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Sommario/riassunto

Neuroplasticity refers to the ability of the Central Nervous System (CNS) to alter its structure and function in response to a variety of physiological and pathological processes such as development, cognition, injury or neurological diseases. Since more than four decades, studies on synaptic plasticity in the context of memory and learning attracted a remarkable interest. Soon after first seminal works on synaptic plasticity were published, research in this field was extended by studies on non-synaptic as wells as structural plasticity towards a goal to understand cellular and molecular determinants of cognition. Over the past two decades, yet two additional crucial players in neuroplastic phenomena started to be intensely investigated – glial cells and the extracellular matrix (ECM). Growing awareness that glial cells, especially astrocytes, are important regulators of synaptic functions gave rise to a novel concept of a tri-partite synapse. Also, over the last two decades, a growing body of evidence has accumulated that the extracellular matrix (ECM) in the brain is strongly involved in regulation of neurons, in particular, in synaptic plasticity. Thus, a concept of tetra-partite synapse was put forward by some neuroscientists. The cross-talk between neuron-glia-ECM system involves enzymatic degradation of proteins or peptides and amino acids occurring in each of these brain constituents by means of a variety of proteases. Importantly, it has been realized that proteases such as serine proteases and matrix metalloproteinases, not only

accompany “robust” phenomena such as cell division, or development or neurodegenerative conditions but may play a very subtle signaling functions, particularly important in memory acquisition. Indeed, the repertoire of substrates for these enzymes covers a wide variety of proteins known to play important role in the neuroplastic phenomena (e.g. BDNF, TNF-a, ephrin systems, various cell adhesion molecules, etc.). In result, the role of metalloproteinases and such serine proteases as tissue plasminogen activator (tPA), neuropsin or neurotrypsin in synaptic plasticity as well as in learning and memory has been particularly well demonstrated. It needs to be emphasized, however, that in spite of a remarkable progress in this field, several basic questions regarding molecular and cellular mechanisms remain unanswered. Potential involvement of so many important players (various proteases and their substrates in neurons, glia and in ECM) points to an enormous potential for plasticity phenomena but makes also studies into underlying mechanisms particularly difficult. In the proposed Research Topic we provide both review of the current state of the art and present some original reports on specific aspects of the role of proteolysis in neuroplasticity phenomena. The present ebook starts with extensive reviews describing involvement of proteolysis not only in synaptic plasticity but also in regulating endogenous excitability and structural changes at the network, cellular and subcellular levels. Cross-talk between neuroplasticity and proteolysis is also emphasized in the context of development and in relation to various pathologies. Whereas in the first part of the present ebook, the major focus is on metalloproteinases, the successive articles address the role of neuropsin and thrombin. The Research Topic is concluded with a series of articles describing the components of extracellular matrix and adhesion proteins and their elaboration by mechanisms dependent directly or indirectly on proteolysis. We do hope that the present ebook will further stimulate the interest in the fascinating investigations into neuroplasticity-proteolysis cross-talk.