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EDITORIAL

Stroke and neuroplasticity: harnessing the brain's adaptive potential for recovery

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In the ever-evolving landscape of rehabilitation for neurological disorders, one concept has gained significant traction in recent years: neuroplasticity. Defined as the nervous system's ability to reorganize and regenerate in response to new information or injury, neuroplasticity offers a beacon of hope for patients suffering from neuromotor disabilities, particularly those resulting from stroke. Traditionally, it was believed that adults could not experience neuroplasticity, but contemporary research has debunked this myth, revealing that the brain's adaptive capacity persists throughout life.

The modern understanding of neuroplasticity is rooted in Donald Hebb's 1949 theory articulated in his seminal work: The Organization of Behavior.[1] Hebb's principle, often summarized as "cells that fire together wire together," explains how repeated and persistent stimulation of a postsynaptic cell by a presynaptic cell enhances synaptic efficacy. This principle laid the groundwork for recognizing the brain's ability to adapt and reorganize, a concept that has profound implications for stroke recovery.

In the context of stroke, neuroplasticity manifests in distinct phases and mechanisms, offering pathways for potential recovery.

The immediate phase occurred in the first 48 hours. Initial stages are marked by cell death and loss of associated cortical pathways. This acute degeneration leads to atrophy in perilesional gray matter and significant structural and functional changes in the contralesional hemisphere. During this period, the brain attempts to utilize secondary neuronal networks to maintain function. After that starts the subacute phase, lasting for some weeks following stroke. In this phase, the recruitment of support cells becomes prominent, transitioning cortical pathways from inhibitory to excitatory. Synaptic plasticity and the formation of new connections are critical during this time, paving the way for potential recovery. Then there is the last subacute phase, weeks to months after stroke. In this period the brain continues to remodel itself through axonal sprouting and further reorganization around the damaged area, emphasizing the ongoing nature of neuroplastic recovery.

Advancements in neuroimaging and neurophysiology have provided tools to measure neuroplastic changes. Several tools are available now to investigate neuroplasticity with different spatial and temporal precision and resolution.

Techniques such as functional magnetic resonance imaging (fMRI), diffusion-weighted imaging (DWI), posi-

TABLE I.—*ReCipe Table.*

Active ingredients	Provider	Modes of delivery	N. sessions	Frequency	Duration	Dose/intensity
Task-oriented specific training upper limb	PT	I	54	6/week	20’	15 repetitions
Trunk control training	PT	I	12	6/week	10’	15 repetitions
High-intensity training for walking	PT	I	50	5/week	30’	Heart rate reserve = 60-80% or ratings of perceived exertion = 15

PT: physiotherapist; I: individually.

tron emission tomography (PET) and repetitive transcranial magnetic stimulation (rTMS) offer important insights into brain activity and structural changes.[2] Additionally, biological markers are used to gauge neuroplasticity and angiogenesis,[3] a process implicated in neurorepair. Some markers are used as promising clinical tools for stroke recovery evaluation in the acute phase (a few days after stroke) as matrix Metalloproteinase 9 (MMP9) and Angiopoietin 2 (Ang2), others find application in the most common post-stroke rehabilitation phase (within 6 months after stroke) like Irisina, Brain-Derived Neurotrophic Factor (BDNF), and Vascular Endothelial Growth Factor (VEGF).

However, not all the processes of structural and functional changes to the brain after stroke have to be considered as a favorable sign for the best recovery, since it is well known that neuroplastic changes can also be maladaptive and negatively affect human function.[4]

Rehabilitation is undoubtedly recognized to be effective for recovery of function and mobility after stroke, when compared *versus* no treatment or attention control,[5] but not all the strategies show the same results.[6] Therefore, we may assume that some interventions are more effective than others in activating neuroplasticity.

Do we have also some evidence that stroke rehabilitation may play a role in enhancing neuroplasticity? In the last years, some papers showed that rehabilitative interventions are able to induce neuroplastic changes in terms of imaging, response to noninvasive transcranial brain stimulations, or concentration of biomarkers. For example, a very recent systematic review on the effect of exercise on BDNF in stroke survivors showed that exercise parameters influence BDNF concentration.[7] In particular, high intensity aerobic exercise can increase more than the non-aerobic ones the circulating BDNF concentrations. Another interesting example is offered by findings of another study on functional connectivity changes in the cortical motor network after rTMS.[8] This study showed that, in early-stage cerebral stroke patients, rTMS seem to induce functional connectivity changes improving motor function recovery.

Unfortunately, research in this field is still in its primordial phase. Moreover, to date the impact of patient’s age on neuroplasticity is unclear, and appropriate dosage of each rehabilitative active intervention is usually not reported in most of the literature.

We believe that, like a carefully calibrated medication, rehabilitation interventions should be tailored to include the best combination of exercises, with optimal dosage, appropriate frequency, and sufficient duration (Table I).

In conclusion, the potential for neuroplasticity in stroke recovery is immense. Despite the complexities and variances in individual cases, the overarching principle remains clear: the brain’s ability to adapt and reorganize offers a promising avenue for rehabilitation. By understanding and harnessing this potential, clinicians and researchers can develop more effective strategies to support stroke patients, ultimately improving their quality of life.

References

1. Hebb DO. The Organization of Behavior: A neuropsychological theory. New York: John Wiley & Sons, Inc.; 1949.

2. Christiansen L, Siebner HR. Tools to explore neuroplasticity in humans: combining interventional neurophysiology with functional and structural magnetic resonance imaging and spectroscopy. Handb Clin Neurol 2022;184:105–19.

3. Wlodarczyk L, Szelenberger R, Cichon N, Saluk-Bijak J, Bijak M, Miller E. Biomarkers of angiogenesis and neuroplasticity as promising clinical tools for stroke recovery evaluation. Int J Mol Sci 2021;22:3949.

4. Johnson BP, Cohen LG. Applied strategies of neuroplasticity. Handb Clin Neurol 2023;196:599–609.

5. Pollock A, Baer G, Campbell P, Choo PL, Forster A, Morris J, *et al.* Physical rehabilitation approaches for the recovery of function and mobility following stroke. Cochrane Database Syst Rev 2014;2014:CD001920.

6. Scrivener K, Dorsch S, McCluskey A, Schurr K, Graham PL, Cao Z, *et al.* Bobath therapy is inferior to task-specific training and not superior to other interventions in improving lower limb activities after stroke: a systematic review. J Physiother 2020;66:225–35.

7. Ashcroft SK, Ironside DD, Johnson L, Kuys SS, Thompson-Butel AG. Effect of exercise on brain-derived neurotrophic factor in stroke survivors: a systematic review and meta-analysis. Stroke 2022;53:3706–16.

8. Chen Q, Shen W, Sun H, Zhang H, Liu C, Chen Z, *et al.* The effect of coupled inhibitory-facilitatory repetitive transcranial magnetic stimulation on shaping early reorganization of the motor network after stroke. Brain Res 2022;1790:147959.

Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions
All authors read and approved the final version of the manuscript.

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