It is now well known that the functional organization of the cerebral cortex is plastic, and that changes in organization occur throughout life in response to normal and abnormal experience. Transcranial magnetic stimulation (TMS) is a non-invasive and painless technique that has opened up completely new and fascinating avenues to study neural plasticity. First, TMS can be used to detect changes in excitability or connectivity of the stimulated cortex which may have occurred through processes such as learning or recovery from a lesion. Second, repeated TMS by itself can induce changes in excitability and connectivity of the stimulated cortex which may be used therapeutically in neurological and psychiatric disease. Third, TMS can induce short-lasting 'virtual lesions' which may directly test the functional relevance of brain plasticity.

Current knowledge of all these exciting possibilities is brought together in this book, written by the world’s leading experts in the field. The book is an essential compendium on plasticity of the human brain in health and disease, for clinical neurophysiologists, neurologists, psychiatrists and neuroscientists.

Simon Boniface is Consultant Neurophysiologist and Director of Neurophysiology, Addenbrooke’s Hospital and Wolfson Brain Imaging Centre, Cambridge, UK.

Ulf Ziemann is Assistant Professor of Neurology, Clinic of Neurology, Johann Wolfgang Goethe-University of Frankfurt, Germany.
Plasticity in the Human Nervous System
Investigations with Transcranial Magnetic Stimulation

Edited by
Simon Boniface
Department of Clinical Neurophysiology
Addenbrooke's Hospital Wolfson Brain Imaging Centre
University of Cambridge
UK

and

Ulf Ziemann
Clinic of Neurology
Johann Wolfgang Goethe-University of Frankfurt
Germany
# Contents

<table>
<thead>
<tr>
<th></th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The nature and mechanisms of plasticity</td>
<td>01</td>
</tr>
<tr>
<td></td>
<td>Mengia-S. Rioult-Pedotti and John P. Donoghue</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Techniques of transcranial magnetic stimulation</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>John C. Rothwell</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Developmental plasticity of the corticospinal system</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>Janet Eyre</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Practice-induced plasticity in the human motor cortex</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>Joseph Classen and Leonardo G. Cohen</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Skill learning</td>
<td>107</td>
</tr>
<tr>
<td></td>
<td>Edwin M. Robertson, Hugo Theoret and Alvaro Pascual-Leone</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Stimulation-induced plasticity in the human motor cortex</td>
<td>135</td>
</tr>
<tr>
<td></td>
<td>Joseph Classen and Ulf Ziemann</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Lesions of cortex and post-stroke 'plastic' reorganization</td>
<td>166</td>
</tr>
<tr>
<td></td>
<td>Paolo M. Rossini and Joachim Liepert</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Lesions of the periphery and spinal cord</td>
<td>204</td>
</tr>
<tr>
<td></td>
<td>Michael J. Angel, Nick Davey, Peter Ellaway and Robert Chen</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Functional relevance of cortical plasticity</td>
<td>231</td>
</tr>
<tr>
<td></td>
<td>Pablo Celnik and Leonardo G. Cohen</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Therapeutic uses of rTMS</td>
<td>246</td>
</tr>
<tr>
<td></td>
<td>Chip Epstein and John C. Rothwell</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Contents</td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>-------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Rehabilitation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>David Gow, Chris Fraser and Shaheen Hamdy</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>New questions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mark Hallett, Eric M. Wassermann and Leonardo G. Cohen</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Index</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Colour plates between pp. 116 and 117</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>© Cambridge University Press</td>
<td></td>
</tr>
<tr>
<td></td>
<td><a href="http://www.cambridge.org">www.cambridge.org</a></td>
<td></td>
</tr>
</tbody>
</table>
Contributors

Editors

Simon Boniface
Department of Clinical Neurophysiology
Addenbrooke’s Hospital
and the Wolfson Brain Imaging Centre
Cambridge CB2 2QQ, UK

Ulf Ziemann
Neurologische Klinik
Johann Wolfgang Goethe-Universität
Theodor-Stern-Kai 7
60590 Frankfurt am Main
Germany

Contributors

Michael J. Angel
Toronto Western Hospital
5W 445, 399 Bathurst Street
Toronto, Ontario,
M5T 2S8, Canada

Pablo A. Celnik
Department of Physical Medicine and Rehabilitation
Johns Hopkins University
136 West Lanvale Street
Baltimore
MD 21217, USA

Robert Chen
Toronto Western Hospital
5W 445, 399 Bathurst Street
Toronto, Ontario,
M5T 2S8, Canada

Joseph Classen
Department of Neurology
University of Würzburg
Josef-Schneider-Str 11
D-97080 Würzburg, Germany

Leonardo G. Cohen
Human Cortical Physiology Section
NINDS
National Institutes of Health
Building 10, Room 5N 234
10 Center Drive, MSC 1428
Bethesda
MD 20892-1428, USA
List of contributors

Nicholas J. Davey
Department of Sensorimotor Systems
Division of Neuroscience and Psychological Medicine
Imperial College School of Medicine, Charing Cross Hospital
Fulham Palace Road
London W6 8RF, UK

John P. Donoghue
Department of Neuroscience
Brown University
Box 1953
Providence
RI 02912, USA

Peter H. Ellaway
Department of Sensorimotor Systems
Division of Neuroscience and Psychological Medicine
Imperial College School of Medicine, Charing Cross Hospital
Fulham Palace Road
London W6 8RF, UK

Chip M. Epstein
Department of Neurology
Emory Clinic
1365 Clifton Road NE
Atlanta
GA 30322, USA

Janet A. Eyre
Department of Child Health
The Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
NE1 4LP, UK

Chris Fraser
Department of Medicine
Royal Bolton Hospital
Farnworth
Bolton BL4 0JR, UK

David Gow
Department of G.I. Sciences and Medicine
University of Manchester
Hope Hospital
Eccles Old Road
Salford M6 8HD, UK

Peter H. Ellaway
Department of Sensorimotor Systems
Division of Neuroscience and Psychological Medicine
Imperial College School of Medicine, Charing Cross Hospital
Fulham Palace Road
London W6 8RF, UK

David Gow
Department of G.I. Sciences and Medicine
University of Manchester
Hope Hospital
Eccles Old Road
Salford M6 8HD, UK

Mark Hallett
Human Motor Control Section
NINDS
National Institutes of Health
Building 10, Room 5N 226
10 Center Drive, MSC 1428
Bethesda
MD 20892-1428, USA

Joachim Liepert
Clinic of Neurology
University of Hamburg
Hamburg
52 2046, Germany

Alvaro Pascual-Leone
Laboratory for Magnetic Brain Stimulation
Behavioral Neurology Unit
List of contributors

Beth Israel Deaconess Medical Center
330 Brookline Avenue, Kirstein Building KS 452
Boston, MA 02215, USA

Mengia-S. Rioult-Pedotti
Department of Neuroscience
Brown University
Box 193
Providence, RI 02912, USA

Edwin M. Robertson
Laboratory for Magnetic Brain Stimulation
Behavioral Neurology Unit
Beth Israel Deaconess Medical Center
330 Brookline Avenue, Kirstein Building KS 452
Boston, MA 02215, USA

Paolo M. Rossini
Department of Neuroscience
Ospedale Fatebenefratelli
Isola Tiberina 39
00186 Rome, Italy

John C. Rothwell
Sobell Department
Institute of Neurology (Box 146)
Queen Square
London WC1N JBG, UK

Hugo Theoret
Laboratory for Magnetic Brain Stimulation
Behavioral Neurology Unit
Beth Israel Deaconess Medical Center
330 Brookline Avenue, Kirstein Building KS 452
Boston, MA 02215, USA

Eric M. Wassermann
NINDS
National Institutes of Health
Building 10, Room 5N 226
10 Center Drive, MSC 1428
Bethesda MD 20892-1428, USA

Ulf Ziemann
Neurologische Klinik
Johann Wolfgang Goethe-Universität
Frankfurt
Theodor-Stern-Kai 7
60590 Frankfurt am Main
Germany
Plasticity of the brain is an increasingly important topic in many areas of neuroscience including development, learning and repair. It is still a challenge to study plasticity directly in the human nervous system. Transcranial magnetic stimulation (TMS), however, has become a suitable non-invasive and painless technique, which can be applied to detect changes in cortical excitability or connectivity as indicators of plasticity. Further, TMS can be used to induce short-lasting virtual lesions in order to test the functional relevance of brain plasticity. Finally, TMS can induce plasticity itself. In this book, we utilize TMS in these ways to investigate and manipulate plasticity in the human nervous system. In so doing, we have been fortunate to gather many of the world’s leading contributors in this field.

The basic nature and mechanisms of plasticity are tackled in the introductory chapter, with particular reference to the animal primary motor cortex. This is followed in the next chapter by an introduction to the technique and physiological effects of human TMS.

In the next section we then apply this background to TMS studies of plasticity in healthy subjects. Chapter 3 is about developmental plasticity of the human corticospinal tract. The next two chapters demonstrate the maintained capability of the adult human brain for plastic change by looking into TMS studies of use-dependent plasticity and learning of motor skills. Finally, the induction of plasticity by TMS itself is the focus of Chapter 6.

The next section is more clinically orientated and examines functional deficits and the principles of recovery of function after cortical lesions, stroke in particular, and lesions of the periphery and spinal cord. This is followed by a demonstration of the functional relevance of cortical plasticity. The concluding two chapters of this section provide a survey of TMS as a potential therapeutic tool for promoting beneficial plasticity in various neurological conditions.
and psychiatric disorders, and the applications of TMS in the process of neurological rehabilitation. The book closes with a look towards the future, speculating on novel and farther reaching avenues for the study and influence of human brain plasticity with TMS.

We would like to thank the contributors for all their time and effort, and chiefly we would like to thank our families for their support, past and future.

Simon Boniface and Ulf Ziemann
Cambridge and Frankfurt, September 2002