
Preface

Despite major advances in prevention, acute treatment, and rehabilitation, stroke remains a major burden on patients, relatives, and economies. The role and potential benefits of experimental models of stroke (i.e., focal cerebral ischemia) in rodents have been recently debated. Critics argue that numerous treatment strategies have been tested successfully in models only to be proven dismal failures when tested in controlled clinical trials.

When methods of systematic review and meta-analysis are applied, however, it turns out that experimental models actually did faithfully predict the negative outcomes of clinical trials. Neuroprotection by hypothermia, on the other hand, first described in animal models, is a good example of a treatment modality that has made it successfully into clinical practice (favorable neurologic outcome after cardiac arrest). Thrombolysis with tissue plasminogen activator (t-PA), the only clinically effective pharmacological treatment of acute ischemic stroke, was first demonstrated and evaluated in an experimental model of stroke. Many other examples document the positive prediction of rodent stroke models even beyond the brain, such as changes in the immune system and susceptibility to infection after stroke. These were first described and can be faithfully modeled in rodents.

Beyond its role in investigating pathomechanisms of stroke and in preclinical testing for the efficacy of novel diagnostic and treatment strategies, rodent stroke is often used as a “model” for how the brain reacts to neurological injury (damage, protection, repair), with implications for many other neurological disorders such as brain and spinal cord injury, epilepsy, and even multiple sclerosis. Concepts such as “neuroprotection”, “preconditioning”, and “ischemic penumbra” are largely the result of experimental stroke research.

Nevertheless, the issue of the relevance of experimental stroke research, particularly in rodents, to human disease, has to be taken seriously. Only recently, a number of problems which are prevalent in this research field and impact on its predictiveness have been identified. These include low statistical power, flaws in experimental design, and negative publication bias, just to name a few. In addition, the validity of experimental stroke research is affected when the effects of age, gender, and comorbidities are ignored in our models.

In this volume, an international consortium of authors aims at critically addressing all these issues on a very practical level. From choosing the model and outcome measures, designing the experiment, conducting and analyzing it, and reporting it in a scientific publication, we are trying to offer food for thought as well as practical advice. This book is the result of a longstanding cooperation of many of the authors not only in scientific questions but also in teaching animal models of stroke and good scientific practice to students and researchers, and it is the result of an intense discussion of matters of validity, quality and quality control. For more than 10 years, several of the authors have been organizing the course “Methods in Cerebral Ischemia Research,” and many are now jointly organizing training and dissemination of practical knowledge in the European Community-funded European Stroke Network (<http://www.europanstrokenetwork.eu/>), and in the Center for Stroke Research (<http://www.strokecenter.de>) in Berlin. The structure and

content of the book reflect both the authors' longstanding expertise in experimental and clinical stroke research and their roles in training the scientific community in the tools of the trade.

We hope that this volume will help its readers understand the limitations and the opportunities of modeling stroke in rodents and enable them to conduct experiments which will not only improve their understanding of the pathophysiology of this devastating disorder but also serve as the basis for developing highly effective treatments.

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