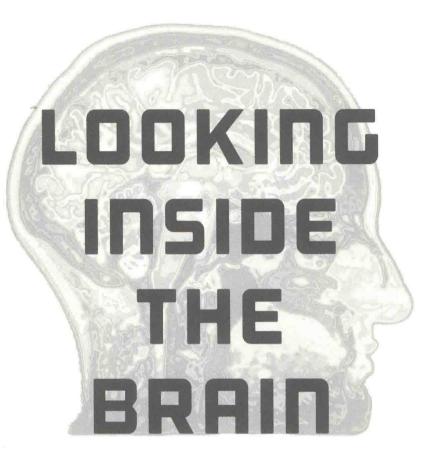
THE POWER OF NEUROIMAGING

DENIS LE BIHAN

TRANSLATED BY TERESA LAVENDER FAGAN



HE POWER OF NEUROIMAGING

DENIS LE BIHAN

TRANSLATED BY TERES AND ENDER FAGAN

PRINCESON ALMAND OXFORD

First published in France under the title *Le Cerveau de cristal. Ce que nous révèle la neuro- imagerie*, copyright © Odile Jacob, 2012

English translation copyright © 2015 by Princeton University Press
Published by Princeton University Press, 41 William Street,
Princeton, New Jersey 08540
In the United Kingdom: Princeton University Press, 6 Oxford Street,
Woodstock, Oxfordshire OX20 1TW

press.princeton.edu

Jacket design by Karl Spurzem Interior design by Lorraine Betz Doneker

All Rights Reserved

Library of Congress Cataloging-in-Publication Data Le Bihan, D. (Denis), 1957–, author. [Le Cerveau de cristal. English]

Looking inside the brain : the power of neuroimaging / Denis Le Bihan ; translated by Teresa Lavender Fagan.

p.; cm.

Originally published in France under the title Le Cerveau de cristal. Ce que nous révèle la neuro-imagerie, copyright © Odile Jacob, 2012.

Includes bibliographical references and index.

ISBN 978-0-691-16061-0 (hardcover : alk. paper)
I. Fagan, Teresa Lavender, translator. II. Title.

[DNLM: 1. Neuroimaging—methods. 2. Brain—physiology. WL 141.5.N47]

RC78.7.N83

616.07'548—dc23 2014036587

British Library Cataloging-in-Publication Data is available

This book has been composed in Garamond Premier Pro and Trade GothicBold Condensed

Printed on acid-free paper. ∞

Printed in the United States of America

1 3 5 7 9 10 8 6 4 2



比为试读,需要完整PDF请访问: www.ertongbook.com

ACKNOWLEDGMENTS

This book would never have existed without the faith and enthusiasm of Odile Jacob, who literally forced me to put my ideas on paper, whereas I was extremely reluctant to do so, mainly because I was so pressed for time. Her team has done a remarkable job. I would like to thank in particular Nicolas Witkowski, who helped me to improve the text, both in terms of style and concision (it seems I have a slight tendency to digress), and who was able to give me the motivation and a rhythm that enabled me to complete the book. It has also been a pleasure to work with Teresa Fagan for the English translation and Eric Schwartz at Princeton University Press for the U.S. edition.

My life's work, upon which this book is based, has been undertaken over a period of around thirty years. Although a great part of my research has been undertaken in France, at the Hôpitaux de l'Assistance Publique in Paris, then at the Commissariat à l'Energie Atomique (CEA), first in the Service Hospitalier Frédéric-Joliot (SHFJ) in Orsay, and currently at NeuroSpin in Saclay, I have particularly warm memories of the years I spent at the National Institutes of Health in Bethesda, Maryland, and at the University of Kyoto.

As for my "prehistory," I owe a great deal to the support and understanding of Marie-Germaine Bousser, Emmanuel Cabanis, Maurice Guéron, Claude Marsault, as well as Denis Lallemand and Maurice Laval-Jeantet, who are no longer with us, who enabled me to simultaneously pursue a medical internship and studies in physics, a period during which I established the foundations of diffusion MRI. I wish also to thank the teams of Thomson-CGR for welcoming me into their fold, in particular Éric Breton and Patrick Leroux.

Throughout the years I have lost count of the many colleagues with whom I have had the joy and the honor to work. Unfortunately, I can't list them all, but I am particularly grateful to my National Institutes of Health (NIH) colleagues, John Doppman and Edwin Becker, who invited me, Robert Turner, Peter Basser, Jeff Alger, Robert Balaban, and Leslie Ungerleider, for all that they taught me. It is clear that the period I spent at the NIH corresponds to a sort of universal golden age in neuroimaging through MRI, with the appearance of fMRI, the groundbreaking developments of diffusion MRI (which

ACKNOWLEDGMENTS

I brought back to France with me), which gave birth to diffusion tensor imaging at the NIH. At the University of Kyoto, diffusion MRI experienced new growth thanks to the unique climate in which I was working. I had, for example, particularly fruitful both scientific and friendly discussions with Hidenao Fukuyama, Toshihiko Aso, and Shin-ichi Urayama at the Human Brain Research Center, and with Kaori Togashi and Mami Iima in the radiology department.

As for André Syrota, his loyalty and constant support throughout these thirty years are indeed priceless. One can only admire what he has made possible over those years. After welcoming me at the SHFJ while I was working on my thesis, he invited me to return ten years later, after my stay at the NIH. And it was he who gave his immediate support to the project I proposed to him for a center of neuroimaging through high-field MRI, which was to become NeuroSpin. He was able to remove countless obstacles and convince the decision-makers, both at the CEA and in the highest levels of the French government. Bernard Bigot, the high commissioner, then chief administrator of the CEA, has also played and continues to play a crucial role in the creation and the development of NeuroSpin and its instruments—in particular, its future 11.7 T magnet.

Much of the work discussed in this book is of course the fruit of the labor of my close collaborators, Cyril Poupon, Stanislas Dehaene and his wife Ghislaine, Andreas Kleinschmidt, Christophe Pallier, Jean-François Mangin, Yann Cointepas, Bertrand Thirion, Lucie Hertz-Pannier, Jessica Dubois, Philippe Pinel, Jean-Baptiste Poline, Franck Lethimonnier, Luisa Ciobanu, Alexis Amadon, Nicolas Boulant, Sébastien Mériaux, Fawzi Boumezbeur, Éric Giacomini (and the list is, in fact, much longer). Their contributions have been enormous, and I thank them wholeheartedly, as I do my students, both past and current, of whom there are too many to mention here. The Iseult project has also been the occasion to create many strong bonds, both professional and of friendship, with our colleagues at the Institut de recherches sur les lois fondamentales de l'Univers (IRFU) at the CEA, notably the teams of Philippe Rebourgeard and Pierre Védrine, who have been involved in the conception and development of our 11.7 T magnet at the IRFU, and with the teams of Guerbet, led by Claire Corot and Philippe Robert for molecular imaging.

ACKNOWLEDGMENTS

Finally, I can't express warmly enough all of my gratitude to my family, who have always believed in and supported me. First, my parents, who always encouraged me, and to whom I regret not having been able to give more back in return through my work; my daughters, Armelle and Carolyn; and my wife, Christiane, without whose constant love, understanding, and encouragement none of this would have been possible. This book is also theirs.





CONTENTS

Acknowledgments vii

INTRODUCTION

ONE	ELEMENTARY PARTICLES 4	
	Broca's Discoveries 5	
	The Birth of Modern Neuroimaging 7	
	The First Revolution: The X-Ray CT Scanner 8	
	Nuclear Magnetism 11	
	The Nuclei Enter into Resonance: From NMR to MRI	13
	The Anatomy of an MRI Scanner 16	
	The Crystal Skull 18	

TWO THE MAGNETIC BRAIN 22

The Computer at Work 22
The Brain's GPS 24
When the Brain Is Constructed 25
The Destiny of Neurons 28
Language and Cerebral Plasticity 30
Genes or Environment? 33
The Phrenology of the Brain 35

THREE SEEING THE BRAIN THINK 38

I Think, Therefore I Irrigate 38
Seeing the Brain with Antimatter! 39
The Glory of PET 41
Positrons on the Verge of Being Replaced by Magnetism 42
Electrons Come to the Aid of Protons 43
The Wrong Track 45
A Question of Oxygen 46
From Rats to Cats... Then to Humans 47
The Prowess of Functional MRI 48
Don't Think of Anything 50
Proof through Statistics 51
The Homunculus Seen in fMRI 52
The Traps of fMRI 53
The Missing "L" 54

CONTENTS

FOUR THE MAGNETIC BRAIN IN ACTION 56

A Cat in the Brain 57 Mental Reading 59

"When Things Are Bad, Look at Yourself in a Mirror" 62

Singing in the Brain 64

What Side Do You Speak On? 67

An Expensive Lie Detector 71

The Intimate Brain 73

Does Free Will Exist? 76

At the Doors of Awareness 78

FIVE THE BRAIN PROBED THROUGH WATER MOLECULES 82

Einstein's Visions 84

NMR Sensitive to Diffusion 86

From NMR to MRI: Diffusion . . . Confusion 87

Diffusion and Cancer 90

Mike's Other Discovery 93

White Matter Takes On Colors 95

An Asynchronous Brain 99

SIX WATER: MOLECULE OF THE MIND? 104

The Firefighters Arrive a Bit Late 104

Swelling Neurons 106

Two Types of Water 109

104.5 Degrees: The Angle of Life 111

Protons Play Leapfrog 114

The Tribulations of Water in Cells 115

A Dance of Spines 118

Mechanical Neurons 121

SEVEN THE CRYSTAL BRAIN 125

Enter the Nanoparticles 126

Many Are Called, Few Are Chosen 129

MRI of the Extreme 133

An Exceptional Instrument for an Exceptional Organ 137

The Birth of NeuroSpin 141

Safety Above All 143

Conquering the Brain 147

In Search of a Neural Code? 150

References 153

Figure Credits 161

Index 163

INTRODUCTION

before realizing that it has taken *Homo sapiens* centuries of reflection before realizing that the brain is the source of thought and awareness, centuries to allow the brain to usurp the organs—the heart or the liver (and its bile)—that had always been considered the centers of emotions. The Egyptians took the brain out of their mummies because they considered it to be merely a radiator. Aristotle, too, thought that the brain served to cool blood that was overheated through an emotional agitation of the heart, a concept that we find in the French expression *perdre son sang-froid*—"to lose one's cool." And yet the brain being so highly protected by the bone of the skull should have put people on the right track much earlier: it is clearly not by chance that nature provided the seat of our nervous system with such armor. Of course, traces of trephination discovered in prehistoric remains suggest that some curious observers had perhaps begun to suspect the truth. But for centuries the skull was associated more with death and its representations than seen as a container sheltering the organ of our thoughts.

And so it wasn't until the relatively recent age of the advent of anatomy, then surgery, that people dared to examine the brain, and to begin to study it. Much of our current knowledge comes from the work of Paul Broca on language in the mid-nineteenth century; from dissections of the brain of deceased patients; and from observing the brain of patients awake during neurosurgical interventions. Understandably, the possibility of seeing the brain of a living patient, let alone the brain of completely healthy subjects, for a long time remained an inaccessible dream. Only science fiction novels and films dared to suggest that one day it would be possible to have direct access to the contents of our thoughts by observing the human brain.

But this didn't take into account the progress that had been made in the realm of physics. Atoms had been discovered, and mysterious rays, such as

INTRODUCTION

x-rays or those emanating from natural radioactivity, had been demonstrated. Following these discoveries theoretical and experimental physicists at the beginning of the twentieth century in a few years put into place physical and mathematical models to explain such strange phenomena and to account for the infinitely small. And so quantum physics was born, a discipline that explained the behavior of atoms and particles, the ultimate components of matter. Armed with these powerful theoretical tools, physicists were able to go beyond what was available in nature: radioactivity became artificial, atomic systems were mastered to produce a new, very powerful light—the laser—and, based on an equivalent principle, radio waves following the magnetization of certain atomic components. Engineers consolidated all these discoveries into developing apparatuses, such as x-ray tubes, enabling them to be reproduced on demand in well-controlled conditions, and to be used for various applications.

This is how physics joined the field of medicine, and in particular the field of medical imaging. The rays and particles discovered by physicists in fact had the ability to travel through our bodies, providing shadows of the structures they had traversed. Radiology made its debut as a medical specialty, and then came "nuclear" medicine. On a medical level, such images of the interior of the human body constituted an initial revolution, but those images remained fairly rudimentary, the organs were more "guessed at" than truly observed. The second revolution came with the marriage of physics and computer science at the end of the last century. Sensors of rays and particles became highly sensitive, and the computer was able to enhance that sensitivity, showing for the first time details of internal organs, and in particular of the brain inside the skull. "Neuroimaging" made great strides in the last quarter of the twentieth century, when it became possible to observe easily and without risk the brains of sick or healthy subjects, including that of a fetus in its mother's womb. Neuroimaging then became functional, revealing the workings of our brain while we are thinking, sometimes enabling access to the contents of our thoughts, or to the thought processes of which we are unaware.

How did neuroimaging become an incomparable method both for the neurosciences and for medical practice? What of our brain, and its functioning, do we really see in these images? How can we detect the signs of illnesses, both neurological and psychiatric, read our thoughts, gain access

INTRODUCTION

to our unconscious? These are the questions we will attempt to answer here. After recalling what our brain is, exactly, and why the concept of imaging is particularly adapted to it, our travels will lead us progressively from the instrument of imaging to what it enables us to see. For neuroimaging is essentially multidisciplinary: physics, instrumentation and engineering, software and sophisticated calculation processes enable that which otherwise would remain invisible to appear before our eyes; the biological sciences contribute, as well, whether it be molecular or integrative biology, neuropsychology or the cognitive sciences, neurology, psychiatry . . . The contributions of these disciplines are most often presented in their historical context, in order to show how science is made and unmade, depending upon human passions or dramas, Nobel Prizes or frustrations. Some chapters are more technical (chapters 1 and 3), but the chapters that follow them provide a glimpse into the huge realm of applications. Neuroimaging is well on its way; it has already changed our society and raised ethical questions. How far can it go? And will it enable human beings, themselves, to understand their own brains?



ELEMENTARY PARTICLES

Before setting out on our discovery of the brain, we must first understand what makes it such a unique organ (figure 1.1). The brain weighs on average close to 1.5 kilograms (3 pounds, for males, a bit less for females) and is made up of two hemispheres, the left and the right, which play somewhat different roles. It is part of a larger whole, the encephalon, which also includes the brainstem, through which neurons travel to communicate with the spinal cord (some neurons that start at the brain and end at the base of the spinal cord are more than a meter long...). Although relatively small in size, the brainstem is crucial because it gathers together vital smaller elements that regulate our life (sleeping, breathing, heartbeats). This is no doubt why it is very protected and difficult to access, because if it is damaged, the result is often fatal. Alongside the brainstem is the cerebellum (the "little brain," which in fact has little in common with the brain). One of its noticeable roles is to smooth out and coordinate our movements; thanks to the cerebellum we are able to walk straight or play the piano.

The human brain is impressive, perhaps less in its size (the brain of an elephant, whose memory is legendary, is larger, at 4 to 5 kilograms [11 pounds]), than in its complexity: the human brain is made up of a large number of folds and bumps, called sulci and gyri, that are not as developed in other animal species, including the great apes. It is to the French surgeon, Paul Broca, that we owe the fundamental discovery that the two hemispheres are not functionally identical, and that the brain is an organ that, although apparently homogeneous, is made up of regions that have different functional speci-