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Rehabilitation and Repair
Introduction

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Brain repair after stroke is entering an exciting stage. The four articles on this topic that follow examine a number of the forefronts, including translational efforts, new drug discovery, brain mapping to measure reorganization in humans, new national structures for expanding trials in this setting, the interplay between repair and experience, and the various therapeutic approaches under investigation.

Dr Larry Goldstein summarizes the many clinical trials conducted on the effects of d-amphetamine in stroke survivors. This drug has been repeatedly shown to be beneficial in animal models, especially when combined with behavioral experience. However, results of clinical trials have been quite variable, possibly related to differences in dosing regimens, timing with respect to physiotherapy, or other factors related to stroke severity. Dr Goldstein emphasizes the critical issues of trial design in evaluating amphetamine trials in stroke recovery, including the importance of coupling drug exposure with the experience of physiotherapy, and concludes that the effectiveness of this drug remains unanswered.

Dr Theresa Jones and colleagues review the evidence for the effects of behavioral experience on the anatomy of dendrites and synapses in the remaining intact cortical tissue after injury. Dr Jones indicates that these effects can be adaptive or detrimental, depending on the type and timing of such experience. Further, behavioral experience, in the form of increased use of the unimpaired limb after unilateral damage, produces bihemispheric effects. Combinatorial therapies, such as cortical electric stimulation, may aid the rehabilitative process by enhancing its effects. Injury, experience, plasticity, and behavioral outcome have a complex interrelationship. Further studies might provide a knowledge base that would allow clinicians to modulate brain plasticity in a manner that maximizes behavioral gains.

Drs Rajiv Ratan and Mark Noble review the potential for new therapeutic strategies to improve recovery after brain and spinal cord injury. They argue that infrastructural support for more efficient bench-to-bedside translation must be generated to facilitate the development of novel therapies. It is proposed that drugs should be developed that target the various biological epochs that follow stroke, emphasizing stroke therapeutic targets along a continuum. A strategy of testing small molecule drugs in high-throughput screening process is described that has yielded several potential candidates for therapy. The issues surrounding application of new stroke therapeutics, such as delivery and route of administration, are also discussed. A broad perspective of the bench-to-bedside pathway for producing new stroke repair therapeutics is considered in this review.

Dr Thomas Kent and colleagues review the evidence for use-dependent learning after stroke. Analogies exist between normal learning and brain plasticity after stroke. Evidence from magnetoencephalography and functional MRI studies are used to examine how recovery of language function after stroke resembles a true return of function versus compensation. Specifically focusing on constraint-induced language therapy, the authors argue that after stroke, language recovery is reflective of use-dependent learning, similar to the learning process that occurs during the acquisition of a foreign language.

As noted by Drs Ratan and Noble, to date there have been few trials in humans of therapies that target brain repair after stroke. Momentum from numerous sources anticipates human clinical trials, with improved methodology, and with useful insights from accompanying measures of brain function. The need for effective restorative therapies is great, as most patients do not reach medical attention in time to receive acute stroke therapies, and the majority of those that do still have significant long-term disability. The pallete of options is large, from growth factors to cells, brain stimulation to activity-dependent approaches, and small molecules to learning-based programs. The future holds great promise for restorative therapies after stroke.

Disclosures

None.

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