

From neurobiology to evidence-based medicine concepts in neurorehabilitation

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Nowadays, it is still difficult to find the correct therapeutic approach for brain protection and recovery in stroke, especially because we do not fully understand all of the endogenous neurobiological processes, the complete nature of the pathophysiological mechanisms and the links between these two categories. Endogenous neurobiological processes, such as neurotrophicity, neuroprotection, neuroplasticity and neurogenesis, are central to protection and recovery and represent the background of endogenous defense activity (EDA). Stroke pathological cascades contain a limited number of pathophysiological processes. It is characterized mainly by excitotoxicity, oxidative stress, inflammation, apoptotic-like processes and important metabolic disturbances. Pathophysiological processes share some common mechanisms with EDA (e.g. excitotoxicity and neurotrophicity together with neuroplasticity have, as a common important driver, the NMDAR activity; inflammation has an important contribution for neuroregeneration, stimulating neuroplasticity, via trophic factors). Postlesional brain regulation is currently better understood. Every lesion in the nervous system triggers in the first minute an endogenous neuroprotective reaction. An endogenous repair process, combining neuroplasticity and neurogenesis follow this as a second answer. All these processes are initiated and regulated by endogenous biological molecules. The biological reality of the nervous system is far more complex. In fact, there is an endogenous holistic process of neuroprotection and neurorecovery that should be approached therapeutically in an integrated way. The current tendency to exclusively frame drug activity in terms of single mechanisms and single focus effect might distract from other paradigms with greater explanatory power and hinder the development of more effective treatment strategies. A change of concept is required in pharmacological brain protection and recovery in stroke therapy. This presentation briefly reviews the current and future considerations in this therapeutic strategy, including an integrated pharmacological approach, focusing on drugs with multimodal activity rather than single mechanism drugs, which usually are chemical drugs. In line with this strategy the current presentation will also highlight the result of CARS Trial, one of the latest double blind placebo randomized controlled trial in the field.