Preclinical Stroke Research
Gains and Gaps

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The Stroke Progress Review Group, commissioned by National Institute of Neurological Disorders and Stroke to review the status of stroke research in 2011, addressed a variety of clinical and preclinical areas, including progress and unmet needs in preclinical investigation. Identified among the latter were the need to develop better molecular, cellular, and animal models of stroke. This finding reflects understandable disappointment that, although such models have been available for >50 years, few advances in the treatment of acute stroke have occurred. Numerous authors have addressed possible explanations for this paradox and recommended new approaches, and the Stroke Progress Review Group produced no new conceptual breakthroughs in this respect. However, there may be value in reflecting again on some of the extant issues.

What should be expected of a disease model? Should it resemble the disease outwardly, reproduce known pathophysiologic features of the disease (which have often been inferred from other models), predict effective treatments, or all of these? Considering that predicting treatment is of most practical benefit, how effective must the treatment be to validate the model? For example, if thrombolitics end up helping only a tiny fraction of all patients with stroke, does their efficacy in rodents help to validate or to refute the rodent model?

How bad are the existing (primarily rodent) models of stroke? A frequently cited review noted that no clinical treatment had emerged from 1026 “neuroprotective” agents deemed successful in animals, reinforcing the perception that “everything works in animals but nothing works in people.” But the authors also noted that the animal studies in question exploit one or more of these other targets. Even if existing models have not produced clinically validated acute neuroprotective treatments, they may still spur efforts to exploit one or more of these other targets.

Experimental models of disease can be useful not only for discovering treatments but also for elucidating pathophysiology. In this respect, the recent record of preclinical stroke research seems much better. When asked to identify recent advances in the field, Stroke Progress Review Group working groups pointed to new insights on interactions among neurons, glia, and vascular cells; systemic, including immune-mediated influences in stroke pathophysiology; and mechanisms of brain plasticity, repair, and recovery after stroke. Even if existing models have not produced clinically validated acute neuroprotective treatments, they may still spur efforts to exploit one or more of these other targets.

**Sources of Funding**
This work was supported by National Institutes of Health grants NS44921 and NS62414.

**Disclosures**
None.

**References**


Key Words: ischemia  ■  neuroprotection  ■  stroke
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Stroke. 2013;44:S114-S115
doi: 10.1161/STROKEAHA.113.002088

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/S114

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