The Promise of Neuro-Recovery After Stroke: Introduction

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The study of brain repair and behavioral recovery after stroke continues to accelerate with points of convergence between findings in humans and results in animal models of stroke. Approaches to motor recovery after stroke can be usefully broken into 3 categories: reduction in impairment with a return to more normal patterns of motor behavior; compensatory responses with the other limb or even muscles within the same limb; and use of neurally controlled prosthetics that substitute for the affected limb. The future choice of any of these approaches to neurorehabilitation is likely to depend on both the severity of the initial impairment and the time since stroke onset.

Stem cells have garnered a great deal of attention because they conjure up the possibility of neural regeneration and the possible reintegration of new neurons into damaged neural circuits. However, evidence suggests that stem/progenitor transplantation in stroke is not replacing damaged brain but instead enhancing or extending the processes of endogenous brain repair after stroke. This more indirect benefit is the subject of the perspective/review submitted by Dr Sean Savitz. His group has focused on bone marrow–derived mononuclear cells and how they may enhance recovery in rodent stroke models. Several studies, including his own, in rodent models have shown that intravenous or intra-arterial delivery of autologous mononuclear cells lead to reduced impairment and slower infarct maturation when given within a week of stroke. The mechanisms of these benefits are not known, but preliminary evidence suggests anti-inflammatory and neuroprotective effects, as well as effects on the endogenous repair processes of neurogenesis and angiogenesis. Dr Savitz led a study showing that harvesting autologous mononuclear cells in patients after stroke and giving them back intravenously is feasible and safe. Subsequent efficacy trials will hopefully show that the enhancement of spontaneous biological recovery demonstrated with mononuclear cells in animal models will generalize to patients after stroke.

We recently argued that the focus during the time-window of maximal spontaneous recovery, which is 1 month in rodent models and 3 months in humans, should be on reduction in impairment and not on compensation. The reasons for this include evidence that compensatory responses may reduce the chance of reduction in impairment, either because time is spent devoted to the wrong thing or because, as suggested by some rodent models, peri-infarct plasticity might be conducive to both compensatory and recovery responses, suggesting a zero sum game. In this issue, Theresa Jones et al present a review of a series of experiments they have performed in a rodent stroke model showing that training the unaffected limb on a skilled prehension task blunts the responses of the affected side to rehabilitative training. Interestingly, the deleterious effect on the affected side by training the unaffected side is prevented with callosal transection. This suggests that changes that occur with learning in one hemisphere can interfere via the callosum with learning in the other hemisphere. These results are disturbing because they suggest yet another reason why it might not be a good idea to teach patients compensatory techniques with their unaffected side in the first few weeks after stroke.

Disclosures

Dr Carmichael has received research grant support from Biotime, Inc.

References


KEY WORDS: compensation ■ impairment ■ neural repair ■ regeneration ■ rehabilitation ■ stem cell
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Stroke. 2013;44:S103
doi: 10.1161/STROKEAHA.111.000373
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/44/6_suppl_1/S103

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