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REVIEW PAPER

NEUROPLASTICITY AND BRAIN NEOPLASMS

Vanja Klarin
University of Zagreb, School of Medicine
0009-0001-6591-2735

Marko Krklec
University of Zagreb, School of Medicine
0009-0004-4009-7449

Abstract

Neuroplasticity is the ability of the brain to reorganize its networks to adapt to changes in neural surroundings. It is an important component of learning and memory, but it is also critical in the process of tissue recovery after brain injury. One of the most common causes of brain injury are tumors of the central nervous system. Thus, the importance of understanding the relationship between plasticity and injuries caused by brain tumors is apparent. Plastic reorganization can affect healthy motor and sensory regions, language networks, the hippocampus, and many other areas, as well as infiltrative neoplastic structures themselves. This literature review aims to analyze the different aspects of neuroplasticity as pertaining to brain neoplasms, in order to better understand the different implications of plastic processes in a tumor-afflicted brain. This understanding could be used to improve postoperative outcomes of resection, find new therapeutic methods, and reveal the mechanisms behind plasticity in disease conditions.

KEYWORDS: brain networks, brain tumors, language, motor cortex, neuromodulation, neuroplasticity

INTRODUCTION

Plasticity has major roles in both physiological and pathological conditions. It is a foundational element of memory formation and learning. Neuroplasticity also has a role in brain pathology compensatory mechanisms, when lesioned areas of the brain can no longer properly perform their function[1] and even the integration of some types of brain tumors into neural circuitry.[2] A sizeable amount of research in neuroplasticity is focused on lesions in areas related to important functions such as language, sensory and motor functions, all of which are often affected by low-grade tumors. Due to their indolent nature, these types of lesions are more suitable for examining neuroplasticity than sudden disorders like strokes, as the latter hinder plastic reorganization.[3] (Figure 1) Patients with slower growing tumors have less severe deficiencies, before and after resection of the affected tissue, due to better reorganization of affected areas. Better rehabilitation also occurs in younger patients which could be associated with the efficiency of plastic remodeling being better in this population.[4,5] The mentioned processes can be visualized by invasive and noninvasive methods such as functional magnetic resonance imaging, electroencephalography, magnetoencephalography and direct cortical stimulation.[6] One of the most useful methods for assessing neuroplasticity is functional magnetic resonance imaging, a noninvasive method which tracks changes of oxygenated blood flow into different parts of the brain active during specific tasks performed by the patients.[7] In this narrative review, we aim to examine the different facets of the mechanisms underlying brain plasticity, in particular with regard to its relation to brain neoplasms.

LANGUAGE

Brain neoplasms can affect several brain regions related to different aspects of language, greatly affecting quality of life. However, these same regions can exhibit neuroplasticity which change the course of disease progression. One of these specific areas is the speech-associated part of the supplementary motor cortex (SMA) in the cerebrum, an area which is believed to be crucial for speech production. Resections of this area in two patients followed by Chivukula et al. with astrocytoma and oligodendroglioma have caused problems with phonation and articulation such as mutism and speech latency, symptoms which are a part of SMA syndrome.[8] Both patients recovered in a little over one year due to the migration of the function of the supplementary motor cortex to the contralesional nondominant side of the cerebrum, which was proved by fMRI mapping. The authors believe that this switching was probably possible due to the connective fibers in the corpus callosum but are not sure if the dominant SMA was involved in the process or not. Contralesional recruitment is thought to be the least efficient form of remodeling due to having the poorest recovery shown in patients. The other form of reorganization is the intrinsic model which uses preserved neural networks in the affected tissue and the ipsilesional recruitment of networks, both of which are thought to be more beneficial. Ipsilesional recruitment implies the assignment of healthy synapses near the lesion to functions that were lost to the injury, whereas contralesional recruitment entails the uncovering of latent brain pathways that are silenced in the healthy brain in order to compensate for the loss of function caused by the tumor.[5]

Glioma infiltration into language networks can also result in the reorganization of corresponding areas of the cerebellum, as well as cerebro-cerebellar neuron circuits. This manifests as increased gray matter volume of the involved cerebellar regions and increased activity of the contralesional cerebro-cerebellar circuitry, presenting a potential therapeutic target for treating language-related deficits in patients who are going through rehabilitation following tumor resection.[9] All in all, language functions and quality of life could be preserved in brain cancer patients in the future by utilizing functional neuroplastic reorganization of language networks to improve postoperative outcomes and induce plasticity in relevant brain regions, thus reducing language deficits to a minimum.

MOTOR FUNCTIONS

Another aspect of brain function that is important for patient quality of life is motor function. Motor deficits that result from tumor infiltration of motor regions can severely impact patients' abilities to perform even basic daily tasks. Therefore, using our understanding of plasticity to minimize motor losses that could result from tumor resection is of utmost importance. A study by Zimmerman et al. revealed that the presence of a brain neoplasm and its proximity to the motor cortex are factors that induce functional reorganization through neuroplasticity.[1] Patients who experienced reorganization of the primary motor cortex (PMC) had less postoperative deficits and better postoperative outcomes.

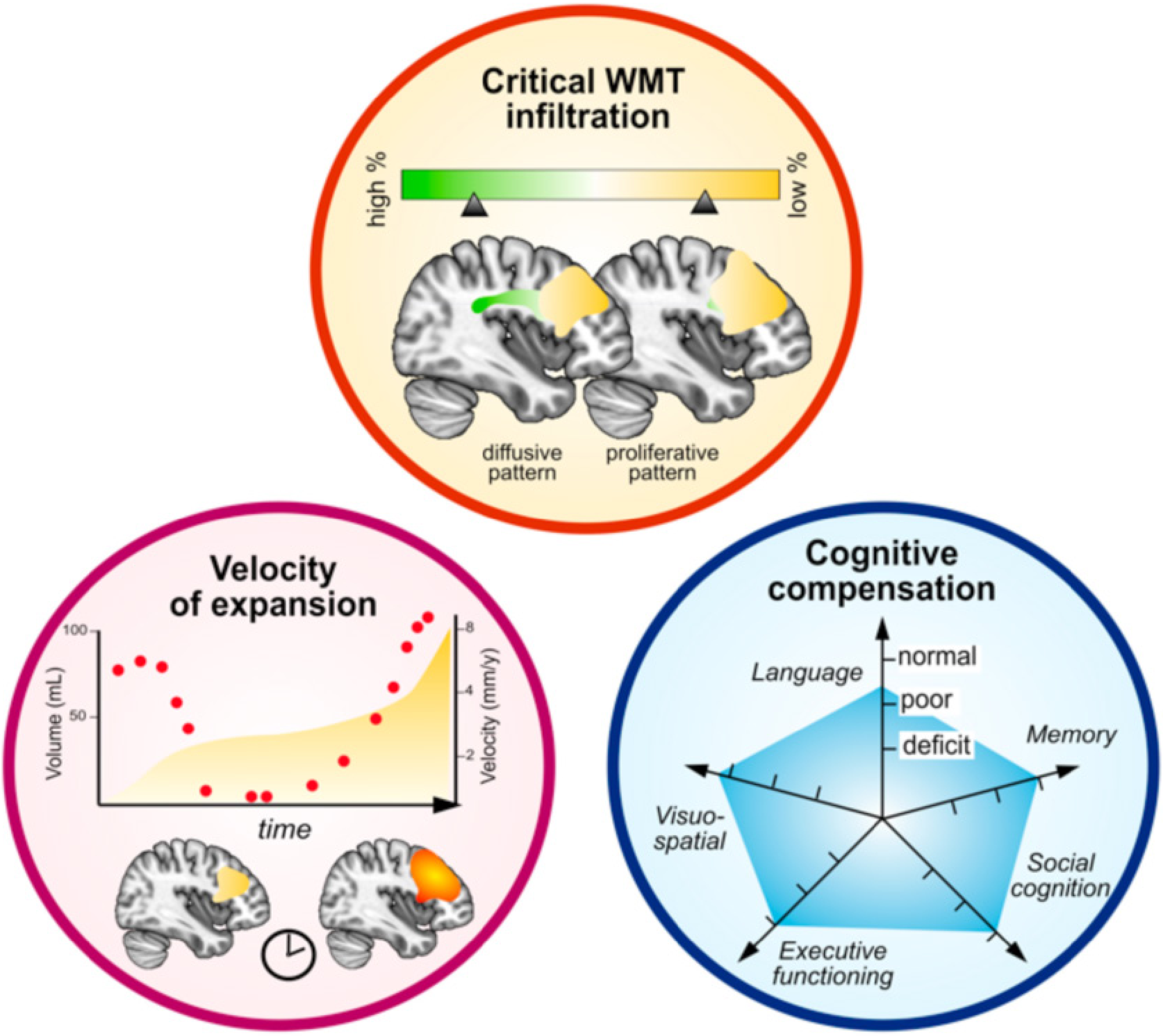

Figure 1. Factors that influence the potential for plasticity in patients with low-grade glioma

These factors refer to the "3Dtm" model by Duffau4 (3D – location of tumor and white matter tract infiltration, t – speed of tumor expansion, m – metaplasticity compensation).

Source: Figure published in Ng S, Duffau H. Brain plasticity profiling as a key support to therapeutic decision-making in low-grade glioma oncological strategies. *Cancers*. 2023;15(14):3698. doi:10.3390/cancers15143698

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However, all patient groups were observed to have a slowed processing speed in these regions. One of the studies focusing on the PMC, specifically the hand region, found two main modes of synaptic recruitment in the motor cortex: contralesional and ipsilesional. Kong et al. examined thirteen patients with low- and high-grade gliomas before and after surgical procedures with fMRI scans and have concluded that different types of remodeling were associated with different tumor size and location.[10] Small tumors which were located further away from the PMC exhibited recruitment of neural networks near the affected area, while bigger and fast-growing tumors caused activation of the contralateral cortex. The authors concluded that high-grade gliomas saturate the plastic capacity of the ipsilateral hemisphere and disrupt the inhibition of the contralateral hemisphere. Patients which exhibited contralesional recruitment also showed greater deficits during clinical exams. Activation of contralesional regions points to the increased importance of uncrossed pyramidal fibers in such conditions.[4]

INTEGRATION OF GLIOMAS INTO NEURAL CIRCUITRY

It is not only healthy neural tissue that can be affected by neuroplasticity. Gliomas, which are brain tumors composed of malignant glial precursor cells, contain cellular subpopulations that resemble oligodendroglial precursor cells (OPCs). These cells form synapses with neurons in physiological conditions.[11] Therefore, it was hypothesized and later proven by Venkatesh et al. that these OPC subpopulations within glioma tissue can form synapses with normal neurons.[2] It was also shown that depolarization of glioma membranes induces tumor proliferation. Glioma growth is also exacerbated by growth factors that are released by neurons in an activity-dependent fashion. Thus, gliomas benefit from forming new synapses with neurons and from being depolarized by those same neurons. This depolarization can occur via two mechanisms: synaptic transmission in neuron-glioma synapses and non-synaptic activity-dependent potassium currents. This way, a vicious cycle is formed, where synaptic depolarization of glioma cells allows the tumor to grow and form even more synapses with neurons, which in turn causes even more depolarization of the malignant cells. Another vicious cycle works in tandem with the first one. Gliomas were found to induce neuronal hyperexcitability[12] through non-synaptic glutamate transmission[13], secretion of synaptogenic factors[14] and by reducing inhibitory interneurons in the tumor microenvironment.[15] This causes more depolarization of tumor cells, which in turn causes tumor proliferation, and as a result even more neurons become hyperexcitable. Blocking these mechanisms of glioma integration represents a potential therapeutic method for slowing the growth of these tumors.[2]

DISCUSSION

In recent times, the neuroscientific community has begun to move away from the traditional localizationist view of the brain which explains cognitive functions as products of individual cortical regions. Instead, more and more researchers are adopting a connectionist philosophy that sees those functions as a result of the interplay and synergy between many different neural networks, all of them contributing varying amounts of processing power. This perspective has been shown to be much closer to reality than the aforementioned localizationist view. An example of this is the often-observed lack of neurological deficits in patients with brain tumors. Neoplasms often infiltrate functional brain regions which would render patients unable to perform corresponding tasks, were the localizationist view true. However, this is often not the case. Brain tumor patients exhibit a degree of plasticity and a lack of full neurological deficits. This indicates that the parallel networks responsible for the processing of a certain task can, to an extent, compensate for each other.[16]

Accordingly, there are many examples of using neuromodulation to induce neuroplasticity in patients before surgical removal of areas lesioned by tumors, which can enhance the quality of the surgery's outcomes. Neuromodulation-induced cortical prehabilitation (NICP) is a method of inducing plasticity by stimulating the patient's unaffected cortex with electrodes while they perform tasks controlled by the affected areas. The method can be both invasive and non-invasive with the former showing better results but having greater risks such as infections and hematomas. By transferring the function of areas to different sites surgeons can resect greater parts of the tissue, reducing the risk of tumor recurrence, without risking the loss of motor or language function in patients.[17]

Incorporating these methods into modern clinical practice could improve the overall quality of available therapies for treating brain cancer patients.

CONCLUSION

In this review, we have described the different facets of neuroplasticity in neoplastic diseases of the brain. Keeping them in mind for the future, clinicians and researchers could utilize these patterns of plasticity to expand neurosurgical options and improve surgery planning, thereby improving postoperative outcomes. These same mechanisms could also be used in controlling tumor growth and minimizing functional damage caused by neoplastic brain processes. Therefore, neuroplasticity should be kept in mind as a pivotal element of tailoring brain tumor surgery, and also of normal brain functioning.

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NEUROPLASTIČNOST I MOŽDANE NEOPLAZME

Sažetak

Neuroplastičnost je prilagodba mozga na promjene uvjeta u moždanom tkivu putem reorganizacije neuronskih krugova. Važan je dio učenja i pamćenja, ali je isto tako bitna u procesu oporavljanja tkiva nakon ozljede mozga. Jedan od najčešćih uzroka ozljeda mozga su tumori središnjeg živčanog sustava. Iz tog razloga vrlo je bitno razumjeti povezanost plastičnosti i ozljeda uzrokovanih moždanim tumorima. Reorganizacija može zahvaćati zdrava motorička, osjetna i jezična područja, hipokampus te mnoge druge regije, kao i same infiltrativne neoplastične strukture. Ovaj pregledni rad nastoji analizirati različite implikacije plastičnih procesa u mozgu zahvaćenom tumorom. Razumijevanje navedenih procesa moglo bi se koristiti u svrhu poboljšanja postoperativnih ishoda, istraživanja novih terapijskih metoda i neuroplastičnosti u uvjetima patoloških procesa mozga.

KLJUČNE RIJEČI: jezik, motorička kora, moždane mreže, moždane novotvorine, neuromodulacija, neuroplastičnost