
Introduction

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Stroke is an important clinical problem with few effective clinical solutions. On average, every 45 sec someone in the United States has a stroke, totaling 700,000 strokes in 2000 alone. Although 25% of all strokes result in death, 75% constitute survival. Of the individuals who survive, 50 to 70% regain some degree of functional independence. However, 15 to 30% are permanently disabled, making stroke a leading cause of serious, long-term disability in the United States (AHA 2002). In 1999, more than 1,100,000 American adults reported difficulty with functional limitations resulting from stroke (CDC 2001). The financial burden of stroke on our society is quite large, with estimates of more than \$50 billion for 2003 (AHA 2002).

Interest in stroke research has increased greatly in recent years. This new interest has been sparked by at least five recent events. First, one of the first effective treatments for stroke is now in widespread use—tissue plasminogen activator (t-PA¹). t-PA is a thrombolytic agent that can, if given in the first few hours after stroke, result in sparing of vulnerable brain tissue. The rapid acceptance of t-PA as an acute therapeutic agent and the importance of diagnosing a stroke very early after its onset have resulted in a number of major efforts directed toward stroke awareness.

Second, there has been considerable interest in developing neuroprotective agents that can act on specific neurotransmitter receptors and potentially impede neuronal death due to excitotoxic events. Although clinical trials to date have been disappointing, a large number of laboratories remain committed to developing pharmacological means to rescue dying neurons.

The third impetus is the rapid development of sophisticated neuroimaging techniques. These techniques (e.g., functional magnetic resonance imaging and magnetoencephalography) are now capable of describing the biochemical and anatomical events that take place in the damaged brain tissue, as well as the functional changes that take place in the uninjured areas.

A fourth impetus to increasing interest in stroke research is the maturation of neuroplasticity principles, which provide a theoretical framework for understanding the process of brain repair and recovery. These principles were derived largely from studies in animal models in the 1970s and 1980s. With improved neuroimaging techniques, many of the initial results have been replicated in humans, providing a firm rationale that rodent and nonhuman primate models can be used to mimic neurological conditions in humans (Cramer 2003).

Although neuroimaging can provide a very detailed picture of the effects of a stroke in the brain and can be used to track changes in the human brain over time, studies of human brains that have undergone stroke have limitations for designing controlled experiments to understand mechanisms or effects of treatment. Strokes in humans are quite varied in the size of the injured area and its location. For example, we still have no definitive way to determine which stroke survivors will benefit from a particular type of therapy.

Fifth, and finally, new therapeutic approaches for the chronic stroke survivor with seemingly permanent disabilities (e.g., constraint-induced movement therapy and amphetamine/physiotherapy) are now under investigation. Very importantly, these approaches were first developed in animal models based on fundamental principles of neuroplasticity. Thus, translational models of stroke in rodents and nonhuman primates show great promise for driving new therapies for restoration of function. The inherent variability in the effects of stroke in humans can be controlled to a large extent in animal models. This potential allows one to determine precise mechanisms of action, leading to logical treatment approaches based on underlying mechanisms.

Animal models of brain injury and recovery are not without their own set of caveats, including the cost and availability of primates as well as scientific concerns regarding the appropriateness and relevance of the animal model. In addition, there are a number of veterinary care issues with any injury and recovery model. Associated animal welfare issues must also be carefully considered.

In this issue of *ILAR Journal*, we have assembled articles by several of the leading researchers in stroke recovery research. The initial group of articles, the first by Dr. Richard Traystman (Traystman 2003) and the second by Drs. Shunichi Fukuda and Gregory del Zoppo (Fukuda and del Zoppo 2003), provide excellent and extensive reviews of current stroke models in rodents and primates, respectively.

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¹Abbreviation used in this Introduction: t-PA, tissue plasminogen activator.

The second group of articles, one by Drs. Jaraslaw Aronowski and Lise Labiche (Aronowski and Labiche 2003) and one by Dr. Christian Xerri and colleagues (Xerri et al. 2003), describe rodent models that are used primarily for acute intervention to lessen deficits. The third group deals primarily with recovery models and intervention beyond the acute period. These articles have been written by Dr. Larry Goldstein (Goldstein 2003), Dr. Tim Schallert and colleagues (Schallert et al. 2003), Dr. Theresa Jones and colleagues (Jones et al. 2003), Dr. Jonathan Marshall and Rosalind Ridley (Marshall and Ridley 2003), and Dr. Randy Nudo, co-editor of this issue, and his colleagues (Nudo et al. 2003).

In this issue, we have sought to provide (1) a resource for stroke researchers, including a basis for both basic research and preclinical models of human stroke; and (2) a review of laboratory animal care issues for laboratory animal research personnel. Many of these models are unique; some utilize primates; some require long surgical procedures and long postinjury survival periods. We have asked each of the authors to comment on these topics, which rarely appear in typical specialized journal articles on stroke. This volume includes not only the articles described above but also features an Appendix of web addresses, where you can extend your exploration into this disease that affects people nationwide. We trust that you will find these additions to the literature to be interesting and informative.

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