Recovery

Introduction

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The brain repair field and its implications for rehabilitation after stroke continue to mature. The 4 articles that follow, including new MRI analyses for studying fiber reorganization, stratification approaches for stroke trials, synaptic-level in vivo imaging in animal models, and potential targets for neural repair therapies, provide ample evidence that our knowledge base regarding stroke recovery mechanisms is accelerating rapidly, that transformative new technologies are providing new insights into mechanisms, and that the future holds substantial promise for the development of restorative therapies in humans.

In the first article, Dr Quan Jiang and colleagues discuss the use of MRI to monitor structural substrates of recovery and restorative treatment after stroke in rats. Specifically, Jiang et al describe the advancement of techniques in diffusion tensor imaging that has resulted in increased attention on white matter reorganization, in addition to its use in defining pathology. However, significant challenges are imposed by complex fiber arrangements in brain tissue, and resolving crossing fibers has become a priority for this field. Jiang et al summarize the application of q-space diffusion tensor imaging, emphasizing its superiority in detecting axonal remodeling, especially during the early stages after injury. This new potential to track axonal remodeling associated with various treatment strategies offers an exciting platform to understand the neural substrates underlying recovery after stroke.

In the second article, Dr Steven Cramer explores the issue of patient stratification in stroke recovery trials. Borrowing from similar approaches in general medicine, a tacit assumption is that repair-based therapies would be most effective if guided by knowledge about the biological substrate targeted by the therapy. Cramer proposes some of the key variables that may be used to distinguish those who would be more likely to benefit from a particular therapy. These include, but are not limited to, injury characteristics, neurophysiological status, comorbid conditions, and genetic profiles. As an example, Cramer describes the relationship between functional gains after therapy and increases in motor cortex activation, as demonstrated in functional MRI patterns. As these and other variables are better understood and considered in a multivariate model, it may eventually be possible to stratify stroke patients to more effectively maximize functional gains.

In the third article, Drs Albrecht Sigler and Timothy Murphy review the recent application of 2-photon imaging in animal models of stroke. Two-photon imaging has revolutionized visualization of structures in live animals, allowing unprecedented detail relatively deep within cortical tissue. The authors introduce readers to many practical aspects of high-resolution 2-photon imaging in live animals after stroke, with particular attention to imaging of fine structures, such as dendrites. The various factors limiting in vivo imaging are discussed. In addition, the authors discuss the use of transgenic animals with fluorescence proteins in the context of high-resolution brain imaging. These new techniques have allowed imaging of fine structures during both the acute and chronic stages after stroke in rodent models and have provided important insights into the dynamics of structural plasticity, such as spine turnover. The authors illustrate how imaging technology is rapidly extending both the temporal and spatial resolutions to visualize poststroke structural events in new ways.

As discussed by Dr Thomas Carmichael in the fourth article, recent studies of neural repair mechanisms have uncovered several new potential targets for therapy development after stroke. These include blockers of axonal growth inhibition, astrocyte or extracellular matrix growth inhibition, RhoA pathway inhibition, axonal growth stimulators, and cognitive enhancers. Carmichael notes that some of the compounds targeting these processes have already shown promise in preclinical stroke models. The role of high-throughput screening in identifying pharmacological agents that may have repair potential is also discussed. Our expanding knowledge of neural repair processes and putative targets after stroke may eventually provide the basis for stroke recovery drugs.

We hope that these articles provide a springboard for recovery research in several new directions, from selecting patients for recovery trials and designing new drugs to facilitate recovery to imaging of the neural mechanisms of recovery itself—imaging of synaptic plasticity and axonal remodeling.
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Stroke. 2010;41:S111
doi: 10.1161/STROKEAHA.110.595223
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/41/10_suppl_1/S111

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