Neuroplasticity and future concepts in managment of Neurological diseases

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- While people for a long time used to believe that the brain became fixed after a certain age, newer research has revealed that the brain never stops changing in response to stimuli

Introduction

- The human brain is now considered to be a highly dynamic and constantly reorganizing system capable of being shaped and reshaped
- It is believed that every experience alters the brain's organization at some level.
- With lifelong capacity to change and rewire itself in response to the stimulation of learning and experience.
- As we age, the rate of change in the brain, or neuroplasticity, declines but does not come to a halt.

Neuroplasticity

- Neuroplasticity or brain plasticity is defined as the ability of the nervous system to change its activity in response to intrinsic or extrinsic stimuli by reorganizing its structure, functions, or connections

A wide range of definitions exist in relation to the term neuroplasticity

- 'The ability to change in structure or function . [6]
- 'The capacity of adaptation or regeneration [7].
- 'The ability to undergo structural and functional changes
- The ability to modify the strength of existing synapses, as well as form new synaptic connections,

Neurogenesis

- Neurogenesis is the ability to create new neurons and connections between neurons throughout a lifetime.
- We now know that new neurons can appear in certain parts of the brain up until the day we die.

Synaptogenesis the ability to create new synapses.

Neuroplasticity concepts{theories}

- Remember

  - Functional changes ⇉→
    structural changes
  - Neurons that fire together {coordinated activity}
    → Wire together {Hebbian plasticity}
  - Use-dependent plasticity [use or lose}
  - Metaplasticity { higher order form of plasticity.}

These mechanisms and principles are essential to create therapeutic strategies to support brain rehabilitation and treat neurological illnesses.

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Mechanisms of Neuroplasticity

- Functional plasticity (e.g., LTP and LTD,..etc)

- Structural plasticity (e.g., axonal sprouting, dendritic remodeling, and neurogenesis,…etc) . These pathways are essential for creating new connections, rewiring brain circuits, and fostering functional recovery.

Mechanism of functional changes

- **Denervation supersensitivity**
- **Long-term potentiation**
- **Long-term Depression**
- **Synaptic strengthening**

Long-term potentiation

- Glutamate binds to postsynaptic membrane receptors, ⇉ stimulation of AMPA →↑ influx of sodium →| magnesium ions are released →| blocks NMDA receptors. →| further release of glutamate →| more sodium ions → ⇧ the positive charge.→ More magnesium ions from NMDA receptors,→ more calcium influx. ⇉ All this leads to activation of 'Protein Kinase C and Calmodulin Kinase → more AMPA receptors → further stimulation of post-synaptic membrane → release more glutamate → enhances 'strengthening of the synapse and thus potentiation has occurred

Long term Depression

- Befor reaching the ceiling level of potentiation

{ saturation} → low-frequency stimulation of the post-synaptic membrane,will lead to the generation of ‘Weaker post-synaptic response’[role of metaplasticity]

Mechanism of structural changes

- Structural changes include sprouting and pruning, Sprouting generally includes increase in synapse number, size, spine density, receptor density, dendritic arbour and axonal arbour density.

- Neurons that are used frequently develop stronger connections. Those that are rarely or never used eventually die.{ use or lose }

- By developing new connections and pruning away weak ones, the brain can adapt to the changing environment.

Markers of Neuroplasticity

- A significant role in the induction of brain plasticity is played by neurotrophins: NGF, BDNF, NT-3, and NT 4 , NT 5.
- Myokines {interleukin-6 (Il-6), irisin, and cathepsin B} may be considered potential biomarkers of brain plasticity,& may answer whether the type of rehabilitation intervention induces brain plasticity{muscle–brain endocrine loop}
- Adipokines {Adiponectin} levels in the blood and CSF of MS patients have been found to be higher than in healthy individuals and correlate with a more severe course and faster progression of the disease. Therefore, adiponectin could become a potential predictive biomarker of faster progression of MS . levels of different adiponectin isoforms in MS patients in response to physical training could be an interesting direction for future research.{ J. Clin. Med. 2023, 12, 1880]

Markers of Neuroplasticity

- Neurogranin, a postsynaptic protein involved in synaptic plasticity and LTP
- Synaptosome-associated protein-25 (SNAP-25), which participates in the control of synaptic plasticity
- Vascular endothelial growth factor (VEGF), a protein involved in the growth of blood vessels and delivery of glucose that has a role in enhancing neurogenesis and synaptic plasticity {Pharmaceutics 2023, 15, 2052.}
- ***NB*** In MS patients, reduced levels of BDNF were shown in both the blood and the cerebrospinal fluid compared to those without organic CNS damage

Rehabilitation and Brain Plasticity

Conventional & novel Rehabilitation techniques effects

Myokines

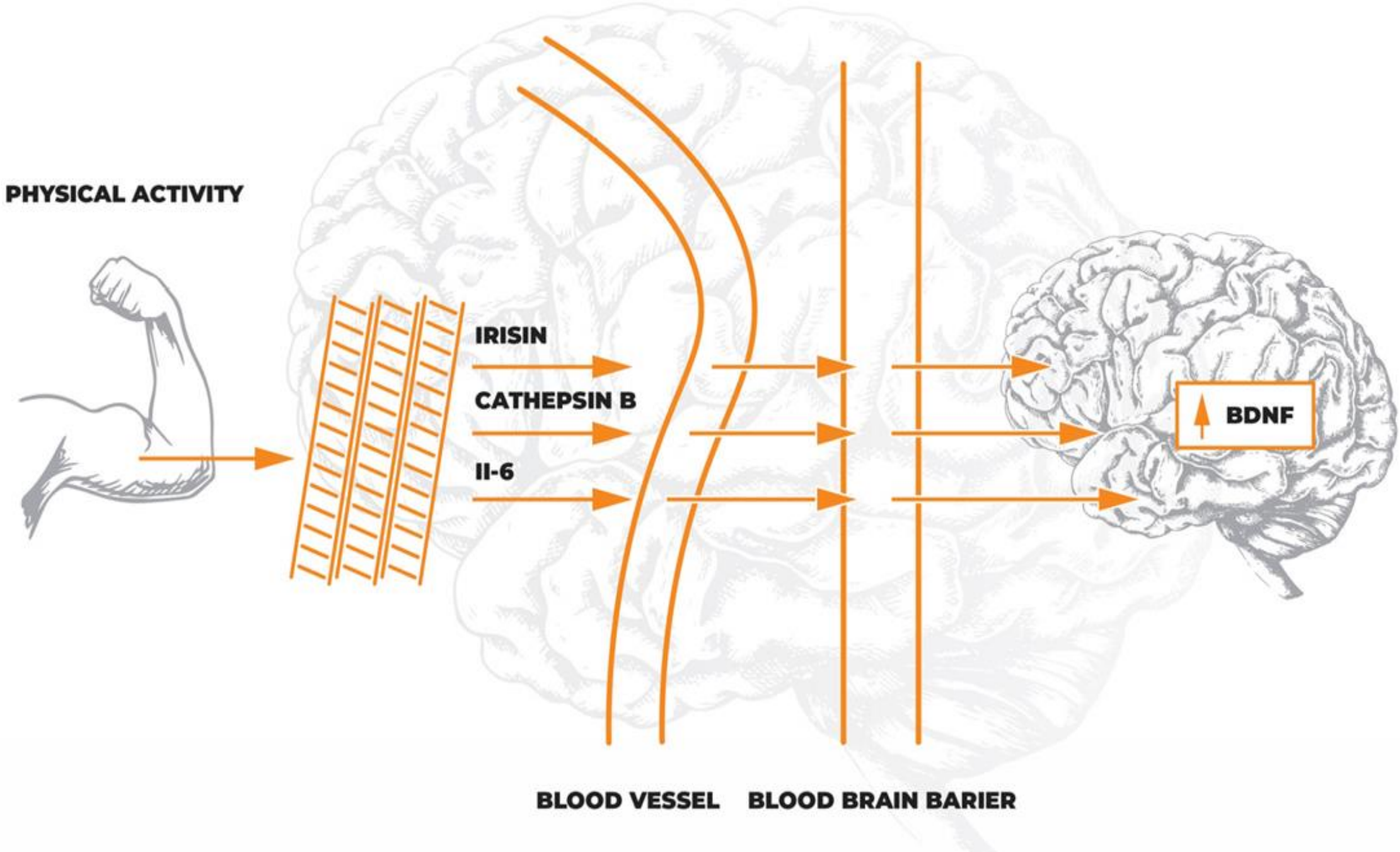
Adipokines

Oxidative Stress & nitroxidative stress

Epigenetic changes

The Mirror Neuron System & VR,AR,MR{telerehabilitation}

Markedly (threefold) increase BDNF synthesis in the human brain


PHYSICAL ACTIVITY
IRISIN
CATHEPSIN B
II-6
BDNF
BLOOD VESSEL
BLOOD BRAIN BARIER

What are the health benefits of physical activity?

dementia by up to **30%**

All-cause mortality by **30%**

cardiovascular disease by up to **35%**

hip fractures by up to **68%**

type 2 diabetes by up to **40%**

depression by up to **30%**

colon cancer by **30%**

breast cancer by **20%**

Benefits of Neuroplasticity

1. • The ability to learn new things
2. • The ability to enhance existing cognitive capabilities
3. • Recovery from strokes, traumatic brain injuries,…..etc
4. • Strengthening areas where function is lost or has declined
5. • Improvements that can boost brain fitness

Why is neuroplasticity important?

What are examples of neuroplasticity?

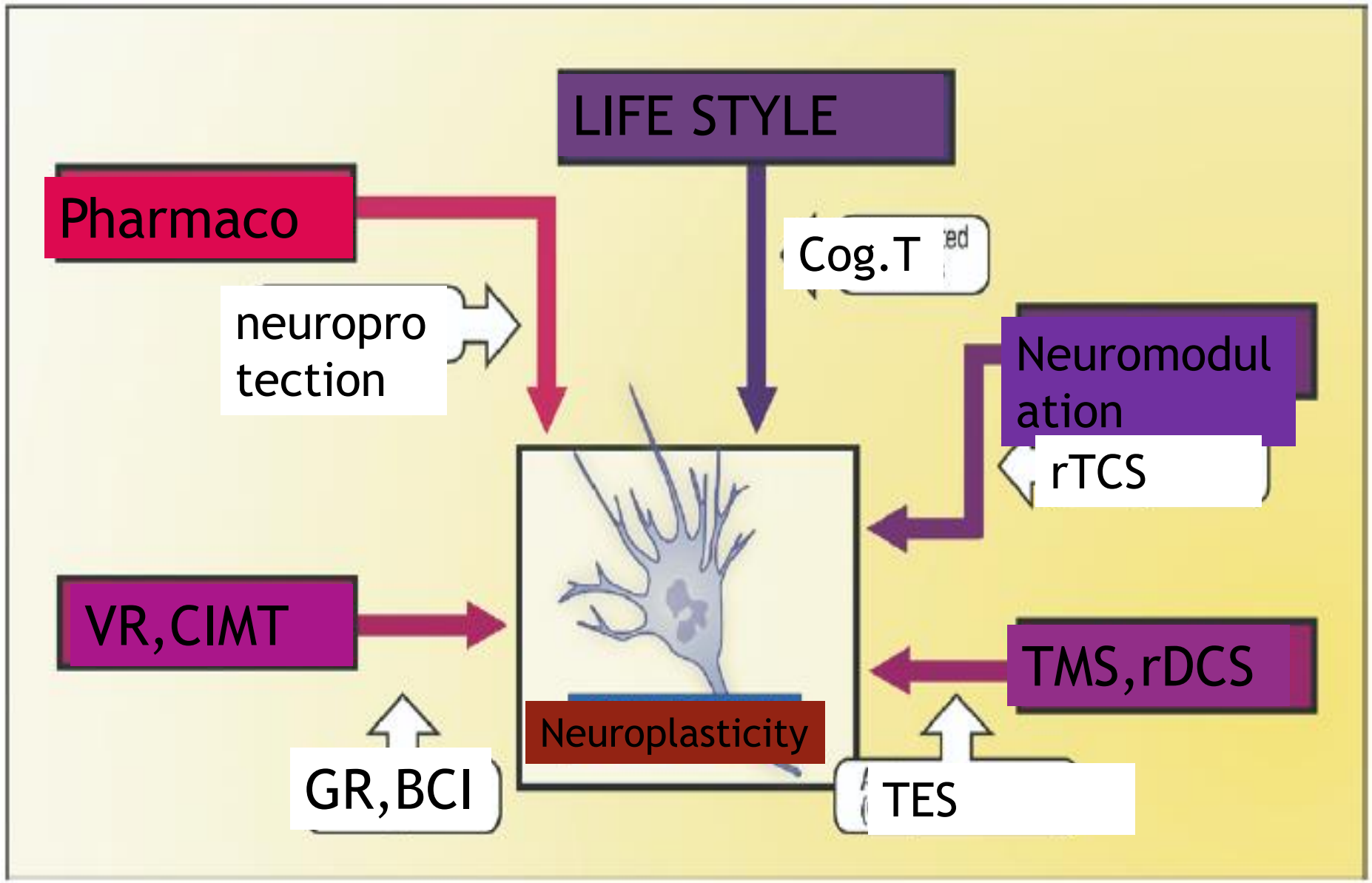
How to Improve Neuroplasticity

How to improve Neuroplasticity
{ promote development of new cells & protect old ones}

- Life style factors
- Neuromodulation techniques
- Pharmacological therapies

Modulating neuroplasticity, halting disease development, and easing symptoms have all been proven possible with {neuroplasticity-based methods}

- Pharmaceutical therapies
- Cognitive training
- Physical exercise
- Non-invasive brain stimulation techniques (e.g., TMS and tDCS)


LIFE STYLE
Pharmaco
Cog.T
neuropro
tection
Neuromodul
ation
rTCS
VR,CIMT
TMS,rDCS
Neuroplasticity
GR,BCI
TES

Enrich Your Environment

- Learning a new language
- Learning how to play an instrument
- Traveling and exploring new places
- Creating art and other creative pursuits
- Reading

- Get Plenty of Rest
- Practice Mindfulness
- Play { games are not just for kids }
- Exercise Your Body
- Exercise Your Brain
- Manage Your Stress

- ***Life style factors***
- - Diet ►Mediterranean Diet
- - Education – cognitive activity
- - Religion activities
- - Social activities - never stay alone
- - Avoid & fight-- low mood, anxiety or depression
- - Stope smoking sooner
- - Stope alcoholics

NB Life style factors → ↑Cognitive reserve ,enhance neuroplasticity ⇉ → structural changes & ↑ Brain reserve

Pharmaceutical therapies

- SSRIs..BDNF have been investigated in stroke for their potential to support neuronal survival, plasticity, and active recovery..
- BDNF. memantine and amantadine, have been investigated in TBI rehabilitation for their neuroprotective and cognitive-improving benefits.
- AchEI, BDNF, and other substances that support neuronal survival and synaptic plasticity are also being investigated in neurodegenerative disorders
- Niacin appears to upregulate BDNF and tropomyosin receptor kinase B (TrkB) expression as well

Problems With Brain Plasticity

Conditions that can limit or hinder brain plasticity

- Substance use
- Brain injury or traumatic experiences that result in post-traumatic stress disorder .
- Lead poisoning can negatively impact brain plasticity.
- Epilepsy, cerebral palsy, tuberous sclerosis, and Fragile X syndrome

Bottom Line

- Neuroplasticity-based methods are crucial to brain rehabilitation , to recover and regain function following neurological insults,
- Recovery for people with neurological disorders, such as stroke, traumatic brain injury (TBI), multiple sclerosis and neurodegenerative diseases, depend mainly on neuroplasticity.

Still there is a hope

Thank You