njih, katerih namen je izboljšanje kakovosti življenja in funkcioniranja ljudi." Uporaba različnih nevromodulacijskih terapij pri poškodbah hrbtenjače spodbuja nevroplastičnost in je namenjena predvsem izboljšanju okrevanja po nepopolnih okvarah ter omejitvenih motnjah po popolnih ali nepopolnih okvarah, kot so spastičnost, nevropatska bolečina, avtonomna disrefleksija in ortostatska hipotenzija. V predavanju bo najprej predstavljen kratek pregled nevromodulacije kot fiziološkega procesa v osrednjem živčevju in kot oblike zdravljenja, sledila bo predstavitev različnih vrst nevromodulacije pri okvarah hrbtenjače, na koncu pa bodo obravnavana nekatera posebna vprašanja.

Ključne besede:

nevromodulacija; okvare hrbtenjače; neurotransmiterji; nevroplastičnost

Terminology

The International Neuromodulation Society describes neuromodulation as "a field of science, medicine, and bioengineering that encompasses implantable and non-implantable technologies, electrical or chemical, for the purpose of improving the quality of life and functioning of humans."

The use of various neuromodulation therapies in spinal cord injuries (SCI) promotes neuroplasticity and mainly aims to improve recovery of incomplete lesions and limit disorders in complete or incomplete lesions such as spasticity, neuropathic pain, autonomic dysreflexia and orthostatic hypotension.

Neuromodulation as a physiological process of the central nervous system

Central Nervous System reacts to environmental cues and regulates body functions with neurotransmission and neuromodulation. Neurotransmitters are binding on fast-acting neuroreceptors of a target neuron at a specific synapse during direct synaptic transmission. Neuromodulators are a subset of neurotransmitters and target slower neuroreceptors (G-protein neuroreceptors). Unlike neurotransmitters, the release of neuromodulators occurs in a diffuse manner ("volume transmission"). This means that neuromodulators impact a region of neural tissue and not only specific neurons. Neuromodulators alters either the cellular or synaptic properties of neurons and control the physiological levels of several classes of neurotransmitters so that neurotransmission

between neurons is changed. Neuromodulators and neurotransmitters act on different types of neuroreceptors causing different functional outcomes.

Major neuromodulators in the central nervous system include dopamine, serotonin, acetylcholine, histamine, norepinephrine, nitric oxide, and several neuropeptides bringing in close “collaboration” and interaction the nervous system with the endocrine system. Neuropeptides are small chain amino acids synthesized and secreted by neurons or neurosecretory cells that act as signaling molecules to nearby neurons. Some neuropeptides can also function as peptide hormones regulating physiological homeostasis (e.g., cognition, blood pressure, feeding behaviour, water balance, glucose metabolism, pain, and response to stress), neuroprotection, and immunomodulation.

Neuromodulation as a treatment

Neuromodulation is also a category of treatment that involves stimulation or direct administration of medications to the nervous system that aims to modulate the activity of target neurons when there is dysfunction of the nervous system due to trauma, diseases, genetic or degenerative reasons.

Under the term “neuromodulation” there are many different modalities of treatment, for different diseases. Pharmacological agents interfering with neuromodulation, stimulation (electrical or other stimulation) of brain and spinal cord, stimulation of nerves, drug delivery systems overcoming barriers.

Neuromodulation treatments may employ/or not advanced medical device technologies. These technologies include implantable as well as non-implantable devices that deliver electrical, chemical or other agents. Neuromodulation is useful treatment with reversible effects on brain and nerve cell activity and has been used in many different diseases: dysfunction of psychic sphere (depression, etc.), cognitive impairments (Alzheimer, etc.), epilepsy, movement disorders (incomplete paralysis, spasticity, dystonia, etc.), neuropathic pain, autonomic nervous system dysfunction (lower urinary tract dysfunction, neurogenic distal bowel dysfunction, cardiovascular dysfunction, etc.).

Neuromodulation for persons with spinal cord injury

Spinal cord injuries due to traumatic or non-traumatic causes lead to devastating disability. Data of SCI incidence around the world are missing. According to data from US, there is a trend toward the increase of incomplete lesions, 47.2 % of all SCIs result in incomplete tetraplegia, 19.6 % in incomplete paraplegia, 20.2 % in complete paraplegia, and 12.3 % in complete tetraplegia, while only 0.7 % result in complete recovery of sensory and motor function. Neuroplasticity reflects the changes of neuronal circuitries and thus the reorganization of the nervous system following SCI. Neuroplasticity after SCI occurs at several anatomical and physiological levels of the central nervous system, i.e. spinal cord, brainstem and cortex and includes changes of

synapsis and synaptic strength, axonal sprouting and intracellular changes. Enhance of neuroplasticity following SCI and inhibition of mal-adaptive neuroplasticity are promoted by neuromodulation. The developments of high technology have given new perspectives in neuromodulation treatments towards the management of sensorimotor and autonomic nervous system dysfunction and gave hope for the improvement of the health-related quality of life.

There are different types of neuromodulation in SCI:

- pharmacological modulation
 - per os (parasympatholytic, sympathomimetic and sympatholytic drugs, selective serotonin reuptake inhibitors, etc.);
 - intrathecal drug delivery systems
 - baclofen for the treatment of severe spasticity,
 - clonidine, opioids for treatment of neuropathic pain;
- electrical modulation (invasive and non-invasive)
 - brain stimulation
 - deep brain stimulation,
 - direct motor cortex stimulation;
 - spinal cord stimulation (for motor control, pain and somatoautonomic reflexes control)
 - epidural electrical stimulation,
 - transcutaneous electrical stimulation,
 - transspinal stimulation-TSS with electrodes over the spinous processes of the lesion;
 - peripheral nervous system
 - afferent nerves (for somatoautonomic reflexes control),
 - efferent nerves (for motor control);
- magnetic modulation;
- optogenetics modulation.

SPECIAL CONSIDERATIONS

Which are the advantages of neuromodulation treatments for patients with SCI?

Neuromodulation therapies are reversible and adjustable unlike neuroablative neurosurgery treatments (surgery in dorsal root entry zone, peripheral neurotomies, cordectomy, sacral anterior root stimulation implants in combination with dorsal root surgery-Brindley method, etc.). Reversible therapeutic management is preferable for incomplete lesions allowing the effects of possible neuroplasticity to limit the need for treatment. Benefits of neuromodulating therapies also exist for progressive diseases ensuring the possibility of adjusting the treatment according to the progression of the disease.

Are neuromodulation treatments too expensive to be incorporated in every health/insurance system?

There is evidence that the early application of neuromodulation treatments may be more cost-effective at controlling certain conditions overall than medical management approaches, specifically spinal cord stimulation for the treatment of neuropathic pain and intrathecal baclofen for the treatment severe of spasticity.

Which is the best way to apply neuromodulation treatment to a person with SCI?

Combining it with other therapeutic approaches which will be followed by a personalized rehabilitation program with specific goals discussed and accepted by the patient and her/his important others.

Is functional electrical stimulation (FES) a neuromodulation treatment or just a replacement therapy for motor dysfunction? FES restores a missing function, i.e., FES for the upper limb dysfunction following cervical SCI. The systematic use of this FES could interfere with neuroplasticity as a neuromodulation treatment.

CONCLUSION

Recovery of neurological function after SCI is largely due to neuroplasticity – making new synapses or altering the strength of existing synapses. Neuroplasticity after SCI is stimulated by the loss of afferent input below the lesion (deafferentation) and by the expression of neurotrophins such as NGF and other neuromodulators.

However, the same neuroplasticity that enables recovery also produces mal-adaptive consequences. Neuromodulation treatments enhance health related quality of life in individuals who suffer neuropathic pain, spasticity, movement disorders, bowel, bladder and sexual dysfunction due to SCI. There is a cumulative evidence that neuromodulation induces neuroplasticity and limits mal-adaptive neuroplasticity and facilitates recovery and rehabilitation.

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