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Editorial

New molecular insights, innovative technologies, and medical approaches in the "Exploration of mechanisms in cortical plasticity"

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Neuroplasticity (NP) has been defined as the neurobiological ability of the central nervous system to adjust its physiological functions in response to a continuously changing environment. Although this concept can be also extrapolated to changes in different molecular pathways at the unicellular level, in multicellular organisms NP leads to the formation of new neural connections, rewiring cortical and subcortical circuits to adapt and survive. NP has been accepted as a sound theoretical basis for some therapies such as rehabilitation after stroke (Asakawa et al., 2017), transcranial magnetic stimulation (Kim et al., 2020), and deep brain stimulation (Asakawa et al., 2019). In the last decades, several discoveries and technical advances across multiple scientific areas have gained new insights on the theme of cortical plasticity. Thus, harnessing the potential of this endogenous biological self-repairing process and restoring brain functionality in the context of acute and chronic neurological diseases has been one of the key promises for translational therapeutic strategies. In this research topic, we intended to recapitulate some of the most recently molecular, technological, and modern medical approaches in the field of cortical plasticity. Hence, seven articles writing from different perspectives were included in the special issue "Exploration of mechanisms in cortical plasticity".

Among diverse molecular mechanisms involved in the NP processes, recent studies have shown an additional role of microRNAs (miRNAs) constructs as a crucial modulator in various pathological and physiological processes. Specifically, *in vitro* neuronal cells exposed to oxygen-glucose deprivation and reoxygenation-induced environments have shown specific patterns of induction and suppression of their microRNAs expression (as well as the activation of Batch1/HO-1 signaling pathways) with specific roles in the adaptative neuroprotective mechanisms against neuronal injury (Yang et al., 2020). On the other hand, the administration of novel herbal compounds across *in vivo* rodent models of chronic cerebral hypoperfusion with cognitive decline conditions has proven promising results, enhancing the NP and up-regulating the expression of synaptic and myelin basic protein biomarkers in grey (GM) and white matter (WM) respectively. Overall, the beforementioned preclinical studies have demonstrated a potential link between the reduction of neuroinflammation (downregulation of activated microglia) and the improvement of cortical NP processes, like memory and learning (Liu et al., 2020). Additionally, the study of the erythropoietin (EPO) receptor has been involved in the early embryonic neural development and the migration of newly generated neurons during adult neurogenesis in mammalian tissues. EPO as a neurohormonal mediator has a role in the regulation of multiple cellular pathways relieving oxidative stress, decreasing apoptosis, and inhibiting inflammatory responses in neuronal tissue, ultimately enhancing the restoration of axonal connectivity in response to neuronal injury (Zhang et al., 2020).

The effects of neuroprotective compounds can be measured in experimental biological systems using noninvasive imaging methods (Gatto et al., 2015). In that regard, the growing use of structural diffusion magnetic resonance imaging (dMRI) technologies and the increasing development of high magnetic fields (Gatto et al., 2018) have been some of the rapidly evolving features of this technology,and one of the most promising tools in neurosciences, particularly applied to (*in vivo)* NP research (Gatto et al., 2020). Recently, to address some of the limitations associated with mono-exponential diffusion models like diffusion tensor imaging (DTI) (Gatto et al., 2020), new sequences have been developed to explore inhomogeneous biological media (GM brain tissue) utilizing alternative non-Gaussian diffusion models (Gatto et al., 2019). In clinical settings, the use of dMRI makes it also possible to study compensatory axonal connectivity mechanisms (hypertrophic olivary degeneration) after vascular-related injuries (Wang et al., 2020).

Further, the combination of dMRI modalities (diffusion tensor tractography) and repetitive transcranial magnetic stimulation (a non-invasive neurostimulation tool that involves applying an electromagnetic coil to the patient's scalp to produce a magnetic field) can also be considered as a potential approach to assessing WM recovery and motor performance after cerebrovascular events (Kim et al., 2020).

The loss of fine motor skills represents a major handicap and an important target for technologies that attempt to increase neuronal restoration and repair. Application of laboratory research technologies on animal models phenotypes imitate human pathophysiologic features, could improve both motor and non-motor symptoms, especially in clinical studies of neurodegenerative diseases (NDDs). Therefore, appropriate behavioral assessments are extremely crucial for the correct understanding of NDDs mechanisms and accurately evaluate the efficacy and safety of novel medical therapies (Asakawa et al., 2016b). These methods can also help to monitor the responses to therapeutic methodologies that enhance associated NP mechanisms (Asakawa et al., 2016a). Ideally, computerized technologies could result in safe, objective, and real-time assessment of biomechanical parameters (Asakawa et al., 2019). Therefore, translational biometric approaches need to be implemented to monitor the recovery of preclinical motor performance in the context of NDDs. Such studies can be applied not only to verify the reliability of motor tests in the assessment of NDDs severity, but also as a key tool to guide the efficacy of medical and surgical treatments (Kobayashi et al., 2020). Nonetheless, the development of the novel behavioral assessments for human patients following the principles of objectification, multi-purpose, and simplification (OMS) is an ongoing challenge for neurologists and neurosurgeons (Asakawa et al., 2019).

The translation of NP strategies to harvest a medical therapeutic potential still represents a major challenge to the neuro-repair and rehabilitation fields (Asakawa et al., 2017). The constant development and evolution across different bioengineering, neurobiological, and medical disciplines are part of the ongoing efforts aimed to solve the fundamental questions and technical difficulties in this scientific arena. Nonetheless, the scarce integration of such research areas is one of many reasons for delays in the generation of therapeutic results. Ultimately, the assembly of multidisciplinary teams using scientific approaches with clear therapeutical objectives, could be the most promising strategy to offer realistic healing alternatives for a growing worldwide population of patients with brain injuries.

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Conflict of Interest

The authors have no conflicts of interest to declare.

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