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Magnetic Resonance Neuroimaging

Methods and Protocols

Humana Press

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Preface

To visualize the inside of a living human brain has been the goal of physicians since ancient times. The advent of noninvasive imaging technology, such as magnetic resonance imaging (MRI), during the latter half of the twentieth century has allowed for the opening of new vistas of the inner workings of the brain to biologists and clinicians on a daily basis. Great strides in unraveling the secrets of the brain have been achieved since the widespread implementation of imaging protocols in universities and hospitals.

The gradual merging of molecular biology and imaging techniques at the beginning of the twenty-first century now affords a detailed investigation of the molecular underpinning of a working brain. The 30 chapters in this book contain experimental MRI protocols that can be used to noninvasively interrogate the healthy and diseased brain. The protocols are divided into general techniques (e.g., measuring relaxivity, magnetic resonance spectroscopy, diffusion tensor imaging, MR reporter genes) and specific applications in brain imaging (e.g., phenotyping transgenic animals, detecting amyloid plaques, fMRI in psychiatry). Most of these methods can be applied to both animal and human studies and may therefore provide a great resource for translational efforts. Clinical neurologists, psychiatrists, and radiologists will find these protocols useful, as will basic scientists working in the field of neuroscience.

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Contents

Section I

Introduction

Chapter 1

From Molecules to Man: The Dawn of a Vitreous Man

Michel Modo and Jeff W.M. Bulte

Abstract

One of the greatest challenges to study the structure, function, and molecules in the living brain is that it is enclosed within the skull and difficult to access. Although biopsies are feasible, they are invasive, could lead to functional impairments, and in any case will only provide a small regional sample that is not necessarily reflecting the entire brain. Since the beginning of the twentieth century, in vivo imaging has gradually, and steadily, matured into non-invasive techniques that enable the repeated investigation of the structural, functional, cellular, and molecular composition of the brain. Not only is this information of great importance to scientists aiming to understand how the brain works, but these techniques are also essential to physicians who use imaging to diagnose and treat disease. The current book is a collection of 29 cutting-edge methods and protocols that are used in the current field of neuroimaging.

Key words: Neuroimaging, magnetic resonance imaging, computer tomography, positron emission tomography.

1. Looking Inside the Living Brain: A Historical Primer

Correct functioning of the brain is central to our everyday lives. Developmental problems or damage to the brain can interfere with someone's ability to take care of basic live functions. However, the study of the brain is hampered by it being enclosed by the skull that prevents us from seeing or studying the brain directly. Initial theories and studies of the brain were based on ill-conceived ideas, but these have gradually paved the way for a thorough scientific study of the brain and mind. Since the beginning of modern medicine, these studies have been highly dependent on technological developments.

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Arguably, the eighteenth-century pseudo-scientific ideas of Franz Gall's cranioscopy, i.e., the appearance (*scopos* in Greek) of the skull (*cranium*), are at the origin of modern brain science. Gall professed that the external appearance of the skull mirrors the enclosed brain (1). Importantly, phrenology (*phrenos* for mind and *logos* for study) further developed this concept and implied that these external anatomical characteristics are indicative of particular behaviors or personality traits (2). Although even during its day doubts about this approach arose and were considered spurious by some (3), phrenology retained a large following and in some cases was used to justify prejudice and political agendas (4). However, in the second half of the nineteenth century, linking damage of particular brain areas with functional impairments surpassed the scientifically unfounded rhetoric of phrenology. Notably, the seminal studies of Phineas Gage by John Harlow (5) and Tan's aphasia by Paul Broca (6) ushered in a new era of science that attempted to directly link an anatomical brain region with its contribution to behavior.

Ever since these seminal studies, postmortem neuropathology has been the foundation of brain science against which in vivo imaging has been compared. The cellular and molecular compositions of the brain are the gold standard of evidence that damage or aberrations occurred in that region. Although postmortem histopathology can be very informative about the locale of damage or abnormalities, it only provides a means to study conditions after someone has passed away. It is hence of no diagnostic value. In contrast, being able to visualize aspects of pathology in vivo not only allows a more rigorous study of the temporal and spatial progression of these pathologies but potentially also provides a means to diagnose particular conditions and establish a differential diagnosis for an appropriate treatment. At present, both specialties of psychiatry and neurology depend on the study of the brain in vivo to elucidate the underlying causes of behavioral dysfunction.

The first step in achieving this in vivo visualization of the brain has been taken at the beginning of the twentieth century with elementary X-ray-based imaging techniques, such as pneumoencephalography (PEG) (7, 8). **Table 1.1** provides a time line of milestones in neuroimaging. Although these early techniques provided insights into the living brain, they were also often causing damage to the patient's brain (e.g., injection of air into the lateral ventricles to provide contrast). Gradually technological developments, such as tomography, where X-rays are rotated around the patient to record (*graphens*) the signal on single sections (*tomos*) (9, 10), heralded new innovations that are still in use today. Already in the 1920s, Edgar Moniz used imaging to noninvasively visualize blood vessels in the brain to identify the location of brain tumors (11). Despite these early pioneering advances,

Table 1.1
Time line of technological and methodological milestones in (neuro) imaging. MRI milestones are in bold

Year	Researcher	Milestone
1895	Roentgen (43)	X-ray image of skull
1910	Bachem and Gunther (44)	First use of contrast media
1916	Dandy (7)	Pneumoencephalography
1924	Hevesy (45)	Radiotracer use in animals
1927	Moniz (11)	Angiography
1931	Vallebona (22)	Stratigraphic imaging
1935	Grossman (9, 10)	Tomographic imaging
1936	**Gorter** (46)	**Paramagnetic relaxation**
1938	**Rabi** (47)	**Nuclear magnetic resonance**
1942	**Bloch** (48) **and Purcell** (49)	**Measured NMR signal**
1953	Brownell and Sweet (50)	Positron imaging in brain tumors
1956	Kuhl (51)	Recorder for radionuclide scanning
1958	Anger (52)	Scintillation camera
1962	Rankowitz and Robertson (53)	PET transverse section instrument
1963	Kuhl (54)	Emission reconstruction tomography
1965	Harper and Lathrup (55)	Tc-99m radiotracer for brain
1971	**Damadian** (56)	**Hydrogen density in tumors measured by NMR**
1973	Hounsfield (13) and Cormack (12)	Computer tomography (CT)
1973	**Mansfield** (57) **and Lauterbur** (58)	**Magnetic resonance imaging (MRI)**
1974	Budinger and Gullberg (59)	SPECT
1974	**Hoult** (60)	**Magnetic resonance spectroscopy (MRS)**
1975	Ter-Pogossian (61) and Phelps (62)	Positron emission tomography (PET)
1975	Kuhl (63)	First quantitative cerebral blood volume measurement
1975	**Ernst** (64)	**Phase encoding for MRI**
1977	Jaszcak (65)	First head SPECT
1977	Ido and Alavi (67)	FDG-PET
1977	**Damadian** (66)	**First MRI scan of patient**
1977	**Mansfield** (68)	**Echo planar imaging (EPI)**
1980	**Redpath** (69)	**Spin-warp technique for MRI**
1981	**Bydder** (70)	**MR contrast agent**
1983	Wagner (14)	First neuroreceptor imaging using PET
1984	**Weinmann** (71)	**Gd-DTPA**
1986	**Nishimura** (72)	**MR angiography**