See related article, pages 294–302.

Stroke research has primarily focused on prevention and acute treatment. Yet, there is a window of opportunity to provide treatments that will increase functional recovery by capitalizing on the brain’s neural plastic responses during postacute and chronic periods.1,2 Papadopoulos and colleagues’ study in this issue of Stroke is consistent with decades of research demonstrating that coupling of D-amphetamine administration with motor practice can enhance motor recovery after brain injury in animal models.3,4 This study elegantly shows that short-term, postacute administration of D-amphetamine sulfate combined with focused physical activity and housing in an “enriched” environment improves motor recovery markedly. These improvements are associated with increased axonal sprouting in corticofugal pathways to the red nucleus and cervical spinal cord from the contralateral forelimb sensorimotor cortex.

Prior animal experiments provide considerable evidence that even a single dose of D-amphetamine induces enduring motor improvements after various types of brain injury.5 Likewise, some clinical studies show that amphetamine administration can be beneficial6,7 and that drugs that have pharmacological effects opposite to that of amphetamine may be harmful.8 Several clinical trials, however, have failed to show a benefit of poststroke amphetamine administration.9–12 One positive7 and one negative12 trial involved similar patients who were treated under similar protocols. It is therefore not surprising that a recent Cochrane report analyzing 10 studies involving 287 patients concluded that there are no clear or straightforward ways to control for the differences between these 2 settings, factors that may in part have contributed to the long list of promising putative neuroprotective drugs that had no benefit when tested in stroke patients.16 Nevertheless, this is exactly the task facing clinical stroke investigators. One possible approach is to introduce the same challenges in preclinical studies expected in clinical trials, including the use of older animals and variability in the location and size of the infarcts. If these features result in a lost or reduced benefit of treatment in animal models, then clinical trial failures would make more sense. There likely are no “magic bullet” treatments that will benefit all patients with stroke equally. This has led to the notion of “proof of concept” Phase 2 clinical trials that first try to determine whether a biological effect expected from preclinical studies occurs in an ideally matched human population.

There are too few treatment options available for people living with the consequences of stroke to dismiss the promise raised by the extensive body of laboratory work indicating the potential for D-amphetamine coupled with specific training to enhance the recovery process. Studies such as that of Papadopoulos and colleagues that contribute to our understanding of the basic neurobiology underlying the interaction between experience and drug administration are critical.

Sources of Funding

Dr Goldstein has received support from the National Institutes of Health and the Veterans Administration for clinical and laboratory-based studies related to the effects of amphetamine on post–brain injury recovery.

Disclosures

None.

References


**Key Words:** basic science ■ behavioral neurology ■ brain recovery ■ experimental ■ pharmacology ■ rehabilitation ■ stroke recovery ■ therapy
Poststroke Treatment: Lost in Translation
DeAnna L. Adkins, Timothy Schallert and Larry B. Goldstein

Stroke. 2009;40:8-9; originally published online November 26, 2008;
doi: 10.1161/STROKEAHA.108.534248
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2008 American Heart Association, Inc. All rights reserved.
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/40/1/8

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published
in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office.
Once the online version of the published article for which permission is being requested is located, click
Request Permissions in the middle column of the Web page under Services. Further information about this
process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/