

NEUROMETHODS

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fMRI Techniques and Protocols

Second Edition

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 **Humana Press**

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Preface to the Series

Experimental life sciences have two basic foundations: concepts and tools. The *Neuromethods* series focuses on the tools and techniques unique to the investigation of the nervous system and excitable cells. It will not, however, shortchange the concept side of things as care has been taken to integrate these tools within the context of the concepts and questions under investigation. In this way, the series is unique in that it not only collects protocols but also includes theoretical background information and critiques which led to the methods and their development. Thus it gives the reader a better understanding of the origin of the techniques and their potential future development. The *Neuromethods* publishing program strikes a balance between recent and exciting developments like those concerning new animal models of disease, imaging, in vivo methods, and more established techniques, including, for example, immunocytochemistry and electrophysiological technologies. New trainees in neurosciences still need a sound footing in these older methods in order to apply a critical approach to their results.

Under the guidance of its founders, Alan Boulton and Glen Baker, the *Neuromethods* series has been a success since its first volume published through Humana Press in 1985. The series continues to flourish through many changes over the years. It is now published under the umbrella of Springer Protocols. While methods involving brain research have changed a lot since the series started, the publishing environment and technology have changed even more radically. Neuromethods has the distinct layout and style of the Springer Protocols program, designed specifically for readability and ease of reference in a laboratory setting.

The careful application of methods is potentially the most important step in the process of scientific inquiry. In the past, new methodologies led the way in developing new disciplines in the biological and medical sciences. For example, Physiology emerged out of Anatomy in the nineteenth century by harnessing new methods based on the newly discovered phenomenon of electricity. Nowadays, the relationships between disciplines and methods are more complex. Methods are now widely shared between disciplines and research areas. New developments in electronic publishing make it possible for scientists that encounter new methods to quickly find sources of information electronically. The design of individual volumes and chapters in this series takes this new access technology into account. Springer Protocols makes it possible to download single protocols separately. In addition, Springer makes its print-on-demand technology available globally. A print copy can therefore be acquired quickly and for a competitive price anywhere in the world.

Saskatoon, Canada

Wolfgang Walz

Preface

fMRI has gained a remarkable role as a tool for studying brain function due to its capability to provide an invaluable insight into the mechanisms through which the human brain works in healthy individuals and to explore the mechanisms associated with recovery of function or clinical deterioration in patients with different neurological and psychiatric conditions. The utility of this technique to monitor the effects of pharmacologic and rehabilitative treatments has also been recently demonstrated.

The second edition of this book aims at providing an up-to-date review of the main methodological aspects of fMRI, as well as a state-of-the-art summary of the achievements obtained by its application to the study of central nervous system functioning in the clinical arena. Future evolutions of fMRI techniques are also discussed. The contributors of this volume are all worldwide renowned scientists and physicians with a broad experience in the technical development and clinical use of fMRI. Although the field is ample, based on a series of very different disciplines and expanding at a dramatic pace every day, I believe that this book provides an adequate background against which to plan and design new studies to advance our knowledge on the physiology of the normal human brain and its change following tissue injury.

Part I of the volume is aimed at providing the basic knowledge for the understanding of the technical aspects of fMRI. It covers the basic principles of MRI and fMRI, the different options that can be used to set up an fMRI experiment, and the steps of fMRI analysis, from the preparation of data to the achievement of interpretable results. This part is therefore essential to introduce the readers to the “fMRI world” and make them able to interpret with enough criticism the results of their own experiments. A chapter is devoted to the advantages, caveats, and pitfalls of fMRI data acquired using high-field MR scanners. In addition, although still in its infancy, the assessment of brain connectomics with functional and structural imaging techniques is considered at length, given its potential for improving the understanding of normal and pathological brain function.

Part II provides an overview of the main results derived from the application of fMRI to the study of healthy individuals. Given its noninvasiveness, safety, and repeatability, fMRI is rapidly replacing, whenever possible, other functional techniques, such as positron emission tomography, to image the function of the normal brain. In addition, due to its spatial resolution, fMRI is commonly preferred to neurophysiological techniques to locate with precision the areas activated during the performance of experimental tasks. What has been achieved in the analysis of the main human functional systems with fMRI is illustrated, including, among many other aspects, behavior, language, memory, emotion, sensation, pain, vision, and hearing.

Part III is more clinically oriented and illustrates the main findings obtained by the application of fMRI to assess the role of brain plasticity in the major neurological and psychiatric conditions. The first chapter is devoted to fMRI studies of multiple sclerosis, since there is a growing body of evidence that brain functional reorganization has an important role, at least in some phases of the disease, in limiting the clinical consequences of MS-related irreversible tissue damage. Therefore, MS can be viewed as a “model” to understand how

pathology can affect the patterns of brain recruitment. The results obtained in other white matter conditions, including isolated demyelinating myelitis and vasculitides, are then presented. The second chapter deals with stroke studies, which have shown consistently that reorganization of surviving neuronal networks is one of the key factors underlying recovery of function. The experimental caveats to be faced when studying patients with severe clinical impairment are also reviewed. The following chapters cover psychiatric and neurodegenerative diseases, a field where fMRI is providing important pieces of information not only for the understanding of the mechanisms underlying disease pathophysiology and genesis of symptomatology, but also for planning and monitoring novel treatment strategies. Then, two conditions, i.e., epilepsy and tumors, where fMRI is gaining an important role in the presurgical evaluation of patients, are discussed. The last contribution of this part describes the potential and some preliminary, but nevertheless promising, results on the use of fMRI in the monitoring of pharmacological treatments and motor rehabilitation.

Part IV is a glimpse into the future and presents novel approaches for the integration of fMRI data with measures of damage assessed using structural MR techniques and the application of fMRI to image spinal cord function. Finally, results derived from the application of graph analysis to assess network abnormalities in patients with several neurological and psychiatric disorders, including dementia, amyotrophic lateral sclerosis, multiple sclerosis, and schizophrenia, are presented.

The hope that has inspired this book is that it will be of help to clinicians and researchers in their daily life activity by providing a “user-friendly” summary of the field and the necessary background against which to plan and carry out future and successful studies. This is, indeed, an ever-growing and exciting field of research, where we have reached a lot in the past few years, but where there is still a long journey ahead of us.

Milan, Italy

Massimo Filippi

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