

PRESENT AND FUTURE NEUROPROTECTION - FUTURE APPROACHES ARE VERY PROMISING

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The old concept that neuroprotection means suppressing pathophysiological processes, the idea that a single mechanism molecule might be effective in clinical practice are obsolete today, and represents the root cause of failure in clinical neuroprotection.

The effects of ischemia on the brain traditionally is conceived as a linear sum of independent pathophysiological processes (excitotoxicity, inflammation, apoptosis-like, oxidative stress, etc) generating the pathways of ischemic cascade.

The pathway approach has produced a very detailed understanding of molecular changes in the postischemic brain injury but it possesses blind spots that are critically related to the failure of neuroprotection.

This has generated the simplistic way of understanding the concepts and as well, all attempts at clinical neuroprotection. The idea that a system is a linear sum of its component parts is called "superposition", and the associated approach is called "reductionism".

The failure of clinical neuroprotection and recovery post-stroke is measuring the failure of the reductionist approach to the problem.

The pathways can and do interact in a variety of fashions, via cross-talk, positive and negative feedback, etc, but the pathway heuristic itself offers no formal means of understanding such interactions.

The expectation of discovering the magic cell death pathway X has affected experimental designs of neuroprotection studies. The causality demonstrated by the application of the plus/minus strategy is ultimately an illusion. To overcome the limits of the pathway view of cell function, a different approach is needed. Such an approach is provided by network concepts applied to complex systems.

The bistable model based on these assumptions seems to be a better instrument for a successful translational approach in post-ischemic lesion and recovery. Current situation urge for consistent improvement in neuroprotection and neurorecovery clinical trials design in stroke therapies.