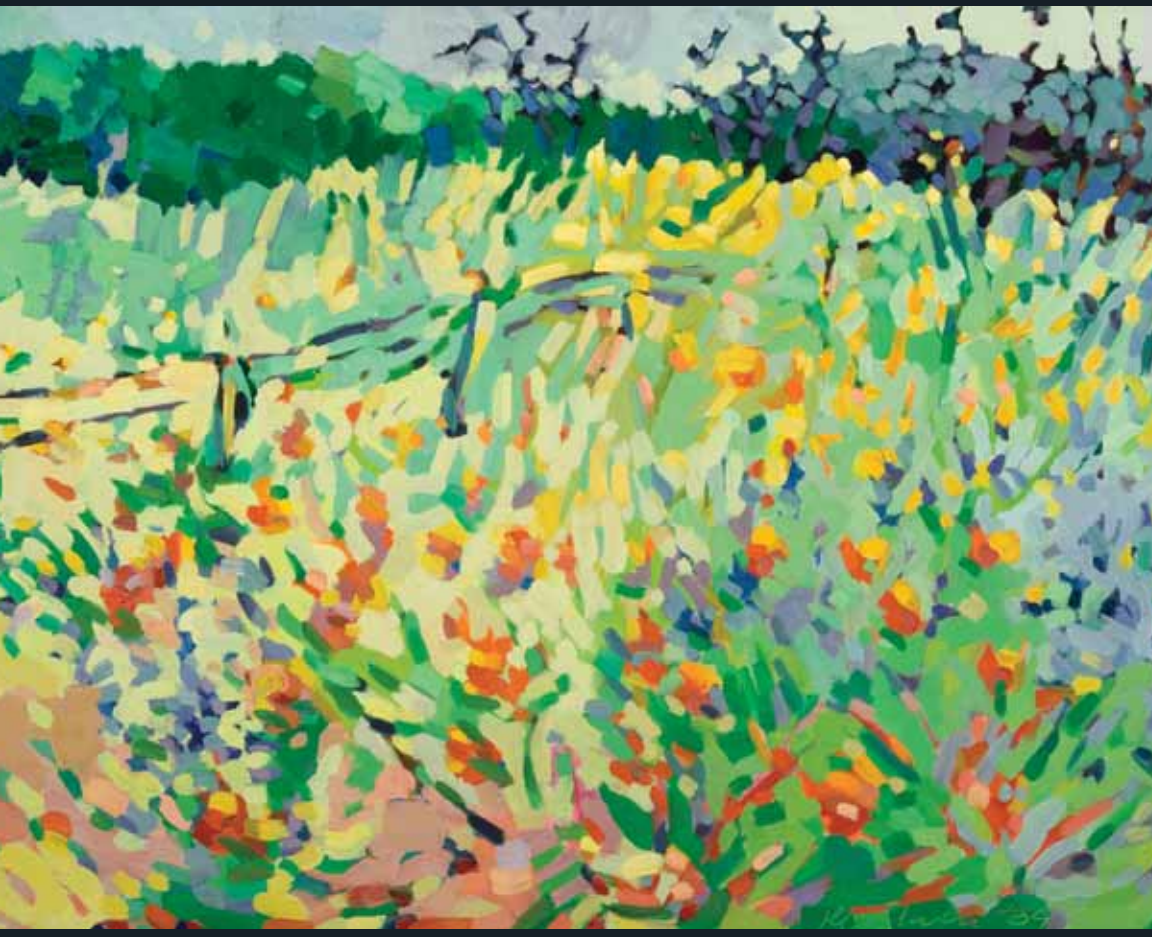
The Cognitive Neuroscience of Mind

A Tribute to Michael S. Gazzaniga



edited by Patricia A. Reuter-Lorenz, Kathleen Baynes, George R. Mangun, and Elizabeth A. Phelps

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Preface

Let's be frank. Michael S. Gazzaniga is the godfather of cognitive neuroscience. That is why, when it comes to Mike, you want to get things right. Imagine, then, the challenge we faced in trying to plan an event that was to be a tribute to Mike. It had to be right. We wanted Mike to be happy. We wanted him to feel the honor, the joy, the impact, the *love*—to understand what he means to us and to the field. But, how to get it right? Should the event be private? Should it be public? Should it happen in Italy, Tahiti, New York? It had to be scholarly but entertaining, grand but intellectual, light but deep. To quote Susan Fitzpatrick, Vice President with the James S. McDonnell Foundation, it had to be an "Extrava-Gazzaniga."

Things started to crystallize once we returned to earth and realized that, really, there's no place like home. The tribute should be part of the Cognitive Neuroscience Society—the society that Mike founded. It should be in San Francisco, the home of the society's inaugural meeting. And of course, Tara Miller, event planner for the society, would be indispensable.

Like all lived days, the day of the tribute came and went: April 12, 2008. Those of you who were lucky enough to join us that day know how truly delightful the day turned out to be. Every talk was a gift to Mike, an expression of appreciation and a celebration of his influence on our universe of ideas. Mike beamed with joy, and with each presentation the warm glow of relief and pleasure flowed more freely from our hearts. The day ranks as one of the most rewarding in our professional lives. And this is to say nothing of the evening banquet that followed–which, naturally, Mike organized because … who else for a party?!!

This book is intended to capture some of the words and sentiments expressed at that tribute, along with contributions from several other scientists who are close to Mike. It is only a fraction of all that could be expressed to honor Mike, but we offer it as a lasting token of our gratitude, an attempt to reciprocate, to say thank you.

In this collection you will read about a range of topics organized under four headings each one bearing the name of one of Mike's many books. We left it up to the authors to decide on their chapter's style, and the relative proportion of "memoir" versus scientific story. Part I, "The Bisected Brain," marks the start of Mike's career and includes contributions with "hemispheric" themes from colleagues and students spanning Gazzaniga's years at Cal Tech (Giovanni Berlucchi, Mitchell Glickstein, Steven Hillyard), Cornell Medical Center (Steve Kosslyn, Kathy Baynes), and Dartmouth (Margaret Funnell). Part II, "The Integrated Mind," begins with a story about the discovery of the integrated mind, written by Joe LeDoux, Mike's student from the State University of New York at Stony Brook. The theme of integration by domination is continued by the other two contributions in this section, by Alan Kingstone, who worked with Mike at Dartmouth, and Michael Miller, originally at Dartmouth and as of 2006 a colleague of Mike's at the University of California, Santa Barbara.

The themes touched on in "The Social Brain" chapters are wide-ranging, from collegial relations originating in Mike's Cornell years (Mike Posner, William Hirst, Elisabetta Ladavas) and at Dartmouth (Todd Heatherton). The substance of these chapters ranges from genes to neurons to social conversations and networks—vertical and horizontal explorations of sociality embracing the breadth of Mike's influence. The final section, "Mind Matters," again spans several levels of observations and reflections on the study of mind, from evolutionary biology (Leo Chalupa) to the multi-methodological approaches of cognitive neuroscience (Mark D'Esposito) to the bioethical (Steve Pinker).

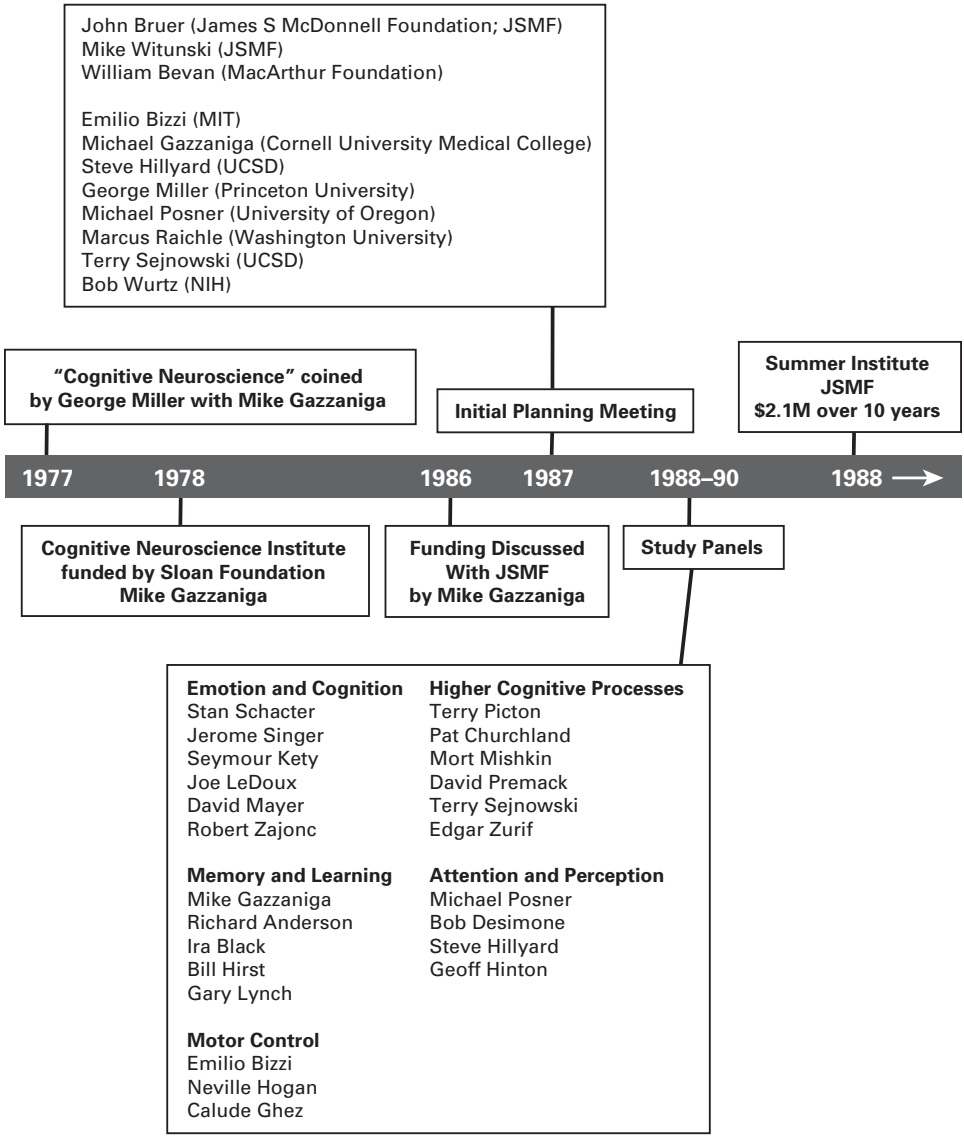
A few special features of the book deserve mention. The painting that is rendered on the cover was created especially for this book, for Mike, by his artist friend Henry Isaac, whose style many readers may recognize from covers of the *Journal of Cognitive Neuroscience*—and from Mike's living room. The jacket also includes a portrait that does an exquisite job of capturing a joyful Mike. We thank Charlotte Smylie, Mike's wife,

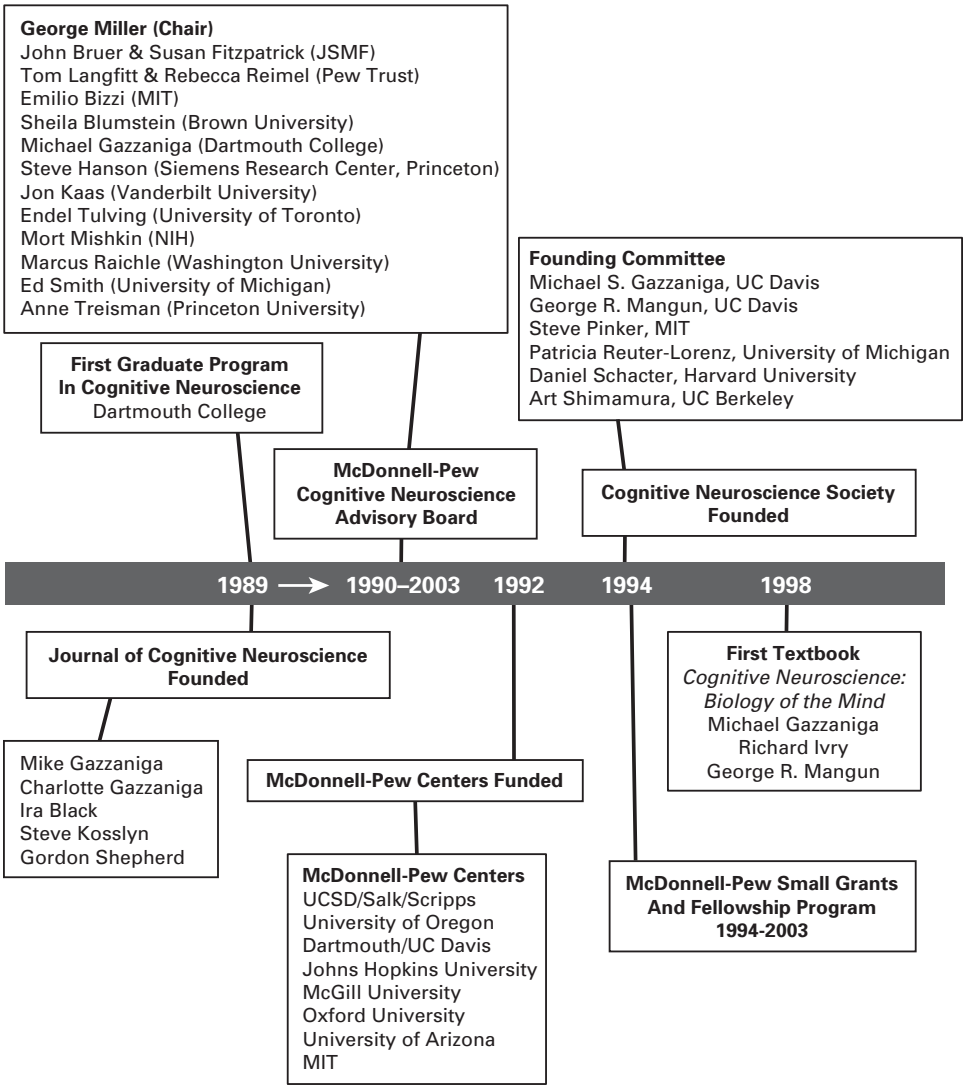
for her help in choosing these works of art, and for her encouragement and guidance throughout the planning of the tribute event. In the front matter is a historical timeline showing major milestones in the establishment of the field of cognitive neuroscience, constructed by Marc Raichle, with input from a number of quarters to verify dates and other facts. Marc used this slide in the marvelous lecture he delivered upon receiving the George A. Miller Prize in Cognitive Neuroscience. He has generously shared it with us in recognition of Mike's abiding influence and guidance of the field since its inception. Each section of this volume is introduced with a poem written by Marta Kutas, a friend and colleague of Mike's since his Cornell years. Finally, the support of Mary Mohrbach, administrative assistant at the University of Michigan, was invaluable to the preparation of this book.

To all of our contributors, we thank you for your candidness, your timeliness, your generosity and enthusiasm for this celebration. Your art and words make up this tribute, and far exceed what we could have dreamed to honor Mike. For those of you who were at the tribute event, we hope this volume brings back good memories and creates new ones. For those of you who know Mike, we hope the events and influence commemorated by this volume speak to you. And to all readers we hope this collection teaches you new things and invites you to glimpse the extraordinary Gazzaniga, a rare scientist, so worthy of the admiration, praise, gratitude, and love expressed in each one of these chapters.

Did we get it right, Mike?

Cognitive Neuroscience Milestones

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Michael S. Gazzaniga received his bachelor's degree from Dartmouth College in 1961 and his Ph.D. from the California Institute of Technology in 1964. Over several decades, Dr. Gazzaniga's research has focused on the study of individuals who have undergone split-brain surgery for treatment of intractable epilepsy, a program of research that began as a graduate student in the laboratory of Dr. Roger Sperry and went on to radically transform the field of psychology. Dr. Gazzaniga has authored and edited more than twenty-five books as well as hundreds of publications and chapters on hemispheric organization and other topics in cognitive neuroscience. Among his many honors, Dr. Gazzaniga served as president of the Association for Psychological Science and was elected to the Institute of Medicine of the National Academies in 2005. Dr. Gazzaniga's vision, ingenuity, and commitment were vital to founding the field of cognitive neuroscience. Among his many foundational ventures, Dr. Gazzaniga created the first graduate program in the field and was integral to establishing and maintaining the Summer Institute in Cognitive Neuroscience, which he has hosted for over twenty years. He is founder of the *Journal of Cognitive Neuroscience*, long serving as its editor-in-chief, as well as the four-volume series *The Cognitive Neurosciences*, published by MIT Press. Along with several of his students, he launched the Cognitive Neuroscience Society in 1993. He is currently a Professor of Psychology and the first Director for the SAGE Center for the Study of Mind at the University of California Santa Barbara.

I

The Bisected Brain

Bisected Brain
Two brains in one skull or so it seems.
But are there really two (separate & equal) conscious streams?
Or some unfathomable nonlinear sum
That makes each cc-connected human brain a uniquely mindful one?

1

Corpus Callosum: Mike Gazzaniga, the Cal Tech Lab, and Subsequent Research on the Corpus Callosum

Mitchell Glickstein and Giovanni Berlucchi

In this chapter we are delighted to honor our old friend Mike Gazzaniga. He pioneered split-brain research on humans, along with Roger Sperry and Joe Bogen, and has constantly and brilliantly contributed to this research up to this day. Their joint work on split-brain patients unequivocally demonstrated the major role played by the corpus callosum in the interhemispheric transfer of information and in the unification of the independent cognitive domains of the two cerebral hemispheres.

Here we attempt to do two things. First we want to convey some of the early history of those discoveries. We hope that we can give a feeling for the science that was being done at Cal Tech, the California Institute of Technology, when Mike came there. Both of us made friends with Mike when we were all much younger. We also want to acknowledge that science moves on. After our personal recollections of early days at Cal Tech, we go on to discuss some of the progress since those early experiments.

Remembrance by Mitch Glickstein

Mike Gazzaniga was an undergraduate at Dartmouth College in Hanover, New Hampshire. Mike's father was a surgeon in the Los Angeles area, and Mike, like his older brother and sister, originally planned to follow the family career and go on to medical school when he graduated from Dartmouth. The plan was spoiled by a summer job he had at Cal Tech between his junior and senior years at Dartmouth. I was a new post-doc with Roger Sperry at Cal Tech, and I met Mike that summer. A bright and enthusiastic kid, he was easy to like; we soon became friends, and we remain friends some fifty years later.

Describing the lab at Cal Tech might help to explain Mike's change of direction. Cal Tech was among the great scientific institutions of the world. Great science and great scientists were all around us. Richard Feynman taught physics; Linus Pauling taught chemistry. These were not remote figures; they were people you saw in the hallways; you attended their lectures. The Biology Department could hold its head up proudly in this august company. The department had been founded in 1928, and it maintained itself as a preeminent world center for the study of genetics. When I arrived at Cal Tech there were twelve professors of biology—three in neuroscience and nine in genetics. Five of the biology professors would go on to win the Nobel Prize in Physiology or Medicine.

In 1958, soon after I arrived to take up a position as a post-doc in Sperry's lab, came the announcement of the first of several Nobel Prizes that would be awarded to Cal Tech professors; George Beadle, the chairman of the Biology Department, receive the prize with Edward Tatum. When I first came to Cal Tech, Beadle was about to start a visiting professorship at Oxford. The first social event I attended at Cal Tech was a luau, held as a sendoff for Beadle. I was told that in a proper Hawaiian luau it is customary to bury a pig and keep the coals above it hot for three days or so to slowly cook the pig. Busy biologists, they had no time for maintaining a fire for three days, so they autoclaved the pig before burying it for three hours. Not a great success. In a later party that I heard about but did not attend, some caviar had been centrifuged prior to the party so that the individual cell constituents could be sampled in isolation. I was told that they all tasted salty.

There was a joy in science. People were happy not just with their own achievements but also with the achievements of their colleagues. One thing that united the Biology Department was the "Introductory Biology" course. The biology faculty recognized that Cal Tech had among its students the brightest and most promising young people in science in the country. For some of these undergraduates science meant physics; what they wanted to do was construct a unified field theory. Some merely wanted to get rich by becoming engineers and inventing some new device that would make them millionaires. The message of "Introductory Biology" was "Biology is just as great and challenging a science as physics and chemistry." Some of the undergraduates were convinced, and went on to become outstanding biologists. The course was organized

by James Bonner, a brilliant lecturer who communicated not just the substance but also the fun of biology. The final exam almost always contained a question that was a variant of "What is life?" The expected answer had to refer to self-replicating organisms. The year I taught in the course the What is life?" question was phrased as follows: "You are walking on an alien planet and encounter an object. How can you tell whether it is alive or not?" One student answer began, "I would ask it if it was alive. If the answer was 'no' I would remain suspicious." The student then went on to the obligatory discussion of self-replicating organisms. All of the lecturers in the course were the full professors of biology (the department at the time had only full professors plus post-docs and graduate students). Sperry disliked lecturing, so he asked me to give our lab's contribution to the course in the two years I was there—an exhilarating and challenging audience. Addicted to slides, I showed a lot of them in my first lecture. In my next lecture, the students had inverted the optics of the slide projector, so that the image appeared on the screen the size of a postage stamp.

Sperry, before going to the University of Chicago as assistant professor of anatomy, had been a post-doctoral student for several years with Karl Spencer Lashley at the Yerkes Laboratory for Primate Biology in Orange Park, Florida. Lashley devoted almost all of his scientific efforts to understanding brain mechanisms in learning. In most of his work he studied the effects of brain lesions on the acquisition or retention of a learned response. No single lesion would abolish a rat's recall of a maze habit or prevent it from learning a maze. Rather, there was degradation in performance or acquisition related to the amount of association cortex removed. Lashley characterized these results with the rather vague designation of their reflecting a principle of "mass action" (Lashley, 1929).

Lashley had also tried other approaches in an attempt to localize a memory trace in the brain. In 1924 he devised a mask that would allow vision to only one eye of a rat. He found that if a rat was trained on a visual discrimination task with one eye open, it knew the correct solution when tested with the other eye open (Lashley, 1924). Lashley suggested to a few of his post-doctoral students that they might see whether a memory trace could be isolated within one hemisphere by cutting the crossing fibers of the optic chiasm and the corpus callosum. Some tried

cutting one or the other structure, but always there was good interhemispheric transfer. When he moved to Chicago, Sperry suggested the experiment to Ronald Myers. Myers cut both the optic chiasm and the corpus callosum of cats. He found that the combined operation blocked the normally strong transfer of visual discrimination learning between the hemispheres (Myers, 1956; see Glickstein & Berlucchi, 2008).

Sperry came to Cal Tech in 1954 as Hixon Professor of Psychobiology, and Myers came with him. By the time I arrived, in 1958, Myers had gone, but the lab was in full swing. I came to work with Sperry after finishing a Ph.D. in psychology at the University of Chicago. Sperry had been one of my teachers in my first year in that program. The usual learning theory that I was taught as a graduate student seemed trivial. Sperry's approach was fascinating. I knew that I understood very little, but I was convinced by Sperry and some of my other teachers that if a problem in psychology could be solved, to do so would require understanding the brain mechanism involved.

The people in Sperry's Cal Tech lab worked on two problems. As a graduate student Sperry had done ground-breaking and iconoclastic studies of nerve regeneration. With a few simple and deft experiments he challenged a widespread but ill-founded optimism about the nature of functional recovery following neuronal damage. Both of Sperry's scientific interests were being actively pursued by his people when I got to Cal Tech in 1958. Chuck Hamilton and Colwyn Trevarthen were studying split-brain monkeys. Harbans Arora was carrying on with nerve regeneration experiments. Sperry could sometimes seem to fall into remarkable scientific luck. In the year I came, the histology technician, Octavia Chin, apologized to Professor Sperry because she "could not get the regenerating fibers to stain the same color as the normal fibers." At the same time Domenica Attardi (called Nica) came to ask for a part-time job in the lab. She was married to Giuseppe Attardi, who had come to Cal Tech to work with Renato Dulbecco. Their eight-year-old son, Luigi ("My name is Louie") was in school, so Nica had a few hours in the middle of the day available for working in the lab. Using Octavia Chin's stain for regenerating fibers Nica did a brilliant study in the Sperry tradition. She made regional ablations in the retina of a fish and cut the optic nerve. The optic nerve in fishes regenerates in a few days. Using the staining technique for regenerating nerves she could follow the regen-

erating optic nerve fibers from the surviving retina along the nerve's course to the optic tectum. She showed that the nerve makes three choices: after crossing in the chiasm and reaching the tectum, it must (1) go medial or lateral along the edge of the tectum; (2) turn onto the tectum or continue alongside; (3) dip into the substance of tectum to synapse. Attardi and Sperry's description predated a genetic analysis that confirmed their general conclusions (Attardi & Sperry, 1963).

When I arrived at Sperry's lab he was ill with a bout of tuberculosis and was in the hospital. His wife, Norma, ferried information and suggestions from the hospital to the lab. She kept talking about "split brains" and I had little idea of what she was talking about. I was saved by two things; a respite before I began an experiment, and a splendid review of the structure and function of the corpus callosum by Frederic Bremer (Bremer, Brihaye, & André-Balisaux, 1956). It was about fifty pages long, and in French—and I knew no French. Armed with a dictionary I translated the paper, writing it all out in longhand. At the end of three weeks I knew much more than when I arrived about the corpus callosum, and I could now read scientific French.

Mike Gazzaniga arrived in the summer of 1960. A bright and likable kid, he took to the work with great enthusiasm. As I recall, his first plan for an experiment was typically ambitious: he hoped to develop a test for monkeys like the one Wada and Rasmussen (1960) had developed for testing hemispheric dominance in humans: injecting a local anesthetic through one carotid artery. A great idea, but technically very demanding. Wonderful if you could switch a hemisphere on and off.

When I and, later, Mike arrived at Cal Tech, people were working with other neuroscience professors. Nico Spinelli had come from Milan and was working on spinal reflexes with Anthonie Van Harreveld. Joe Bogen was on leave from a neurosurgical residency, also working with Van Harreveld doing research on an appalling drug called bulbocapnine whose effect seemed to mimic catatonic schizophrenia. Both looked over enviously at the Sperry callosum group. When Joe Bogen went back to his neurosurgery residency he reviewed the early studies of Van Wagenen, which had attempted to control epilepsy by cutting the corpus callosum. Sensing that the operation might assist in limiting the spread of epilepsy, he and his colleague began a series of operations in which they cut the callosum in epileptic patients. Mike fitted in perfectly with the need to

have someone who was not only skilled and motivated but also, above all, was a person who could communicate with these patients in a most human way. It was Mike's outgoing and warm personality as well as his intelligence and skill that led to the successful studies he carried out with those patients.

I moved on from Cal Tech, first to Stanford for a year and then to the University of Washington in Seattle. Meanwhile, Mike returned to Dartmouth College for his senior year. He wrote to me from Dartmouth that he was not going to apply to medical school but instead planned to return to Cal Tech as a graduate student, working for a Ph.D. degree with Roger Sperry. (Mike told me that his father was less than pleased with the plan, suggesting that Mike get a medical degree as planned, and then hire a Ph.D. if he felt the need.)

It might be appropriate to write briefly about the personality of Roger Sperry, the way it affected the research in the lab at Cal Tech, and the relationship with his ex-students. My own experience with Sperry when I was at Cal Tech was of a productive and happy interaction. Sperry would suggest a research direction to one or another of us, and then leave us to get on with it. Always he had good instincts, a gut feeling for what was a scientifically promising direction. By nature a somewhat introverted man, Sperry got on with us all on a personal level. I used to go fishing in the sea from Long Beach with him. When Mike came to the lab, he seemed to be the only one who could actually make Roger smile. Despite his easy relationship with Mike and his other students within the lab at Cal Tech, Sperry seemed to resent anyone who claimed credit for the work after they had left his lab. At times this resentment could border on the vitriolic; even after he had received the Nobel Prize and was universally recognized as a major contributor to the understanding of brain and behavior, he hated to share credit for the discoveries of the group.

Remembrance by Giovanni Berlucchi

The beginning of my friendship with Mike does not date back as far as that of Mitch Glickstein, but still has lasted for the respectable duration of forty-five years and—my good fortune—continues still. When I joined Sperry's group at Cal Tech as a postgraduate student from Pisa in 1964,

Mike was deeply engaged in the work that was to produce the foundation of split brain research in humans. He was also doing some experiments on monkeys, and I think that it was at that time that he developed the idea of cross-cuing, some sort of external commissure that could allow the two hemispheres to communicate by means of behavior rather than through anatomical connections. Most of the people who were in the Division of Psychobiology at Cal Tech when Mitch Glickstein was there had already left when I arrived, but Mike and also Chuck Hamilton were still there, and both of them made it easy for me to integrate into the activity of the group, which included Harbans Arora, Emerson Hibbard, Richard Mark, Evelyn Lee Teng, Arthur Cherkin, and an undergraduate student named Murray Sherman, whom I was to meet again a few years later at the University of Pennsylvania in the Department of Anatomy chaired by Jim Sprague. The neurosurgeon Joe Bogen who had been instrumental in reviving the callosotomy treatment of epilepsy frequently visited the lab and told me amusing and instructive stories about his hemispherectomized cats. Sometime during my stay at Cal Tech I first met Mitch Glickstein when he came down from Seattle to give a seminar on, I think, reaction time to cortical stimulation, during which he exchanged a few dialectic jabs with Sperry. We met again at a corpus callosum meeting in Bratislava in 1969 and have been friends ever since.

At Cal Tech my lab was contiguous with those of two Dutchmen who would become lifelong friends of mine: Han Collewjin, who at that time was working with Anthonie Van Harreveld, and Ries van Hof, who at that time was working with Cornelius Wiersma. Van Harreveld and Wiersma had emigrated from Holland to the United States before World War II and had become distinguished professors at Cal Tech. Chuck Hamilton, whose kindness toward me I will never forget, impressed me greatly with his scholarship and experimental prowess, and I would never have predicted that his talents would be miserably wasted years later in a Texan university. Mike Gazzaniga was a joy to be with for his humor, joviality, and wide-ranging interests. I am sorry that I did not write down some of the million jokes that he used to crack on our way to and from the Cal Tech cafeteria, where one could encounter legendary figures of science such as Richard Feynman, Max Delbrück, Murray Gell Mann, James Bonner, Ray Owen, Robert Sinsheimer, Giuseppe Attardi,

and others. I am sure that Mike could have written a script for a Mel Brooks movie. Although Mike's parents were of Italian descent, he is a Californian to the bone. One of his jokes was that in Italian his surname means "big or small penis, depending on the occasion," but I can assure you that this is totally false; Gazzaniga is a rather common surname in northern Italy and probably comes from a small Lombard town with that name. Sperry was always nice and helpful to me, though a bit awe-inspiring for his obvious genius and dry Socratic attitude. At the beginning of our stay in Pasadena he entrusted my wife and my three-year-old son to the care of Inuccia Dulbecco, advising us not to mention her former husband, Renato, the future Nobel Prize winner, because he had just divorced her and moved to La Jolla with a new wife. To me Sperry looked more like an austere European professor than an easygoing American one. (I heard that when one of his former students, after becoming a full professor at a Californian university, asked him whether, as a colleague, she could call him Roger, he replied, "Gee, I don't know, I never called Doctor Lashley Karl"). I was grieved by the split (no pun intended) between Sperry and Mike and, like Mitch Glickstein, I believe that the personality clash was totally unnecessary and could have been avoided.

After I left Cal Tech Mike and I collaborated in Pisa and elsewhere, and in some of his wonderfully humorous books he has told the story much better than I could do. Mitch Glickstein says that Mike was the only one who could make Sperry smile. I don't laugh easily, but Mike has always been able to give me a good laugh and to keep me in good spirits. Knowing that he likes the big picture in science and is hardly interested by experimental details, we are somewhat afraid that what follows may be a bit of a bore to him. He is of course welcome to skip it if he wants to. Yet we like to offer to him this limited review of recent anatomical and physiological data to give a hint of how extensive, productive, and unending is the influence exerted on neuroscience by the split-brain research that he initiated with Sperry and Bogen so many years ago.

Recent Research on the Corpus Callosum

Gazzaniga should be credited with bringing our contemporary understanding of cerebral asymmetry and hemispheric interaction to bear on

such complex philosophical problems as the enabling of the human condition by the corpus callosum, the perception of causality, and the recognition of the self (Gazzaniga, 2000, 2005). While these topics at the boundary between neuroscience and philosophy are fascinating in their own right and likely to open entirely novel views of the perennial mind-brain problem, on a humbler level some "bottom-up" fundamental questions regarding the anatomo-functional organization of the corpus callosum and other systems of hemispheric interaction in cognition and behavioral control are still outstanding. These questions are now been addressed with the aid of considerable technological advances in the structural and functional analysis of the living human brain, to which Mike has also contributed in a significant way. Knowledge of interhemispheric communication has also been promoted by technical, empirical, and theoretical progress at the molecular and cellular levels in experimental animals. In the next section we deal with some old issues that as a result of such advances in the knowledge of interhemispheric communication in the human and animal brain can now be considered from relatively novel perspectives.

The Callosal Projection Neurons

In adult animals, neurons projecting to the corpus callosum appear to form a rather uniform population, either morphologically or functionally, regardless of their laminar position in the cortex (Ramos, Tam, & Brumberg, 2008). Most of them are pyramidal neurons, though with varying phenotypes, since the proportion of nonpyramidal neurons is no greater than 5 percent (Martinez-Garcia, Gonzalez-Hernandez, & Martinez-Millan, 1994). Although all pyramidal cortical neurons are supposed to be excitatory to their targets, in fact, 10 to 15 percent of nonpyramidal cortical neurons are inhibitory and GABAergic (aspiny nonpyramidal neurons). Yet in adult animals very few GABAergic, presumably inhibitory nonpyramidal neurons project to the corpus callosum. Immunochemical assessments of percentages relative to the total population of callosal fibers vary from 3 to 5 percent (Gonchar, Johnson, & Weinberg, 1995) to 0.7 percent in rats and 0.8 percent in cats (Fabri & Manzoni, 2004). A transient contingent of inhibitory GABAergic callosal fibers (up to 21 to 57 percent) has been reported in fetal or neonatal rats, where they may have some as yet unknown role in the formation

of neuronal networks (Kimura & Baughman, 1997). However, this contingent is destined to be eliminated during postnatal development, probably by the process of corpus callosum pruning discovered by Innocenti (1986). In mice the determination of callosal neurons has been attributed to their expression of a DNA binding protein (Satb2) without which their axons fail to extend into the corpus callosum and instead are misrouted to subcortical centers (Alcamo et al., 2008). The potential importance of the lack of this protein for human callosal agenesis has yet to be assessed.

In general, basic anatomical knowledge about the neuronal organization of the human corpus callosum is less extensive than of experimental animals, and is largely limited to the fiber composition (Aboitiz, Scheibel, Fisher, & Zaidel, 1992), the much protracted myelination process, which lasts well into adulthood (Pujol, Vendrell, Junque, Marti-Vilalta, & Capdevila, 1993), and the pattern of fiber degeneration in the cortex or the callosum itself following localized cortical lesions (De Lacoste, Kirkpatrick, & Ross, 1985; Clarke & Miklossy, 1990). Much less is known about the neurons in the human cortex which give rise to callosal projections, but indirect evidence indicates that in humans as in animals callosal fibers mostly belong to pyramidal neurons. A peristriate strip in the occipital cortex of humans and macaques alike is characterized by clusters of large pyramidal cells in layer III that presumably project homotopically to the opposite cortex via the corpus callosum (Braak & Braak, 1985). This is suggested by the finding that in macaques a callosal section or a contralateral cortical lesion causes an apparent disappearance of such neurons, most probably because they either shrink or die from retrograde degeneration (Glickstein & Whitteridge, 1976). In agreement with this, two human brains with an agenetic lack of the corpus callosum were found to display a virtually total lack of the distinctive large pyramidal cells in layer III of peristriate cortex (Shoumura, Ando, & Kato, 1975). Different phenotypes of neurons projecting to the corpus callosum were found in the cingulate cortex of human fetuses, but all these phenotypes could be characterized as pyramidal neurons (deAzevedo, Hedin-Pereira, & Lent, 1997).

Recently Jacobs et al. (2003) analyzed pyramidal neurons in the supragranular layers of three cortical areas (Brodmann areas 4, 10, and 44) of two patients who had died several years after a surgical calloso-

tomy. Especially in area 44 of the left hemisphere (Broca's area) they found a large number of pyramidal neurons with abnormally long basilar dendrites (taproot dendrites) and attributed this abnormality to the epileptic condition or, more likely, to the neurons' reaction to the removal of their callosal input. A third equally likely possibility is that such abnormal dendrites were developed by callosal projection neurons which did not undergo retrograde degeneration following callosotomy because they retained axon collaterals within the ipsilateral hemisphere. In sum, the assumption seems justified that (excitatory) pyramidal cortical neurons constitute the main if not exclusive source of callosal projections in humans as much as in experimental animals.

Cortical Excitation and Inhibition by the Corpus Callosum

Considerations of the potential excitatory and inhibitory action of the corpus callosum are in order when behavioral data from experiments on interhemispheric interactions are interpreted to suggest that one hemisphere may massively inhibit or facilitate the other hemisphere, or that given cortical areas on one side of the brain may exert similar uniform but more restricted effects, either facilitatory or inhibitory, on the corresponding contralateral cortical areas. The terms "facilitation" and 'inhibition" are used in this connection in a loose sense, simply to mean that a particular behavioral performance, presumably controlled by one hemisphere, appears to be respectively worsened or improved when that hemisphere is freed from interhemispheric influences (Bloom & Hynd, 2005). Although at a descriptive level the terms "facilitation" and "inhibition" are convenient labels for these *behavioral* effects, they should not be taken to refer to the *physiological* actions of callosal fibers on their neuronal targets. Electrophysiological evidence in experimental animals indicates that barring some dubious exceptions, all callosal fibers are excitatory to their direct target neurons in the cortex (Matsunami & Hamada, 1984). Thus callosal fibers can directly (monosynaptically) activate corticofugal pyramidal neurons, mostly through axo-spinous synaptic contacts, as well as local nonpyramidal neurons, including GABAergic neurons, which in turn can inhibit corticofugal pyramidal neurons (Carr & Sesack, 1998; Karayannis, Huerta-Ocampo, & Capogna, 2007). Callosal monosynaptic excitation works by means of glutamate receptors, including NMDA receptors possibly connected with

synaptic enhancement (Cissé, Crochet, Timofeev, & Steriade, 2004), and the disynaptic inhibition from callosal inputs uses both GABA A and GABA B receptors (Kawaguchi, 1992; Chowdhury, Kawashima, Konishi, Niwa, & Matsunami, 1996; Chowdhury & Matsunami, 2002). Because of its multiple neuronal targets, the physiological action of the callosal projection to a given cortical area is an obligatory mix of a monosynaptic and di- or polysynaptic excitation and a di- or polysynaptic inhibition such that the callosal input can hardly be attributed the function of upregulating or downregulating the total output of a given cortical area. Indeed, Asanuma and Okuda (1962) found that in discrete cortical regions such as the motor cortex the pattern of activity set up by the callosal input is spatially organized in a concentric fashion, with focal excitation surrounded by inhibition.

A similar spatial organization of excitation and inhibition generated by callosal inputs has recently been found in the auditory cortex of bats, which contains neurons tuned to the combination of the emitted biosonar pulse and its echo with a specific echo delay. The activity of these neurons is modulated by the corpus callosum according to a pattern of bilateral cortical interaction consisting of a focused facilitation mixed with a widespread lateral inhibition, and balancing the delay maps of the two hemispheres in the analysis of orientating echo sounds (Tang, Xiao, & Suga, 2007).

With regard to physiological excitation and inhibition by the corpus callosum in humans, some information has been provided by studies using the transcranial magnetic stimulation technique for activating the cortex in a noninvasive manner. Appropriate magnetic stimulation of the motor cortex of one side produces electromyographic responses in the intrinsic muscles of the contralateral hand; callosal inhibition or excitation of motor cortex can be inferred from changes in the threshold for obtaining such responses as a result of conditioning stimuli applied to the motor cortex of the other side. Although some of these studies have reported that inhibition is the only consistent effect of such transcallosal stimulation (for example, Ferbert et al., 1992), others have found that inhibition is systematically preceded by excitation (Ugawa, Hanajima, & Kanazawa, 1993; Salerno & Georgesco, 1996), in agreement with the evidemce from animal experiments that callosal excitation can be monosynaptic whereas callosal inhibition always involves at least

two synapses. However, the interpretation of these results is made difficult by the possible antidromic (and therefore nonphysiologic) activation of callosal neurons.

Functional magnetic resonance imaging (fMRI) of the brain also seems at present inadequate for attempting to relate callosal effects to cortical excitation or inhibition (for one of these attempts see Putnam et al., 2008). As an active process cortical inhibition involves an expenditure of energy whose relations to local metabolism and blood flow are still at least partly unknown (Buzsáki, Kaila, & Raichle, 2007; Logothetis, 2008). A local increase in cortical blood flow can therefore result from either prevalent neuronal excitation or prevalent neuronal inhibition, whereas a decrease in blood flow may index deactivation rather than inhibition. Recent studies combining fMRI with other technologies seem to offer more plausible models of interhemispheric connectivity which eschew the interhemispheric excitation-inhibition dichotomy (Baird, Colvin, Vanhorn, Inati, & Gazzaniga, 2005; Stephan, Marshall, Penny, Friston, & Fink, 2007). Further, the concept of neuronal assemblies extending in the two hemispheres (Pulvermüller & Mohr, 1996; Knyazeva et al., 2006), which has been invoked for explaining the bihemispheric advantage effect in word reading (Mohr et al., 1994) and face recognition tasks (Mohr, Landgrebe, & Schweinberger, 2002; Schweinberger, Baird, Blümler, Kaufmann, & Mohr, 2003), is fully compatible with an involvement of both neuronal excitation and inhibition in bilateral coordination within the assemblies.

In conclusion, because of their excitatory action on different types of cortical neurons, including inhibitory interneurons, the action of the callosal fibers on the output of a given cortical area can never be purely excitatory or purely inhibitory. Although behavioral performance undoubtedly appears to benefit from hemispheric cooperation in certain tasks and from hemispheric dissociation in other tasks (see, for example, Banich & Belger, 1990), the attribution of the cooperation to physiological excitation and the dissociation to physiological inhibition of the cortex by the corpus callosum is empirically and logically unwarranted. The phrenological concept that the entirety of neurons of a cortical area, let alone of the cortex of a whole hemisphere, can be simultaneously excited or inhibited makes little sense in the light of orthodox cortical physiology.

Constructing Functional Maps in the Corpus Callosum

As early as 1922 Mingazzini had proposed an anatomo-functional subdivision of the corpus callosum in an anterior portion, portio verbalis et praxica, primarily involved in the cooperation of speech controlling centers in the two hemispheres; a middle portion, portio praxica, necessary for the effective coordination of synergic movements of the limbs of the two sides; and a posterior portion, portio sensorialis, subserving the unification of the visual and auditory fields of the two hemispheres and the transmission of perceptual information from the non-dominant hemispheres to interpretative centers restricted to the dominant hemisphere.

Modern anatomical investigations in animals have provided evidence for a topographic organization of fibers within the corpus callosum, such that the callosal projections from anterior cortical areas occupy anterior callosal sectors and vice versa for the callosal projections of posterior cortical areas. However, the topographic segregation of fibers related to different cortical areas within the corpus callosum is by no means complete (Pandya & Seltzer, 1986; Lamantia & Rakic, 1990). Until recently there was little evidence from classical anatomical methods about an orderly topographical organization of the human corpus callosum. Based on inferences from animal evidence and a degeneration study in humans (De Lacoste et al., 1985), Witelson (1989) proposed a division of the corpus callosum whereby the anterior half corresponds to the genu, which carries fibers related to prefrontal, premotor, and supplementary cortices, and the anterior mid-body, which carries fibers related to the motor cortex; whereas the posterior half corresponds to the posterior mid-body, which carries fibers related to anterior parietal cortex; the isthmus, which carries fibers related to the posterior parietal and superior temporal cortex; and the splenium, which carries fibers from inferior temporal and occipital cortices.

If callosal connections perform the same function as the cortical area to which they are related, one would expect, for instance, that the anterior callosal mid-body has to do with motor control, the posterior mid-body has to do with somesthesis, the isthmus has to do with audition, and the splenium has to do with vision. In other words, lesions affecting a specific sector of the corpus callosum should cause specific deficits of interhemispheric communication related to the function of

the cortical area connected with that sector. A particularly embarrassing result for this view of the corpus callosum as a collection of specialized functional channels organized in an orderly topographic sequence was reported several years ago by Gordon, Bogen, and Sperry (1971).

They found that two patients submitted to section of the anterior two thirds of the corpus callosum for relief of epilepsy did not present any of the many signs of interhemispheric disconnection exhibited by patients with complete callosotomies. This was true not only for vision, which was expected to be normal according to anatomy, but also for somesthesis, audition, and even (in one patient) olfaction, all served by cortical areas supposedly connected across the midline by callosal fibers lying in the sectioned parts of the callosum anterior to the splenium. Also, in the taste modality the splenium seems to be dominant for the interhemispheric exchange of gustatory information (Aglioti et al., 2001). Conversely, lesions restricted to the splenium have been shown to cause deficits outside the visual modality, such as the interplay between prosody and syntax in speech comprehension (Friederici, von Cramon, & Kotz, 2007) and left ear suppression in dichotic listening tasks (Pollmann, Maertens, von Cramon, Lepsien, & Hugdahl, 2002).

Pollmann, Maertens, and von Cramon (2004) have argued that splenial lesions may cause nonvisual and supramodal deficits by interrupting the callosal connections of the temporo-parietal junction, which is presumably important for the allocation of attention to behaviorally relevant signals. An alternative interpretation is offered by recent revolutionary findings about the anatomo-functional topography of the human corpus callosum based on the novel technique called tractography by diffusion tensor imaging (DTI). DTI tractography is based on the detection of the preferential (anisotropic) diffusion of water molecules along the main direction of parallel bundles of axons and their myelin sheaths. It allows one to measure the location, orientation, and anisotropy of particular tracts within the white matter, in particular the in vivo visualization of pathways within the corpus callosum and, when coupled with cortical imaging, with their relations with cortical areas. Callosal connections of identified cortical areas appear to occupy definitely more posterior positions within the corpus callosum than was originally thought. Thus, the callosal connections of the primary motor cortex do

not course in the anterior mid-body, as assumed by Witelson (1989) and others, but rather in the posterior mid-body and the isthmus (Zarei et al., 2006; Wahl et al., 2007). As to the posterior callosum, Dougherty, Ben-Shachar, Bammer, Brewer, and Wandell (2005), Zarei et al. (2006), and Hofer and Frahm (2006) have made it clear that occipital callosal connections occupy only the very back tip of the splenium, whereas the rest of the splenium is constituted by projections from parietal and temporal areas. As a result of these findings, Hofer and Frahm (2006) have proposed a revision of the Witelson's schema whereby the anterior half of the callosum is taken up by prefrontal, premotor, and supplementary motor connections, and all the remaining connections are crowded in the posterior half. In the revised schema, the splenium, corresponding to the posterior quarter of the callosum, is shown to contain parietal, temporal and occipital connections extensive enough to account for the occurrence of non-visual and supramodal deficits following splenial lesions. In addition to the demonstration of cortico-callosal topography, DTI tractography has the potential of assessing the structural bases of efficiency of interhemispheric connectivity and to allow correlations between such assessments and behavioral measures of interhemispheric communication such as the crossed-uncrossed difference, the redundant target effect and the ear advantage in dichotic listening (Schulte, Sullivan, Müller-Oehring, Adalsteinsson, & Pfefferbaum, 2005; Westerhausen, Woerner, et al., 2006; Westerhausen, Kreuder, et al., 2006). Further, DTI tractography can also be used to study callosal integrity in pathological conditions such as alcoholism and Alzheimer's disease and to analyze interhemispheric pathways in callosal dysgenesis. For example, in partial callosal agenesis DTI of the callosal remnant shows misrouted connections across the midline and the formation of abnormal white-matter tracts, which may interfere with normal brain functioning (Tovar-Moll, Moll, De Oliveira-Souza, Bramati, Andreiuolo, & Lent, 2007). This may perhaps explain why functional compensation is paradoxically greater in complete than in partial callosal agenesis (Aglioti, Beltramello, Tassinari, & Berlucchi, 1998).

Functional magnetic resonance imaging of the human corpus callosum can also help assign particular functions to particular callosal sectors. Surprisingly, BOLD (blood oxygen level-dependent) signals can also be detected in the white matter, and Tettamanti et al. (2002), Weber et al.

(2005) and Omura et al. (2004) have obtained evidence for activations in the splenium during interhemispheric transfer tasks. If transit of action potentials along callosal fibers proves beyond a doubt to be accompanied by a local change in blood flow, this will become a method of choice for constructing functional maps of the corpus callosum.

Epilogue

Science is a human endeavor. Here we have traced one thread of the scientific study of the corpus callosum to its roots at Cal Tech and some of the people involved, especially to Mike Gazzaniga and his contributions. Since those early days our understanding of the links between mind and brain has continued to grow.

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Interhemispheric Cooperation Following Brain Bisection

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My lifelong involvement with Mike Gazzaniga and cognitive neuroscience began during my junior year at Cal Tech, when I took a class entitled "Psychobiology," taught by Professor Roger W. Sperry. In those days (1963–1964), "psychobiology" was the term used to refer to the study of mind-brain relationships, a field that we now know and love as cognitive neuroscience. After the course ended, Dr. Sperry was kind enough to let this ill-clad and untutored undergraduate work in his psychobiology laboratory, where so many fundamental discoveries about the neural bases of cognition and consciousness were in the process of being made. This proved to be a life-transforming experience.

In the Sperry lab at the time there were two very talented graduate students, Mike Gazzaniga and Chuck Hamilton, who became my first mentors in psychobiology. Mike was working with Dr. Sperry and Dr. Joseph Bogen on neuropsychological studies of patients who had undergone cerebral commissurotomy as a treatment for intractable epilepsy, and Chuck was doing basic research on the functions of the corpus callosum in nonhuman primates. With their complementary cognitive styles, Chuck and Mike made a great team. , Even then, Mike had a fertile and restless imagination that generated grand ideas a mile a minute. Chuck, on the other hand, was more circumspect and analytical and would rein in Mike's more outlandish propositions. I was privileged to listen to their dialogs and diatribes, which formed an essential part of my early scientific education.

Chuck went on to make fundamental discoveries about the sensory and cognitive specializations of the left and right hemispheres in monkeys (Hamilton, Tieman & Farrell, 1974; Hamilton, 1977, 1983; Hamilton & Vermiere, 1988a, 1988b; Vermiere & Hamilton, 1998) and the role

of the forebrain commissures in interhemispheric integration (Hamilton & Gazzaniga, 1964; Hamilton, 1967; Hamilton, Hillyard, & Sperry, 1968; Hamilton & Lund, 1970; Hamilton & Tieman, 1973). Meanwhile, Mike forged ahead with the studies of the commissurotomy patients that have done so much to illuminate the neural substrates of the human mind. Indeed, Mike's first paper with Bogen and Sperry (1962) laid down the essential and enduring insights derived from their initial studies of the split-brain patients, namely: (1) sectioning the forebrain commissures creates two separate mental systems, one in each hemisphere, (2) the two hemispheres have different cognitive specializations, with the left hemisphere dominant for language and logic functions and the right for visual pattern perception and spatial relationships, and (3) an intact corpus callosum is required to integrate these disparate functions of the two hemispheres and produce a unified conscious mind. Here I briefly review some of the advances that Mike and his colleagues have made over forty years of exploring these phenomena.

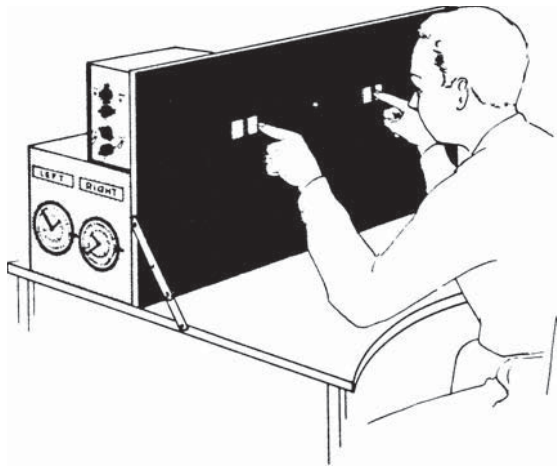
How Much Do the Surgically Separated Hemispheres Interact?

It was evident from the early studies of the commissurotomy patients (Gazzaniga, Bogen, & Sperry, 1962, 1963, 1965) that the separated hemispheres continued to cooperate in controlling everyday motor activity, which remained bilaterally coordinated. Depending on the situational demands, either the right or the left hemisphere could dominate the control of the lower motor system. There was also evidence, however, that perceptual experiences and learned associations that were lateralized to one hemisphere were not shared with the other. The key question then arose as to which sensory and cognitive functions could be carried on independently in the separated hemispheres and which functions were bilaterally coordinated or integrated, the latter perhaps reflecting the participation of intact subcortical connections. In other words, to what extent did the separated mental systems in the right and left hemispheres function independently following commissurotomy?

This question was investigated for the first time using chronometric techniques by Gazzaniga and Sperry (1966). Subjects were presented with two simultaneous discrimination tasks (red-green in one visual

field and black-white in the other) and responded by pushing the designated correct choices with the ipsilateral hands as fast as possible (figure 2.1a). In the dual-task condition the two pairs of stimuli were flashed briefly (for 150 ms) and simultaneously on translucent panels using an archaic device known as a tachistoscope. In a single task-control condition, only the red-green discrimination was presented to one visual field. As shown in figure 2.1b, the average reaction times (RTs) for making dual, simultaneous discriminations was substantially increased relative to the single-task condition in the intact control subjects, whereas no significant increase was found for the commissurotomy patients. That is, the surgically separated hemispheres could perform their respective discriminations independently, with no apparent interference from the concurrent task in the other hemisphere. This finding reinforced the view that cerebral commissurotomy creates two separate mental entities that are capable of making independent perceptual judgments and initiating goal-directed motor responses in parallel with no interference.

An even more impressive demonstration of the independent perceptual and mnemonic capabilities of the separated hemispheres came from a study carried out many years later by Jeff Holtzman in Mike's laboratory (Holtzman & Gazzaniga, 1985). On each trial a letter X was moved through four sequential positions in two 3 × 3 grids, one presented to each visual field (figure 2.2a). Following these initial presentations, after a short delay an X was moved through four positions in only one of the visual fields, and the subject's task was to report whether the second spatial pattern was identical to or different from the initial pattern presented in the same visual field. It was found that neurologically normal subjects were highly accurate (about 90 percent correct) at making this matching judgment when the initial patterns were identical in the two visual fields, whereas the split-brain patient J.W. was somewhat less accurate, about 75 percent (figure 2.2b). When the initial patterns were different in the two visual fields, however, the performance of the intact subjects fell abruptly to chance (about 50 percent), whereas J.W. maintained about the same level of accuracy, 75 percent, as with identical patterns. These results show that intact subjects do well when the overall information load is low (identical patterns in the two fields), but the normally unified hemispheres have limitations in encoding the increased



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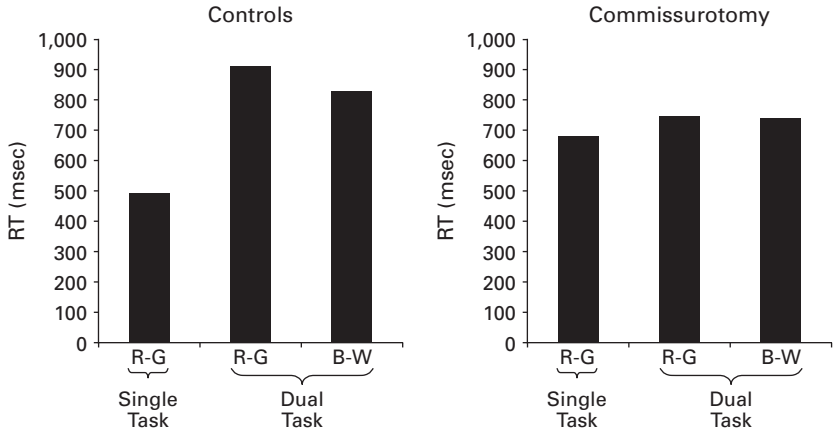

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Figure 2.1
(a) Testing apparatus in the study by Gazzaniga and Sperry (1966). Two-choice discriminations were performed simultaneously in the left and right visual fields, with the ipsilateral hand responding to the correct choice. Central fixation was maintained during testing. (b) Mean reaction times (RTs) for performing the single discrimination (control) task (R-G = red or green) and the simultaneous dual discrimination in intact control subjects (N = 6) and commissurotomy patients (N = 4). Increased RT for dual- versus single-task performance was significant in control subjects but not in the patients.

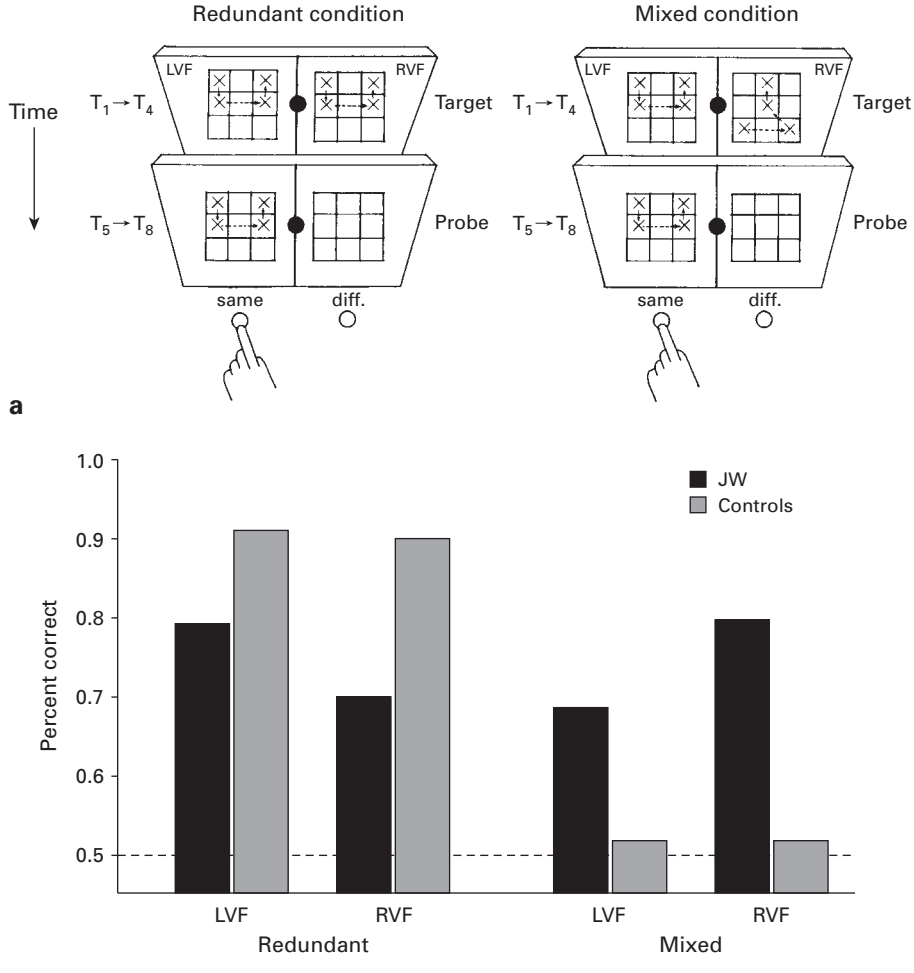


Figure 2.2
(a) Experimental setup in the study by Holtzman & Gazzaniga (1985). During time periods T1 to T4 the target X moves through four sequential positions in both visual fields simultaneously. During subsequent periods T5 to T8 the probe X moves through four positions in one visual field only, and the subject judges whether the probe sequence matches the initial target sequence. (b) Probability of correct matching for commissurotomy patient J.W. and for a group of intact control subjects. Note that control performance accuracy falls precipitously when the patterns in the two visual fields are different ("mixed" condition), whereas J.W. does equally well in the mixed and redundant conditions.

information load when the patterns differed in the two fields. In contrast, the separated hemispheres of the patient J.W. each encoded the viewed pattern efficiently regardless of whether the opposite pattern was the same or different. These results showed that the surgically separated hemispheres each had independent perceptual encoding and short-term memory storage functions, such that the total amount of information that could be remembered was substantially greater than in the normal unified brain.

A closely related question investigated by Holtzman, Volpe, & Gazzaniga (1984) was whether the separated hemispheres had the ability to direct attention independently to different regions of their respective visual fields. This was tested in variations of the Posner cued spatial orienting paradigm, like the one shown in figure 2.3. On each trial an arrow cue was presented to the left or right of a central fixation point, and the direction of the arrow indicated whether a subsequent target number was more likely to appear in the left or right visual field. The conditions to be compared were when the target was presented to the same visual field (hemisphere) as the cue (the "within" condition) or to the opposite visual field (the "between" condition). It was found (figure 2.3b) that reaction times for judging the target number as odd or even were speeded up when the target occurred in the visual field cued by the arrow (valid trials). Most important, this RT facilitation was the same whether the target was seen by the cued hemisphere or by the uncued hemisphere. It thus appeared that the unilateral cue information facilitated processing at the attended location in both hemispheres. Evidently, even in the absence of the forebrain commissures the two hemispheres do not act independently in the spatial orienting of attention. Instead, these findings provide evidence for a unitary, bilateral attentional orienting system, presumably coordinated through subcortical structures or pathways.

A strikingly different result was obtained by Mike and his San Diego collaborators, however, in a task that involved the deployment of spatial attention during visual search (Luck , Hillyard, Mangun & Gazzaniga 1989; Luck, Hillyard, Mangun, & Gazzaniga, 1994). In this conjunction search task, arrays of two, four, or eight items were presented either unilaterally (all in the left or right visual field) or bilaterally (half in each visual field; figure 2.4a). On each trial the subject searched for a "red-

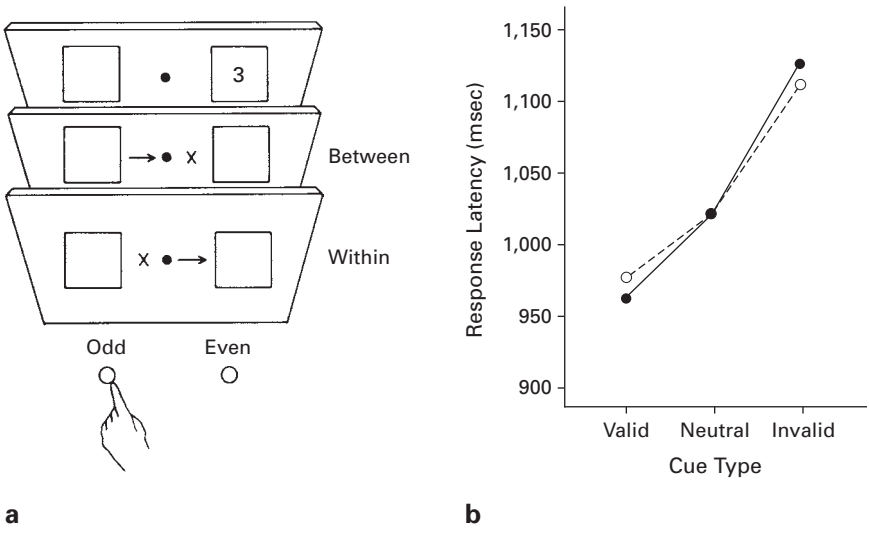
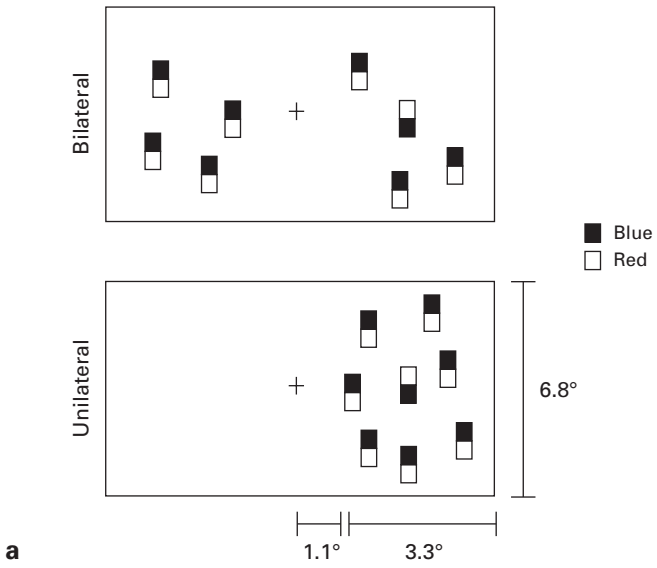


Figure 2.3
(a) Posner cuing task used by Holtzman, Volpe, and Gazzaniga (1984). The attention-directing arrow cue could be presented either in the same visual field as the subsequent target ("within" condition) or to the opposite field ("between" condition). (b) Mean reaction times for valid trials (target appeared where arrow pointed), invalid trials (target appeared opposite to where arrow pointed), and neutral trials (no arrow shown), averaged over commissurotomy patients P.S. and J.W. Note that cue validity effect was the same, whether or not the target appeared in the same field as the cue.

on-top" target intermingled with "blue-on-top" distractors and responded to such targets with the ipsilateral hand. As expected for a visual conjunction search, RTs for finding the target increased linearly as a function of the number of items (set size) under all conditions. The slopes of these set-size functions, which indicated the speed of visual search, were found to be the same for unilateral and bilateral displays in the intact control subjects (figure 2.4b). In contrast, for the commissurotomy patients the slopes of the set size functions were half as steep for bilateral relative to unilateral presentations, indicating that these patients searched the bilateral arrays about twice as fast as the unilateral arrays. This pattern of results was consistently observed in all four patients studied (Luck et al. 1994), indicating that they could, in fact, divide attention effectively between the stimulus arrays in their respective visual fields. It was as if each hemisphere possessed its own independent "spotlight" of attention for scanning its own half of the visual array, which could then be carried



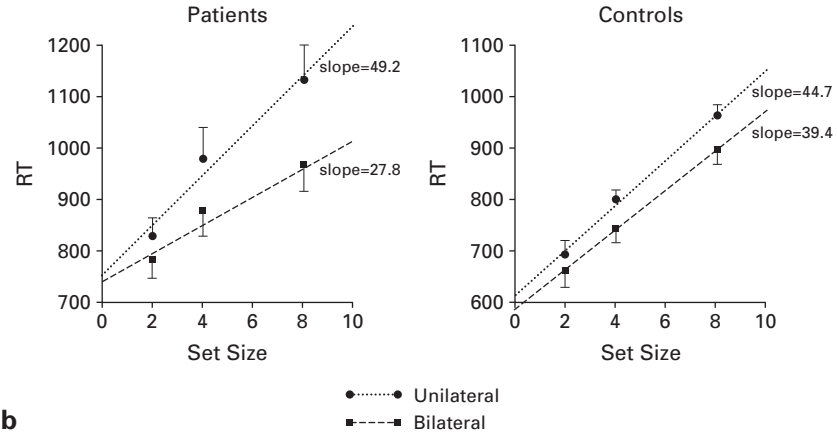


Figure 2.4
(a) Examples of stimulus arrays in visual search experiment by Luck et al. (1989). The top panel shows a bilateral array and the bottom panel a unilateral array with eight search items. Search arrays were presented for 2.5 seconds each. Unilateral and bilateral arrays of different set sizes were randomly intermixed, and one target was present on a random 50 percent of the trials. (b) Increasing mean reaction times as a function of search set size for six normal control subjects (top graph) and two commissurotomy patients (lower graph) in an experiment by Luck et al. (1989). For the patients the slope of the set-size function was about half as steep for the bilateral arrays (dashed lines, circles) as for the unilateral arrays (solid lines, squares).

out about twice as fast as in the intact brain with its unitary focus of attention.

The findings of Luck et al. (1989, 1994) appear to contrast sharply with Holtzman et al.'s (1984) conclusion that spatial attention maintains a unitary focus after section of the forebrain commissures. The implication is that the cued orienting of attention is mediated by a different brain system from that engaged during target search within a visual array. Whereas the cued orienting of attention toward an anticipated target appears to engage subcortical pathways linking the two hemispheres, the attentional scanning of a visual scene following its presentation seems to be carried out `independently by each hemisphere viewing its own visual half-field. These two examples highlight one of the general principles that has emerged from research on the split-brain patients, namely, that some cognitive functions involve an interplay between cortical and subcortical systems that link the two hemispheres, whereas others may be carried out exclusively within one hemisphere. This idea is sketched in figure 2.5. In addition to the control of attention during visual search, functions that can be lateralized to one hemisphere with

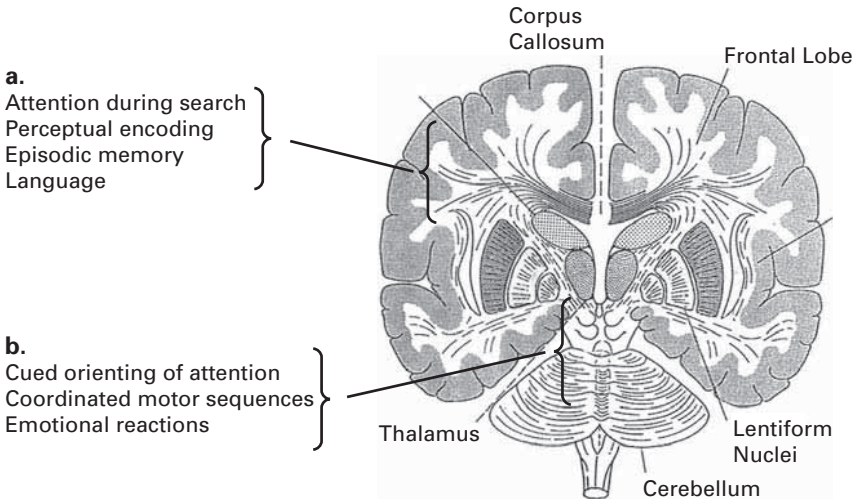


Figure 2.5
Schematic diagram indicating that some cognitive functions (examples of which are listed under a) may be carried out independently in the separated hemispheres while other functions (listed under b) engage subcortical pathways that link the hemispheres following section of the forebrain commissures.

little or no interference from the other include perceptual encoding (Gazzaniga & Hillyard, 1973), episodic memory (Holtzman & Gazzaniga, 1985), and both receptive and expressive language (Gazzaniga 1983). To demonstrate such lateralization, however, it is essential to rule out elaborate cross-cueing strategies developed by some patients that enable one hemisphere to gain access to the information held in the other (Gazzaniga & Hillyard 1971). In contrast, processes that generally engage subcortical pathways that link the separated hemispheres include the cued orienting of attention (Holtzman, Volpe, & Gazzaniga, 1984), rapid sequencing of bilateral motor actions (Pashler et al., 1994; Ivry, Franz, Kingstone, & Johnston, 1998) and emotional expression (Gazzaniga & Smylie, 1984).

The Unity of Conscious Experience

Mike has never been one to shrink from confronting the most imposing problems in mind-brain science. One of the fundamental questions he has wrestled with is how to account for the subjective unity of our conscious experience. From his studies of commissurotomy patients, Mike concluded that the human mind is made up of a complex mosaic of perceptual, cognitive, and emotional processes, each with its own particular neural substrate (Gazzaniga, 1989). How is it, then, that these diverse modular functions are incorporated into the subjective feeling of a unified conscious self? Mike's approach to this conundrum has been to propose that the language-rich left hemisphere has an interpretive capability that seeks coherent explanations for events that occur in the world and for our emotional and behavioral reactions to them. This left-brain "interpreter" constructs a plausible narrative of our actions, thoughts, and emotions, and this narrative provides the thread of unity to our conscious experience (Gazzaniga, 1989, 2000). Although this interpreter hypothesis grew from Mike's studies of split-brain patients, which showed that the left hemisphere would often invent plausible explanations for actions initiated by the isolated right hemisphere, it has widespread applicability to our everyday lives. This drive to seek explanations and generate interpretations is indeed a general human tendency, and Mike's insight was to realize that this interpreter based in the left

hemisphere could serve as the "glue that keeps our story unified and creates our sense of being a coherent, rational agent" (Gazzaniga, 2000).

In this context, a major function of the corpus callosum is to communicate the modular operations of the right hemisphere to the left hemisphere's interpreter, thereby creating an interplay between the hemispheres that forms the basis for unified conscious experience. More recently, however, Mike has proposed another far-reaching hypothesis about the corpus callosum, namely, that this communication link between the hemispheres may also play a pivotal role in the evolution of human cognition. The subtitle of the article in *Brain* in which this idea was developed (Gazzaniga, 2000) is "Does the corpus callosum enable the human condition?" a phrase that at first struck me as overblown hyperbole of the sort that Chuck never would have tolerated. As I got into it, however, this evolutionary hypothesis began to seem inspired, and perhaps even profound. Mike's basic idea is that the corpus callosum allows evolution to experiment by means of mutations that create new modular cognitive functions in one hemisphere while preserving the previous function in the other hemisphere, in case the new one doesn't work out. As he put it, the corpus callosum allows for a "no cost extension" of previously existing cognitive modules. The mutations and adaptations that are successful then become laterally specialized functions that reside primarily in one hemisphere. This proposal thus not only explains why some very important cognitive functions such as language are strongly lateralized to one hemisphere but may also account for the rapid emergence of advanced cognitive skills in the Hominidae.

Mike's article in *Brain* (Gazzaniga, 2000) not only propounds this provocative hypothesis about the evolutionary significance of the corpus callosum but also happens to provide a superb overview of the conclusions he has drawn from more than forty years of split-brain research. What shines through this body of work is Mike's unerring knack for identifying the central questions in mind-brain science and for answering them through ingenious experiments. No one has contributed more than Mike to our understanding of the neural underpinnings of the human mind (figure 2.6).

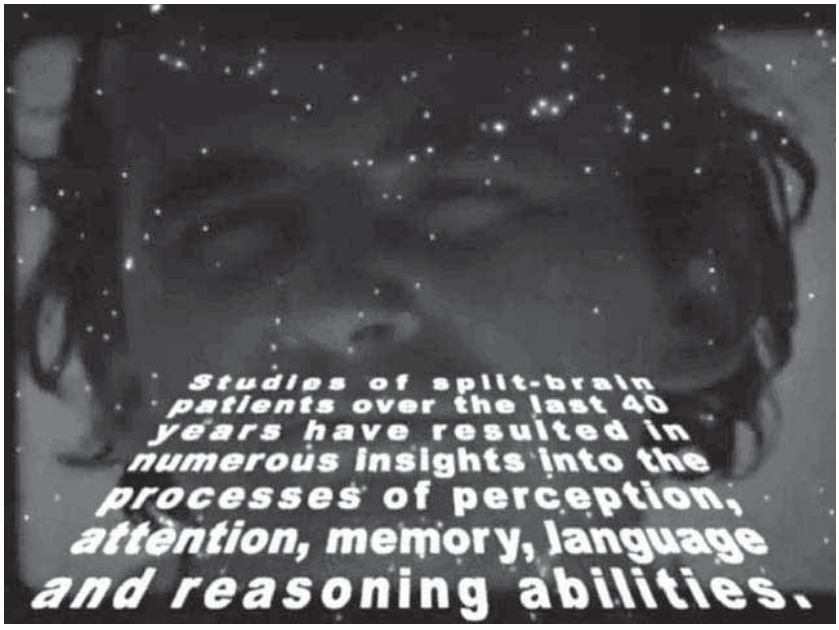


Figure 2.6
Mike Gazzaniga has been a visionary pioneer in exploring the inner galaxies of the human mind. The quoted passage is from Gazzaniga (2000).

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3

Where Is the "Spatial" Hemisphere?

Stephen M. Kosslyn

I met Mike somewhere between twenty-five and thirty years ago, when Edgar Zuriff set us up to have a lunch in a really nice restaurant in New York. We talked about the brain and the cerebral hemispheres. I was, I must confess, a tiny bit skeptical about this talk of cerebral hemispheres. I associated this topic mostly with pop psychology. But Mike made a good case that it was exciting, stimulating work, and he invited me to come up to Lebanon, New Hampshire, with him to test a split-brain patient. In that pre-neuroimaging era, studies with split-brain patients were the most solid evidence for hemispheric specialization, and I was intrigued. This was during what Mike later referred to as his "Travels with Charlie" days (most readers may be too young to know what I'm referring to here, but Mike knows what I'm talking about). Mike had a huge Winnebago that he would park out front of patient J.W.'s kitchen window, and snake cables through the window to power the Apple II computer he used for testing.

I vividly remember the first session of testing J.W. We were considering the possibility that both hemispheres could generate and use mental images, but did so in different ways. I was really blown away. I was standing behind the patient, watching him respond as the computer presented the tasks. This wasn't like my usual "$p < .05$" finding; these were huge, visible effects. This felt like "bench science." I was really impressed, and this experience working with Mike nudged me first into neuropsychology, then into cognitive neuroscience—and it's not likely that I would have gone that way otherwise.

The work I discuss in this chapter was inspired by the early split-brain work that I did with Mike. Although I don't discuss that early split-brain work here, I want to acknowledge that I never would have done any of

this research if not for Mike. I want to thank him for his enthusiasm, guidance, and that gentle nudge.

I begin with a simple question: Where is the spatial hemisphere? Before we can even begin to answer this question, we need to back up a step and ask: Is this the right question to ask? Is "spatial" just one thing? And if it's not, if the brain can represent spatial information in more than one way, does it make sense to ask where the spatial hemisphere is? One theme of this chapter is that this is the wrong question to ask, that in fact the brain represents spatial information in multiple ways, and that at least two types of spatial representations are lateralized differently in the brain.

This chapter has four parts. First, I consider the rationale for hypothesizing that the brain uses two distinct types of spatial representations. As part of this analysis, I offer a hypothesis about why these two types of representations would be lateralized to different cerebral hemispheres. Second, I summarize empirical research that tests these ideas in perception, using a variety of techniques. Third, I review empirical research that extends these ideas to visual mental imagery. If imagery arises from representations encoded during perception, then we should be able to obtain converging evidence for the two hypothesized types of representations during imagery. Finally, I summarize computational models that provide yet another type of converging evidence in support of the hypotheses.

Two Types of Spatial Representations?

A fundamental insight from cognitive neuroscience is that faculties that appear to be unitary and undifferentiated, such as memory and perception, are not; rather, they are carried out by systems of distinct processes. Consider memory: We distinguish between short-term and long-term memory, between episodic and semantic memory, between implicit and explicit memory, and so forth (see Schacter, 1996). Why should we expect only a single form of spatial representation?

Categorical Versus Coordinate Spatial Relations Representations

Some simple observations lead me to hypothesize two classes of spatial representations. First, it is clear that different information is required to

accomplish different tasks. For instance, to read English words you need to know the arbitrarily assigned associations between patterns of marks on a page and meanings. In contrast, to walk across the street you need to be able to recognize moving objects, estimate their speeds and trajectories, and control your own movements.

Second, it is also clear that different representations make different information explicit and accessible (Marr, 1982). For instance, Arabic numerals make powers of 10 explicit and accessible, whereas Roman numerals do not. Thus, different representations will be more or less useful for helping us to accomplish different tasks. For instance, if you want to multiply two numbers, you are better off using Arabic numerals.

These two simple observations lead me to posit two different types of spatial representations. Consider first what sort of representation would help us to recognize jointed flexible objects when they appear in different contortions. For instance, imagine a human form with arms extended and standing on tip-toe. Now imagine the same form, but squatting down, with arms crossed over the chest. If you could lay these two images on top of each other, they wouldn't match very well. Nevertheless, we have no problem identifying both as the same object. How could this be accomplished? Notice that in spite of the differences, we haven't added or subtracted any parts, and the spatial relations among the parts are still the same—if we characterize these spatial relations at a sufficiently abstract level. For instance, the thigh bone is still "connected to" the shin bone in all those positions.

In short, if we describe the individual parts and their (relatively abstract) spatial relations, we can produce the same description for flexible jointed objects when they are in different configurations—which could then be matched to the corresponding description stored in long-term memory, thereby allowing us to identify objects. Based on this notion, my colleagues and I have hypothesized that the brain can encode and store *categorical spatial relations* representations, which assign relative positions to an equivalence class. For example, consider the relation between you and the words you are now reading: If you are two feet or four feet from them, moved to the left side or right side or anywhere in between, they are still "in front of" you. "In front of" is a categorical spatial relation: It abstracts out one aspect of the relation, and throws away everything else. Thus, the different specific positions you take are

treated as equivalent, with respect to the categorical spatial relation of "in front of."

The same is true for other categorical spatial relationships, such as "left of," "above," and "inside." You can produce invariant descriptions of jointed objects if you use categorical spatial relations among the parts; such relations will allow you to use the same description for the object as it contorts.

Consider next different sorts of tasks, namely reaching and navigating. There are very different requirements on the information necessary to perform these tasks than on the information necessary to produce the same description of jointed objects in different configurations. Now you need the very information that you threw away when you assigned a relation to a spatial equivalence class. It's not enough to say that one part is connected to another, or that this part is in front of or behind another part. Rather, you need to know precisely how two objects are positioned relative to each other, so that you can reach to it or avoid bumping into it (as appropriate for your goals). For reaching and navigation you need to specify the location and metric coordinates relative to an origin, such as of Cartesian or polar coordinates.

On the basis of this notion, my colleagues and I have hypothesized that the brain can encode and store *coordinate spatial relations* representations, which assign objects or parts to a precise metric location relative to an origin. For example, consider the relation between you and the words you are now reading: If you are two feet or four feet from them, moved to the left side or right side or anywhere in between, you would need to move your arm, hand, and index finger differently to point to the first word at the top of the page. Using the categorical spatial relation "in front of" won't help you point precisely; you need to know precisely how far away and at what angle, relative to your body, the target is. Thus, the different positions you take as you move are treated as distinct, and are represented separately.

Lateralization of Spatial Relations Representations

This kind of reasoning led to the notion that there are two candidate types of representations: categorical spatial relations representations assign relative positions to an equivalence class, such as above or left of, whereas coordinate spatial relations representations specify location in metric coordinates relative to an origin.

Reasoning also led my colleagues and me to hypothesize that these two types of representations are lateralized differently in the brain. Why would we hypothesize that a type of spatial representation might be processed more efficiently in a single cerebral hemisphere? Our argument rests on the idea that implementing processes in a single hemisphere allows the brain to coordinate efficiently across both halves of the body, especially when the behaviors involve complex sequences, which are likely to be performed via an "open loop" computation (i.e., without movement-by-movement feedback; see Lashley, 1951).

A good example of such a behavior is speech production. As you speak, you don't want the right half of your brain to be controlling the left part of your mouth and the left part of your brain to be controlling the right part. You need to have the two sides of your mouth tightly coordinated. Thus, it makes sense to have a single speech output controller that governs both sides of the mouth.

Some evidence for this hypothesis comes from people who stutter. For least some of them, they stop stuttering if part of the frontal lobe in one hemisphere is removed (Jones, 1966). These cases may serve as a counterexample: these people have two controllers that compete, and hence the speech output can become tangled.

From this perspective it makes sense that a single lateralized structure —Broca's area, in the left frontal lobe—plays a key role in speech output control. What might be the connection between Broca's area and categorical spatial relations representations? The crucial idea for present purposes is that categorical spatial relations are easily named and related to language; we can always find a word or two to describe these relations. If the speech output controller receives input from linguistic representations, and such representations are easily used for categorical spatial relations, then the left hemisphere may be more efficient at using categorical spatial relations representations.

In contrast, coordinate spatial relations are important for reaching and navigation. Both of these abilities require searching the environment, and doing it quickly and "sampling without replacement." That is, one needs to find a sought object before reaching for it, and one needs to find and note pathways and obstacles before navigating. The right hemisphere appears to have a map of the entire visual field (see De Renzi, 1982; Mesulam, 1981), and such a map would be well suited for a search control process that samples the visual field without

replacement–coordinating search to cover both halves of the field. This search controller would need to receive input about specific locations, and coordinate spatial relations representations would be the appropriate sort of representation. Thus, we can hypothesize that the right hemisphere may be more efficient at using coordinate spatial relations representations. (Note, however, that although these hypotheses about lateralization apply to right-handed people and to the majority of left-handed people, some lefties are reverse lateralized—in which case I would reverse the hypotheses about lateralization. That said, in the remainder of this chapter, I will focus solely on right-handed people and the majority of left-handers when discussing hemispheric localization.)

Both the analysis of why different sorts of spatial relations representations would be useful and the hypotheses about how such spatial relations representations might be lateralized in the brain are highly speculative. Before trying to develop these hypotheses in more detail and with greater rigor, it would be useful to discover whether they lead to fruitful predictions. Thus, the following two sections of this chapter summarize empirical research that was sparked by these ideas. For the most part I've focused here on research from my own laboratory; Laeng, Chabris, and Kosslyn (2003) and the special issue of *Neuropsychologia* in which Kosslyn (2006) was published contain additional pieces of converging evidence.

Spatial Relations Representations in Visual Perception

The most straightforward prediction from the previously summarized line of reasoning is that the left hemisphere should be more adept at encoding and processing categorical spatial relations representations whereas the right hemisphere should be more adept at encoding and processing coordinate spatial relations representations. Such findings would not only provide evidence for the hypotheses about lateralization but also would thereby support the distinction between the two types of representations: if there were only a single way to represent spatial information, we would expect either no lateralization or would expect that one of the hemispheres would generally be better than the other at encoding spatial relations. If we find that one hemisphere is better at encoding and processing categorical spatial relations and the other is better at

encoding and processing coordinate spatial relations, this is evidence that the two sorts of representations are distinct.

In this section, I briefly summarize three classes of convergent evidence that support the predictions.

Divided-Visual-Field Studies

The back of the eye is actually a part of the brain that was pushed forward during development. The left part of each retina can be viewed as an extension of the left hemisphere, and the right part of each retina as an extension of the right hemisphere. Thus, if a stimulus is presented in the right visual field while a person is staring straight ahead, the image of the stimulus will strike the left part of the retina in both eyes and the encoded information will be projected first to the left hemisphere. If the left hemisphere is more efficient at encoding the stimulus and performing the task than the right, the person will be faster and perhaps more accurate than if the stimulus goes first into the right hemisphere—and vice versa, if the right hemisphere is more efficient than the left in the relevant respects.

Kosslyn, Koenig, et al. (1989) flashed stimuli very briefly (well under the 200 milliseconds required to make an eye movement) in the left or right visual field, so that they were processed initially by the right or left hemisphere, respectively. In separate experiments, we administered three categorical tasks: the participants decided whether a dot was on or off a blob, whether an X was to the left or to the right of an O, or whether a dot was above or below a horizontal line (this task was developed by Michimata & Hellige, 1989). In each of these categorical spatial relations tasks, the participants responded more quickly when the stimuli were presented in the right visual field (so that they were processed initially by the left hemisphere) than when they were presented in the left visual field. In addition, in each of these experiments we administered a corresponding coordinate task: deciding whether a dot was closer or farther than 2 mm from a blob, whether a plus sign was closer or farther than 1 inch from a minus sign, or whether a dot was closer or farther than 3 mm from a horizontal bar. In each of these coordinate spatial relations tasks, the participants responded more quickly when the stimuli were presented in the left visual field (so that they were processed initially by the right hemisphere) than when they were presented in the right visual field.

By varying the difficulty of the distance discrimination, we were able to demonstrate the predicted interaction between task and hemisphere when either task was easier than the other. Thus, we can rule out the possibility that the left hemisphere is simply better in general at processing difficult tasks and the right hemisphere is better in general at processing easy tasks.

In another study we returned to the rationale for hypothesizing the existence of two kinds of spatial relations representations. In particular, I argued that categorical spatial relations representations allow one to produce the same description when jointed objects appear in different configurations, and hence such representations are useful for identifying such objects. My colleagues and I (Laeng, Shah, & Kosslyn, 1999) showed pictures of common objects either in standard or contorted configurations. The task was simply to respond yes or no to each picture, indicating whether or not an auditorily presented name was appropriate for the object.

The results from this study were straightforward: The participants evaluated contorted pictures more accurately when they were presented in the right visual field, and hence the input was delivered directly to the left hemisphere. This finding is just what we predicted should happen, if in fact categorical spatial relations play a key role in representing and identifying jointed objects when they assume unusual configurations. In sharp contrast, we found the opposite result when we showed standard configurations; now the participants were more accurate when the pictures were presented in the left visual field, and hence the input was delivered directly to the right hemisphere.

This finding that the right hemisphere is better at evaluating standard shapes makes sense if this configuration is stored as a single representation in this hemisphere, and the stimuli can be matched directly to this representation. Why would this be the case? Coordinate spatial relations may be associated with single exemplars; the metric distance to an object often is only useful for a specific object (for example, a table with a certain shape). If so, then ease of encoding coordinate spatial relations may be associated with ease of encoding specific exemplars (see Jacobs & Kosslyn, 1994).

Neuroimaging Studies

Neuroimaging studies have provided converging evidence for both the distinction between categorical and coordinate spatial relations represen-

tations and their hypothesized lateralization in the cerebral hemispheres. The more activated a specific part of the brain is, the more blood it draws in; hence, by measuring blood flow, we can assess the degree to which neurons in specific regions were activated while a person performed the task. For example, we (Kosslyn, Thompson, Gitelman, & Alpert, 1998) used positron emission tomography (PET) to monitor regional cerebral blood flow as participants encoded and processed the two types of spatial relations. Participants saw a bar, and an X that could appear at different distances above or below the bar. In the categorical spatial relations condition, the participants decided whether the X was above or below the bar; in the coordinate spatial relations condition, they decided whether the X was closer or farther than a half inch from the bar.

When we directly compared activation in the two conditions, we found that all areas that were activated in the right hemisphere were more strongly activated by the coordinate task than the categorical one. And all of the areas that were more strongly activated by the categorical task than the coordinate one were in the left hemisphere. That said, there was some activation in the posterior left hemisphere that was stronger for the coordinate task. The areas of activation in general focused on the parietal and frontal lobes, which is interesting, given the clear role of the parietal lobe in encoding spatial information and the role of the frontal lobe in working memory (see Smith & Kosslyn, 2006). A subsequent functional magnetic resonance (fMRI) study produced convergent results, finding lateralized activation of the sort we predict (Baciu et al., 1999).

Effects of Brain Damage

Another piece of convergent evidence was reported by Laeng (1994). He studied patients who had localized brain damage, and found that those who had damage to the left hemisphere made more errors when they had to encode categorical spatial relations than when they had to encode coordinate spatial relations. In contrast, patients who had damage to the right hemisphere showed the opposite pattern. The damage was typically in the parietal or frontal lobes–which lines up nicely with the areas we found activated in the neuroimaging studies.

In addition, Slotnick, Moo, Tesoro, and Hart (2001) tested patients while their left or right hemispheres were pharmacologically inhibited (for medical reasons), and found that they made more errors assessing categorical spatial relations when the left hemisphere was inhibited and

more errors assessing coordinate spatial relations when the right hemisphere was inhibited.

Spatial Relations Representations in Visual Mental Imagery

Many of the same neural systems are used in visual perception and visual mental imagery (for a review, see Kosslyn, Thompson, & Ganis, 2006). Mental imagery is based on information that was encoded via perception, which typically has been stored in long-term memory and is subsequently activated when one is trying to remember (or reason about) a perceptual characteristic. For present purposes, the most relevant finding about mental imagery is that visual mental images are actively constructed. That is, creating an image is not like accessing a jpeg file in a computer. Rather than simply retrieving a stored representation, images are produced by arranging different parts to form a whole (Kosslyn, 1980, 1994; Kosslyn, Cave, Provost, & von Gierke, 1988).

For example, in one study participants first memorized upper-case block letters in 4×5 grids (Kosslyn, Cave, Provost, & von Gierke, 1988). Following this, they participated in a task where, on each trial, they were cued with the name of one of the letters and then saw a 4×5 grid that contained an X mark in a single cell. Their task was to decide whether the letter, if it were present in the grid as they had memorized it, would cover the X mark (this task was devised by Podgorny & Shepard, 1978).

The results provided strong support for the claim that visual images are constructed a segment at a time. The participants not only required more time to evaluate letters that had more segments (e.g., *F* required more time than *L*) but also required different amounts of time to evaluate whether the letter would cover the X depending on the location of the X. Participants were faster to evaluate X probes that fell on segments of letters that previously had been drawn (by a different group of participants) earlier in the sequence (e.g., they were faster when the X fell on the vertical line at the left of the *F* than when it fell on the horizontal segment at the top). It was as if the participants were mentally placing the segments one at time in the same order they had previously been drawn, and more time was required to get to segments later in the sequence. In contrast, the participants did not require different amounts of time to evaluate X marks on different segments when they actually

saw light gray letters in the grids and evaluated the X marks on the basis of perception, and so the time difference was not caused by a scanning effect. Moreover, in another condition the participants were given the letter name and were asked to visualize the upper-case version in the 4 × 5 grid as they had previously studied it, and were to press a button after they had fully formed an image of the letter. At this point, the X was presented. Now the location of the X did not affect the time to respond. This makes sense if the initial finding arose because we "caught the generation process on the fly," and assessed the order in which segments were inserted into the image.

The evidence suggests that mental images are constructed a part at a time. If so, then spatial relations representations presumably are used to assemble the parts into an image. Given our previous findings, we were led to hypothesize that there should be two distinct ways to generate images, by using categorical spatial relations representations to arrange the parts or by using coordinate spatial relations representations to arrange the parts. If so then—contrary to common wisdom—mental imagery should not solely be the purview of "right-brain" thinking. Rather, the right hemisphere should be better at forming images based on coordinate spatial relations representations, whereas the left should be better at forming images based on categorical spatial relations representations.

Divided-Visual-Field Studies

We thus predicted that the left hemisphere should be better at generating visual mental images when categorical spatial relations are used to arrange parts whereas the right hemisphere should be better at generating images when coordinate spatial relations are used to arrange parts. To test this prediction, we began by asking participants to encode a description of a form, and that description relied on categorical spatial relations. Specifically, we asked participants to memorize a description of a set of bars in a 4 × 5 grid. For example, the description might be something like "a vertical bar extends from the upper right corner downward to the bottom; connected at the bottom, a horizontal bar goes to the left and stops one column short of the far left side; attached to the top of the left side of this bar is a short vertical bar, extending two squares up." The participants memorized two such descriptions, which were labeled with the digits "1" and "2." We induced them to use

categorical spatial relations by making them name the spatial relations and by leading them to use these relations to construct the image in advance.

In the coordinate condition, we showed the participants not a 4 × 5 grid, but rather only the four corners (little right-angled brackets). We then presented a line segment within this space, and asked the participants to remember precisely where it was. We then removed this segment and presented a second. We told them that they should visualize the first segment, and then "mentally glue" the second segment to the first, to form a pattern. Then the second segment was removed, and we presented a third, and again asked them to "mentally glue" it to their image of the two segments just memorized. To learn the patterns correctly, the participants had to remember precisely where each segment was located in the space, which requires coordinate spatial relations. The participants memorized two such patterns, each of which was named with a digit.

After memorizing the stimuli, participants received the identical task with the identical stimuli. In the task itself we presented a digit to cue the relevant stimulus, and then up flashed up a set of four corner brackets (the corners of the 4 × 5 grid), with a single X mark within the space they demarcated. The task was to decide whether the cued stimulus, if it were in the space defined by the brackets, would cover the X. The stimuli were lateralized to the left or right visual field.

The results were as predicted: When the stimulus was processed initially by the left hemisphere (i.e., was presented in the right visual field), the participants were more accurate if they had learned the stimulus using descriptions. In contrast, if the stimulus was processed initially by the right hemisphere (i.e., was presented in the left visual field), the participants were more accurate if they had learned the stimulus by mentally amalgamating the segments, based on their precise positions in space. We replicated this result, with variants of the task (Kosslyn, Maljkovic, Hamilton, Horwitz, & Thompson, 1995).

Neuroimaging Study

We performed a PET study, using precisely the same procedure and task that were just described, but in this case the stimuli were shown in the center of the field (Kosslyn, Thompson, Sukel, & Alpert, 2005). The results were clear-cut: More activation occurred in the left hemisphere

when the images were formed on the basis of previously stored descriptions, whereas more activation occurred in the right hemisphere when the images were formed on the basis of having memorized the precise positions of the segments. And, again, the activation was primarily in the parietal and frontal lobes.

In short, mental imagery is not solely a right- or left-hemisphere function. Both hemispheres can produce mental images, but they do so in different ways.

Computational Modeling of Spatial Relations Representation

The research just summarized was inspired by informal analyses. We fleshed out and firmed up these ideas, and also discovered new implications of them, by developing and implementing computational models.

Incompatible Mappings?

A key assumption of this project is that different types of representations make different information explicit and accessible. In so doing, they may specify incompatible sorts of information, which is why they need to be processed separately (see Rueckl, Cave, & Kosslyn, 1989). In the present case, categorical spatial relations representations are useful because they specify what is preserved under various transformations. In order to do this, these representations must throw away the very information that is central to coordinate spatial relations representations, namely the specific distance and direction of two related parts or objects.

One set of models we constructed explicitly tested the assumption that the two kinds of representations rely on incompatible processing. These models relied on simple three-level feed-forward networks that were trained using back propagation (e.g., Gurney, 1997). We used such models not because we think that each of the nodes corresponds to a neuron but rather because of the evidence that the process of mapping an input vector to an output vector captures something about how the brain performs such mappings. We asked whether a single network would perform both sorts of mappings, categorical and coordinate, better than a network that was split, so that the two mappings were independent.

In these models, the input layer was a one-dimensional vector where two contiguous central units were always activated to represent a "bar,"

and another unit, which changed from trial-to-trial, was activated to represent an X mark. The networks learned to classify the X relative to the bar, either as above or below it (for the categorical task) or closer or farther than a criterion distance (for the coordinate task; see Kosslyn, Chabris, Marsolek, & Koenig, 1992). There were two pairs of output units; one pair indicated the categorical judgment (above or below), and one indicated the coordinate judgment (closer or farther). The trick was that the nodes in adjacent layers of the networks either were fully interconnected or were split so that the hidden layer had two parts, the nodes in each of which were in turn connected only to the pair of output units that indicated one of the two types of judgments; we tested various sorts of split networks, varying the ratio of connections allocated for the different judgments.

As predicted, the split networks were more accurate in establishing the requisite mappings. This finding indicates that there is interference between the two kinds of mappings, which is evidence that they are in fact qualitatively different. In a control study, we showed that split networks actually did worse than the fully interconnected ones when they made two judgments of the same type, where there was no such interference.

Bases of Lateralization

At the outset I speculated that a speech output process and a search control process are likely to be lateralized because a single source of control is best when rapid open-loop processes cross the midline. To test this idea, my colleagues and I (Kosslyn, Sokolov, & Chen, 1989) built a model that began with the two controllers' being innately lateralized, the speech output controller being more effective in the left hemisphere and the search controller being more effective in the right hemisphere. We assumed that each of these controllers typically inhibits its analog in the other hemisphere, thereby allowing control to originate from a single hemisphere.

We also formalized what we dubbed the "snowball effect," relying on the following three key ideas: (1) When either controller receives input it can use, it sends feedback to the subsystem that sent that input. This feedback strengthens that subsystem and its connections to the controller. (2) The feedback is more effective in the same hemisphere as the controller. Why? There are many possibilities; for example, perhaps

crossing the corpus callosum degrades information slightly, or one hemisphere tends generally to inhibit the other. (3) Once a subsystem has become lateralized in this way, it then plays the same role as the speech output and search controllers, now providing more effective feedback to subsystems that send it usable information. Thus, over time and experience, lateralization should percolate deeper into the system.

We simulated many scenarios, which documented the viability of this snowball effect to account for patterns of cerebral lateralization and also illustrated ways in which individual differences in lateralization could arise, depending on the settings of precise parameter values.

New Predictions

The snowball effect can result in lateralized changes far from the control processes that are innately lateralized. We decided to test a somewhat counterintuitive prediction, focusing on the notion that the left and right hemisphere might selectively monitor output from visual neurons that have different-sized receptive fields. Why? First, regarding the right hemisphere, we hypothesized that output from neurons with larger, overlapping receptive fields is more useful for computing coordinate spatial relations than categorical spatial relations. These predictions follow from the observation that large overlapping receptive fields promote "course coding" to derive very precise metric information (Kosslyn et al., 1992). Second, regarding the left hemisphere, we hypothesized that outputs from neurons with smaller, less overlapping receptive fields, can divide space into little pockets—which could easily be categorized by categorical spatial relations, such as above versus below or left versus right.

To check whether these intuitions hold conceptual water, we again implemented network models (Kosslyn et al., 1992). As predicted, the networks judged coordinate spatial relations better when the stimulus was filtered through large, overlapping receptive fields than when it was filtered through small, nonoverlapping ones, and vice versa for the categorical task.

We now had the grounds for making firm predictions about humans. If this line of reasoning is correct, then people should monitor larger patches of space in the left visual field (feeding directly into the right hemisphere) than the in the right visual field (feeding directly into the left hemisphere). My colleagues and I (Kosslyn, Anderson, Hillger, &

Hamilton, 1994) tested this prediction with a very simple paradigm. We showed people a short straight line segment, tilted 45 degrees to the left or to the right, followed a brief time later by a second such line segment; both segments were in the left visual field or both were in the right visual field. The task was simply to decide whether the second segment was tilted the same way as the first. The trick was that we varied the distances between the two segments.

The models gave us clear predictions: If the right hemisphere monitors outputs from neurons with relatively large receptive fields, it should perform comparably when segments are close together or far apart. This is in fact what we found. In contrast, if the left hemisphere monitors outputs from neurons with relatively small receptive fields, then it should perform worse when segmentsare far apart (and hence were processed by different neurons). This is also precisely what we found. These findings are consistent with reports that the hemispheres are sensitive to different ranges of "spatial frequencies" (Kitterle, Christman, & Hellige, 1990; Niebauer & Christman, 1999) and different-sized stimuli (Robertson & Lamb, 1991). However, we also found that such differences could be reversed by context and instructions—which indicates that the hemispheres may differ in part in their default biases for monitoring outputs from classes of visual neurons, not in their absolute potentials.

Finally, I must note that several studies of categorical versus coordinate spatial relations have not yielded the predicted laterality effects (although I also note that a meta-analysis supports the present conclusions; for reviews, see Kosslyn et al., 1992, and the special edition of *Neuropsychologia* in which the Kosslyn, 2006, paper was published). The findings just summarized might help to explain these failures: If the task does not allow space to be carved into small pockets that define categorical spatial relations, or if overlapping receptive fields cannot be used to specify specific locations, then the hemispheric advantages should disappear.

Conclusions

The core ideas that motivated this work are that different information is required to perform different tasks, and that different sorts of repre-

sentations make explicit and accessible the information needed to perform different tasks. These observations led to the hypothesis that the brain uses two types of representations of spatial relations: Categorical spatial relations are abstract, assigning relative positions to a category, and are useful for producing the same description of jointed objects when they are in different configurations. Coordinate spatial representations are specific, indicating the metric distance between two points, and are useful for guiding navigation or reaching. In addition, we hypothesized that the two sorts of representations are lateralized differently in the brain, with categorical spatial relations being encoded and processed more effectively in the left hemisphere and coordinate spatial relations being encoded and processed more effectively in the right hemisphere.

I briefly summarized research we performed to test these hypotheses, which used a variety of techniques to provide convergent evidence for the hypothesized lateralization during perception. In addition, I argued that mental images can be constructed using either type of spatial relation representation, with the result that neither hemisphere is generally "better" at generating visual mental images. Finally, modeling revealed that the intuitions that guided the work could be unpacked and formalized. Moreover, we derived a new prediction, which was supported when we tested human participants.

This project has shown that commonsense approaches to cerebral lateralization, which lead one to try to characterize the hemispheres in terms of large-scale abilities (such as using spatial information) are lacking. We made progress by taking an information-processing approach, and decomposing processing into more fine-grained components.

To conclude, we return to the question we asked at the outset: Where is the spatial hemisphere? The answer is: There is no single "spatial" hemisphere. This was the wrong question to ask. We are better off asking about the specific ways in which each hemisphere deals with spatial information.

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4

Recovery from Aphasia: Is the Right Hemisphere a Cure or a Crutch?

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It is hard to believe that it is more than twenty-five years since I turned up on the steps of Mike's lab at Cornell University Medical College in New York City, hoping to corral an aphasic population for my dissertation research. Aphasia is a disorder of language that often afflicts persons with damage to the left hemisphere of the brain. Mike was gracious but puzzled as to why anyone would want to be in his lab and not work with split-brain subjects. He offered me just that opportunity when J.W. and V.P., two of the completed callosotomy patients, came to town. Mike was persuasive in presenting his view that this was the most exciting research population in the world in terms of understanding human cognition. What he was interested in at that time was whether or not there was any evidence of use of syntax in the isolated right hemisphere.

He didn't even have to ply me with liquor to persuade me to take on this question. At the time, how the brain used different classes of words in language comprehension and expression was being vigorously investigated in the aphasia literature. Early work with split-brain patients and divided-field studies had suggested that the right hemisphere could understand single words, but showed little ability to put words together, or as Mike was soon to demonstrate, make simple inferences or solve problems. Was it an inability to understand how grammar was used to structure sentences that limited right-hemisphere cognition?

Around this time the lab was switching from true "tachistoscopic" displays, using slides and Gerbrands timers, into the brave new world of computers. With Jeff Holtzman to show me the ropes regarding lateralization and making those blazing new Macs display words on their little green screens, I got to work and came up with some experiments. This

was a far cry from running undergraduate students in the basement of Uris Hall at Cornell in Ithaca.

The weeks when a split-brain patient was in the lab were hectic and exciting. Everyone rushed to get experiments ready to run, filing into and out of Mike's office to make a case for their work. Bumbling graduate students like me were on standby. If something didn't work, or there was unexpectedly extra time, we would have a shot at seeing whether our experiments might show something interesting about the right hemisphere's capacity. Always, as you looked at your data, there was this tall guy looking over your shoulder with the question, "What have you got? Anything interesting?" Results never came fast enough for Mike then, and they still don't now. If your experiment was working, were you asking something significant enough to merit more time the next day? If it wasn't working, why not? Could it be fixed? And then at the end of the day, there was the chance to take J.W. or V.P. to dinner. For me, living on my modest NIH stipend, the chance to see the inside of a decent restaurant was not to be sneezed at. But best for me, my early experiments showed that the right hemisphere did have some sensitivity to syntactic information and that the right hemispheres of both J.W. and V.P. were able to make grammaticality judgments about a range of structures. Despite this ability neither was able to use this information in comprehension (Baynes & Gazzaniga, 1988; Gazzaniga, Smylie et al., 1984). I was hooked.

Of the various sources of data about the right hemisphere's language capacity, the commissurotomy population—those who have had the two hemispheres of their brains surgically separated—has some advantages over hemispherectomy patients or patients with focal brain injury. It is the only example of an isolated right hemisphere that developed in conjunction with a left hemisphere, so might be expected to represent "normal" right-hemisphere development. However, of the patients with well-developed right-hemisphere language, the age of seizure onset varied from twenty months to nineteen years, and surgery did not take place until years later. Hence, lateralization may be influenced by the presence of the seizure disorder (Gazzaniga, Nass, Reeves, & Roberts, 1984). In contrast, cognitive recovery in the hemispherectomy population (those who have had one hemisphere removed) was most successful when surgeries were completed early, usually when patients were under five years

of age. In the developing brain, the right hemisphere was sometimes quite capable of acquiring language, permitting children who survived the surgery to grow up, go to high school and college, and hold jobs. (For review see Baynes, 1990). Only under laboratory conditions, when the language of these successful cases was minutely examined, was it possible to show that there are areas of language that the right hemisphere is less able to support (Ogden, 1996; Vanlancker-Sidtis, 2004). Despite early optimism regarding plasticity and the equipotentiality of both hemispheres, newer series of surgeries have demonstrated that there is great variability in both linguistic and intellectual outcome after surgery to remove either hemisphere (Bishop, 1983; Curtiss & de Bode, 2003). Minimally, the outcomes of hemispherectomy represent a proof that some combination of skills can exist in the right hemisphere without the left. Under some conditions, still not completely specified, the right hemisphere can develop a useful language system commensurate with the general intelligence level of the individual in question.

In the case of split-brain patients with an isolated right hemisphere (RH), it was clear early on that there were radical differences in skill within that population and that there were in fact many patients who postsurgically had little language capacity at all (Gazzaniga, 1983). Within those right hemispheres that did support language, there was marked variability, but often semantic knowledge was present. The right hemisphere indeed knows things about the world, what words mean, what relationships exist between words and things, how objects are used and where they occur. But the ability to use other components of the language system—more strictly linguistic elements such as the grammatical processes that help us understand how words relate to each other in phrases and sentences and the phonological processes that help us structure the rapid and transitory stream of sound into words and sentences—are less likely to be present and are more variable in quality when they are present (Baynes, 1990; Sidtis, Volpe, Wilson, Rayport, & Gazzaniga, 1981). The split-brain population has also offered clear examples of the modularity of language processing. There are cases where a subset of language skills is uniquely located in the right hemisphere. One left-handed patient became agraphic (unable to write) after her callosotomy was completed. In this case, the motor programs needed to produce written language were in the right hemisphere and were cut

off from the otherwise language-dominant left hemisphere to use for daily life (Baynes, Eliassen, Lutsep, & Gazzaniga, 1998). Hence, any discussion of language lateralization should consider how the component parts of the language system are lateralized and not assume an all-or-none unitary language system.

Although the premise of the provision of a nonverbal means of response was based on the belief that the normal right hemisphere was mute, it became clear over time that there were instances where the right hemisphere was initiating verbal responses. Early instances of responses hypothesized to represent right-hemisphere speech were shown to be varieties of a "Clever Hans" effect when experimental paradigms were more carefully controlled (Gazzaniga & Hillyard, 1971; Gazzaniga, Holtzman, & Smylie, 1987). P.S. was the first patient observed to make verbal responses to LVF (left visual field) stimuli (Gazzaniga, Volpe, Smylie, Wilson, & LeDoux, 1979). The second split-brain patient observed to produce speech in response to LVF stimuli was V.P. Within one year of her surgery she was able to make limited verbal responses to LVF words and pictures (Gazzaniga, Smylie, Baynes, McCleary, & Hirst, 1984). J.W., long the prototypical split-brain patient with normal left-hemisphere language and a mute but literate right hemisphere, was observed to produce some vocal output to LVF displays while in the Purkinje eye tracker in the late 1980s. This was striking because this device displays an image of the stimuli that moves synchronously with the movement of the eyes. This clever bit of technology keeps the image stable and lateralized relative to eye position.

J.W.'s development of the ability to make spoken responses to LVF stimuli was particularly striking as it occurred shortly after the laboratory moved from New York City to Dartmouth College in New Hampshire. This location was more convenient to J.W.'s home and he was coming in on an almost weekly basis rather than for a week once every six months or so. The experiments I was running with him often focused on semantic relations and sometimes semantic priming. Was it possible that the development of this ability nearly ten years after his callosotomy surgery had been aided by regular semantic stimulation? If this was so, could some manipulation like this be used to increase the level of recovery from aphasia after left-hemisphere stroke?

Aphasia and the Right Hemisphere

Thirty years ago most neurologists believed that useful functional recovery from a stroke or other injury that resulted in the loss of brain tissue would occur in the first six months after injury. Slower minor improvements might take place over the first year, but after that there would be no dramatic recovery of function. Plasticity was virtually nonexistent; once physiological recovery was completed, the abilities and disabilities displayed at that point were permanent.

Nonetheless, interest in the right hemisphere as an aid in recovery from aphasic deficits has been kept alive by intriguing case studies over the years. In the 1970s, Kinsbourne (1971) reported three patients who had recovered from aphasia after a left-hemisphere stroke. Each was subjected to a bilateral sodium amytal test during which the ability to phonate was curtailed following the right hemisphere injection, but was undisturbed following the left-hemisphere injection. Normally, the left hemisphere injection disturbs speech production whereas speech can continue after a right hemisphere injection. Kinsbourne concluded that these patients' right hemispheres supported their language output following stroke. Shortly thereafter, Cummings and colleagues (Cummings, Benson, Walsh, & Levine, 1979) reported the case of a fifty-four-year-old male who became severely aphasic after a left-hemisphere stroke. After three years in a nursing home, he was reexamined, at which time he had developed the use of words and short phases with greatly improved comprehension. These authors attributed his recovery to the right hemisphere. Two other patients who became densely aphasic following a left-hemisphere stroke experienced recovery attributed to the right hemisphere after a second right hemisphere stroke rendered them speechless (Basso, Gardelli, Grassi, & Mariotti, 1989). These cases suggest that there are times when the right hemisphere can be crucial in recovery, but note that they are few in number relative to the many stroke victims who do not progress substantially. Also, reports indicate recovery is limited to improved comprehension and some single words or short phrases. So despite intriguing evidence that the right hemisphere could play a role in language recovery, the bulk of the evidence during this period suggested that role was limited and recovery located in the right hemisphere would be limited as well.

Mike's work taught me to be skeptical about what the right hemisphere could contribute. He was intrigued by the existence of dual minds, but keenly aware of the cognitive limitations of the isolated right hemisphere (Gazzaniga, 1985; Gazzaniga & Smylie, 1984). Nonetheless, the split-brain literature demonstrates variable literacy in the right hemisphere and the hemispherectomy literature reveals conditions where language development in an isolated right hemisphere is close to normal. It took progress in the animal literature to stimulate a reexamination of expectations regarding functional recovery and neural reorganization. In one early study, rats were trained to run a beam in response to noxious stimuli and then received lesions to the motor cortex. They received doses of saline solution, varying amounts of amphetamine, or amphetamine and haloperidol. Some continued to receive training on the beam while others were confined to small cages. The combination of the larger doses of amphetamine and continued practice yielded better recovery (Feeney, Gonzales, & Law, 1982). In Michael Merzenich's lab, owl monkeys were trained to make tactile discriminations based on repetitive stimulation of a small patch of skin on one hand. Examination of the receptive fields of their brains revealed that the area associated with the stimulation had grown 1.5 to 3 times larger than the comparable area on the untrained hand (Recanzone, Merzenich, Jenkins, Grajski, & Dinse, 1992). So not only could practice enhance behavioral recovery, it could also change cortical organization. These results are now well established and have stimulated the development of human treatment approaches (Mahncke et al., 2006; Merzenich et al., 1996).

New imaging methods developing in parallel also demonstrated right hemisphere activation during many tasks traditionally associated with language. Numerous studies reported greater right hemisphere activation in aphasic subjects relative to healthy subjects during language tasks, but still questioned the role of right hemisphere activation in recovery (Belin et al., 1996; Karbe et al., 1998; Cao, Vikingstad, George, Johnson, & Welsh, 1999). Other studies showed right hemisphere activation in recovered subjects or early in the course of recovery (Thulborne, Carpenter, & Just, 1999) and early right hemisphere activation has predicted a good response to treatment (Richter, Miltner, & Straube, 2008). Six Wernicke's aphasics showed increased activation both of the left inferior frontal gyrus and the right hemisphere homologs of the damaged

areas (Weiller et al., 1995). In this study, right hemisphere involvement was seen as representing activation of semantic knowledge, perhaps via the automatic spreading activation of the semantic system. Electrophysiological measures also indicated greater right hemisphere activation in aphasic subjects after injury, with greater right lateralization after recovery in patients with Wernicke's aphasia and greater left lateralization in recovered Broca's aphasia patients (Thomas, Altenmuller, Marckmann, Kahrs, & Dichgans, 1997). As Wernicke's patients have problems with language comprehension and difficulty generating the semantically appropriate word, increased right hemisphere activation during recovery may represent support of auditory comprehension and semantic knowledge. In contrast, Broca's aphasics have more difficulty producing speech and often experience problems both producing and understanding grammatical information. These skills are more strongly left lateralized and their improvement may depend more on left-hemisphere recovery. Thomas suggests that recovery models may have to incorporate different strategies for different lesion sites and different deficits.

These diverse observations inspired attempts to develop training methods that would engage the right hemisphere semantic system in recovery. Studies with split-brain patients have shown a well-developed semantic system even in patients with relatively little reading ability (Baynes, Tramo, & Gazzaniga, 1992; Gazzaniga, et al., 1984). Likewise, split-field studies with normal subjects consistently show semantic priming in both visual fields, although the type and speed of priming differ (Beeman et al., 1994; Burgess & Simpson, 1988; Chiarello, Burgess, Richards, & Pollack, 1990). However, it is usually the case that the accuracy and response time of the left visual field–right hemisphere is poorer that that of the right visual field–left hemisphere. Semantic, associative, and functional relations appear to be similarly organized (after all, in the normal state of affairs the two hemispheres do work together). If the left hemisphere is damaged, might it be possible to engage the right hemisphere's semantic system in the recovery process?

Contemporary models of lexical access incorporate semantically and phonologically driven activation to prepare words for production (Dell, 1986;; Wheeldon & Monsell, 1994). These models assume that the competitive process of activation goes awry in aphasic speech because of errant activation, of inhibition, or of selection (Schnur, Schwartz,

Brecher, & Hodgson, 2006). If these models are correct, aphasic individuals may benefit from practice in semantic decision making free of the additional burden of actual lexical selection and word production. This process provides aphasic speakers the opportunity to strengthen neural associations and increase activation of target words and sounds. If the right hemisphere semantic system is organized like the left but is slower to respond, perhaps intense rapidly paced practice with as many as 300 decisions required per session could provide a pathway to increased activation and improved lexical access.

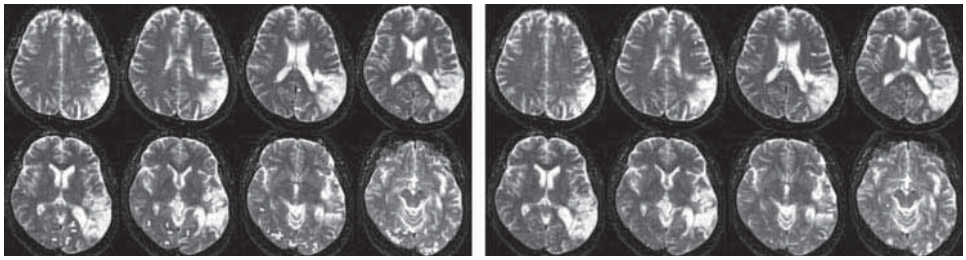
Working on these assumptions, we developed an implicit training method based on repeated forced-choice semantic and phonological decisions. Our first study trained chronic aphasic patients in semantic decision making without requiring any vocal response. Eight chronic aphasics were grouped according to the predominant error type (semantic or phonological) during naming. All received both implicit semantic training and implicit phonological training. In the semantic training, the participants made decisions about categorical, associative, or functional relations based entirely on pictures. In the phonological training, the participants had to choose the correct initial or final sound or the appropriate nonword rhyme of a pictured object. Both semantic and phonological training had a measurable effect on naming ability that was specific to the patient's error type. Phonological training had the largest effect on participants with a predominance of phonological errors, but no significant effect on the naming of participants who made mostly semantic errors. Semantic training was effective for both groups. Moreover, results generalized to naming on the Boston Naming Test. This is a striking result given the modest length of time spent in each training method (three weeks with three 30- to 45-minute sessions a week) and the fact that there was no explicit naming practiced (Baynes, Share, Redfern, Ludy, & Dronkers, 1995; Dukette et al., 1998). This training method had been developed with J.W.'s case in mind and the initial hypothesis was that semantic training would be more effective because this decision-based training could encourage the use of the undamaged right hemisphere, but the phonological method was clearly effective as well.

The same type of semantic training was applied intensively to a single subject, A.T., with pre- and post-training fMRI scanning. A.T., a

Wernicke's aphasic with a large posterior left hemisphere lesion, was asked to perform tasks that required judgments about perceptual, categorical, or associative aspects of target pictures. The intensity of the intervention was increased for this case study. The participant was trained for one to one and a half hours per day, five days a week, for one month. The intervention required A.T. to complete about 300 semantic decisions in each session. During the four weeks of intensive treatment, he progressed from 28 percent correct to 77 percent on training sets and from 5 percent to 48 percent correct on the Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983). His wife reported that communication at home was much improved, and narrative analysis demonstrated that his ability to use nouns readily in sentences also improved (Davis, Harrington, & Baynes, 2006).

In addition, A.T. completed pre- and post-training fMRI scans during verb generation, lexical decision, and text listening. Changes in fMRI activation during verb generation were apparent on the pre- and post-training session (figure 4.1, plate 1). Specifically, after training, increased activation was seen in the left inferior frontal cortex (LIFC) and there was a decrease in the scattered bilateral occipital and posterior parietal activation (figure 4.1a). The increased LIFC activation may reflect the marked increase in naming ability that A.T. experienced. In contrast to this verb-generation task, there was no change on the pre- and post-imaging of lexical decision, which was performed without error prior to training (figure 4.1b). Hence, the increased activation during the verb-generation task likely reflects the behavioral improvement in naming. Note that the posterior RH activation pre-training was not observed after training, so behavioral improvement was accompanied by increased LH participation.

A.T.'s behavioral outcome is very encouraging for the use of implicit training methods, but the improvement was not accompanied by increased right hemisphere participation. Earlier studies had observed increased right hemisphere activation after recovery from Wernicke's aphasia (Thomas et al., 1997), but A.T. did not show this increase, despite training intended to engage right hemisphere semantic networks. A.T.'s result also differed from studies that showed an increase in perilesional activity following recovery. Instead of increased activation near the lesion site, our subject had shown an increase in activity in the areas normally



a **b**

Figure 4.1 (plate 1)
Comparison of activation between pre- and post-therapy sessions for the Verb-Generation Task (a) and Lexical Decision Task (b). Images are in radiological view (left is right). Key: yellow = pre-therapy; red = post-therapy; blue = overlap between pre- and post-therapy.

activated during verb generation—the left inferior frontal cortex. The exact role of this area is uncertain, but it is more likely involved in semantic selection than in semantic storage. Hence, some recruitment of right hemisphere semantics during the retrieval process may have permitted the final stages of word selection to take place more normally.

The failure to see a role for the right hemisphere in a single patient should not be a surprise. Both the split-brain literature and the hemispherectomy literature document considerable variability. However, variations in right hemisphere language representation may fall into patterns. Whereas split-brain patients are far too rare to permit much generalization, many more patients undergo Wada examination (which tells doctors which hemisphere controls language in the individual's brain by anesthetizing a single hemisphere at a time) than complete callosotomy surgery. In one large series, Mike's student Gail Risse has observed patterns of representation across the hemispheres. Risse, Gates, and Fangman (1997) looked in detail at the results from sodium amytal testing in a series of 368 epilepsy cases. She selected cases with evidence of bilateral language and looked at the modality of the representation across hemispheres (table 4.1). Four language activities were sampled: automatic speech (counting backward, saying the days of the week, reciting a nursery rhyme), naming (saying the name of a real object), auditory comprehension (modified Token Test, a test designed to assess verbal comprehension of commands of increasing complexity requiring manip-

Table 4.1
Patterns of language representation in patients with bilateral language during a Wada procedure

	Automatic Speech	Naming	Auditory Comp	Reading
Group 1	>Left	Left	Left	Left
Group 2	Left	Left	>Left	Left
Group 3	>Right	>Right	>Right	>Right
Group 4	Both	Both	Both	Both

Note: ">" indicates "relatively better in."
Source: Adapted from Risse et al. (1997)

ulation of colored plastic tokens), and reading (words written on cards). She found that patients fell into four groups. With clearly left- or right-dominant individuals eliminated, only a subset of the possible permutations of combinations of abilities actually occurred. The Wada assessment is restricted in the amount and quality of information that can be collected during the brief period of anesthesia. However, this work suggests that bilateral language is under some constraints whose character might be clearer were we able to assess the psycholinguistically demonstrated language components, such as lexical semantics, phonology, morphology, and syntax, in terms of their possible patterns across hemispheres. This knowledge could advance rehabilitation methods that make optimum use of right hemisphere capacities.

My research group continues to develop our implicit rehabilitation method and has used it successfully with a range of disorders, from verb retrieval to phonological alexia (Baynes, Truong, Jonathan, Farias, & Davis 2008; Davis, Farias, & Baynes, 2009). It remains to be seen whether right hemisphere participation will be evident with larger studies using psycholinguistically motivated imaging protocols. Nevertheless I remain very optimistic about using intensive treatments based on psycholinguistic models to engage healthy neural tissue, be it left or right hemisphere. Improved imaging techniques and advancing knowledge of the genetic basis of language may indicate early on after a stroke what aspects of language can be expected to require rehabilitation, on the basis of lesion site and of a genetic analysis that identifies the probable language distribution. Believe it or not, Dr. Gazzaniga?

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5

The Interpreting Hemispheres

Margaret G. Funnell

One of the best things about working with Mike Gazzaniga was the people he surrounded himself with. There were, of course, all of the "big names" in the field who would come to visit the lab or give talks—Endel Tulving, for example, spent a term at Dartmouth at Mike's invitation. But more than that, it was the people Mike hired to work in his lab who were incredible. When making hires, Mike was never interested in listening to what people thought they wanted to work on—he was more interested in their intellectual curiosity and the way their minds worked. He always said that if he brought good people together, great things would happen. And he was right. Even a casual perusal of Mike's curriculum vitae makes it clear that this strategy was highly successful. The other thing about Mike is that he is not a detail guy—I don't think I have ever seen him sitting down to work out the minutiae of an experimental design. Mike is an idea guy. And as those of us who have worked for him know, he has LOTS of ideas. Truth be told, not all them are good ideas, and graduate students and post-docs often learned this the hard way. I know I'm not the only one who spent months trying to make one of his ideas work, only to be gently told by someone "older and wiser" to just quietly drop it. Most of his ideas are good and often great, though, and his vision is one of his defining characteristics. I remember one time when I submitted a grant, and two of the three reviews were fairly negative, complaining about the lack of detail in the experimental methods and analyses. The third reviewer, though, had a different take on it. He, too, noted the lack of detail, but argued that in Mike's case, the lack of detail should not be relevant. He pointed to the years of cutting-edge research that had come out of Mike's lab and concluded that we should be awarded the grant despite the lack of experimental

detail and despite the fact that it was unlikely that we would do any of the experiments we proposed to do. That reviewer managed to convince the others, and we got the grant. The reviewer was right, too—I don't think we actually did any of the experiments we proposed!

I started working with Mike because of my doctoral dissertation. I wanted to follow up on a memory study my advisor, Janet Metcalfe, and I did with Mike's split-brain patient, J.W., while Mike was at Dartmouth in the early 1990s (Metcalfe, Funnell, & Gazzaniga, 1995). By the time I was ready to begin my dissertation, though, Mike had left Dartmouth for UC Davis. I needed his permission to test J.W., and so I sent him a copy of my thesis proposal. He sent it back to me via Federal Express with a note on it—"You're hired." I hadn't actually been applying for a job, but since Mike was on his way back to Dartmouth to head the Center for Cognitive Neuroscience, I was happy to accept the job as a post-doc (once I had finished my dissertation, that is). After I completed my doctoral degree, the first experiment I designed for J.W. in Mike's lab was to explore memory differences in the two hemispheres. I set up a practice test of sorts just to demonstrate to J.W. what type of perceptual discrimination he would be asked to remember. Each trial included two identical objects aligned vertically—they were either in the same orientation or one was the mirror-image of the other. Much to my astonishment, he was completely unable to make this simple discrimination with his left hemisphere, although his right hemisphere could do the task almost perfectly. I told J.W. that I would be back in a minute, and I went and told Mike what had happened. Not surprisingly, he didn't believe the result, either, and came in to test J.W. himself. The result was the same. That task, initially intended as just a practice set, led to several productive years of research as Paul Corballis, Mike, and I explored the extent of the hemispheric difference in visuospatial processing.

In a series of papers, we laid out the differences between the two hemispheres in visuospatial processing. Although the left hemisphere is clearly capable of sophisticated visual processing—after all, reading is predominantly a left-hemisphere function—we found that it represents spatial information relatively crudely compared to the right hemisphere. The right hemisphere is vastly superior to the left in a variety of visuospatial tasks, including mirror image discrimination (Funnell, Corballis,

& Gazzaniga, 1999); simple perceptual discriminations, such as orientation, vernier-offset, and size discrimination (Corballis, Funnell, & Gazzaniga, 2002); and in temporal discrimination (Funnell, Corballis, & Gazzaniga, 2003). These studies led Paul Corballis to theorize a right-hemisphere interpreter (Corballis, Funnell, & Gazzaniga, 2000) that complements Mike Gazzaniga's left-hemisphere interpreter (Gazzaniga, 2000). Whereas the left-hemisphere interpreter makes sense of the cognitive and linguistic world, the right-hemisphere interpreter makes sense of the visuospatial world, with both making inferences and filling in missing information about their specialized domain. Corballis and his colleagues found evidence for such an interpretive process in the right hemisphere in a series of experiments on amodal completion (Corballis, Fendrich, Shapley, & Gazzaniga, 1999).

The notion of the right-hemisphere interpreter started with the discovery of basic perceptual differences between the two hemispheres, which then led to consideration of the higher-level implications of these differences. In the case of the left-hemisphere interpreter, the process was the other way around. Mike Gazzaniga introduced the idea of the left-hemisphere interpreter to explain the left hemisphere's propensity to make inferences and draw conclusions on the basis of incomplete information. It was not clear, though, what underlying processes might give rise to the left-hemisphere interpreter. An obvious place to start was language, since it was via language that the left hemisphere expressed its interpretive capacity. One way to begin answering this question is to look for hemispheric differences in the cognitive processes that might underlie or at least be related to the left-hemisphere superiority for linguistic processing, and therefore to the left-hemisphere interpreter.

Testing with split-brain patients is most often accomplished in the visual domain, because it allows the investigator to take advantage of the contralateral organization of the visual system. Presenting information briefly to one visual field ensures that only the contralateral hemisphere perceives the information. In split-brain patients, the corpus callosum is severed and so the hemispheres are unable to share information (although there is evidence of some low-level information transfer via subcortical pathways; see Corballis, 1995). In a lateralized-visual-field task, the responses of the two hemispheres can be compared to each

other to determine whether there is a hemispheric difference in the processing required by the task.

Since the modality was to be vision, the question was, what processes might underlie the cognitive processes necessary for left-hemisphere interpretation. In order to function effectively in our daily lives, we must be able to make sense of vast quantities of information. To do this, we rely on a variety of perceptual and conceptual processes. One aspect of perceptual processing is the ability to recognize objects, which is clearly an essential step in information processing. Being able to recognize an object, however, is not enough. It does not solve the problem of how to efficiently cope with the amount of visual information confronting us. This is where conceptual processing comes into play. Processing at the conceptual level allows us to recognize similarities and differences among objects, and to identify types of objects. The ability to divide the world into categories reduces the amount of information to be processed, thereby significantly increasing the efficiency of processing. In order to make complex categorical distinctions, for example, it is necessary to recognize concrete and abstract relationships among objects, represent objects conceptually rather than only perceptually, and remember these representations over time. These are some of the same conceptual processes that underlie language and maybe the left-hemisphere interpreter, and so I wondered whether they might also be lateralized to the left hemisphere.

A number of methodologies are available to study hemispheric differences in function. Research involving patients with unilateral brain lesions provided some of the first insights into these differences, and functional neuroimaging has added to that knowledge base. In addition, a number of studies have investigated the cognitive capacities of the two hemispheres of split-brain patients. In one such study, Teng (1998) found that both hemispheres were able to learn a discrimination task in which two rods were matched by either size or texture. When the contingency was reversed, however, a striking hemispheric difference emerged. The left hemisphere learned each reversal quickly, but the right hemisphere had significant difficulty when the contingency was reversed. This suggests that although both hemispheres are capable of learning a particular discrimination, only the left is proficient when the contingencies are altered. The ability to learn this type of discrimination relies on recogniz-

ing that objects can have similarities and differences along a number of dimensions. This process is clearly essential to the ability to make complex categorical distinctions. The right-hemisphere deficit evident when contingencies are reversed may reflect an overall deficit in the conceptual processes that underlie categorization.

After considering the possible building blocks of the left hemisphere's interpretive capacity, I elected to investigate hemispheric differences in the ability to form complex relational categories. Tasks of this sort involve recognizing and understanding abstract relationships between items rather than focusing on concrete characteristics. The ability to form relational categories relies on cognitive processes such as identifying dimensions of similarity, representing objects conceptually, and holding these representations in the mind during a delay. Although both hemispheres are equally able to identify similarities and to represent objects conceptually, the right hemisphere has difficulty switching between dimensions of similarity, suggesting that its representation of objects may not be as conceptually rich as that of the left hemisphere. To test this idea, J.W., a split-brain patient, participated in a series of experiments designed to assess the ability of the right and left hemispheres to form relational categories and to generalize this learning to other tasks.

J.W. was forty-seven years old at the time of testing. He had undergone a two-stage callosotomy at the age of twenty-five to control his epilepsy. A CT scan prior to the callosotomy revealed no evidence of any neurological abnormality. Postsurgical magnetic resonance imaging (MRI) confirmed that his corpus callosum was fully severed, and also revealed no evidence of any other brain damage (Gazzaniga et al., 1985). J.W. has an IQ within the normal range, completed high school, and has no history of any type of learning disability (Gazzaniga et al., 1985). To test each hemisphere individually, stimuli were flashed to either the right or left visual field for 150 ms. These arrangements ensure that stimuli were perceived only by the hemisphere contralateral to the visual field of the presentation. In addition, in this task, no verbal instructions were presented. Since the left hemisphere is specialized for language, providing verbal instructions would have given the left hemisphere an advantage over the right. Instead, when J.W. made an incorrect response, a loud tone sounded. Pre-testing with a different task demonstrated that both hemispheres were able to use auditory feedback to learn how to do a

computer-based task. Since neither hemisphere had the benefit of instructions and both were able to learn using auditory feedback, any hemispheric difference found in the task is likely to be the result of a true hemispheric difference rather than an artifact of the experimental design.

In the relational matching task, J.W. was shown a target pair in which the two items were either both the same color or were different colors. He was then presented with two pairs of probe items and was instructed to press the top key to select the top pair and the bottom key to select the bottom pair. The correct response was the one that demonstrated the same relation (i.e., same or different color) as the target pair regardless of the specific colors of the items (see figure 5.1, plate 2). As noted above, J.W. was provided no explicit instructions as to how to select the correct response pair, but when he responded incorrectly, a loud tone would sound. His left hemisphere was able to quickly and easily learn this task. In contrast, the right hemisphere showed no indication of learning even after 800 trials. Three weeks later, performance in both hemispheres was virtually identical to the original results (see figure 5.2).

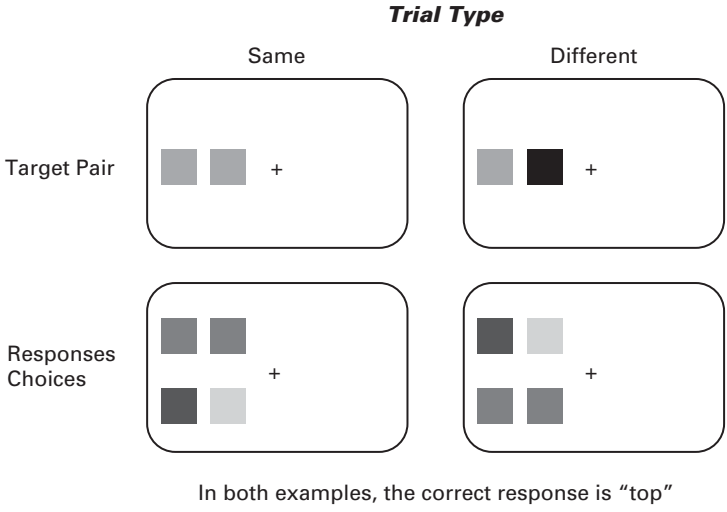

Figure 5.1 (plate 2)
Example of the stimuli for the relational category-matching task. The left-hand panel depicts a trial in which the squares in the target pair were the same color, and the right-hand panel depicts a trial in which the target squares were different colors. In both types of trials, the correct response is "top," as the two squares on the top are related to each other in the same way that the two target squares are related to each other.

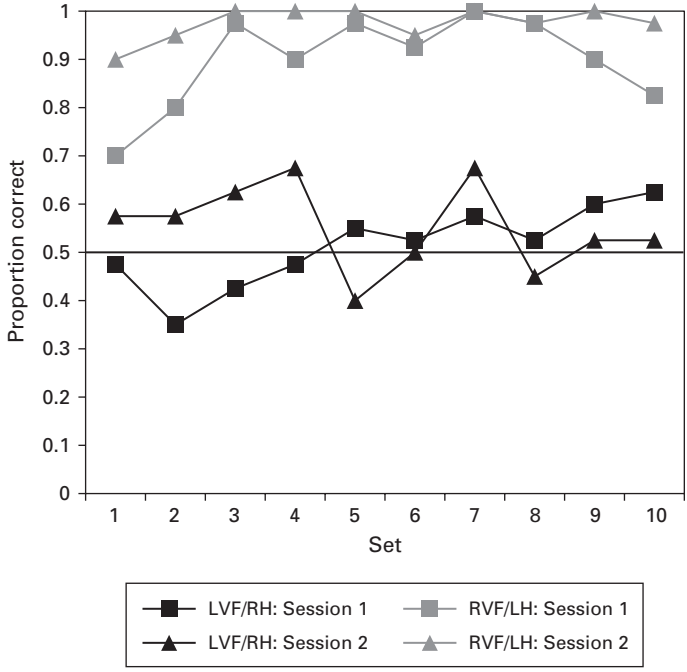

Figure 5.2
Accuracy data for the initial testing Sessions 1 and 2 were separated by one week, and J.W. completed ten sets of forty items per hemisphere in each testing session. Because these experiments involve analysis of single-subject data in which each hemisphere serves as a control for the other, the data were analyzed using multidimensional chi-squared analyses (Winer, Brown, & Michels, 1991) which allows higher-order interaction effects to be evaluated in a manner directly analogous to analysis of variance. J.W.'s left hemisphere performed significantly better than his right hemisphere (chi square = 265.86, $p < 0.01$).

So the right hemisphere couldn't learn the task on its own. But could it be taught to do the task with explicit training? An incremental training procedure was designed to explore this question. As in the initial test, J.W. was given no verbal instructions but received auditory feedback immediately after each response indicating whether he had been correct or incorrect. In the first stage, the target was a single item (e.g., blue square) and the response choices were two single items, one appearing above the other. One item was identical to the target and the other was a different color (e.g., red square). The identical item was the correct response. The right hemisphere learned this task within two sets. In the second stage of the training, the target was a pair of squares that were

the same color (e.g., two blue squares) and the response choices were two pairs of squares, one pair appearing above the other. One pair was identical to the target (e.g., two blue squares) and the other pair consisted of two squares that were different colors (e.g., one red square and one green square). The identical pair was the correct response. The right hemisphere learned this task immediately.

Both of the first two training stages involved matching by color. The third stage moved on to matching by relationship. The target was a pair of squares that were the same color (e.g., two blue squares) and the response choices were two pairs of squares, one pair appearing above the other. One pair consisted of two squares that were the same color as each other but not the same color as the target pair (e.g., two red squares). The other pair consisted of two squares that were different colors (e.g., one yellow square and one blue square). The pair with matching colored squares was the correct response. This task is identical to the original relational category task, except that the target pair never differ in color. In other words, J.W. was trained on the items for which the relationship was matching target squares, but not trained on those in which they were a different color. J.W.'s right hemisphere mastered this task within four sets.

During the training, the left hemisphere consistently performed at ceiling in all stages. The right hemisphere's performance was poorer than that of the left hemisphere in the initial part of each training stage, but it was capable of mastering each task. Following the three training stages, J.W. was retested on the initial relational category task. He completed four sets of this task, his left hemisphere performing significantly better than his right. His right hemisphere did show clear evidence of learning, however. Prior to training, the right hemisphere performed at chance, and after training, the right hemisphere achieved almost 80 percent accuracy.

Another question was whether this learning would be maintained over time. J.W. was retested in the relational category task, one week, one month, two months, and one year after the training and post-testing (see figure 5.3). At each of the first three time points, J.W. completed two sets of the relational categories test. At one year post-training, J.W. completed four sets of the task. At each time point, the left hemisphere's performance was at ceiling and was superior to the right hemisphere for

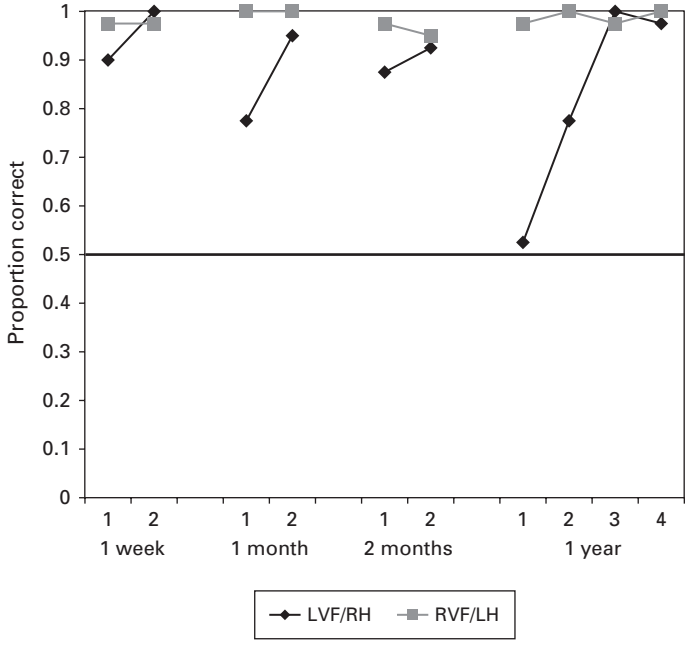

Figure 5.3
Accuracy data for post-testing on the relational category-matching task J.W.'s completed two sets of the task at one week, one month, and two months post-training. He completed four sets of the same task one year after the training sequence was completed. For the data from the one-year time point, the right hemisphere performed at chance on the first set, but showed rapid improvement on the subsequent sets and demonstrated mastery of the task on sets 3 and 4. The effect of set was significant (chi square = 11.62, $p < .01$) as was the effect of visual field (chi square = 9.31, $p < .01$) and the interaction between set and visual field (chi square = 10.99, $p = .01$).

every set. However, each time the right hemisphere was able to regain its post-training level of performance, suggesting that the right hemisphere may be relearning the task on each of the post-testing dates. This is particularly apparent at the one-year point. Although the right hemisphere initially showed no evidence of being able to do the task after one year, the rapidity with which it relearned the task suggests that some knowledge of the task was maintained over time, although this knowledge was not immediately accessible.

J.W.'s left hemisphere was able to learn the relational-category task rapidly without incremental training or explicit instruction. His right hemisphere required incremental training, but did learn the task. Both

hemispheres showed evidence that some degree of learning was maintained over time. The next issue was to determine whether the two hemispheres simply learned how to do the relational category task using colors, or whether a more abstract comprehension of the task was achieved. To find out, J.W. was tested in three relational category tasks similar to the color task. Instead of the key relationship being color, however, it was different in each of the three tasks. In the first task, the stimuli were all squares but the same/different relationship was based on the texture. In the second task, the stimuli were all the same color but had different shapes—for example, circle, square, triangle. In the third task, both the shape and the color of the stimuli varied, but the same/different relationship was based only on color, and the shape of the stimuli was irrelevant to the task. Aside from the change in stimuli, the tasks were identical to the initial task. J.W.'s right and left hemispheres were able to successfully perform the texture and shape relational-categories tests. Although the right hemisphere initially had difficulty with the task, it quickly learned the task requirements. Overall, the pattern of results in the three generalization tasks indicates that once the two hemispheres learned the relational category task (the right required specific training to learn it whereas the left did not), they were able to generalize this learning to stimuli that varied along other dimensions.

To summarize, the left hemisphere was able to quickly learn the relational category task based on auditory feedback with no explicit instructions. In contrast, the right hemisphere showed no evidence of learning, even after 800 trials. With explicit incremental training, however, the right hemisphere was able to learn the task. Post-test performance of the right hemisphere was significantly better than chance, but still not at the level of the left hemisphere's performance. In addition, testing at later time-points suggests that the right hemisphere's learning was not as well maintained as that of the left hemisphere. One year after the initial testing, the left hemisphere showed no decrement in learning; the right hemisphere performed poorly initially at follow-up time points, but did relearn the task each time.

Why does the right hemisphere have so much more difficulty learning a relational-category task than the left? I suggest that this hemispheric difference is the result of the difference between the two hemispheres in the capacity for linguistic processing. Linguistic capability requires sym-

bolic representation and rule-based learning. The ability to associate an arbitrary sound or symbol with an abstract concept is essential to forming a lexicon, and rule-based learning is critical for syntactic comprehension because grammar is essentially a system of rules. Understanding and forming relational categories involves recognizing the abstract relationship between the two items in the pair and learning the rule that links them. Although this is not specifically a linguistic task, it relies on some of the same conceptual processes as language.

Evidence that linguistic ability may be related to the formation of complex relational categories can be inferred from studies with nonhuman primates. Information processing at the perceptual level is highly similar across species, but this is not the case at the conceptual level. There are significant interspecies differences in the type and complexity of conceptual processes that can be brought to bear on the processing of incoming information. The evidence from investigations of the cognitive components underlying categorization suggests a phylogenetic progression, with primates possessing the greatest capacity for making complex categorical distinctions. Even great apes and chimpanzees, however, are unable to make the higher level, multidimensional and complex distinctions that are routine for adult humans. It has been argued that nonhumans, including higher primates, are unable to make these higher-level and more complex distinctions because they lack the linguistic capabilities that are uniquely human (Cartmill, 1994).

Formation of complex relational categories relies on learning the abstract demands of a task rather than a specific response. No nonprimate species has demonstrated this ability (D'Amato, Salmon, & Colombo, 1985) but there is evidence that non-human primates are capable of learning a relation-matching task, which is one of the building blocks of the ability to form complex relational categories (Premack, 1983, with chimpanzees; Burdyn & Thomas, 1984, with squirrel monkeys; Smith, King, Witt, & Rickel, 1975, with chimpanzees). To better characterize the relationship between linguistic ability and the ability to form relational categories, Oden, Thompson, and Premack (1990) compared the performance of chimpanzees with and without formal language training. Chimpanzees who had no formal language training performed at the same level as a chimpanzee who had formal language training. The non-language-trained chimpanzees, however, did have experience with

arbitrary tokens that were consistently associated with abstract relations. The critical factor in understanding and forming relational categories, therefore, seems not to be language per se, but rather the ability to associate an arbitrary symbol with an abstract concept. Because language by definition involves associating arbitrary symbols with abstract concepts, formal language training results in improved performance on relational matching tasks, but language training is not necessary for understanding and forming relational categories.

It is well established that the left hemisphere in most right-handed humans is specialized for language. The right hemisphere, however, is not wholly without linguistic capacity (see Baynes, chapter 4 in this volume). Evidence from neuroimaging studies and patient populations has demonstrated that the right hemisphere has a lexicon and is capable of making semantic judgments about words, but is impaired in syntactic abilities (Gazzaniga, Smylie, Baynes, Hirst, & McCleary, 1984). Because the right hemisphere has a lexicon, it is clearly capable of associating arbitrary symbols with concepts. Its lexicon is not, however, as extensive as that of the left hemisphere, and there is also evidence that its lexicon is organized differently. Beeman and his colleagues found that, given a word, the right hemisphere weakly activates a large number of directly and indirectly related concepts. In contrast, the left hemisphere activates only concepts closely related to the input word (Beeman, 1993; Beeman et al., 1994; see also Gazzaniga & Miller, 1989). This may in part account for the right-hemisphere deficit in the formation of relational categories. The way the two hemispheres represent objects and the similarities among them appears to be fundamentally different. Categorical distinctions in the right hemisphere may be less tightly constrained than those of the left, and therefore associations of symbols with concepts may be less well determined.

The hemispheric difference in associating symbols with concepts and in extrapolating and applying rules may explain why the right hemisphere does not have the same sort of interpretive capacity that the left hemisphere possesses. These capabilities also underlie language, thus linking linguistic capacity with the left-hemisphere interpreter. The right hemisphere, however, has its own, albeit different, interpretive capacity that the left hemisphere does not possess. The right hemisphere, but not the left, is able to fill in missing information and draw conclusions about

visuospatial information. This right hemisphere capacity for interpretation in the visuospatial domain is likely based on its superior visuospatial processing abilities. In the intact brain, these two interpreters work together seamlessly to make sense of the world around us. It is only when the corpus callosum is severed that each hemisphere's contribution to our sense of personal unity is revealed.

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II

The Integrated Mind

Integrated Mind
From what is known of brains split
scientists can infer the integrated it.
In the neural codes traversing callosal roads
informational balance maintained
neural operations constrained to interact
via a silent pact from which emerges a sense of free will and unity
that governs each (hu)man's mentality
purging disharmony from a large modular community
and creating its own personal view of reality.

6

From the Integrated Mind to the Emotional Brain

Joseph LeDoux

"There's not much work on emotion in brain science these days." With those words, uttered in 1976 or thereabouts, Mike Gazzaniga set me on the career path that I remain on today.

Why did Mike's statement, probably in a bar somewhere over a glass of Jack Daniels, have such an impact? First of all, Mike was my Ph.D. adviser at the State University of New York, Stony Brook. I adored him, so everything he said had an impact on me. But there must have been more, since I didn't become a Young Republican. Another factor was that I had taken a biology seminar with Harvey Karten on the comparative anatomy of the brain. Harvey waxed wild on lots of topics, and one afternoon spent quite a while telling us why we should not study the visual system or the hippocampus, since those systems were already overpopulated with researchers. "Find something that nobody's doing, and make your mark there." I thought at the time that Harvey's suggestion made sense, but how do you actually find that mysterious topic that is unstudied yet important enough to spend your time on? Mike's comment filled in the blank.

But there was something else. I happened to be really interested in topics such as emotion and motivation. The way I got into science and found my way to Stony Brook was through Robert Thompson, a professor of psychology at Louisiana State University. While working on a master's degree in marketing, I took Thompson's course "The Brain Mechanisms of Motivation and Memory." Thompson had worked with Karl Lashely, the father of modern behavioral and cognitive neuroscience. Thompson was searching for the locus of memory in the brain, mainly through tasks that were motivated by fear, and I ended up working in his lab. My favorite project involved a

comparison of the effects of brain lesions on learned versus innate fear responses.

Thompson's letter of recommendation got me into the Ph.D. program in psychobiology at Stony Brook, even though I had no academic preparation for this field of study. But once at Stony Brook, I put my interest in emotion and motivation aside, at least for a while. Cognition was king then, and I turned my attention there. But Mike's casual statement about emotion, which came toward the end of my graduate career, made me think I could study what I was most interested in rather than just doing what was popular at the time. In this chapter, I summarize how Mike helped me achieve this goal.

Updating the Bisected Brain

Mike Gazzaniga was not my original adviser at Stony Brook. Although I had gone there to study the brain, I had, unbeknownst to myself, been accepted into the program by a researcher who did ethological studies of primate behavior. Although he was a well-known researcher, this was not what I wanted to do.

I had become friendly with Nick Brecha, who was a second-year student working in Mike's lab. He gave me one of Mike's papers, an article in *American Scientist* about split-brain research (Gazzaniga, 1972). I was blown away by this article, and desperate to join Mike's lab. Nick made the introductions. Mike later told me he almost told me to "take a hike." I had shoulder-length hair, which probably rubbed his conservative side the wrong way, and I also reminded him of someone he didn't like. But he was busy, always traveling, and took a trip before he could dismiss me. While he was gone, I wrote a two-page summary of what I wanted to do in his lab (look at the effects of cutting the anterior corpus callosum on the acquisition of learning sets in monkeys). When he returned I gave him the proposal. He liked the experiment okay, and agreed to let me pursue it. But what he really liked was the fact that I had written it up and, I guess, that it was coherent.

A few days later he called me into his office. He told me that his book *The Bisected Brain* (Gazzaniga, 1970) needed updating and asked if I would be interested in being a coauthor. So here I was, maybe two months into my graduate career in psychobiology after having had no

previous training in science and my Ph.D. adviser was asking me to coauthor a book with him.

Mike has a strong Italian background. He believes in family. And once you were in his family, you were special. This worked in two ways. He saw you as special and treated you that way. But also, you began to see yourself as part of his family. And that was indeed a special feeling.

I think we both thought the rewrite of the book would be a simple updating job. I'd do my monkey study and in my spare time would add a little to each chapter and that would be that. But soon things changed.

From *The Bisected Brain* to *The Integrated Mind*

To get me started on the monkey project, Mike turned me over to Richard Nakamura. Richard was a cigar-smoking senior graduate student and lab chief (in those days you could smoke in buildings, and even in labs, while doing experiments). Richard patiently began to teach me how to do primate brain surgery (or a least the preparation, since the actual cutting of the corpus callosum was usually done by Mike). He also showed me the ropes of behavioral testing of monkeys. I remain very friendly with Richard, who is now in charge of the intramural research program at the National Institute of Mental Health.

A few months into the monkey study, Mike asked me how it was going. I told him it was going okay, but was very slow, and we hadn't gotten very far. He knew this already, as it was the basis for what he was going to say next. He asked if I would be interested in switching to the human split-brain project. The students working on that would be graduating and he needed someone who was at the beginning of his graduate career to take over. I wasn't overly enthusiastic about this, as I really liked the precision of animal work compared to studies of human clinical patients. At the same time, I realized this was a unique opportunity, since so few people had ever seen a split-brain patient. So I accepted his offer and switched over to the patient work. Gail Risse, another graduate student, helped get me started.

Pretty soon after joining the project, several new patients underwent split-brain surgery at Dartmouth to control their epilepsy. Until this point, the patients coming out of Dartmouth were not suitable as a

scientific subject population. But the new patients seemed to open up new research opportunities. We started making monthly trips up to New England to study these patients at their homes, parking our mobile test lab (a camper trailer pulled behind a bright orange Ford van) in their driveways.

Patient P.S. was especially important. He could use both sides of his brain to read but only the left hemisphere to speak. Previously, the right hemisphere had been thought of as a lesser partner, with cognitive capacities like a monkey's or chimp's, but not like a human's. The left hemisphere clearly had self-awareness, but whether high-level conscious was possible on the other side as well seemed dubious. With P.S. we were able to ask whether the right side was self-aware because his right hemisphere could read. So we flashed questions to his right hemisphere and his left hand would reach out and, using Scrabble tiles, spell the answers. In these simple tests we found out that P.S.'s right hemisphere had a sense of self (he knew his name) and had a sense of the future (he had an occupational goal), both important qualities of conscious awareness. It was particularly interesting that the right and left hemispheres had different goals for the future. Might there indeed be two people in one head?

In the process of testing the interactions between the two sides, one day in our camper trailer lab Mike made an important observation. We were giving the right hemisphere written commands (stand, wave, laugh), and P.S. responded appropriately in each case. Had Mike not been there that's probably as far as it would have gone. We would have been happy to have shown that the right hemisphere could respond to verbal commands. But Mike's incredibly fast and creative mind immediately realized there was more to it. He started asking P.S. why he was doing what he was doing. Remember, only the left hemisphere could talk. So when the command to the right hemisphere was "stand," P.S. would explain his action by saying he needed to stretch. When it was "wave," he said he thought he saw a friend. When it was "laugh," he said we were funny. That was the birth of Mike's theory of consciousness as an interpreter: a reason for doing these things was made up to justify the impulse to take a certain action.

This led to more experiments to directly test the idea. On the next trip we simultaneously presented different pictures to the two hemi-

spheres and told him to point to the card that matched the pictures. In the classic example, we presented a snow scene to the right hemisphere and a chicken claw to the left. The left hand pointed to a card picturing a chicken and the right hand to a card picturing a shovel. P.S. explained his choices saying he saw a chicken claw so he picked the chicken, and you need a shovel to clean out chicken shit in the shed. The left hemisphere, in other words, used his behavioral responses as the raw data to concoct an interpretation that was then accepted as the explanation of why he did what he did.

For the left hemisphere of a split-brain patient, everything done by the right hemisphere is an unconscious act. Mike proposed that our behaviors are controlled by systems that function unconsciously, and that a key function of consciousness is to make sense (interpret) our behavior. This was his theory of the interpreter. I'll discuss what influenced Mike to have this view later.

We made trips to New England regularly, and studies of these patients, especially P.S., were generating data fast and furiously. As the data rolled in, and the new ideas such as conscious interpretation of unconscious behavior, began to emerge, it became obvious to us that a simple updating of *The Bisected Brain* was not the way to go. *The Bisected Brain* had described the ways that behavior is affected when the brain is split. It was all about the split brain. But the new studies we were doing, and especially the ideas that were emerging (mostly from Mike) to explain the data, were suggesting how information from split-brain patients helps us understand how the mind and brain normally work. So our idea (I think this one may actually have been mine) was to give the new book a title that would directly contrast with *The Bisected Brain*. That, of course, was *The Integrated Mind* (Gazzaniga and LeDoux, 1978).

Each chapter was on a topic we had been studying, including interhemispheric transfer of sensory processing, language and cognition, emotion, and consciousness, to name some. I struggled to write these chapters in interesting and creative ways. I'd end up with a draft, and Mike usually had to rewrite it to make it work. Still, when we went to the publisher with the final product, he argued strongly that I should be the first author. The editor would have none of that. He had commissioned Gazzaniga, and he wanted Gazzaniga's name up front. I actually

felt better about that since it was really Mike's creativity that made the book what it was.

The Social Psychology Connection

In his quest to find connections between things, Mike often took the approach of hooking up with some really smart people and trying to learn from them. As a graduate student at the California Institute of Technology he put on debates and became a lifelong friend of William F. Buckley. Mike shared Buckley's political convictions, and Mike from time to time would call on Buckley for advice on various matters. But he also became friends with liberals too—the comedian Steve Allen, for example.

But Mike's academic friends are more relevant here. One was David Premack. In the 1970s Mike turned Premack's (1962) theory about the relative nature of reward into a split-brain experiment. Later, when Premack began to study chimp language, Mike adopted some of Premack's techniques as a way of helping aphasic patients learn to communicate.

The psychologist who probably had the most influence on Mike was Leon Festinger, a social psychologist who in the late 1950s had proposed the theory of cognitive dissonance (Festinger, 1962). I believe that Mike and Leon became friends when Mike was at New York University just before moving to Stony Brook. NYU is a few blocks from the New School, where Festinger worked. According to Festinger's theory, when we find ourselves in a situation where we have competing or apparently inconsistent thoughts or behaviors, a state of dissonance results. Because dissonance is unpleasant, we are motivated to try and explain what is going on and to do things to reduce it. Mike's theory of the interpreter, based on the observations about left hemisphere of split-brain patients confabulating explanations of right-hemisphere-produced behavior, was a direct extension of cognitive dissonance theory. Mike's book *The Social Brain* (Gazzaniga, 1985) clearly reflects these influences, as does his later book, *Mind Matters* (Gazzaniga, 1988), which laid our the interpreter theory in detail.

Mike's friendship with Festinger is all the more interesting given that Festinger was a diehard Greenwich Village lefty. But that's how Mike

was and is—a wonderful combination of strong opinionated and open-mindedness. When intelligence is pitted against politics, the former wins every time for him.

Back to Emotion

One of the studies we did on P.S. was especially important in shaping my future work. We presented words with emotional significance to him to either the left or the right hemisphere. The words were either commonly accepted words with good or bad connotations—such as Mom, God, devil—or things he often talked about —the name of a girl he had a crush on, President Nixon. Regardless of which hemisphere saw the word, P.S. was required to give a verbal rating of the word on a five-point scale, ranging from "like very much" to "dislike very much." When the stimulus was seen by the left hemisphere, the rating was a straightforward evaluation of the word. But when the word was presented to the right hemisphere, the left hemisphere protested that it saw nothing. So we asked him to just take a guess about the rating. The ratings overlapped remarkably. Even though the left hemisphere did not see the word it nevertheless seemed to have access to the emotional significance of the word.

How did this happen? It's important to digress for a moment and consider the nature of neuroscience at the time. The field had long been mired in a debate about whether brain functions were localized or distributed. These were mutually exclusive ideas in the age when most data about brain function came from people who had brain lesions. The split-brain work helped shift the emphasis to connections between areas rather than areas per se. Norm Geschwind, the world's leading behavioral neurologist, had been promoting the idea that many neurological disorders could be understood in terms of disconnections between brain areas. Mike turned me on to Geschwind's review in *Brain* on disconnection syndromes (Geschwind, 1965a, 1965b). I studied this paper endlessly, and was particularly fascinated by his discussion of a study by Weiskrantz (1956). He found that damage to the amygdala, a region deep in the temporal lobe, disrupted the ability of monkeys to link stimuli to their rewarding or aversive consequences. Damage to the amygdala disconnected stimulus and emotional processing. Mort Mishkin pursued

these ideas in a series of studies in monkeys in the 1970s (Jones & Mishkin, 1972; Mishkin & Aggleton, 1981).

Back to P.S. In P.S. and other patients in the Dartmouth series of split-brain surgeries, certain parts of the cerebral commissures were left intact in an effort to minimize the extent of the surgery and reduce potential side effects. In particular, in P.S. the anterior commissure had been left intact. This structure interconnects regions of the temporal lobe, including the amygdala. Having read Geschwind, Weiskrantz, and Mishkin, it seemed possible that in P.S. the words were semantically processed in the right hemisphere and this led to the activation of the right amygdala. The right amygdala then sent a signal, via the anterior commissure, to the left amygdala. The left hemisphere then used this signal to assign a rating to the stimulus.

We were very excited about this possibility because is suggested that there are different pathways in the brain for processing the cognitive representation of a stimulus and the emotional significance of the same stimulus. The leading theory about emotion at the time was Stanley Schachter and Jerome Singer's cognitive theory (Schachter and Singer, 1962), which proposed that emotion is a cognitive interpretation of nonspecific emotional cues. In this theory, joy and fear involve similar physiological states in the brain and body and what distinguishes these is one's cognitive interpretation of the nonspecific state. Schachter and Singer were, like many social psychologists, greatly influenced by Festinger, and theirs was a kind of dissonance theory since it proposed that the nonspecificity of emotional arousal created a state of dissonance and that through cognitive interpretation of the social context we explain why we are emotionally aroused, thereby reducing the dissonance. Our results, on the other hand, suggested instead that there is specific encoding of different emotional states within the brain.

But it's important to distinguish two things about emotion at this point. The Schachter-Singer theory was really about feeling states and was thus a theory of emotional consciousness. But our findings were instead about how emotional stimuli are processed unconsciously in the brain and how such unconscious processing might then contribute to conscious feelings. Conscious feelings, we felt, were, in the tradition of Festinger and Schachter and Singer, a left-hemisphere cognitive and

language-based interpretation. Thus, we were refining rather than rejecting the cognitive view.

The Emotional Brain

Given my prior interest in emotion, the emotion study in P.S. started me on my career. But I was pretty certain I didn't want to pursue this research in humans, since the tools for doing any kind of detailed study of the human brain were very limited at the time. So I returned to animal research. My work on fear mechanisms in the rat for the past twenty-plus years are all a footnote to ideas that germinated under Mike's mentorship. This work eventually led to a book, *The Emotional Brain* (1996). Mike was a master book writer, and always encouraged me to write my own book. So following his lead, I did just that.

Thanks, Mike

The rest of the story is about me rather than Mike, so I'm going to stop here, at least for now. I just want to close with a great big hug to Mike. He's been a mentor and friend for a long time, and I value him in both roles. Thanks, Mike. You're the best.

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7

Mike's Attentional Network

Alan Kingstone

Contrary to popular belief, the price of admission into Michael Gazzaniga's network in the early 1990s was a dime. I had recently received my Ph.D. from the University of Manchester, England, and had moved from there to Halifax, Nova Scotia, to work with Ray Klein at Dalhousie University. With Ray my interest in doing research on human attention grew, and with it, a desire to test individuals with disorders in human attention. Ray suggested that I contact his former supervisor, Michael Posner, for advice on where I might find a spot to get some experience doing research with patients, and Michael Posner pointed me toward Michael Gazzaniga, noting that there was no better place to go than Michael Gazzaniga's lab for this type of research experience.

So in the blissful ignorance bestowed upon the very young, and those that hold Ph.D.s, I picked up the telephone, used my dime, and called Michael Gazzaniga. He answered, and deduced in about one millisecond that I didn't know anything about the brain and its relation to human cognition. The conversation went something like this:

Mike: Do you know anything about the brain? [This, I was to learn, is classic Michael; he cuts straight to the heart of an issue, or as was often the case where I was concerned, the weakness of an issue.]

Alan: No. [This was not going the way I had hoped!]

Mike: Don't you think that's a problem?

Alan: No. I'll learn.

Mike: Come on down. Lets see what you've got to offer.

Truly. That was it. A short time later I found myself flying to Montreal, and then catching a train on a beautiful spring morning through the magical countryside of Vermont down into White River Junction. From

there it's just a ten-minute cab ride to Dartmouth College, in Hanover, New Hampshire. And by the time I stepped out of the cab and onto that truly remarkable Ivy League Dartmouth Campus—a campus that manages to blend the old and new together in such a seamless manner—I was completely and absolutely sold. And I began to suspect the truth—that my life had already begun to change forever, and for the better.

The next day I set off for Mike's lab. At that time, in the early 1990s, Mike and his team were conducting their research in a white clapboard, side-gabled house that had been built by Mrs. A. Pike in 1874. There at Pike House I met several of the future stars in cognitive neuroscience: people like Patti Reuter-Lorenz and Ron Mangun, and of course, Michael Gazzaniga himself. He had me give a little talk to his group, and then whisked me off to an elegant French restaurant, where he offered me a spot in his lab. "Say yes, and come do your thing" was his offer. I accepted of course. We shook hands, and that was that.

Research

I was now part of Mike's research team. And, as I was to discover, part of his incredibly extensive and loyal research network. In this world everything seems possible. Literally every week a world-class scientist would come through the lab, hang out, and work. The opportunity to chat with them over lunch, or at Mike's house for dinner, lent itself to a relentless stream of new thoughts, questions, and ideas. I had truly never been in a more intellectually rich and stimulating world!

In this environment one is drawn to the lab. Patti Reuter-Lorenz (who was soon off to a faculty position at the University of Michigan), Bob Fendrich, and Ron Mangun were three individuals who immediately stepped forward and helped me get my research with split-brain patients up and running. They were each fantastically generous with their time and gave me many invaluable "tricks of the trade" tips for testing split-brain patients. The greatest help, however, came from the writings of Jeffrey D. Holtzman, a young scientist and close friend of Mike's. In the 1980s Holtzman conducted a number of ingenious attention research studies on split-brain patients and found that the two disconnected hemispheres shared a common attentional system. Tragically, he died

very suddenly and I never had the honor of meeting him. But by reading Holtzman's papers I came to admire and respect his research immensely. As I shall discuss, Holtzman and Gazzaniga's work defined the attention issues that would be studied for decades to come.

When the corpus callosum is surgically sectioned for the relief of intractable epilepsy, all major cortical connections between the two hemispheres are severed. Subcortical structures such as the superior colliculus and the thalamus retain their interconnections, though these are much less extensive than the corpus callosum. Studies of these patients can tell us about the functions each hemisphere carries out independently of the other. In the absence of an intact corpus callosum, any activities that require integration between the hemispheres must now rely only on intact subcortical connections. These patients have been studied to understand lateralization of function in processes such as speech, emotion, memory, and perceptual processing, and, in the ground-breaking work of Holtzman and Gazzaniga, human attention.

Most split-brain patients possess language only in the left hemisphere. The few who possess language in both hemispheres provide a unique opportunity for cognitive abilities to be compared between the hemispheres. Although language comprehension exists in both hemispheres, language production is typically restricted to the left hemisphere (in other words, the right hemisphere is mute). Visual information presented entirely in one visual field projects exclusively to the opposite, or contralateral, hemisphere. In other words, stimuli presented in the left visual field (LVF) are seen exclusively by the right hemisphere, while stimuli in the right visual field (RVF) project directly to the left hemisphere.

This remarkable disconnection between the hemispheres raises the possibility that a split-brain patient might actually outperform intact subjects in situations where the information presented to the two hemispheres might normally cause confusion. Holtzman and Gazzaniga (1985) presented the split-brain patient J.W. with one 3×3 matrix positioned in each visual field. On each trial an X was flashed sequentially in four of the nine cells in each matrix. The pattern in the two fields could be either the same (redundant condition) or different (mixed condition). Subsequently a probe sequence appeared in one matrix and the subject was required to respond, by pressing a key, indicating whether the probe pattern matched the stimulus pattern that had just occurred

in that matrix. Comparison subjects with fully connected hemispheres responded correctly about 90 percent of the time for the redundant condition but they were at chance in the mixed condition. In contrast, J.W. performed at about 75 percent accuracy in both conditions. Because of his disconnection the split-brain patient did not benefit from the redundant information between the visual fields and so he performed worse than the controls; but he did not suffer from the conflicting information in the mixed condition and so here he outperformed the controls. It appears as if for the split-brain patient each hemisphere was functioning on its own, neither benefiting from corroborating information from the other hemisphere nor questioning conflicting information. At first glance, the split-brain patient appears to have attentional resources at his disposal that are not possessed by subjects with intact brains.

A Paradox

It is unlikely that sectioning the corpus callosum in and of itself would increase the attentional capacity of the subject. However, it is possible that after disconnecting the hemispheres, each hemisphere would come to control its own attentional network. Research on this issue had revealed a paradox.

To investigate the independence of attentional processing in the disconnected hemispheres, Holtzman, Volpe, and Gazzaniga (1984) tested split-brain patients in a spatial cuing experiment in which the left hemisphere was cued (by a left- or right-pointing arrow) to orient attention to the LVF or RVF, while the right hemisphere was cued simultaneously (with a left- or right-pointing arrow) to direct attention to the LVF or RVF. Results showed that the time to respond to a visual target was delayed when the two hemispheres received different attentional instructions than when the two hemispheres received the same cues (that is, two left-pointing arrows or two right-pointing arrows). This indicated to Holtzman that the disconnected hemispheres share a common attentional system (see also Holtzman & Gazzaniga, 1982).

However, Luck, Hillyard, Mangun, and Gazzaniga (1989, 1994) subsequently produced data that bring this conclusion into question. They found that split-brain patients can search through visual displays twice as fast as healthy observers when items are divided evenly between visual

fields, as though each disconnected hemisphere possesses its own attentional search system. Armed with the knowledge that both findings are valid, these studies raise a paradox: How can the disconnected hemispheres share a common attention mechanism (as suggested by Holtzman & Gazzaniga, 1982, 1985) and yet orient attention independently (as suggested by Luck et al., 1989, 1994)?

A Solution to the Paradox

The clue as to how these studies could be reconciled was provided by Reuter-Lorenz and Fendrich (1990). In their experiment, split-brain patients fixated a central dot on a computer screen that displayed four empty squares. The squares were aligned in a row on the horizontal axis with two squares to the left and two squares to the right of fixation. One of the squares was brightened briefly (a peripheral cue) and then after a delay of a half second an X was presented at the location of one of the squares. The split-brain's task was to push a button when an X was detected. The box that brightened (that is, the cue) correctly indicated where the X would occur on 70 percent of the trials, and on the remaining target trials the X appeared with equal probability at one of the three uncued locations (10 percent probability at each location). The uncued location could be in the same field (hemisphere) as the cue, or in the opposite field (hemisphere). Results indicated that split-brain patients were fastest to respond to a target at the cued location, and were slowed, in a way that was normal for intact observers, when the target appeared at an uncued location that was in the same field as the cue. However, when the target appeared at the uncued location in the opposite field, there was an unusually large delay in responding to the target for the split-brain patients. These data are consistent with Holtzman and Gazzaniga's idea that the two hemispheres share a common attention system, in that orienting attention by one hemisphere compromises the performance of the other hemisphere. However, in a final experiment, Reuter-Lorenz and Fendrich (1990) repeated their experiment, but on this occasion the cue did not predict where the target would appear, that is, the target onset had a 25 percent chance of appearing at any given location regardless of whether that location it was cued or not. Performance was again best when a target appeared at the cued location, but now the

performance for targets at uncued locations was comparable between the visual fields. Reuter-Lorenz and Fendrich concluded that each hemisphere could independently deploy attention when a target was equally likely in each visual field. In contrast, when the probability of a target was high at a cued location, the two hemispheres acted as if in competition for the same attentional system.

The Reuter-Lorenz and Fendrich (1990) study draws a distinction between attending to a location because a cue indicates that there is a high probability that a target will occur there, and attending to a location despite the fact that a cue indicates a target is no more likely to occur there than anywhere else. The former type of orienting is said to be driven in a top-down manner by strategic, volitional attention processes; the latter is said to be driven by bottom-up involuntary attentional processes. Is it possible that the paradox in the split-brain literature reflects a difference between the attentional processes that have been activated, such that top-down orienting involves competition between the hemispheres, but automatic orienting is performed independently?

Kingstone, Enns, Mangun, and Gazzaniga (1995) tested this idea by extending the Luck et al. (1989, 1994) search investigation. Recall that Luck and colleagues found that split-brain patients search through visual displays twice as fast as normal observers when items are divided evenly between visual fields, as though each disconnected hemisphere possessed its own attention system for performing visual search. Kingstone and colleagues (1995) replicated this standard search effect and extended it by including the possibility for what is called strategic or "smart search," that is, the selection of a small number of candidate targets on the basis of their shared feature information (Egeth, Virzi, & Garbart, 1984). Figure 7.1 illustrates the difference between standard and "smart search" displays (as well as the difference between bilateral (figure 7.1a) and unilateral (figure 7.1b) displays). Note that in figure 7.1a the target, a black circle, is hidden among roughly an equal number of black square and gray circle distractors (this is standard search). However, in figure 7.1b, it takes less time to find the black circle target because it can be found simply by smart searching among the small set of four black square distractors (excluding the large set of eleven gray circles). Smart search occurs when a target can be found efficiently by applying this strategic form of scanning.

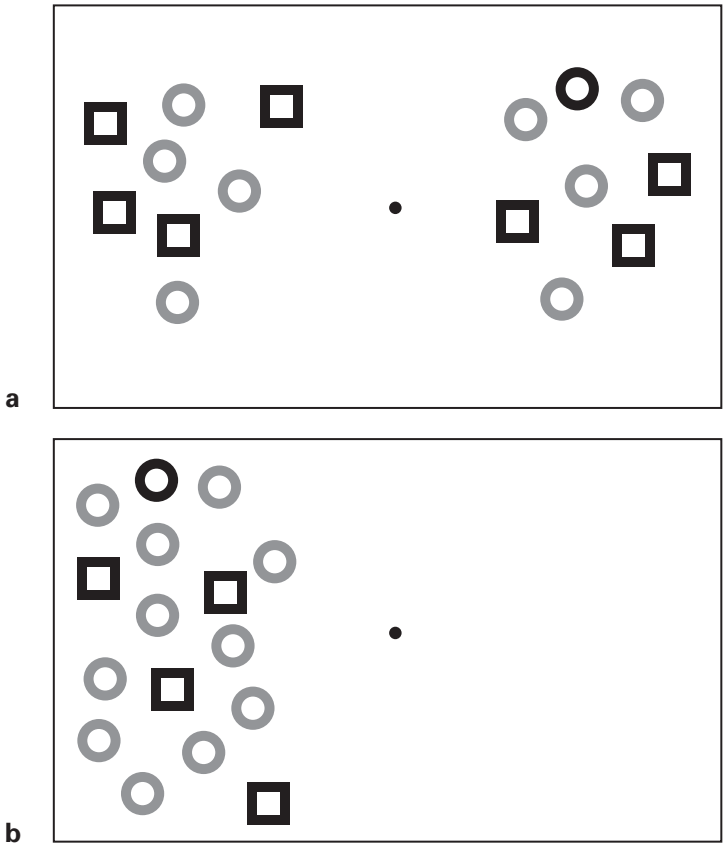

Figure 7.1
Arrays used to test searching behavior for a black circle. A bilateral standard search array (top panel, a) and a unilateral guided search array (bottom panel, b) are shown for a black circle target with display size equal to 16 (these samples are not to scale).

For split-brain patients, but not for comparison subjects, the search rate for unilateral displays was twice that for bilateral displays, consistent with Luck et al. (1989, 1994). However, Kingstone et al. also found that the means by which each split-brain hemisphere searched its respective field differed. When provided with the opportunity to perform smart search, only the left hemisphere seized this opportunity.

One interpretation of these findings is that strategic search is the unique property of the left hemisphere. An alternative interpretation, motivated by Reuter-Lorenz and Frendrich (1990), is that lateralization

of strategic search to the left hemisphere may actually reflect competition between hemispheres for volitional control of attention. The right hemisphere may be *capable* of engaging in smart search, but it may be actively inhibited from doing so when the dominant left hemisphere is employing this function. This idea was tested by re-running the guided visual search experiment with the split-brain patient J.W. and eliminating the opportunity for the left hemisphere to perform smart search (accomplished simply by eliminating all the guided search displays presented to the RVF). Remarkably, J.W.'s right hemisphere was now found to perform strategic guided search behavior!

In sum, the paradox in the split-brain literature reflects a difference between the attentional processes that have been activated. Top-down volitional control results in competition between the hemispheres, and that control is preferentially lateralized to the left hemisphere. Automatic bottom-up attentional orienting can be performed independently by the two hemispheres.

A General Principle of Split-Brain Performance

One day Mike gave a talk to the lab about the split-brain patients that he had tested in the past. One video showed a clip of a patient seated before a computer screen, where two words were shown on the screen: the left hemisphere received the word "clock" and the right hemisphere received the word "six." The task for the split-brain participant was to draw, with the left hand, what word or words had been shown. The subject picked up the pen in his left hand and drew a picture of a clock and then he set the time at 6. This video clip suggested to us all that the information for the two words had, remarkably, been shared between the two hemispheres and then drawn by the left hand (right hemisphere).

But maybe not. Mike and I met the next day and entertained an alternative. What if the sharing of that information between the hemispheres was just an illusion? Instead of combining the word information between the left and right brain each hemisphere was simply drawing what it had been shown on the paper, so that the only place the information had really been shared was in the outside world on the paper. To test this idea we created a bunch of words that could be combined liter-

ally on the paper, or integrated in the mind to create a very different item to be drawn. For instance, the two words "hot" and "dog" could be drawn separately and integrated on the paper as a dog with the sun shining overhead. Alternatively, the words could be combined in the brain and drawn as a frankfurter. When we tested a split-brain patient the results were perfectly clear. For word pairs like "hot" and "dog," "fire" and "arm," "toad" and "stool," and "sky" and "scraper," the participant never produced a picture of a wiener, a gun, a tall building, or a mushroom. When the two were drawn, they were always depicted literally (see figure 7.2; Kingstone & Gazzaniga, 1995). In the "clock" plus "six" case, the integration between the hemispheres was an illusion. It had only occurred on the paper.

This fascinating result holds another gem that tends to be overlooked. Whether or not two words were drawn depended on which hand held the pen. When the right hand (under left-hemisphere control) held the pen, one word was drawn—the left hemisphere's word. The right hemisphere was blocked by the left hemisphere from seizing control of the right hand and drawing the word it had been shown. However, when the left hand (right hemisphere) held the pen, then two words were drawn. The right hemisphere could draw its word but the left hemisphere could also grab control of that left hand and draw its word as well. Like volitional orienting, we find that this ability of the left hemisphere to exert its control over the right hemisphere may be a general principle of the disconnected hemispheres. This conclusion was very recently confirmed by my good friend and colleague Michael Miller, who showed unequivocally that when a hemisphere was challenged directly to gain control of the ipsilateral limb, the ability to do so was preferentially lateralized to the left hemisphere (Miller & Kingstone, 2005).

Opening Doors

Working with Michael Gazzaniga opened the door to a faculty position in Canada, and so many other doors as well. For instance, not long after I moved to Canada, Roberto Cabeza (now at Duke) and I hosted a small functional neuroimaging conference in Banff, Alberta. After that 1999 meeting we began to play with the idea of turning the papers presented at the meeting into a book. Roberto wrote to a famous colleague he

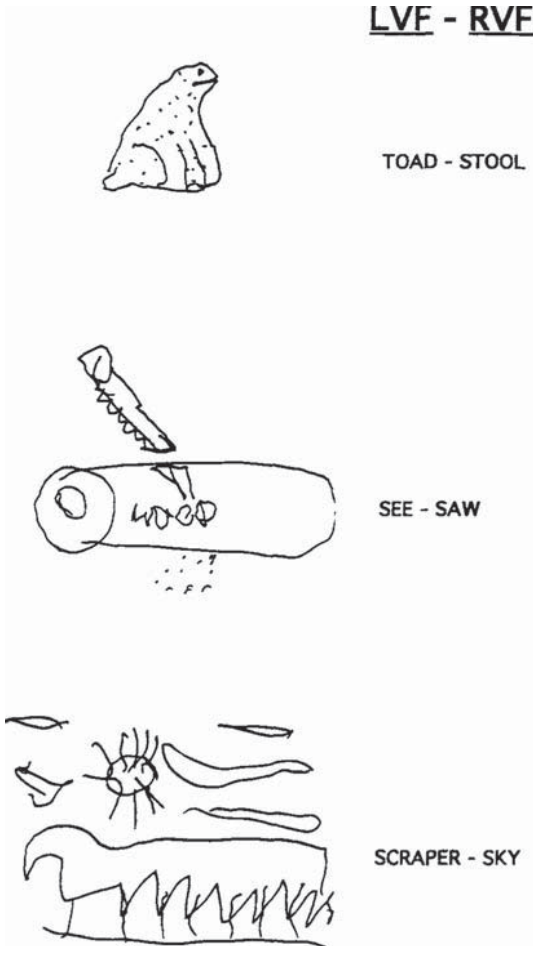

Figure 7.2
J.W.'s drawings of words presented to his left or right visual field. The presented words were conceptually ambiguous (that is, the words "toad" and "stool" may be drawn as a toad sitting on a stool or as a single emergent object—a mushroom). All pictures were drawn by the split-brain participant J.W.'s left hand. (Top) Drawing of the left-visual-field (LVF) word "toad" (ipsilateral to the drawing hand). (Middle) Drawing of the right-visual-field (RVF) word "saw" (contralateral to the drawing hand). (Bottom) Drawing combines both words, "scraper" and "sky" (ipsilateral + contralateral).

knew to see what he thought of the idea, and that colleague told him it would never happen, as we were far too junior. I wrote to Mike. He said he thought that this was a great idea and he would contact MIT Press and see if they were interested. They were, and in two years our book was out (Cabeza & Kingstone, 2001). It was a great success, and MIT Press was so happy with it that they asked us to revise the book for a second edition, which we were honored to do (Cabeza & Kingstone, 2006). I am sure that these handbooks on functional neuroimaging would not exist if it were not for Mike.

More recently still, it was Mike who put forward Michael Miller and me as editors of the new annual review journal *The Year in Cognitive Neuroscience*, published by the New York Academy of Sciences. The first volume was released in 2008 at the annual meeting of the Cognitive Neuroscience Society. Similarly, subsequent volumes will be released at future annual meetings. Again, I have Mike to thank for my involvement in these publications.

I never, ever imagined that my first simple phone call to Mike would bring about such a profound shift in my life. It has been more than an honor to work with Mike. It has been a lot of fun. He has such a natural desire to be with other people, to share ideas, and to push beyond the small limits of everyday living that his excitement for life and discovery is contagious. I look back on the years working him as having passed far too quickly and look forward to the many years that lie ahead. He is a remarkable mentor, a dear friend, and a truly amazing man.

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8

My Dinner with Mike

Michael B. Miller and Scott A. Guerin

If the filmmaker Louis Malle can make a two-hour movie, *My Dinner with André*, consisting entirely of a dinner conversation between André Gregory and Wallace Shawn captivating, then somebody should film a dinner conversation with Michael Gazzaniga. The scene might look something like this: twelve interesting people are sitting around a very large dining room table in a beautifully and tastefully decorated home; everyone is satiated with fine wine and excellent food, the conversation is intellectually stimulating and thought-provoking (even more so than Wally's dinner with André), and the scene ends with Mike summarily dismissing everybody from the party promptly at 9:00pm. The highlight, of course, is Mike's ability to focus everybody's attention on the "big" issue and to get to the heart of a matter without wasting any time. It is this quality that draws people to him and makes his books so popular. So, in tribute to Mike, we pose the "big" question that launched Mike's career: Why does disconnecting the hemispheres have so little impact on the mind of the patients? This is a question that Mike solved forty-five years ago, and yet, paradoxically, he still grapples with it to this day.

Origins of the Problem

The first callosotomy surgeries were performed by the neurosurgeon William Van Wagenen in the 1940s, and these patients were later studied by the neurologist A.J. Akelaitis. These first callosotomies were very dangerous because only a thin layer of cells separates the corpus callosum from the ventricles. But these doctors also believed there was a psychological danger: they worried that severing the corpus callosum would

result in a dual consciousness—two minds fighting for control of the same body. Yet this did not happen—the patients appeared and felt perfectly normal (Akelaitis, 1945). How could this drastic surgery, which has such a profound effect on cats and monkeys, not affect the minds of humans? As a graduate student with Roger Sperry, Mike solved this conundrum by introducing lateralized procedures to the study of human callosotomy patients (Gazzaniga, Bogen, & Sperry, 1962). These procedures allowed researchers to study each hemisphere in isolation for the first time, leading to the discovery of the classic "disconnection" syndrome—presenting information to a single hemisphere caused that information to be inaccessible to the other hemisphere. Mike discovered that whereas the left hemisphere retained all of the patient's language and problem-solving skills, the right hemisphere was aphasic and mentally impoverished, although it retained some specializations of its own. This work by Mike spawned decades' worth of research on hemispheric specialization and integration (Gazzaniga, 2000). It clearly showed the impact of isolating the two hemispheres on the mind.

Yet on another level, Mike still grapples with the question. Despite the discovery that Mike reported in 1962 about the effects of disconnection on each hemisphere, Mike also noted in that report that "the operation appears to have left no gross changes in temperament or intellect, and the patient has repeatedly remarked that he feels better generally than he has in many years." This initial observation of split-brain patients still endures to this day. Not only do patients appear normal to others, but they also report that their mental life is unaffected by the surgery, other than the obvious relief of mental anguish from debilitating seizures. So, we are still left to ponder this question: Why does disconnecting the hemispheres have so little impact on the mind of the patients?

Awareness of Deficits Following Callosotomy

The simple answer is that the right hemisphere does not add anything to the functioning of the speaking left hemisphere. However, that is a very unsatisfying answer, given what we know today about some of the specialized functions of the right hemisphere, including part-to-whole

relations (Nebes, 1972), spatial relationships (Nebes, 1973), apparent motion detection (Forster, Corballis, & Corballis, 2000), mental rotation (Corballis & Sergent, 1988), spatial matching (Corballis, Funnell, & Gazzaniga, 1999), mirror image discrimination (Funnell, Corballis, & Gazzaniga, 1999), veridical memory recollections (Phelps & Gazzaniga, 1992; Metcalfe, Funnell, & Gazzaniga, 1995), amodal completion (Corballis, Fendrich, Shapley, & Gazzaniga, 1999), causal perception (Roser, Fugelsang, Dunbar, Corballis, & Gazzaniga, 2005), and face processing (Levy, Trevarthen, & Sperry, 1972; Gazzaniga & Smylie, 1983; Miller, Kingstone, & Gazzaniga, 2002; Miller & Valsangkar-Smyth, 2005). So although the right hemisphere may not be the linguistic savant that the left hemisphere is, it is not as if it were merely dead weight, as if its only function were to balance the head properly. It seems far-fetched to suggest that the mental experience of the speaking left hemisphere is entirely unchanged as a result of loosing all communication with its nonspeaking neighbor.

A more enticing possibility is that the disconnection does have an impact on the mind of the patients, but they are unaware of it. Just like cortical blindness patients and neglect patients, split-brain patients may have a form of anosognosia—the denial of a deficit. While blindness and neglect are obvious deficits to the people observing the patients, the deficits of the left hemisphere after being disconnected from its partner on the right may be more subtle and less obvious to the split-brain patients, and to those observing them. For example, the left hemisphere appears to be severely impaired on simple face recognition tests (Miller, Kingstone, & Gazzaniga, 2002). So split patients may have a slight form of prosopagnosia after surgery but they may learn to cope by relying more on other cues to identify people—such as a person's hairstyle, a distinctive mark, the sound of the person's voice—so that their deficit is not fully apparent to others. But surely there must certainly be a qualitative difference in the conscious experience of the patient. Yet, despite being completely disconnected from all those specialized modules mentioned above, the speaking left hemisphere does not appear to miss the right hemisphere whatsoever (Gazzaniga & Miller, 2008).

Mike has suggested previously that this phenomenon may be revealing a unique and perhaps startling aspect of our conscious experience

(Cooney & Gazzaniga, 2003; Roser & Gazzaniga, 2006; Gazzaniga & Miller, 2008). The brain consists of hundreds if not thousands of modules, each of which is specialized to process specific information (for example, faces). These modules are widespread throughout the cortex and many of the modules may be directly connected to other modules to form circuitries. Each module or circuit of modules enables the processing and representation of a specific aspect of the conscious experience. The totality of output from these various neural circuitries makes up the entirety of conscious experience. From moment to moment, the contributions of each circuit varies depending on the demands of the environment. Consciousness is an emergent property that arises out of thousands of specialized systems. Yet we do not experience the chattering of a thousand voices, but rather a single, unified voice. Mike attributes this to the "interpreter"—a specialized mechanism that continually interprets and makes sense of our behaviors, emotions, and thoughts as they occur. This interpreter appears to be uniquely human and specialized to the left hemisphere.

In the unique case of the split-brain patient, entire modules or circuits have been removed from the conscious experience. According to Mike's view, just described, consciousness is completely dependent on local, specialized components. Ordinarily, if a module or circuit is damaged, then the whole system is alerted that something is wrong. For example, if the optic nerve is severed, then the patient will notice immediately that she is blind. However, if an entire system is removed, as in the case of cortical blindness, then the modules normally responsible for detecting that something is wrong in the first place may be damaged. As a result, there is no alert and there is no acknowledgment that something is missing (out of sight, out of mind). Similarly, the left hemisphere of the split-brain patient may be impaired as a result of the disconnection from the right, but it cannot acknowledge that deficit. The left hemisphere does not miss the right hemisphere because it is unaware of what it is missing. Indeed, if self-awareness is itself yet another set of modules in our brain, then it will likely be limited by the natural architecture of the brain. Given that dividing the cerebral hemispheres is an unnatural act in the extreme, being able to detect changes in oneself that result from this surgery may simply be beyond the natural repertoire of human self-awareness.

Memory Following Callosotomy

However, despite our general assertion that the speaking left hemisphere seems unaware of any deficits as a result of the surgery, there is one complaint that some patients have expressed about their postsurgery mental life: their memory seems to be worse. For example, we recently tested a thirty-one-year-old male who had a full callosotomy in 1995. His IQ and other neuropsychological measures were in the normal range, and he presented with the typical disconnection syndrome of a split-brain patient. During questioning about the effects of the surgery on his mental life, he stated that everything seemed perfectly normal except that his memory was worse than before his surgery. He said that since his surgery, when he watches a movie, he can only recall a few details three or four days later, whereas before the surgery he could remember many more details.

The literature on memory impairments as a result of the split surgery is somewhat mixed. In 1974, Zaidel and Sperry reported on the memory impairment of eight patients who underwent complete commissurotomy, which included sectioning of the anterior commissure. They noted in their report that relatives and other close associates reported many lapses in memory in these patients, including reports that the patients could not "recall where they have placed personal items" and that "they repeat the same anecdotes many times to the same audience." They tested these patients on several standard neuropsychological tests of memory, including the Wechsler Memory Scale, and found that the patients performed below the normal range and about twenty to thirty points below their scores on the standard intelligence tests. Damage to the fornix may have played a role in these impairments. Today it is known that lesioning the fornix in rats leads to memory impairments (Wiig, Cooper, & Bear, 1996).

Mike and Joseph LeDoux, who was his student at the time, followed up on that report by conducting the ultimate control in patient studies: testing the patient prior to and after his surgery (LeDoux, Risse, Springer, Wilson, & Gazzaniga, 1977). They found that their patient, D.H., a fifteen-year-old male at the time of his surgery, performed just as well after the surgery as he did before it on several standardized memory scales and several experimental memory tasks. They also found no

difference in the performance of other complex cognitive tasks. This led them to conclude that the discrepancy between reports was due to methodological issues and that their "data suggest that efficient cognitive functioning is more dependent upon intrahemispheric integrity than on interhemispheric integrity. As such, the role of the great cerebral commissures in the richer aspects of mental life continues to elude specification" (p. 102).

But Mike wasn't finished. In 1991, Mike and his postdoctoral researcher, Elizabeth Phelps (Phelps, Hirst, & Gazzaniga, 1991), took another stab at those elusive "memory impairments." They tested several patients pre- and post-operatively who underwent partial commissurotomies. In some patients, the anterior portion of the corpus callosum was sectioned. In others, the posterior portion, including the hippocampal commissures, were sectioned. On tests of story recall and picture reproduction, impairments were observed after surgery only in the posterior patients and not in the anterior patients. Furthermore, anterior patients were unimpaired on tests of recognition and recall of words. Recognition and recall of words was also tested in two complete commisurotomy patients and was compared to normal controls. In those tests they found normal performance on the recognition tests but impaired performance on the recall tests. These results suggest two things. First, sectioning the corpus callosum—particularly the posterior portion, the sectioning of which also damages the hippocampal commissures—can clearly result in memory impairments. Second, these impairments appear to be primarily restricted to recall, with the available evidence suggesting that simple recognition abilities remain intact. They hypothesized that if the two hemispheres have different mnemonic representations and different processing capabilities, then disconnection of the two hemispheres may have a more detrimental effect on recall than on recognition, since it is known that recall is more sensitive than recognition to elaboration and the organization of the to-be-remembered stimuli (Kintsch, 1968; see also Guerin & Miller, 2008).

Later in the 1990s, Endel Tulving took an even more extreme view of hemispheric differences in mnemonic processing. Based almost entirely on neuroimaging data that had been collected up to that point, Tulving proposed the HERA (hemispheric encoding/retrieval asymmetry) model of the neural processing underlying episodic memory (Tulving et al.,

1994), memories about events in one's own life. Besides being an excellent meta-analysis, the model heavily influenced the neuroimaging work on memory that was conducted throughout the 1990s. The model stated that episodic encoding is predominantly a left-hemisphere function whereas episodic retrieval is predominantly a right-hemisphere function. At the time, one of us, Michael Miller, was a student of Mike's. The natural problem for us was that—if this is true—then split-brain patients should be severely amnesic (Gazzaniga & Miller, 2000). But of course, other than the slight impairments noted, they are not.

Mike, Alan Kingstone, and Michael Miller tested the encoding asymmetry of the HERA model directly in two split-brain patients (Miller, Kingstone, & Gazzaniga, 2002). The encoding asymmetry in Tulving's model was based on fMRI and PET activations that were found predominantly in the left prefrontal cortex but not the right. However, most of these tasks involved a levels-of-processing manipulation using words (comparing "deep" encoding of words to "shallow" encoding of words). The levels-of-processing framework suggests that the durability of a memory trace is a function of the depth of semantic analysis and that stimuli encoded with a more elaborate semantic mental operation will be better remembered that stimuli encoded with a perceptual mental operation only (Craik & Tulving, 1975). We hypothesized that the hemispheric asymmetry observed in the neuroimaging studies may have been produced by the use of verbal stimuli. Therefore, in two split-brain patients we tested the left and right hemispheres separately on two levels-of-processing tasks. One task involved the deep and shallow encoding of words and the other task involved the deep and shallow encoding of faces. We found a benefit of the deep encoding of words in the left hemisphere but not in the right, as predicted by the HERA model. But we also found a benefit of the deep encoding of faces in the right hemisphere but not the left, which was not predicted by the HERA model. This basic finding was later replicated in a fMRI study of normal subjects (Wig, Miller, Kingstone, & Kelley, 2004). Our conclusion was that both hemispheres are capable of encoding and retrieving information, and any asymmetries in that capability between the two hemispheres may be due to the type of material.

But this difference between the two hemispheres may point to a broader distinction between the memories of the two hemispheres, one

that we have already alluded to. The memories of the left hemisphere are based heavily on language, abstract concepts, and an abstracted "gist" of what has occurred. Very little perceptual detail is retained in the left hemisphere, but a meaning-based narrative of the past is retained. As a result, the left hemisphere is prone to false memories because it is quick to confuse things that are conceptually similar. The right hemisphere is the precise opposite: it retains exquisite detail—almost to a fault. It will rarely confuse things that are conceptually similar, but this also likely means that it fails to grasp the broader meaning of what has happened (Phelps & Gazzaniga, 1992; Metcalfe, Funnell, & Gazzaniga, 1995). It may be that the right hemisphere has memory errors of its own—such as confusing things that are *perceptually* similar—but this has yet to be tested. If we could talk to the split-brain patient's right hemisphere, would it tell the same story about yesterday as the left hemisphere? Probably not. The split-brain patient has two qualitatively different experiences of the past—one constructed by the left hemisphere, the other by the right. And yet, the speaking left hemisphere is none the wiser, content that her perceptually impoverished view of the past is as it should be, and as it always has been.

But if Mike's account of our consciousness is at all correct, then perhaps our memories are not much different from that of the split-brain patients. Perhaps our memories are also divided and we are also none the wiser. Just as in splits, the left and right halves of our brain store different aspects of the past, with the left focusing on conceptual and verbal aspects of objects and the right focusing on visual form (Garoff, Slotnick, & Schacter, 2005). Indeed, many accounts of episodic memory stress that it is widely distributed throughout the cortex. Although we typically think of the hippocampus as underlying episodic memory, the cortex also plays a very important role and likely underlies some of the more complex and uniquely human properties of memory that have fascinated thinkers for centuries. Indeed, in conventional thinking, the hippocampus is seen as enabling the formation of a distributed cortical memory trace. The hypothesis is that different aspects of a memory are stored in the cortical regions originally responsible for processing that information: visual information is stored in the visual cortex, auditory information is stored in the auditory cortex, and more abstract amodal information is stored in the associative cortex.

Once the consolidation task is complete, the hippocampus is no longer required (Squire, Stark, & Clark, 2004). Much like conscious experience itself, episodic memory consists of the totality of information stored in countless modules throughout the brain. Yet, much like consciousness itself, our perception of the past appears to be unified nonetheless. But is it?

This view of memory—which is really just a special case of Mike's view of the mind in general—would suggest that many of the previous accounts of hemispheric asymmetries in memory and the mnemonic abilities of split-brain patients are probably too simple. It is clear that both the left and right hemispheres can encode and retrieve memory—at least as measured by simple recognition tests—so the HERA model is much too extreme. But each hemisphere by itself is not an entirely self-sufficient memory system. When it comes to difficult recall, it appears that the left hemisphere requires the assistance of the right, via the posterior callosum, the hippocampal commissure, or both. Because each hemisphere has a slightly different view of the past, the memories encoded in each are not redundant. The combined memory may specify a more unique cognitive context in which the to-be-remembered item is encoded and may similarly provide for a larger pool of potential cues on which to draw during retrieval. Finally, the mnemonic experience of the right hemisphere remains obscure. Although the right hemisphere can recognize simple items, this reveals little about the complexity of the underlying representations—in particular, whether they entail self-awareness. If the right hemisphere could talk, what sort of life would it talk about? At present, it is not even clear that the right hemisphere possesses the same sense of a unified past as the left hemisphere.

Nine O'Clock

Meanwhile, the table has been cleared and Mike is close to declaring the party over. But while there is still some port left in our glasses, we come back to our original question: Why does disconnecting the hemispheres have so little impact on the minds of the patients? The work that Mike initiated forty-five years ago clearly demonstrates that severing the corpus callosum does have a tremendous impact on the mind, yet it also

demonstrates the remarkable way in which the left hemisphere fills in sudden gaps in its experience. And despite its occasional complaints about where it left its keys and why it can't remember the plot of that movie it just saw, its conscious experience still seems unified, intact, and unchanged.

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III

The Social Brain

The Social Brain
Mind matters.
Consciousness, less so
if it is considered the trigger of "go."
For it's a post-event
sent to keep sanity,
to placate human vanity,
providing mental unity
from a screaming modular community.

9

Genetic Variation Influences How the Social Brain Shapes Temperament and Behavior

Michael I. Posner, Mary K. Rothbart, and Brad E. Sheese

In his 1985 book, *The Social Brain*, Mike Gazzaniga laid out the basic idea that brain networks execute the tasks of daily life. A generation of neuroimaging research has confirmed this idea and provided specific information about the implementation of many of these networks in the human brain. For example, we know much about the processing of faces, fear, music, arithmetic, and reading (for a more complete list with references see Posner & Rothbart, 2007).

In his new book, *Human: The Science Behind What Makes Us Unique,* Gazzaniga (2008) argues that the human brain is unique in part because, through a left-hemisphere interpreter system highly related to language, it creates a narrative that forms the basis of a coherent self. In this chapter we assess what we know about how the interpreter system influences the developing human personality.

Variation in the structure and function of developing brain networks are thought to underlie children's temperament. Temperament refers to individual differences in reactivity present in early infancy and in the ability to regulate those reactions, which is thought to emerge more slowly during development. Temperament thus serves as the basis for later differences in personality (for a review see Rothbart & Bates, 2006).

Psychology has often kept the study of normative behavior and the study of individual differences separate. What is the basis for individual differences? According to one view, differences among individuals rest entirely on experience. For example, expertise in a skill such as chess is said to depend solely on very high levels of practice (Simon, 1969). Simon argued that 50,000 hours of practice was needed to produce a chess master. Little was said about which individuals might be induced to carry

out this high level of practice. Similarly, behavioral theorists have linked individual differences to the reinforcement history of the child.

In contrast to this extreme emphasis on experience, some believe temperamental differences originate in the genes. Although we all have common genes, there are differences among people in the specific form (alleles) of some of these genes. Differences in the efficiency of neural networks underlying personality and skill may be rooted in differences in alleles. Some studies rely on comparisons between monozygotic and dizygotic twins to determine the amount of variance associated with genetic variability. However, if one is unable to specify which genes affect temperament and determine their relationship to brain networks, the role of genes remain somewhat mysterious. As a result of imaging methods (Posner & Raichle, 1994) and of the human genome project (Venter et al., 2001) it is now possible to associate specific variations in genes with the activity of neural networks, some of which are related to reactive and some to regulatory aspects of temperament (Posner, Rothbart & Sheese, 2007; Rutter, 2007). This approach provides the opportunity to bring together the study of human brain networks and of individual differences in efficiency in these networks within a common framework.

In this chapter we first consider dimensions such as fear and positive emotionality that involve basic emotional responses to positive and negative events (emotional reactivity). These functions are carried out by brain networks that appear relatively early in development. We then discuss the ability to regulate thoughts and emotions according to the development of the executive attention network. This network helps to implement the interpreter systems outlined by Gazzaniga (2008). We consider how genes and experience jointly shape our behavior. As one example, we discuss in detail findings relating alleles of the dopamine 4 receptor gene to risk taking, activity level, and impulsivity. Finally, we speculate on how genes and environment together come to shape the social brain.

Reactivity

From birth infants differ in their activity level and response to threat. These dimensions can be observed by parents and others and reliably

reported in questionnaires such as the Infant Behavior Questionnaire (Gartstein & Rothbart, 2003; Rothbart, 1981). Factor analysis extracted higher-level factors that provide the basis for individual differences in positive emotion (also called extraversion or surgency) and negative affectivity. Although these two higher-order factors are correlated, they represent two somewhat distinct reactive tendencies that serve as a basis for the Big Five personality factors, which have the same or similar names.

Imaging studies in adolescents and adults have provided some strong hints as to the neural bases of individual differences in reactivity and regulation. In her work, Whittle (Whittle, 2007; Whittle et al., 2008) correlated dimensions of adolescent temperament, including surgency and negative affectivity, with brain structure size and blood oxygenation-level dependent signal (BOLD) strength during rest. High BOLD measures of activation during rest were correlated with lower surgency. This correlation was found in an area of the anterior cingulate cortex that lies at the boundary between areas related to emotional and cognitive self- regulation (Bush, Luu, & Posner, 2000). Since this study involved adolescents, it is unknown whether these signals reflect more reactive aspects of temperament or the ability of adolescents to control aspects of positive affect. Work by Canli et al. (2005) has implicated the amygdala in response to positive faces, which in turn is correlated with self-reports of surgency in young adults. Canli and associates also reported that the strength of functional connectivity between the anterior cingulate cortex (ACC) and parietal structures is also related to surgency.

There is similar evidence of overlap between reactivity and self-regulation in reports of degree of negative affect. The amygdala is associated with reactive fear states in animals. In her studies, Whittle (Whittle, 2007; Whittle et al. 2008) found that higher negative affect produced structural differences in the dorsal ACC. These differences are in brain areas involved in self-regulation. She also found temperament effortful control as measured from adolescent self-report to show a positive relation to brain size in the dorsal ACC, amygdala, and hippocampus and a negative relation to BOLD activity at rest in the ventral ACC.

The results to date show the importance of limbic areas and the anterior cingulate cortex in relation to aspects of reactivity and self-regulation. Because of the long developmental period prior to

adolescence it is difficult to separate the reactive and regulatory influences. We have been carrying out longitudinal studies beginning in infancy in an effort to trace the origins of self-regulation.

Self-Regulatory Networks

We have studied the brain network that is involved in the regulation of affect and cognition (Posner, 2008; Posner, Rothbart, Sheese, & Tang, 2007). The more dorsal area of the anterior cingulate cortex has been shown to be active primarily in cognitive tasks that involve conflicting responses, such as the Stroop task. When tasks have a more emotional component, however, they activate a more ventral part of the cingulate (Bush, Luu & Posner, 2000). We have argued that in humans the anterior cingulate cortex serves as a part of an executive attention network involved in the control of both cognition and emotion, regulating the processing of information from other networks. Support for this idea comes from studies of the connectivity of the anterior cingulate cortex with other brain areas discussed in the next section.

Connectivity

A possible difference between humans and other primates in their control of cognition and emotion may lie in differences in the degree of connectivity that the anterior cingulate has to other parts of the brain. As mentioned, the more dorsal part of the ACC has been identified with cognitive control, and the more ventral part with emotional control. One way to examine this issue is to image the structural connections of different parts of the ACC using diffusion tensor imaging (DTI). Myelin is the fatty sheath that forms around the axons of neurons to speed neuronal transmission. This form of imaging uses the diffusion of water molecules in particular directions due to the presence of myelinated fibers, thus providing a way of examining the physical connections present in human brains. A DTI analysis of humans confirms animal studies indicating that the dorsal part of the ACC is connected to cortical areas of the parietal and frontal lobes, while the ventral part of the ACC has strong connections to subcortical limbic areas (Posner, Sheese, Odludas & Tang, 2007).

It is also possible to use fMRI to examine the functional connectivity between brain areas during the performance of a task (Posner et al., 2007). Two recent studies illustrate the use of fMRI to trace the interaction of the ACC with other brain areas. In one study subjects were required to switch between auditory and visual modalities (Crottaz-Herbette & Mennon, 2006). Activation of the dorsal ACC was coupled either to visual or auditory sensory areas, depending on the modality selected. Another study (Etkin, Egner, Peraza, Kandel, & Hirsch, 2006) required subjects to resolve conflict related to negative emotion. The ventral anterior cingulate cortex was shown to be coupled to the amygdala in this form of conflict resolution. Studies that have required people to control their positive (Beauregard, Levesque & Bourgouin, 2001) or negative emotional reactions (Ochsner et al., 2001) to stimuli have shown strong activation in the anterior cingulate in comparison with viewing the same stimuli without exercising control.

Comparative anatomical studies point to important differences in the evolution of cingulate connectivity between nonhuman primates and humans. The anterior cingulate cortex is a very ancient structure, and seems to have undergone considerable change in recent evolution. Anatomical studies show the great expansion of white matter, which has increased more in recent evolution than has the neocortex itself (Zilles, 2005). One type of projection cell, called the Von Economo neuron, is found only in the anterior cingulate cortex and a related area of the anterior insula (Allman, Watson, Tetreault, & Hakeem, 2005). It is thought that this neuron is important in communication between the cingulate and other brain areas. This neuron is not present at all in macaques and expands greatly in frequency from great apes to humans.

The two brain areas in which Von Economo neurons are found (cingulate and anterior insula) are also shown to be in close communication in human studies, even when participants are in the resting state (Dosenbach et al., 2007). Moreover, there is some evidence that the frequency of the neurons' activity also increases in development between infancy and later childhood (Allman, Watson, Tetreault, & Hakeem, 2005). In our view, this neuron and the rapid and efficient connectivity it provides may be an important reason why self-regulation in adult humans can be so much stronger than in other organisms. In addition,

the development of this system may be related to the achievements in self-regulation that we have documented between infancy and age seven to eight. In the next section we trace this development.

Development of Self-Regulation

We have been especially interested in the origins of self-regulation in infancy. Studies by Diamond, (1990) and Wynn (1992) found that infants can control their reaching toward objects and detect error. Posner and Rothbart (2007 have been interested in determining whether the executive attention network that includes the midfrontal cortex is involved in these functions during infancy. The development of executive attention can be easily assessed both by questionnaire and cognitive tasks after about age three to four, when parents can identify the ability of their children to regulate their emotions and control their behavior in accord with social demands. In infancy, however, it has been difficult to pose questions about effortful control because most regulation seems automatic or involving the caregiver's intervention. Obviously, infants cannot be instructed to press a key in accordance with a particular rule.

Error detection is one way to study self-regulation. Berger, Tzur & Posner (2006) examined the ability of infants of seven months to detect error. Infants observed a scenario in which one or two puppets were hidden behind a screen. A hand was seen to reach behind the screen and either add or remove a puppet. When the screen was removed, either the correct number of puppets or an incorrect number were present. Wynn (1992) found that infants of seven months looked longer when the number was in error than when it was correct. Whether the increased looking time involved the same executive attention circuitry that was active in adults was unknown. Berger replicated the Wynn study but used 128- channel electroencephalography (EEG) to determine the brain activity that occurred during error trials in comparison with the activity involved when the infant viewed a correct solution. Results indicated that the same EEG component over the same electrode sites differed between correct and error trials in infants and adults. Since this EEG component had been shown to come from the anterior cingulate gyrus (Dehaene, Posner, & Tucker, 1994), it appears that the same brain anatomy is involved in infant error detection as found in adult studies.

Of course, the result of activating this anatomy for observing an error is not the same as found in adults for self-made errors. Adults actually slow down after an error (Rabbitt, 1968) and adjust their performance appropriately while infants do not do this (Jones, Rothbart & Posner, 2003). However, it suggests that even very early in life the anatomy of the executive attention system is at least partly in place.

We also began a longitudinal study with infants of six to seven months (Sheese, Rothbart, Posner, White, & Fraundorf, 2008) in which we studied eye movements that occurred when attractive stimuli appeared in a fixed sequence of locations on a screen in front of the infant. On most occasions the infants moved their eyes to the stimulus, but on some occasions they moved their eyes to the location where the stimulus would occur prior to its presentation (in anticipation). We believe the anticipatory movements were an early form of voluntary response because they actually anticipated the visual event. We previously found that three-and-a-half-year-olds showed a positive correlation between performance on conflict trials in a voluntary key-press tasks and the tendency to make correct anticipations to the visual-sequence task (Rothbart, Ellis, Rueda, & Posner, 2003).

In the first session of our longitudinal study at six to seven months we examined how the frequency of anticipatory movements in the visual-sequence task was related to self-regulation during presentation of novel toys and presentation of a frightening mask (see Sheese et al., 2008, for additional details). Anticipatory looking was related to more hesitant initial approach to the toys, including longer latencies to initial reaching, and longer durations of looking without physically touching the toy. These results were particularly interesting because anticipatory looks have extremely low latencies with respect to the stimulus (either before the stimulus or within 130 milliseconds), yet they are associated with longer latencies in reaching for the toy. Controlled reaching is probably of importance in the development of the ability to reach to locations other than along the line of sight, which has been traced in infancy (Diamond, 1990). Anticipatory looking was also positively related to greater use of sucking as a self-soothing mechanism during the presentation of threatening mask stimuli. Overall, our results indicate that anticipatory looking is related both to caution in reaching for novel toys, and aspects of the regulation of distress in infancy. These results support the

idea that executive attention is present in infancy and serves as one basis for the regulation of emotion.

Genetic Contribution

Since the success of the human genome project it has become increasingly possible to specify particular genes and to examine their relation to the structure and function of specific neural networks. The Attention Network Test (ANT) is a computerized assessment of the efficiency of three distinct attention networks—alerting, orienting, and executive attention (Fan, McCandliss, Sommer, Raz & Posner, 2002)—that uses cues to indicate when and where a target might occur. The target is a central arrow pointing left or right, and the person is instructed to respond with the key in the direction of the arrow. Flankers can be either congruent (pointing in the same direction) or incongruent with the arrow, thus introducing conflict. Subtractions of reaction times to cue or target conditions are used to measure the efficiency of alerting (no cue–double cue), orienting (cue at target–central cue), or executive attention (incongruent flankers–congruent flankers). Neuroimaging studies have shown that differences in performance on the ANT are related to differences in the activation of distinct brain networks thought to support alerting, orienting, and executive attention (Fan, McCandliss, Fossella, Flombaum, & Posner, 2005).

Using the ANT to assess the efficiency of each attention network, we have been able to examine genes that may contribute to the functioning of the attention networks. We first used the ANT in genetic studies to assess attention in monozygotic and dizygotic same-sex twins (Fan, Wu, Fossella & Posner, 2001). We found strong heritability of the executive attention network. These data supported a search for genes related to executive attention. We then used the association of the executive attention network with the neuromodulator dopamine as a way of searching for candidate genes that might relate to the efficiency of the network (Fossella et al. 2002). To do this, 200 persons performed the ANT and were genotyped so that we could examine frequent polymorphisms in genes related to dopamine. We found significant association of two genes, the dopamine D4 receptor (DRD4) gene and the monoamine oxidase A (MAOA) gene, with executive attention. We then conducted

a neuroimaging experiment in which persons with different alleles of these two genes were compared while they performed the ANT (Fan, Fossella, Sommer, & Posner, 2003). Groups with different alleles of these genes showed differences in the ability to resolve conflict as measured by the ANT and produced significantly different activations in the anterior cingulate, a major node of the executive attention network.

Recent studies have extended these observations. In two different studies employing conflict-related tasks other than the ANT, alleles of the catechol-o-methyl transferase (COMT) gene were related to the ability to resolve conflict (Blasi et al. 2005; Diamond, Briand, Fossella & Gehlbach, 2004). A study using the child ANT also showed a significant relation between the DAT1 and executive attention (Rueda, Rothbart, McCandliss, Saccamanno & Posner, 2005). In addition, research has suggested that genes related to serotonin transmission also influence executive attention (Canli et al., 2005; Reuter, Ott, Vaidl, & Henning, 2007). Future studies should determine other genetic influences and examine their interaction and modes of operation.

The relation of genetic factors to the functioning of the executive attention system does not mean that the system cannot be influenced by experience. Rather it appears that some genetic variation allows for additional influence from parenting and other experiences. In our longitudinal study, we found that the 7-repeat allele of the dopamine 4 receptor gene interacted with the quality of parenting to influence such temperamental variables in the child as activity level, sensation seeking, and impulsivity (Sheese, Voelker, Rothbart & Posner, 2007). With high-quality parenting, two-year old children with the 7-repeat allele showed average levels of these temperamental traits, and those with poorer quality parenting showed higher levels. Other research has shown similar findings for parenting on the externalizing behavior of the child, as rated by the parents in the Child Behavior Checklist (Bakermans-Kranenburg & van IJzendoorn, 2006).

There is evidence that the 7-repeat allele of the DRD4 gene is under positive selective pressure (Ding et al., 2002). Our results suggest a possible reason for this in that genetic variation makes it more likely that children will be influenced by their culture through parenting style. This idea could be important for understanding why the frequency of genetic alleles has changed during human evolution. In accord with this idea, a

recent study showed that only those children with the 7-repeat of the DRD4 showed the influence of a parent training intervention (Bakersman-Krannenburg, IJzendoorn, Pijlman, Mesman, & Juffer, 2008).

In our experiments, the DRD4 7-repeat allele did not influence the executive attention network but seemed to act more directly on temperamental characteristics. However, preliminary results with eighteen-to-twenty-month-old children show that toddlers with high-quality parenting and a genetic predisposition for low rates of dopamine metabolization show the greatest performance on our assessments of executive attention. These results highlight the idea that the development of attention networks reflect both genetic instructions and early environmental inputs.

Genes do not directly produce attention. What they do is code for different proteins that influence the efficiency with which modulators such as dopamine are produced and/or bind to their receptors. These modulators are in turn related to individual differences in the efficiency of the attention networks. Humans have a great deal in common in the anatomy of their high-level networks, and networks that are common to all humans must have a basis within the human genome. The same genes that are related to individual differences in attention are also likely to be important in the development of the attentional networks common to all humans. Some of these networks are also common to nonhuman animals. By examining these networks in animals it should be possible to use a variety of molecular methods to understand in more detail the role of genes in shaping networks.

The Social Brain

Evidence that genetic expression is influenced by the social environment shows the close interplay of biology and culture in shaping behavior. The brain is an organ both shaped by thousands of years of evolution and molded by the parental and cultural environment that surrounds it. In his work Gazzaniga (1985, 2008) pointed the way to understanding how brain networks related to social interaction and how control systems led the interpreter to influence human behavior. However, this work did not detail the specific mechanisms of control. Our studies have begun to

show the mechanisms through which the goals represented by the interpreter system can act to influence behavior.

In our work we have outlined a specific neural network that serves to regulate a wide range of thought and emotion. This provides a mechanism for linking the work of the interpreter system to the control of other brain networks. The unique nature of the anterior cingulate cortex connectivity provides insight into cognitive control in humans. Our work has further supported the link between goals and behavior by describing how genes and social experience interact to shape brain networks of control and changes in behavior during child development. We hope this work makes a contribution to the understanding of the brain's social networks, which have so interested Michael Gazzaniga throughout his career.

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10

The Contribution of Malleability to Collective Memory

William Hirst

Why is human memory unreliable and malleable? Scientists and engineers have designed computers with much more accuracy than human memory possesses. Why can't human memory be more like a computer's?

As psychologists have known at least since 1932, when Frederic Bartlett published *Remembering: A Study in Experimental and Social Psychology*, human memories decay over time and are shaped by present attitudes and social interactions occurring between initial encoding and final retrieval. Bartlett was so impressed by memory's unreliability and malleability that he rejected the storage metaphor of memory. The storage metaphor works well for computers, because that is what they do: store information. The inaccuracy of human memory makes the storage metaphor limited, according to Bartlett. People may form mnemonic traces in the brain, but these recordings change over time, as new experience or the acquisition of new information modifies previous memories. Memories, then, become integrated accumulations of past experience, which Bartlett called *schemata*, rather than discrete, unalterable traces. At the time of retrieval, this mishmash of the past, the schemata, is further modified as the rememberer reshapes memories to conform to present attitudes. Because of the constantly changing way the past is represented, at the time of memorization and remembering and at every point in between, a memory becomes not a reappearance of stored-away traces but a product of reconstruction occurring at the time of remembering.

Why would Mother Nature allow such a cockamamie system? Although evolution does not always converge on an optimal system, in the case of memory, what it converges on seems to be dismally poor. Dan Schacter (1999) went so far as to describe human memory's

unreliability and malleability as a sin. Why would Mother Nature condemn us to sin?

Mike Gazzaniga (1985) supplied an answer to this conundrum in his book *The Social Brain*, in which he discussed the exquisite relation between brain structure and the social nature of man. This observation is relevant to the memory puzzle raised here because it suggests that the unreliability and, in particular, its corollary, the malleability, of memory, may serve a positive function, specifically, a social function. The malleability of memory may allow individually discrete memories to become shared over time, thereby promoting what Halbwachs (1925/1992) called a collective memory. A collective memory can in turn both guide the construction of a collective identity and contribute to the development of strong social bonds. The malleability of memory may not be a sin, as Schacter (1999) would have us believe, but a virtue.

On the Definition and Formation of Collective Memory

Collective memories are "community-based" equivalents of autobiographical memories. Autobiographical memories are individually held memories that help shape personal identity (Conway & Pleydell-Pearce, 2000), whereas collective memories are memories shared across a community that help shape the identity of that community (Hirst & Manier, 2008). According to this definition, two things are important when considering collective memory: (1) how a community comes to share individually held memories, and (2) how these shared memories bear on collective identity. The identity-shaping aspect of collective memory is important because not all shared memories are collective memories. Most Spaniards, for instance, know the value of pi, but the value of pi is not a Spanish collective memory. On the other hand, most Spaniards also remember the Madrid bombing of March 11, 2004, but unlike the value of pi, this memory clearly bears on Spanish collective identity. It can properly be called a Spanish collective memory.

In this chapter I focus on the first aspect of the definition of collective memory: How does a memory become shared across a community? A memory cannot bear on collective identity if it is not shared in the first place, and thus, a virtue of memory's malleability lies in the role this

malleability plays in constructing shared memories. Shared memories may be valuable because they contribute to collective identity and facilitate social bonding, but this contribution is realized in large part because memory's malleability promotes their creation.

There are, of course, many ways memories can become shared. As Bartlett (1932) noted, the attitudes held at the time of an experience and at remembering will affect how this experience is initially represented in memory and subsequently remembered. If members of a community hold the same attitudes, then they will initially create shared memories of shared experiences and will remember the shared experiences similarly. Such shared attitudes and shared memories, however, cannot always be guaranteed.

Even members of the same community rarely share all the same attitudes. They will often mnemonically represent an experience and subsequently reconstruct a memory differently. The Japanese film director Akira Kurosawa nicely illustrated this point in his classic film *Rashomon*, but one does not need to turn to artistic representations to illustrate the point. Mundane examples abound, such as couples adamantly disagreeing about their shared past.

If shared experience can often lead to distinctly different memories, how can collective memories ever be formed? The question occupying this chapter is whether social interactions can transform distinct memories of shared experiences into shared memories. I will center my attention on a frequently occurring social interaction: conversations about the past. What happens to dissimilar memories as people talk to each other about them? The contention here is that, through conversation, dissimilar memories become shared, and as more shared memories emerge, collective memories deepen and social bonds increase. Indeed, one could go even further and assert that if conversations can be encouraged across communities, new communities can be built, in part, because initially disparate renderings of the past can be reshaped into shared representations. When viewed in these terms, malleability can unquestionably become a virtue.

I limit my discussion of the effect of conversation on collective memory to the influence speakers have on their own and listeners' memories. Because of the nature of these influences, initially distinct memories

become shared between speaker and listener, and a collective memory is formed between speaker and listener. This elemental influence of a speaker can extend between the pair of one speaker and one listener to larger communities. A speaker's influence can become widespread if she addresses a large number of people. Moreover, a chain of influences can also be set up, with one speaker reshaping the memory of a listener, who in turn becomes a speaker who can influence another listener. This sequence of conversational interactions can multiply in complex ways and, after numerous conversations, may lead to a convergence onto a shared community-held rendering. Studies of the epidemiology of beliefs and the spread of beliefs across a network suggest that this posited convergence is not only a realistic possibility but may be quite frequent (Sperber, 1996; Watts, 2003). What we want to emphasize here is that, if individuals begin with distinct renderings of the past, mnemonic convergence is only possible because of memory's malleability.

I first consider the effects of speaker on speaker and then the effects of speaker on listener. As we shall see, these effects are subtle, operating in some situations and not others. I am interested in documenting the extent of memory's malleability and the conditions under which memories becomes malleable. There is no reason to expect that these conditions are somehow designed to promote the formation of collective memories, or encourage social bonds. They may merely be products of the way the mechanisms underlying malleability evolved. But whatever their origin, there is little doubt that they can facilitate or constrain the degree to which individually held memories become shared memories.

The Effect of Speaker on Speaker: The Saying-Is-Believing Effect

Speakers will usually tune what they say to the attitude of a listener. For instance, when speakers tell a colleague about a political candidate, they tend to emphasize the negative if the listener has a negative attitude toward the candidate, the positive if the listener's attitude is positive (Echterhoff, Higgins, & Levine, 2009). Such audience tuning can lead to changes in the mnemonic representations the speaker holds. As speakers recollect the past, they reshape their own memories to conform with what they say rather than with what they initially remembered. In our

example, depending on whether the tuning was negative or positive, a speaker will subsequently remember the candidate either negatively or positively.

Interestingly, this saying-is-believing effect does not arise simply because speakers tune what they say to an audience. A genuinely interpersonal account is needed. Speakers must be motivated to create a shared reality with their audience in order for the saying-is-believing effect to emerge. That is, they must want to experience a commonality between their own and others' representations and evaluations of the world (Echterhoff et al., 2009). When speakers' motivation for tuning is other than the creation of a shared reality, for instance, receiving a cash payment for tuning, speakers' memories do not change despite pronounced tuning (Echterhoff, Higgins, & Groll, 2005). Along the same lines, when the listener is an out-group member and hence not a strong candidate with which to create a shared reality, no saying-is-believing effect emerges (Echterhoff, Higgins, Kopietz, & Groll, 2008). When German students addressed Turks, a socially stigmatized out-group, they made a greater effort at audience tuning, relative to German speakers communicating with a German and thus a fellow in-group member. Despite the increase in audience tuning, the communication between Germans and Turks had no effect on the memories of the German speakers.

Thus, speakers' audience tuning is not enough to change their memories. The speaker must be motivated to create a shared reality. They must, if you like, want to form a collective memory with the listener. Talking is simply not enough.

The Effect of Speaker on Listener

As we shall see, the situation is different for the effect of speaker on listener. There are at least three ways the malleability of memory permits (or blocks) the ability of a speaker to reshape the memory of a listener: social contagion, induced forgetting, and resistance. *Social contagion* refers to incidents in which speakers impose memories on listeners. The imposed memory could alter an existing memory or introduce a new one. *Induced forgetting* refers to incidents in which what the speaker says leads the listener to forget material. The speaker is not so much

imposing a memory on the listener as making it difficult for listeners to access what they previously knew. In both situations the speaker and the listener come to share similar memories because the listener adopts the memories of the speaker, or speaker and listeners forget the same material. Social contagion and induced forgetting, then, are means of creating collective memories and their counterpart, collective amnesia. *Resistance* is the opposite of social contagion and induced forgetting: It occurs when people want the past to be their own, not what others want it to be. Here listeners will, often with great effort, work to limit the influence of a speaker. In some ways, one might view resistance as a means of limiting the social bonds that malleability can help engender, but, as we shall see, resistance to malleability may promote sociality as much as malleability itself.

Social Contagion

Experimental work on the phenomenon of social contagion began with Elizabeth Loftus's demonstrations of the post-event misinformation effect (for a review, see Loftus, 2005), although she did not initially frame her work in these terms. In a standard experiment, participants first see a slide show of a traffic accident and then hear a post-event narrative. Say the slides might depict a stop sign at a corner, whereas the narrative alludes to a yield sign. Participants are then given a memory test in which they indicate whether they saw in the slide show a stop sign or a yield sign. Participants are more likely to falsely remember seeing a yield sign in the original slide presentation if they heard about it in the post-event narrative. They come to remember seeing things that were not there. Even when the post-event narrative is embedded in a free-flowing conversation between two or more people, the same effect can be found: speakers in a conversation will impose memories on listeners (Cuc, Ozuru, Manier, & Hirst, 2006). Something as mundane as a conversation can alter the memory of listeners in a way that will lead the speakers and listeners to share the same memories.

Speakers can implant a wide range of material into the memories of listeners. For instance, listeners can come to remember, incorrectly, that they were lost in a shopping mall as children simply by listening to a relative insist that the incident took place. Moreover, they not only

come to believe the incident happened, but remember details that the relative did not report. In one documented case, the implantee remembered walking up to an elderly gentleman and asking for his help, even though the detail was never mentioned by the implanter (Loftus, 2005). Researchers have also induced people to remember knocking over the wedding cake at a relative's wedding, meeting the Warner Brothers cartoon character Daffy Duck at Disneyland, going on a hot-air balloon ride during childhood, or putting Slime into a teacher's desk in elementary school (Loftus, 2005). None of these events occurred to the subjects, yet they reported possessing vivid and compelling memories of them.

Of course, not every conversation serves as an ideal medium for implantation, and as a result not every conversation will promote the formation of a collective memory. The malleability of memory may promote the formation of collective memory, but the content and depth of a collective memory is likely to be situationally specific.

Conversational dynamics determine in part the content of collective memories in at least two ways. First, participants in a conversation rarely remember all that they are capable of remembering: what a group remembers may be more than any individual may remember alone, but it is less than the sum of the mnemonic capacities of each individual member (Weldon, 2001). As Marsh (2007) put it, "retelling is not remembering." As a result, a collective memory emerging from a conversation will always be less than the sum of individual memories.

Second, participants' contributions can be distributed differently. Participants may contribute equally in some conversations, while, in other conversations, one participant will dominate, or be the dominant Narrator (Hirst, Manier, & Apetroaia, 1997). In the former instance, memories shared by all participants are more likely to emerge in a group recounting than are memories unique to one conversation participant (Wittenbaum & Park, 2001). As a result of this sampling bias, a collective memory emerging from equal-distribution conversations will consist mainly of the memories shared by all participants before the conversation began. The conversation will only serve to strengthen already existing collective memories. With the presence of a dominant narrator in the conversation, however, this person's memories are likely to be introduced into the group recounting (Cuc et al. 2007). The conversation now

transforms existing collective memories into the rendering of the past the dominant narrator held before the conversation. Conversational dynamics matter when forming a collective memory.

The status or personal characteristics of speakers and listeners also matter. For instance, speakers are more successful at imposing their memories on others when listeners perceive the speakers as experts (Smith & Ellsworth, 1987). Experts, then, can have a disproportionate influence on the content of a collective memory. As to the characteristics of the listener, both younger children and the elderly are more susceptible to misinformation than are young adults (Ceci & Bruck, 1993; Roediger & Geraci, 2007). Susceptibility also varies with personality factors such as agreeableness, extroversion, or an inclination to feeling over thinking (Frost, Sparrow, & Barry, 2006). Finally, those with high levels of mental dissociation or who have suffered posttraumatic stress disorder also show susceptibility (Clancy, Schacter, McNally, & Pitman, 2000).

Thus, social contagion, a significant means by which individual memories are transformed into shared memories, rests in part on the malleability of human memory. Because of this malleability, speakers can implant memories into a listener and by so doing promote the formation of a collective memory. The success of a speaker in implanting memories will depend, among other things, on conversational dynamics and on the status and characteristics of speakers and listeners. The collective memories a community forms, then, are more likely to be shaped by experts and dominant narrators, are more likely to be formed among the young and the old, and are more likely to emerge among those who are less reflective and more introverted. Although these biases may not be all to the good, they unquestionably capture some of the underlying dynamics of community formation and social bonding.

Induced Forgetting

Collective memories are built not only of collective remembering but also of collective forgetting. We are concerned here with the unmentioned material that lurks below the surface of any act of conversational remembering, the intentional or unintentional "silences" that permeate all conversational remembering (Zerubavel, 2005).

What happens to the memories held by both speaker and listener when they go unmentioned by a speaker? Clearly, unmentioned information will be subsequently remembered worse than mentioned information, because of the benefits of rehearsal. Does, however, a speaker's failure to recall information actually induce forgetting of the unrecalled material? And under what conditions? Would it be better for a political figure who wants the public to forget his claim that Iraq possessed weapons of mass destruction (WMDs) to avoid talking about the buildup of the war in Iraq altogether—hoping not to elicit memories of WMDs—or to speak about the buildup, but neglect to mention WMDs? When is induced forgetting most likely to occur?

Cuc, Koppel, and Hirst (2007) have shown that it is better to mention the buildup but omit mention of the WMDs. Prior to this work, Anderson, Bjork, and Bjork (1994) asked participants to study individually category-exemplar pairs, such as ANIMAL-CAT, and then, again individually, to practice selectively some of the studied pairs by retrieving the missing information in cues such as ANIMAL-C___. A final individual memory test followed, in which participants were cued with all the categories featured in the original study list. Selective practice involved some categories and not others. For instance, participants selectively practiced the studied pair ANIMAL-CAT, but not the studied pair VEGETABLE-PEA, nor any other VEGETABLE pair. In addition, within a practiced category, some exemplars were selectively practiced (e.g. ANIMAL-CAT) whereas others were not (e.g., ANIMAL-DOG). Anderson et al. showed that when participants selectively practiced previously learned material, they not only found it easier to recall in the final memory test the practiced material than the unpracticed material but also, surprisingly, found it easier to recall *unrelated unpracticed* material (for instance, all the VEGETABLE pairs) than *related unpracticed* material (e.g., ANIMAL-DOG). Anderson et al. argued that when rerieving CAT in the practice phase of the experiment, participants experienced response competition from other studied ANIMAL pairs, such as ANIMAL-DOG. In order to retrieve CAT successfully, participants had to inhibit the retrieval of DOG. This inhibition lingers. As a result, related, unpracticed pairs became harder to remember on subsequent memory tests than unrelated unpracticed pairs. Without the selective practice, the retrieval-induced forgetting would never occur.

Cuc et al. (2007) extended Anderson et al.'s work to a social setting. Now two participants studied the material, each individually. During the practice phase, one participant completed the unfinished pairs as before (referred to as *the speaker*), while the other participant merely listened. Cuc et al. reasoned that if listeners concurrently retrieve with the speaker, then the speaker's selective practice might induce forgetting, now not just in the speaker but also in the listener. Because speakers and listeners experience the same induced forgetting, Cuc et al. termed the forgetting observed in listeners *socially shared retrieval-induced forgetting*. The issue for Cuc et al. was not what cognitive mechanisms are involved in socially shared retrieval-induced forgetting. The mechanisms are probably the same inhibitory processes featured in *within-individual retrieval-induced forgetting*. Rather Cuc et al. sought the social conditions that might lead a listener to retrieve concurrently with a speaker.

They found that concurrent retrieval and hence socially shared retrieval-induced forgetting varies with conversational goals and the monitoring strategies of the listener. When listeners monitor for the accuracy of what a speaker is selectively recalling, socially shared retrieval-induced forgetting occurs, because in order to judge accuracy the listener must undertake the same retrieval task as the speaker. On the other hand, when monitoring for superficial features such as the fluidity of the speaker's response, no socially shared retrieval-induced forgetting is observed. Cuc et al. also asked participants to study individually stories instead of word pairs and then instructed them to recount jointly the story before administering a final individual recall test. In the joint recounting, some aspects of the story were remembered, while other aspects went unmentioned. The task of joint recounting encouraged all participants to monitor for accuracy. As a result, the free-flowing conversational act of remembering, which served as selective practice, produced socially shared retrieval-induced forgetting in the final individual memory test.

Under the right monitoring conditions or conversational goals, then, both listeners and speakers will forget similar memories, a forgetting induced by the speaker's selective recounting (for a related result, see Coman, Manier, & Hirst, 2009). Although the consequence of this form of malleability might be thought of as a collective amnesia rather than

collective remembering, collective amnesias can promote social bonds just as effectively as collective memories. The collective amnesia applies to material that is related to what was talked about and remembered, only this other material was not talked about and was forgotten. As a result, retrieval-induced forgetting has the added benefit of making what was talked about more memorable, since competing material has become inhibited.

Resistance

Socially shared retrieval-induced forgetting is difficult to resist, but social contagion is not, at least in many instances. Listeners will sometimes realize that a speaker who is remembering a previous event they both experienced is imposing her version of the past on them, come not to trust the speaker, and consequently, *resist* her influence. Such resistance can limit the ability of authorities and powerful entities to shape the collective memory of a community.

Experimenters often elicit resistance by issuing pre- and post-warnings, warnings presented either before or after exposure to post-event information supplied by a speaker. These warnings explicitly inform a listener that the speaker intentionally means to mislead (Echterhoff, Hirst, & Hussy, 2005). Almost all researchers have found that pre-warnings limit social contagion. An effect of post-warnings on social contagion is more difficult to produce, but can still be found.

Neither post-warnings nor pre-warnings are uniformly effective, however. Even resistance has its limits in curbing the tendency of memory to be malleable. Post-warnings can limit social contagion, but they can also increase the incorrect rejection of old material (Echterhoff, Groll, & Hirst, 2007). Moreover, in certain conditions, pre-warnings can increase rather than decrease the level of social contagion. Although listeners can ignore speakers suspected of misleading when the latter talk only a little, it is more difficult to do so, without being rude, when they talk a lot. So listeners might decide not to ignore what suspicious dominant narrators say, but rather to increase their effort to discriminate what occurred in the original event from what the dominant narrator is saying later on (Greene, Flynn, & Loftus, 1982). If listeners possess a good memory of the original event and can easily discriminate what

actually happened in that event from what was stated later, this strategy is effective. But when listeners have a poor memory of the original material, they may have difficulty discriminating new from old. Their increased effort may lead to a better memory for the newly introduced information, and as a result, a rememberer may mistakenly judge that the newly formed robust memory occurred in the original material (Muller & Hirst, in press). With the co-occurrence of a dominant narrator and a listener with a poor memory, a pre-warning might lead to an increase in social contagion rather than a decrease.

Co-occurrences of this kind are all too common. A person of authority often dominates a discussion of a topic of which those listening to her have only a tentative grasp. Disturbingly, as the experiment just described suggests, as people become suspicious of a speaker's authority, they may become more, rather than less, vulnerable to her influence. The malleability of memory can be quite pervasive, even in situations where people wished it weren't.

Paradoxically, when resistance is effective, it can foster the construction of strong new social bonds, not just break existing ones. This is especially true when the resistance is collective. Here the group effort may not only create a sense of intimacy among members because they are undertaking the same task but also, in the course of the resistance, lead to an alternative rendering of the past, one shared by the group. This countermemory may serve not only as a tool for resisting the collective memory urged by the authority, but may also be a means of creating social bonds that the authorities fervently wanted to avoid, as well as a means of fostering an alternative or new rendering of the group's past.

The Role of Intention

In many instances, participants bring to a conversation specific goals and intentions. When a participant is a speaker in a conversation, her intentions and motivations will moderate how much what she says will affect her own memory, but may have little effect on the memories of other participants in the conversation. Specifically, what she as a speaker says will reshape her own memories only when she is motivated to create a shared reality with other participants in the conversation. On the other

hand, whatever her intentions as a speaker are, what she says can still influence how others in the conversation subsequently remember. Even the intentions of the listeners may not always affect the degree to which a speaker can influence their memory. Certainly, listeners do not need to be motivated to create a shared reality with a speaker for the speaker to exert an influence. To be sure, if a listener distrusts a speaker—indeed, intentionally wants to resist any possibility of a shared reality with the speaker—then the listener's attitude can have a substantial impact on the effect the speaker may have. Nevertheless, as noted, even here the effect of the attitude of the listener may be limited. It appears that even though human memory allows people to circumvent its inclination toward malleability, it is difficult to do so, especially if you are a listener.

Final Remarks

Human memory has been endowed not with computer-like accuracy, but with unreliability and malleability. How this malleability unfolds is complex, and I have told only part of the story in this chapter. What is clear, however, is that it allows listeners and speakers to share the same memory, and as conversations expand across a community, it allows a community to possess a shared rendering of the past. The resulting collective memory can help in the construction of collective identities and the formation of social bonds. From this perspective, memory's malleability is not a sin, but a virtue, a virtue that Mike Gazzaniga appreciated when he wrote about the social brain.

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11

How the Sense of Body Influences the Sense of Touch

Elisabetta Làdavas and Andrea Serino

Elisabetta's Story

It has been more than twenty-seven years since I phoned Mike at Cornell University Medical College in New York City, from Toronto, to ask whether I could do a postdoctoral fellowship in his lab. Although already well known internationally, Mike was still very young, and expanding intellectually. He listened to my long explanation without losing interest (or so I thought at the time). But even then he was as accommodating as he is now—he told me that even Italians are welcome in his lab! So, I moved from the frozen streets of Toronto to the sidewalks of New York City. Mike's lab was very active, and soon after arriving I traveled with him, Charlotte Smylie, and Jeff Holtzman to Dartmouth to study split-brain patients during a New Hampshire winter. My perspectives were being broadened, but I was not being very successful in avoiding the cold.

Mike and company were all surprised that I was not interested in split-brain patients and in the "big" questions they were grappling with: whether the self is unique from other forms of semantic and episodic representation; whether there is a role for a left-hemisphere interpreter in the generation of a unified sense of the self; or whether Descartes and Bill Buckley would have hit it off if they were both alive today.

Instead, I was interested in discrete questions such as the role of different coordinate systems in spatial coding. I met with Mike to discuss the results of a just-finished study of neglect patients. Soon after I began my description, his eyes took on that far-away, glazed-over look I often saw in the very patients I was describing to him. He then came out of his reverie and said, "It's better to discuss these data over an aperitif." What I learned that day has kept me in free drinks for twenty-six years.

When my old friends and colleagues invited me to a conference to honor Mike, my initial reaction was "Sorry, but I cannot present data on what I am doing in the lab, because soon after I begin speaking Mike will move the entire audience to the bar. The physiological mechanisms by which the superior colliculus selects visual stimuli for examination won't keep him entertained." But during a visit, Charlotte, always encouraging and always optimistic, tried to reassure me: "I'm sure Mike would like your recent data on . . ." But even she could not complete that sentence. So, for an entire eight-hour flight back to Italy I tried to think of a topic that would please Mike. It still amazes me how rewarding it is to capture Mike's imagination. He is a very special person. Here is the story dedicated to him!

Visual Enhancement of Touch

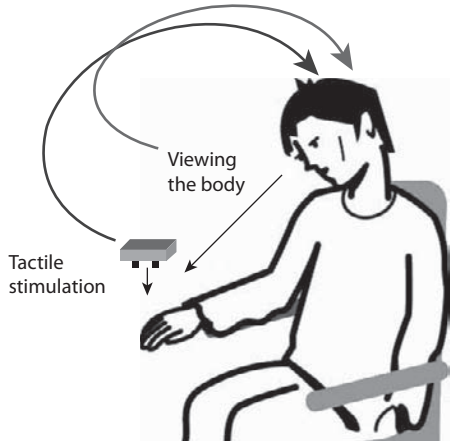
Vision can influence primary levels of tactile processing (for a review, see Spence & Driver, 2004), and visual information pertaining to the *body* seems especially effective in modulating tactile sensation. Several lines of evidence support this notion. First, viewing the body accelerates tactile processing. Tipper et al. (1998) showed that reaction times to tactile stimuli on the hand were faster when subjects could see their stimulated hand in a video monitor, even when the tactile stimuli themselves were invisible. Second, tactile acuity is improved when visual information is available. Kennett, Taylor-Clarke, and Haggard (2001) assessed tactile acuity using two-point discrimination thresholds (2pdt) on the forearm, administered while subjects either viewed their own forearms or a neutral object presented in the same spatial location as their arm. Tactile stimuli were always invisible to the subject. Tactile acuity improved when subjects viewed their stimulated arm, as compared to viewing the neutral object or when blindfolded. These results show that viewing the body during invisible tactile stimulation improves tactile processing; this effect, defined as the visual enhancement of touch (VET), has been replicated a number of times (for a review see Serino & Haggard, 2009).

The enhancement of tactile perception in the presence of visual information may occur at the level of the primary somatosensory cortex. Taylor-Clarke, Kennett, and Haggard (2002) used event-related poten-

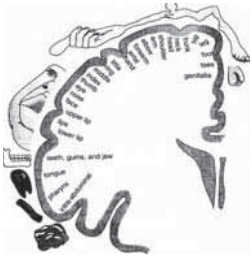
tials to compare cortical activity in somatosensory regions during the 2pdt task, while subjects viewed either their own stimulated arm or a neutral object. The researchers found that viewing the stimulated arm was associated with an increase in early somatosensory event-related potentials. Likewise, Schaefer, Heinze, and Rotte have used magnetoencephalography to demonstrate that viewing the index finger being touched while receiving an unseen tactile stimulation results in a differential activation of the somatosensory cortex region representing the index finger, as compared to conditions of no visual stimulation (Schaefer, Heinze, & Rotte, 2005a) or of asynchronous visuotactile stimulation (Schaefer, Heinze, & Rotte, 2005b). A causal role of SI modulation in VET was suggested when the VET effect was abolished by transcranical magnetic stimulation over primary but not secondary somatosensory cortex (Fiorio & Haggard, 2005).

A recent psychophysical study showed that VET strength reflects the co-location of the neural representation of body parts in the somatosensory cortex more closely than their bodily co-location (Serino, Padiglioni, Haggard, & Làdavas, 2008). In this study, subjects viewed either their own hand or a neutral object, while 2pdt tasks were performed on the hand, the face, and the foot. These body parts were chosen on the basis of their location in the SI body representation: the hand and face representations lie adjacent to each other on the lateral aspect of the postcentral gyrus, whereas the foot representation is distant and more medial (Penfield & Bolderey, 1937). When subjects were viewing the hand, 2pdt scores improved on the hand and the face, but not on the foot. Instead, when the subjects viewed the foot, the enhancement of tactile detection was found on the foot but not on the face or the hand. This pattern of results lends further support to the hypothesis that visual modulation of tactile processing occurs within the somatosensory cortex. In addition, it suggests that VET not only acts on the somatosensory cortex representation of the viewed body part, but also extends *locally* to the adjacent region of the somatosensory cortex, even when the relevant neurons have receptive fields on quite distant body surfaces.

Because it is well known that tactile acuity depends on the receptive field size of SI neurons (Brown, Koerber, & Millecchia, 2004), the work just reviewed suggests that viewing the body might influence somatosen-

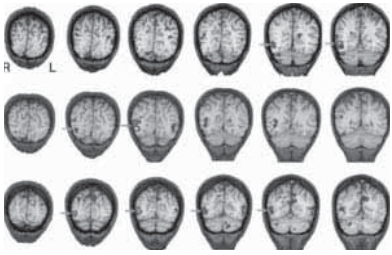


Subjects perceive a tactile stimulus on their body while they view their stimulated body part.



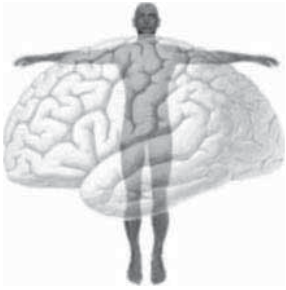
SI

This double stimulation concurrently activates both unisensory tactile areas (SI) and high order visual areas responding to visual bodily-stimuli, such as the Extra-striate Body Area (EBA).



EBA

Somatosensory and visual signals then converge in multisensory brain areas in parietal and pre-frontal cortex integrating multimodal information about the body.



Multisensory body areas may the back-project to somatosensory areas, thus enhancing tactile processing.

Figure 11.1
A model for the brain mechanism underlying visual enhancement of touch. Source: Modified from Serino & Haggard (2009).

sory neurons by reducing the size of their receptive field. A direct test of this prediction was made by positioning vibrotactile maskers at different distances from a tactile target stimulus as a behavioral proxy for SI receptive field size (Haggard, Christakou, & Serino, 2007). The assumption was that maskers would interfere with the tactile task only if they fell within the receptive field of the putative population of somatosensory neurons responsible for spatial representation of the target. Viewing the body reduced the effect of distant maskers and enhanced the effect of close maskers, relative to viewing a neutral object, suggesting that tactile receptive fields were reduced in size when the subject was viewing his or her body.

Therefore, the visuotactile interaction underlying VET may function to improve tactile acuity. Further support for this idea comes from a number of recent studies that demonstrate that tactile perception is affected by visual information only when it is necessary to increase spatial sensitivity (Press, Taylor-Clarke, Kennett, & Haggard, 2004) and that the VET effect is strongest in individuals with poor tactile ability (Serino, Farne, Rinaldesi, Haggard, & Ladavas, 2007). It appears that the visuotactile interactions occur when the tactile stimulus is close to perceptual limits (see also Longo, Cardozo, & Haggard, 2008).

In summary, visual enhancement of touch is a robust phenomenon, demonstrated for different body parts and with different tactile indices when tactile tasks require spatial judgments or judgments close to perceptual limits. In these cases, integration of visual and tactile information is necessary to increase accuracy. In figure 11.1 we propose a possible model for the brain mechanism underlying the VET effect. Somatosensory signals from a given body part are processed in a limited portion of the somatosensory cortex containing neurons with a receptive field centered on that body part; visual information specifically related to the body is processed in high-order visual areas, located in extrastriate visual cortices (Downing, Jiang, Shuman, & Kanwisher, 2001; Downing, Wiggett, & Peelen, 2007). We propose that such tactile and visual unisensory signals reach multimodal areas in parietal and prefrontal cortices (Graziano, Cooke, & Taylor, 2000; Bremmer et al., 2001; Ro, Wallace, Hagedorn, Farne, & Pienkos, 2004; Macaluso & Driver, 2005), where they are integrated. From these multimodal areas a modulatory signal backpropagates to primary somatosensory regions, probably inducing

a retuning of the receptive field size of somatosensory neurons. We speculate that visual information concerning the body is integrated with touch to better define the bodily space to which tactile information is referenced.

Visual Remapping of Touch

The VET effect suggests an important functional relationship between tactile perception and the representation of the body. To further understand this relationship, we studied whether visual observation of a touch on a part of another's body could affect tactile perception as well. Neuroimaging studies showed that observation of a body being touched can evoke brain activity in primary and secondary somatosensory cortices, as well as in some portions of frontal and parietal cortex, as part of the mirror system (Keysers at al., 2004; Blakemore, Bristow, Bird, Frith, & Ward, 2005; Ebisch et al., 2008). However, most subjects do not report tactile perception when observing touch on the body of others. An interesting exception is some synesthetic subjects, visuotactile synesthetes, who experience tactile sensation when they see other people's bodies being touched (Banissy & Ward, 2007). Notably, brain activity induced by observation of touch is greater in synesthetes than in nonsynesthetes (Blakemore et al., 2005). It is possible that the different perceptual experiences of synesthetic and nonsynesthetic subjects might reflect different degrees of activation in the tactile system rather than different mechanisms of visuotactile integration.

Since visuotactile integration is maximum when tactile information alone is not sufficient to drive a clear percept (Serino et al., 2007; Longo, Cardozo, & Haggard, 2008; see also Làdavas, 2008), effects due to the observation of touch might be unmasked in nonsynesthetic individuals if the tactile stimuli were administered near the perceptual threshold. We compared observation of touch on one's own face, on another person's face, and on a nonbody stimulus (a picture of a house). To test touch around the perceptual threshold, we used a classic experimental paradigm, the tactile confrontation task, developed for testing extinction in brain-damaged patients. In this task, a subject is touched on one or both sides of his or her body and must report the location of the touch. Patients with extinction usually fail to report the contralesional stimulus

during double stimulations, because of competition for attentional resources between the two hemispaces (Bender, 1952; Làdavas, 2002). To apply this paradigm to healthy subjects, we electrically stimulated them on the right, the left, or both cheeks with stimuli of unequal intensity to simulate extinction. We predicted that in dual-stimulation trials, the stronger stimulus would occasionally extinguish the weaker one. Thus, under bilateral stimulation, when tactile perception was close to perceptual threshold, an effect of vision on touch could be unmasked. During this task, subjects watched a movie showing their own face (self condition), another person's face (other condition), or a house (house condition), centered on a computer screen. Human fingers either touched (touch condition) or approached (no-touch condition) the image, on the right, the left, or both sides (See figure 11.2, upper panel). Subjects pressed a button with the hand corresponding to the side where they felt the tactile stimulus. When observers saw a face being touched by hands, rather than a face being approached by hands, they demonstrated enhanced detection of subthreshold tactile stimuli on their own faces, i.e., perception of bilateral tactile trials increased. This effect was specific to observing touch on a body part, and was not found for touch on a nonbodily stimulus, namely, a picture of a house. In addition, the effect was stronger when subjects viewed their own faces rather than other persons' faces (see figure 11.2, lower panel).

In summary, in nonsynesthetes, observing a face being touched can activate the tactile system such that visual information can alter their perceptual thresholds. These findings suggest that the same mechanism underlies the effect of observation of touch on tactile processing in both synesthetes and nonsynesthetes; the difference between these groups might be only that sensitivity to the effect is stronger in synaesthetes. We call this effect *visual remapping of touch* (Serino, Pizzoferrato, & Ladavas, 2008).

The stronger effect for viewing one's own face further suggests that visual remapping of touch increases if the observer's body and the observed body match. Remapping a sensation from one sensory modality to another sensory modality is probably facilitated if the two modalities share a common reference system, that is, the same body. Hence, visual remapping of touch depends not only on visual information about touch but also on visual information about the body. The following

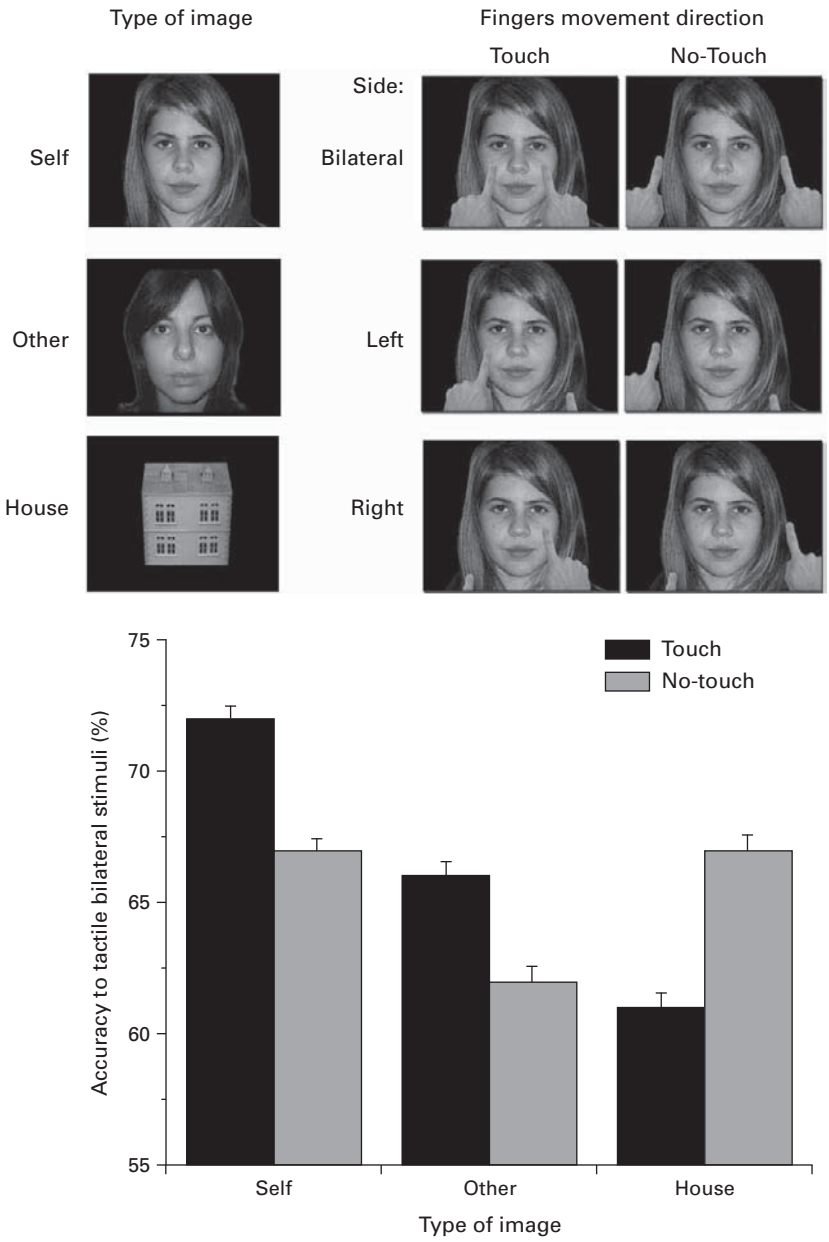


Figure 11.2
Visual remapping of touch. Experimental paradigm (upper panel) and results (lower panel). Viewing a face being touched enhances tactile perception on the face; the effect is stronger when viewing one's own face.
Source: Modified from Serino, Pizzoferrato, & Ladavas (2008).

experiments investigate how visual information about the body modulates visuotactile integration.

Visual information about the body is critical in social interactions of everyday life. Images of the body provide physical information about oneself and conspecifics and play a key role in self-esteem and identity (Rumsey & Harcourt, 2005; Schilder, 1935). This information might be critical in categorizing other individuals as similar or dissimilar to one's self. For instance, when viewing another person, physical features of his or her face immediately help to determine whether that person belongs to one's own ethnic group or to a different ethnic group. Might this ethnic categorization of others influence the degree to which visual information about touch is remapped onto one's own body? Specifically, does visual remapping of touch vary when viewing persons belonging to one's own or to another ethnic group?

To study this issue, Caucasian and Maghrebian subjects were asked to observe a face while they received subthreshold tactile stimuli on their own faces (Serino, Giovagnoli, Làdavas, 2009) as in Serino, Pizzoferrato, and Làdavas's (2008) study. The observed face belonged to the same or to a different ethnic group and in this sense was similar or dissimilar to that of the observer. If the ethnic similarity between the observed's body and the observer's body influences visual remapping of touch, then tactile perception should be boosted when people observe touch directed toward a member of their own ethnic group. Indeed, tactile detection of bilateral stimuli was enhanced when Caucasian observers viewed a Caucasian face compared to when they viewed a Maghrebian face. The effect was exactly reversed for Maghrebian observers. Importantly, this effect was specifically related to the observation of touch, not a general arousal effect. No tactile modulation relative to ethnic membership was found when participants viewed a face being approached by human fingers, but not being touched (see figure 11.3, upper panel; plate 3). Thus ethnic similarity between the self and other bodies modulates visual remapping of touch.

Visual information about the body provides not only physical information about similarity but also semantic information that can be used to determine degree of similarity with another being. Sociopolitical affiliation might be an important factor in evaluating similarity to others. Might political affiliation influence visual remapping of touch? Is tactile

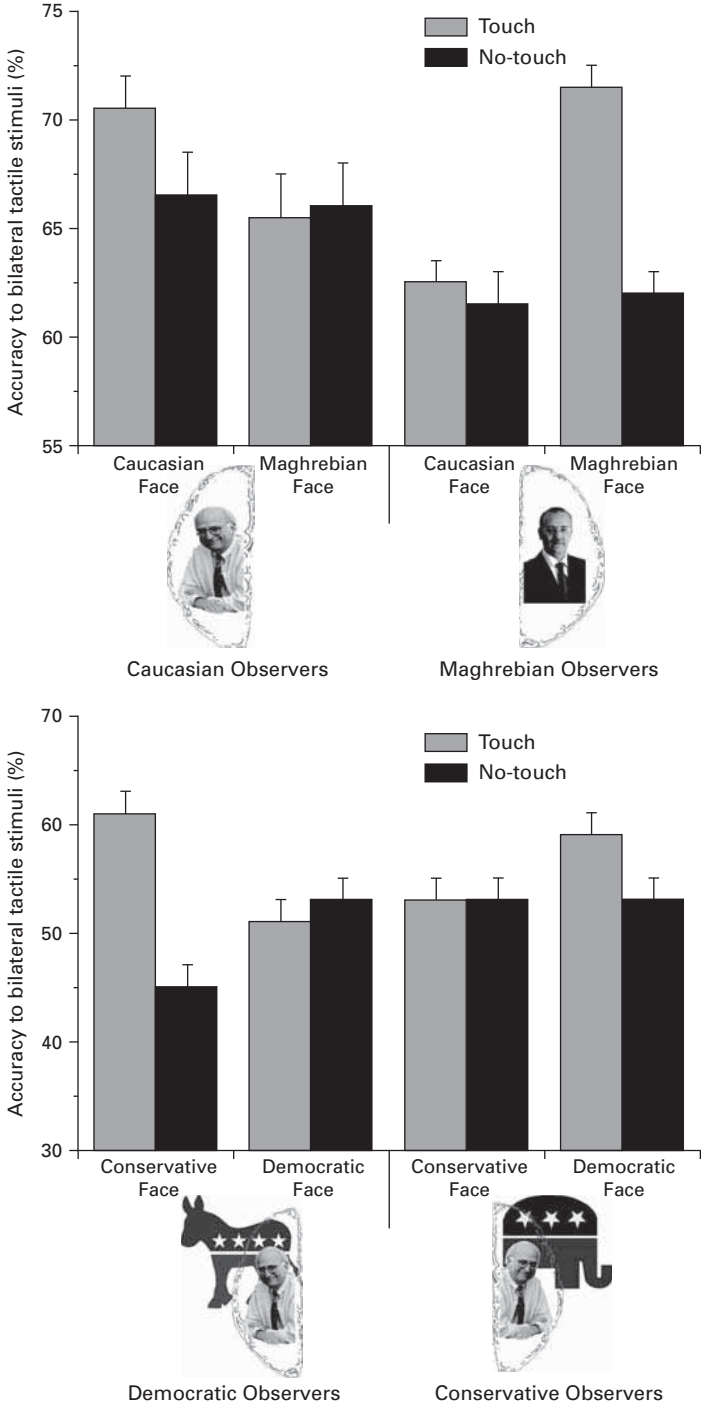


Figure 11.3 (plate 3)
Visual remapping of touch varies as a function of the similarity between the observer's and observed face: an effect of ethnic (upper panel) and political (lower panel) similarity.
Source: Modified from Serino, Giovagnoli, & Làdavas (2009)

perception modulated differently when the political views of a person being touched vary from those of the observer?

The next experiment investigated whether the high-order, semantic concept of similarity was able to modulate visual remapping of touch (Serino, Giovagnoli, & Làdavas, 2009). Participants were recruited from the local headquarters of liberal and conservative parties. These liberal and conservative activists were asked to look at a face of a leader of either a liberal or a conservative party being touched by hands while the subjects received subthreshold tactile stimuli on their faces. This manipulation was intended to create one target whose political views were similar to those of the observer and another target whose views were dissimilar. If political dimension is an important factor in determining similarity between self and others, visual remapping of touch should be stronger when people observe touch directed toward a known member of their own political group than when they observe touch directed toward a known member of the opposite political group. The results supported this prediction. Detection of subthreshold tactile stimuli was enhanced more when liberal political activists viewed a face of a liberal leader, than when exposed to a face of a conservative leader. The opposite pattern was found for conservative observers. Again, the effect was specific for the observation of touch. No modulation of tactile perception was found when the observed face was not touched but was only approached by human fingers (see figure 11.3, upper panel).

In both experiments, the null effect when the viewed face was not touched should be emphasized, because this excludes a generic effect of arousal or familiarity related to seeing similar or dissimilar faces. Nor can the presented results be explained on the basis of a perceptual bias in the visual stimuli. In particular, pleasantness of the shown face might implicitly influence subject's attitude toward the stimulus or the willingness to remap visual information onto one's own body representation. To control for this potential confounding effect, the visual stimuli were drawn from pictures rated for pleasantness by thirty naïve judges and matched on this variable (see Serino, Giovagnoli, & Làdavas, 2009). At the end of the two tactile experiments, participants judged the faces they had seen during the tactile task for pleasantness. Although no difference was found when Caucasian and Maghrebian observers judged the pictures of other unknown Caucasian and Maghrebian persons, a bias was

found in politically active participants. Liberal and conservative observers both judged as more pleasant faces of leaders of their own party. Nonetheless, the effects of ethnic and political membership on visual remapping of touch were analogs in the two experiments, showing that a sensation seen on another body is remapped onto one's own body if the other is perceived to be similar to oneself. Taken together these findings suggest that visual remapping of touch is an automatic process, modulated by high-order representations of the self and other, but independent of explicit judgment.

When an individual observes the face of another, he or she automatically categorizes it as belonging to the same or to a different group as the observer: face-to-face interaction is indeed a crucial aspect of group representation (Lickel et al., 2000). It is well known that in-group versus out-group categorization influences one's own judgments and behaviors toward others (see for reviews Hewstone, Rubin, & Willis, 2002; Brewer & Brown, 1998). Recent evidence suggests that in-group out-group categorization modulates automatic activation of approach or avoidance behaviors toward others (Castelli, Zogmaister, Smith, & Arcuri, 2004; Paladino & Castelli, 2008). This mechanism might have a great impact for survival and therefore might have been selected through evolution (Allport, 1954): the human species has evolved relying on cooperation between individuals in small, strongly interconnected groups (for example, Krebs & Denton, 1997), most of the time in competition with members of different groups. These results suggest that this basic form of self/other and in-group/out-group categorization also influences automatic multisensory integration between touch and vision. The visuotactile interaction underlying visual remapping of touch may be one facet of a basic, primitive empathy that supports social bonds.

In summary, observing touch on a body induces a remapping of tactile input onto the observer's tactile system, resulting in an enhanced ability to perceive a tactile stimulus. The amount of enhancement depends on the perceived similarity between the body of the observer and that of the observed. The effect is maximum for observing one's own body; when observing the body of others, the effect is stronger to the degree that the other body is perceived as similar to the self. Similarity is defined both in terms of physical features of the body and also on the basis of more abstract, conceptual representations of others in relationship to the self.

The neural mechanism underlying this effect is not yet clear. Neuroimaging studies show that observing touch modulates the activity of primary (Blakemore et al., 2005) or secondary somatosensory (Keysers et al., 2004; Ebisch et al., 2008) regions. This enhanced somatosensory activity might potentially boost tactile perception, increasing sensitivity to the detection of incoming sensory events. Indeed, it is well known that tactile sensitivity is determined by the response of neurons in primary somatosensory cortex (Mountcastle, Talbot, Sakata, & Hyvärinen, 1969; de Lafuente & Romo, 2005). Here, we show that tactile perception, as measured with our tactile confrontation paradigm, is modulated by the visual processing of abstract levels of facial identity, such as ethnic membership or known political affiliation. Such complex analysis of visual information cannot be computed within somatosensory cortices, but could be computed in high order visual and associative cortices. For instance, Uddin and colleagues showed that neural activity in parietal (inferior parietal lobe) and frontal (inferior frontal gyrus) areas increases when one views one's own face compared to the face of another person (Uddin, Kaplan, Molnar-Szakacs, Zaidel, & Iacoboni, 2005; Uddin, Iacoboni, Lange, & Keenan, 2007). Furthermore, functionally discrete subregions of medio-prefrontal cortex that process information about others as a function of how similar their sociopolitical views are to one's own (Mitchell, Macrae, & Banaji, 2006; Jenkins, Macrae, & Mitchell, 2008) have been identified. These prefrontal and parietal regions might be critical in linking visual information about a face with the self. The same regions might directly project to somatosensory cortices to modulate visual remapping of touch.

An alternative hypothesis is possible. Even if the activity of primary somatosensory cortex determines the sensory quality of a tactile percept, tactile awareness seems to depend on the activity of other brain regions in the prefrontal and parietal cortices (for neurophysiological data on monkeys see de Lafuente & Romo, 2005, 2006; for data on healthy and brain-damaged humans see Preissel et al., 2001; Kobayashi, Takeda, Kaminaga, Shimizu, & Iwata, 2005; Sarri, Blankenburg, & Driver, 2006). These regions might receive a modulatory signal from the frontoparietal areas discriminating between self-related and other-related visual information. If this is the case, visual remapping of touch might depend on a network of high-order associative areas in the prefrontal and

parietal regions. These two hypotheses might not be mutually exclusive: visual information about touch might both influence the activity of primary sensory areas responsible for tactile sensitivity (Macaluso & Driver, 2005; Schroeder & Foxe, 2005) and modulate higher-level processes in the fronto-parietal network subserving tactile awareness. Future research will shed light upon the dynamics of the neural mechanism underlying visual remapping of touch.

We have described two types of visuotactile interactions, visual enhancement of touch and visual remapping of touch. Both effects show how visual information related to the body is integrated within the somatosensory system to improve tactile perception. In VET, body-related visual information is used to define the body space where sensory stimuli are perceived (Serino & Haggard, forthcoming). In visual remapping of touch, observation of touch activates somatosensory systems which become able to perceive tactile stimuli that were previously subthreshold. Our new results demonstrate that multisensory integration also incorporates information about self-perception and the social categorization of others. But as with all new knowledge, it raises new questions: Mike may let Italians into his lab, but does he find liberals pleasant?

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12

Building a Social Brain

Todd F. Heatherton

Michael Gazzaniga had an immeasurable impact on my life and my career, as he had on those of the other contributors to this volume. Shortly after Mike returned to Dartmouth in the mid-1990s, he appeared at my office door and invited me to join him in producing an introductory psychology textbook. How could I know that agreeing to doing so would lead to so much more than coauthoring a book? During the next dozen or so years Mike and I enjoyed lively discussions over frequent lunches, sometimes talking academic politics, more often talking science. From these experiences I took from Mike at least three essential points about studying the mind:

• Psychologists have generally paid insufficient attention to the adaptive function of mind and behavior. According to Mike we need to be asking not "How does this aspect of the brain work?" but "What is this aspect of the brain for? What problem did it solve for our human ancestors?" Although I was always disposed to evolutionary accounts of behavior, Mike's articulate theories on the evolution of complex behavior provided me with new ways of thinking about the issues I study. To understand the social brain requires thinking about how behavior has been constrained by social context over the long course of human evolution.

• The use of functional neuroimaging techniques, developed over the past two decades, provides researchers with the capacity to study the working brain in action, thus providing a new window for examining previously inaccessible mental states, including the phenomenological experience of self. In the late 1990s, Mike helped spearhead an effort to convince the administration to install an MRI (magnetic resonance imaging) machine in the basement of our new psychology building. Thus,

Dartmouth became the first psychology department in the world to have its own research-dedicated scanner. With Mike's encouragement and the guidance of some wonderful cognitive neuroscience collaborators, my research program has increasingly focused on using fMRI (functional magnetic resonance imaging) to study the social brain and its components.

• Much of human experience occurs through the lens of interpretation. Not only do people lack direct access to the motives and thoughts of others, they have limited access to their own underlying cognitive and neural processes. Thus, much of human experience consists of making sense of events after they have occurred. The interpreter model of mind has many implications for understanding the social brain, as Mike so elegantly argued in his classic work from 1985, *The Social Brain.*

Another important lesson from Mike is that in science you should do what you like and like what you do. Mike's numerous contributions to the science of mind, such as founding journals and societies, launching new centers, and creating new fields, all capitalize on his enormous talents and the fact that he loves what he does. Moreover, Mike encourages those around him to keep focused on their big ideas and to take risks to pursue their academic goals. It is in this spirit that I present a model of the social brain that I have been developing over the past few years. It should come as no surprise that the author of *The Social Brain* has influenced much of my approach.

Building the Social Brain

My overall approach follows a social brain sciences perspective, which merges evolutionary theory, experimental social cognition, and cognitive neuroscience to elucidate the neural mechanisms that support social behavior (Heatherton, Macrae, & Kelley 2004). From an evolutionary perspective, the brain is an organ that has evolved over millions of years to solve problems related to survival and reproduction. Because we are a social species, humans have evolved a fundamental need to belong that encourages behaviors reflective of being good group members (Baumeister & Leary, 1995). From this perspective, the need for interpersonal attachments is a fundamental motive that has evolved for adaptive pur-

poses. Effective groups shared food, provided mates, and helped care for offspring. As such, human survival has long depended on living within groups; banishment from the group was effectively a death sentence. Thus, the human brain is social at its core. Many of the cognitive, sensory, and perceptual systems —although not strictly social—are acutely attuned to social stimuli, such as the way in which people readily spot faces in clouds, inanimate objects, and grilled cheese sandwiches. Indeed, studies suggest that the brain gives "people" privileged status as it processes objects in the environment. For example, our work has shown that there is a distinct functional neuroanatomy for semantic judgments made about people compared to similar judgments made about other objects (Mitchell, Heatherton, & Macrae, 2002).

What do you need to make a social brain? Or what does the brain need to do to allow it to be social? Given the fundamental need to belong, there needs to be a social brain system that monitors for signs of social inclusion or exclusion and alters behavior to forestall rejection or resolve other social problems (Heatherton, in press; Heatherton & Krendl, 2009; Mitchell & Heatherton, 2009). Such a system requires four components, each of which is likely to have a discrete neural signature First, people need *self-knowledge*—to be aware of their behavior so as to gauge it against societal or group norms. Thus, having a self serves an adaptive function for group living. Second, people need to understand how others are reacting to their behavior so as to predict how others will respond to them. In other words they need "*theory of mind,*" the capacity to attribute mental states to others. This implies the need for a third mechanism, one that *detects threat,* especially in complex situations. Finally, there needs to be a *self-regulatory* mechanism for resolving discrepancies between self-knowledge and social expectations or norms, thereby motivating behavior to resolve any conflict that exists.

In this chapter I briefly explore the functional neuroanatomy associated with these four components of the social brain: self-awareness, theory of mind, threat detection, and self-regulation. Unlike many other aspects of cognition, most of what we know about the social brain has been uncovered in the last decade and a half. Fortunately, the emergence of social neuroscience has been both rapid and far-reaching, and thus, despite its infancy, this approach has resulted in a substantial number of reliable empirical findings about the social brain.

Self-Awareness

Survival in human social groups requires people to monitor their behaviors and thoughts in order to assess whether they are in keeping with prevailing group (social) norms. Social neuroscience has made excellent strides in identifying brain regions that are involved in processing information about the self (Heatherton, Macrae, & Kelley, 2004). Both neuroimaging and patient (lesion) research has identified various regions of the prefrontal cortex as being crucial for the normal functioning of self. For instance, a series of imaging studies conducted over the past ten years has documented a substantial role of the medial region of the prefrontal cortex (MPFC) in processing self-relevant information (Craik et al., 1999; Heatherton et al., 2006; Johnson et al., 2002; Kelley et al., 2002; Macrae, Moran, Heatherton, Banfield, & Kelley, 2004; Moran, Heatherton, & Kelley, 2009; Moran, Macrae, Heatherton, Wyland, & Kelley, 2006; Schmitz, Kawahara-Baccus, & Johnson, 2004; Ochsner et al., 2004). This region is more active when, for example, people report on their personality traits, make self-relevant judgments about pictures, or retrieve autobiographical memories of past events. The issue of whether the self is somehow "special" is somewhat contentious (see Gillihan & Farah, 2005), but the imaging literature is quite clear regarding tasks that involve self-awareness; imaging studies (Gusnard, 2005) show that they activate the MPFC. It is important to note that converging evidence from patient research indicates that frontal lobe lesions, particularly to the MPFC and adjacent structures, have a deleterious effect on personality, mood, motivation, and self-awareness. Patients with frontal lobe lesions show dramatic deficits in recognizing their own limbs, engaging in self-reflection and introspection, and even reflecting on personal knowledge.

I hasten to add that that there is no specific "self" spot of the brain, no single brain region that is responsible for all psychological processes related to self. Rather, psychological processes are distributed throughout the brain with contributions from multiple subcomponents determining discrete mental activities that come together to give rise to the human sense of self (Turk, Heatherton, Macrae, Kelley, & Gazzaniga, 2003). From this perspective, then, the sense of self is an emergent conscious experience of ongoing neural activity that occurs in a social world.

Studying people with brain damage, who are often unaware of their deficits, supports this idea. For instance, people who have eye injuries notice that they have vision problems because visual areas of the brain notice that something is wrong. But if you damage a part of the brain responsible for vision, such as occurs for blindsight, then there is no output from that region to consider and nothing is noted as being wrong. Cooney and Gazzaniga (2003) explain this phenomenon by arguing that a left-hemisphere interpreter can make sense only of information that is available, so even though we might find the behavior of the hemi-neglect patients bizarre, they see the state of their world as perfectly normal. Studies like these show us that the experience of the brain injury patients often does not include awareness of the deficit, which supports the idea that consciousness arises as a result of the brain processes that are active at any point in time. Critically, Gazzaniga (2000) has argued that the interpreter may play a prominent role in the experience of self: "Insertion of an interpreter into an otherwise functioning brain creates many by-products. A device that begins by asking how one thing relates to another, a device that asks about an infinite number of things, in fact, and that can get productive answers to its questions cannot help but give birth to the concept of self" (page 1320).

My view of self has been highly influenced by Gazzaniga's interpreter model. Various psychological processes in discrete brain regions are active, depending on various environmental triggers, such as food, and internal body states, such as hunger. Other cognitive processes that are also active—such as autobiographical and prospective memory—include our goals, dreams, and aspirations. Although speculative, I believe it is possible that the MPFC operates by binding together various physical experiences and cognitive operations that have implications for the self. The prefrontal cortex receives input from all sensory modalities, and is therefore the brain region where inputs from internal sources conjoin with information received from the outside world. This region may act in a metacognitive fashion to monitor all stimuli, whether internal or external, so that our conscious sense of self at any particular moment reflects a workspace determined by which brain regions are most active.

One consequence of this model is that our sense of self is limited to functioning brain circuits that support psychological activity. So, for

example, until the frontal lobes are sufficiently developed there is only a minimal sense of self-awareness. Likewise, people often are unable to understand their personal failings and inadequacies, perhaps because people cannot recognize their own incompetence because they lack the capacity and expertise to identify and recognize competent behavior (Dunning, Johnson, Ehrlinger, & Kruger, 2003). Likewise, those who are socially anxious may have a dysfunctional connection between subcortical limbic structures associated with emotion, especially the amygdala, and prefrontal regions that normally regulate them, with a resulting sense of self that is overwhelmed by negativity. Finally, those who have frontal injuries have social deficits that they are not aware of because the very brain regions necessary for theory of mind and threat detection are unavailable to inform whether the self is living up to societal or group norms, and therefore such people lack insight and have impaired social emotions (Beer, Heerey, Keltner, Scabini, & Knight, 2003).

Hence, just as Gazzaniga's (1985, 1989) proposed interpreter gathers available evidence and tries to make sense of the world, I propose that the self serves a similar function, although it is biased to make sense of the world in a way that casts the self in a positive light (Baumeister, 1998). Indeed, substantial evidence points to a strong motivation for self-enhancement that is supported, in part, by cognitive biases and illusions. The adaptive significance of a positivity bias in an interpretive structure remains an open question, as do other questions such as why only some neurological activity contributes to a unitary experience of self.

Theory of Mind

In addition to recognizing our own mental states, living harmoniously in social groups requires that we be able to interpret the emotional and mental states of others (Heatherton & Krendl, 2009). For example, social emotions require that we be able to draw inferences about the emotional states of others (even if those inferences are inaccurate). For instance, to feel guilty about hurting a loved one, people need to understand that other people have feelings. Similarly, interpersonal distress results from knowing that people are evaluating you (thereby giving rise to emotions such as embarrassment), which at its core means recognizing

that other people make evaluative judgments. The ability to infer the mental states of others is commonly referred to as mentalizing, or having the capacity for theory of mind (ToM). ToM enables the ability to empathize and cooperate with others, accurately interpret other people's behavior, and even deceive others when necessary. The rapidly emerging neuroimaging literature on theory of mind has consistently implicated the MPFC as a central component of the neural systems that support mentalizing (Amodio & Frith, 2006).

Interestingly, neuroimaging research has demonstrated that the ability to mentalize relies heavily on similar neural networks engaged in processing self-relevant information, notably the MPFC. The area of greatest activity in the MPFC tends more often to be the more dorsal region in theory-of-mind studies than in self-reference studies, where the activity tends to be more ventral. Sometimes overlap between ventral and dorsal MPFC is observed when perceivers are asked to infer the mental states of targets—other people—who are most similar to them (Mitchell, Banaji, & Macrae, 2005). This finding suggests the possibility that mental simulation is engaged during theory-of-mind tasks, posing the question, "What would I do if I were that person?" This points to the possibility that the MPFC plays a similar role in both self-awareness and theory of mind. Although activity in other brain regions has been observed during ToM tasks—notably the superior temporal sulcus, the temporoparietal junction, and, less often, the amygdala—the dorsal MPFC appears to play a central role in the ability to make mental state attributions about other people. Indeed, this area reliably differentiates between people-people and people-computer interactions, even when the pairs are engaging in the same tasks. That is, "people" are given privileged status by the dorsal medial region of the prefrontal cortex as it processes information coming from the environment (see Mitchell, Heatherton, & Macrae, 2002)

Detection of Threat

Over the course of human evolution, a major adaptive challenge to survival was other people. Put simply, other people can be dangerous. There are two basic social threats: those from the in-group and those from the out-group. The nature of these threats is distinctly different; the major threat from the in-group is social exclusion. As mentioned earlier, humans

have a fundamental need to belong, because during the course of evolutionary history being kicked out of the group was a potentially fatal sentence. By contrast, out-group members are threatening because they want to take your group's resources or they may even want to kill you. Thus, the social brain requires threat mechanisms that differentiate in-group from out-group, or that are differentially sensitive to the nature of the social threat. A variety of brain regions have been identified as relevant to the detection of threat, but the two most prominent regions are the amygdala and the anterior cingulate cortex. Both regions have been implicated in social cognition.

Let's start with the out-group threat. In the social neuroscience literature, the most common area identified as relevant to threat from out-group members is the amygdala. For instance, studies have associated amygdala activity with negative response by whites to African Americans (Phelps et al., 2000; Richeson et al., 2003). People who possess stigmatizing conditions that make them seem less than human, such as the homeless, also activate regions of the amygdala (Harris & Fiske, 2006). We also have found amygdala responses to the physically unattractive or people with multiple facial piercings (Krendl et al., 2006). Considered together, it is clear that evaluating out-group members involves activity of the amygdala. So, what does the amygdala do in the social context? It has long been thought to play a special role in responding to stimuli that elicit fear (LeDoux, 1996). From this perspective, affective processing in the amygdala is a hard-wired circuit that has developed over the course of evolution to protect animals from danger. For example, much data support the notion that the amygdala is robustly activated in response to primary biologically relevant stimuli such as faces, odors, tastes, and so forth, even when these stimuli remain below the subjects' level of reported awareness (Whalen et al., 1998). Although there are other stimuli that elicit amygdala activity—biologically relevant positive objects such as food or sexual stimuli—the key role of the amygdala in learning what to fear may explain its involvement in detection of out-group threats.

How about threat from in-group members? If humans have a fundamental need to belong, then there ought to be mechanisms for detecting inclusionary status (Leary, Tambor, Terdal, & Downs, 1995). Put another way, given the importance of group inclusion, humans need to

be sensitive to signs that the group might exclude them. Thus, it was perhaps not surprising that a recent study implicated brain regions commonly associated with physical pain as crucial for the experience of social pain. Specifically, Eisenberger, Lieberman, and Williams (2003) found that a region of the dorsal anterior cingulate cortex (dACC), which is well established in the literature as involved in the experience of physical pain, was responsive during a video game designed to elicit feelings of social rejection when virtual interaction partners suddenly and surprisingly stopped cooperating with the research participant. Although these findings are intriguing, they clash with prior research and theorizing on the anterior cingulate cortex. In numerous prior studies, the dACC has been most closely associated with cognitive conflict, such as occurs when expectancies are violated (Bush, Luu, & Posner, 2000) whereas activity in the ventral anterior cingulate cortex (vACC) is more typically associated with social and emotional processes. Thus, one complication in interpreting the Eisenberger, Lieberman, and Williams findings is whether the method used to induce social rejection also likely violated research participants' expectations. Put simply, the participants expected to participate. When this did not happen, it violated expectancies, producing cognitive conflict. The experiment left unanswered whether the activation patterns they observed in that study were produced by cognitive conflict or social rejection.

We sought to address this issue by designing studies that allowed for an independent examination of the neural underpinnings of social rejection and expectancy violation (Somerville, Heatherton, & Kelley, 2006). Using an elaborate cover story we led subjects to believe that they had been evaluated by others as likable or not and we asked people to make similar judgments about those who had evaluated them, without their knowing what judgments the others had made. This approach permitted a factorial analysis that examined neural responses to feedback as a function of expectancy violation (when feedback matched or did not match participants' first impressions) and social feedback (when feedback was negative and when positive). Results revealed a double dissociation between the dorsal and ventral ACC regions. The dorsal ACC was uniquely sensitive to expectancy violations, with greater response when the fictitious feedback was inconsistent with participants' impressions. This was true regardless of whether the feedback was a rejection

or an acceptance. Conversely, a region in the ventral ACC was uniquely sensitive to social feedback, with significantly greater response to negative feedback than positive feedback, irrespective of expectancy violations.

Of course, social rejection is a complex phenomenon that includes, for most people, a violation of the central human expectation of social inclusion. As Leary's theory dictates (Leary et al., 1995), any situation in which people act in ways that permit the possibility of social exclusion should produce cognitive conflict, in part to signal people that they need to alter their behavior to avoid rejection. Various views of the anterior cingulate cortex have proposed that it helps resolve conflict by instigating other executive processes (Botvinick, Cohen, & Carter, 2004). This suggests that the anterior cingulate cortex should be important for self-regulation, a topic I consider shortly. What is apparent is situations that elicit threats of exclusion produce a cascade of neural responses associated with negative affect and cognitive conflict, which may promote behaviors that forestall social rejection. Given the role of the ventral ACC in processing the valence of self-descriptive terms, its abnormalities in depression, and its involvement in social rejection, further explorations of this region will be especially valuable for exploring the affective basis of self.

Self-Regulation

People who defy group norms—such as by cheating, lying, or being incompetent—often experience social emotions that indicate that something is wrong. We feel embarrassed when we goof, guilty when we harm, and ashamed when we get caught. Likewise, encounters with outgroup members can leave us wary or even afraid, even if we can ultimately override our prejudices and treat them fairly. The important point is that emotions that arise from social interactions serve as guides for subsequent behavior. This is what makes something like feeling guilty adaptive (Baumeister, Stillwell, & Heatherton, 1994). Feeling socially excluded, which threatens the need to belong, motivates behavior to repair social relationships. Feeling ashamed about considering cheating on our partner helps reign in temptations. In other words, social emotions promote self-regulation, which allows us to alter our behavior, make plans, choose from alternatives, focus attention on pursuit of goals,

inhibit competing thoughts, and regulate social behavior (Baumeister, Heatherton, & Tice, 1994).

Neuroscience research indicates that various regions of the prefrontal cortex are responsible for the human capacity for self-regulation (see the review by Banfield, Wyland, Macrae, Munte, & Heatherton, 2004). For instance, functional neuroimaging studies have implicated the anterior cingulate cortex in decision monitoring, initiating the selection of an appropriate novel response from several alternatives, performance monitoring, action monitoring, detection or processing of response conflict, and internal cognitive control (Wyland, Kelley, Macrae, Gordon & Heatherton, 2003). More recently, we found an important role for the ACC in efforts to suppress unwanted thoughts (Mitchell et al., 2007). What we observed was that the ACC was transiently engaged following the occurrence of unwanted thoughts, whereas dorsolateral prefrontal cortex was most active during ongoing efforts to suppress those thoughts. This finding is in keeping with the important role of prefrontal regions in executive functions more generally, all of which are necessary for successful self-regulation. Since the days of Phineas Gage we have known that the damage to certain prefrontal regions is associated with poor impulse control and self-regulatory difficulties more generally.

More recently, we have been using fMRI to study self-regulatory failures such as those that occur with smoking or dietary relapse. For example, laboratory research indicates that providing high-calorie foods to chronic dieters leads them to eat a great deal more than they would if their diets were intact. By contrast, nondieters eat less because they are filled by the food. We have recently used fMRI in a food-cue-reactivity paradigm (showing nondieters and dieters pictures of tempting foods) and found substantial differences in nucleus accumbens activity as a function of the high-calorie preload (Demos, Kelley, & Heatherton, in preparation). We found that somehow dieters are able to view attractive food cues without activating reward circuitry while their diets are intact (although how they do this is currently unknown). In sharp contrast, dieters who have just drunk a large milkshake that should have induced satiety, and that eliminated a reward response among nondieters, showed much greater reward-related food cue reactivity. Studies such as these begin to provide information relevant to people's

efforts to regulate their thoughts and actions, which are key aspects of the self-regulatory component of the social brain.

Summary

In this chapter I have proposed that building a social brain requires four components, each of which involves distinct functional brain regions. First, people need self-awareness—to be aware of their behaviors so as to gauge them against societal or group norms. The available evidence indicates that ventral MPFC is especially important for the experience of self. Second, people need to have a theory of mind—to understand how others are reacting to their behavior so as to predict how others will respond to them. This capacity for theory of mind has been most closely associated with a region of the medial prefrontal cortex that is more dorsal than that observed for self-referential processing. Third, they need to be able to detect threats. Threat detection involves at least the amygdala and the anterior cingulate cortex, although the precise nature of their roles in threat detection remains somewhat unclear. For instance, the amygdala may be especially important in ambiguous situations, such as when people are anticipating negative social judgments, whereas the anterior cingulate cortex may be more important once negative feedback has been received. The fourth component is the ability to self-regulate. This involves a number of prefrontal brain regions, including the anterior cingulate cortex, the lateral prefrontal cortex, and the ventral-medial prefrontal cortex. It is possible that these areas play different roles in self-regulation failure, depending on whether the failure is related to an impaired sense of self (ventral-medial prefrontal cortex), impaired theory of mind (dorsal prefrontal cortex), or failure to detect threat or conflict (anterior cingulate cortex).

There is much yet to discover about the social brain. Three decades ago, when Mike, with Joe LeDoux, published *The Integrated Mind* (Gazzaniga & LeDoux, 1978) , and later in his important volume *The Social Brain* (Gazzaniga, 1985), Mike foreshadowed current efforts to use the methods of neuroscience to understand what it means to be a member of our social species. An important contribution from Mike's approach was his development of the interpreter concept, which has gained broad support from many areas of scientific inquiry. The

interpreter idea is central to my thinking about the social brain, as it helps to reveal the interpretive nature of social interaction, for it is necessary to make sense not only of one's own behavior but also that of other people. In closing I express my gratitude to Mike for the many lunches and the many opportunities to see his social brain in action.

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IV

Mind Matters

Mind Matters
Homunculus
what do you want from me?
From us? From we?
Who can I be
but you—whom I (must) deny.
Do you why?
Are you one or many?
Any that has a different voice?
Any that can offer an alternative choice?
Any that wait for me to decide
whether to automatically react, thoughtfully enact, or
merely hide somewhere inside?
Any that can help clear up the confusion
emerging from the neural collusion
that leads me not only to feel
that "I" am real
but to insist
that "I" exist!

13

Different Ontogenetic Strategies for Different Species: Insights from Studies of the Developing Visual System

Leo M. Chalupa

I first met Michael Gazzaniga in a spectacular setting, a sixteenth-century palace on the Grand Canal in Venice. He was hosting a meeting on a provocative topic: "What's unique about the human brain?" Mike did his best to steer the discussion into intellectually fertile domains, but the participants, while paying some lip service to the features that might distinguish the human brain, for the most part gave their standard "stump" talks. The person working on the visual cortex spoke about the organization of the visual cortex, the expert on the hippocampus delivered his lecture on memory circuits, and so forth. As the final speaker, and the newest member of Mike's circle of meeting attendees, I pretty much followed suit. But in keeping with the general theme of the meeting I did focus on some data that my laboratory had collected showing that the cellular mechanisms underlying the formation of connections in the macaque monkey's visual system differed in unexpected ways from those that had been documented in rodents and carnivores. This led to an invitation by Mike to write a lead article on this topic for the *Journal of Cognitive Neuroscience*, a journal he founded and at that time was serving as editor in chief.

I recently finished reading Mike's new book, simply titled *Human*. (Gazzaniga, 2008). It deals in a brilliant yet very approachable manner with essentially the same question as the Venice meeting: "Might there be unique features to the human brain?" So some twenty years after the Venice meeting, Gazzaniga gives us his take on this subject. Having known Mike for all these years, I can tell you that this is a signature of his modus operandi. He floats an idea, and if it turns out to be a keeper, sooner or later the completed project materializes as a result of his efforts. The same thing happened when he first floated the idea for

starting a society for cognitive neuroscience. That was also in a memorable setting, a wonderful restaurant in Aspen, Colorado. Mike offered to buy the wine for about a dozen of us who had gathered for dinner after a hard day skiing and attending sessions at the Winter Conference on Brain Research. Maybe it was the wine, but as I recall, no one was much taken with the idea of starting another scientific organization. All sorts of reasons were given why this would not fly. Mike didn't press the matter further, but fortunately for the field this did not dissuade him from launching one of the most successful societies in all of science.

But I digress. Let me return to Mike's most recent book. The fact that it took about two decades for the book to appear after the Venice conference should not be taken as a sign of procrastination. No one who knows Mike would ever consider such an explanation as even remotely plausible. Rather, it is more a case of waiting for the opportune time to devote his energies to the topic under consideration. As was aptly demonstrated by the Venice conference, an earlier attempt to meaningfully address the question Mike posed would have fallen short of the intended outcome. Until recently, we simply lacked the vital information to deal with the matter in a satisfactory manner. In this case, as cogently discussed in *Human*, it took the molecular revolution in the neurosciences to provide us with plausible explanations based on genetic data of how changes in the brain could have evolved to give us the organ that makes the writing of this article possible. As Mike relates in the first chapter of *Human*, many neuroscientists are loath to seriously consider the concept that the human brain differs in some significant and fundamental way from that of other animals. This notion is especially prevalent among developmental neurobiologists, which happens to be my specialized field of endeavor. Why is that? For one thing, it is virtually impossible to do experiments on the developing human brain, so we rely on model organisms. These include fruit flies (*Drosophila* spp.), worms (*Caenorhabditis elegans*), mice (wild type and genetically modified), carnivores (cats and ferrets), and nonhuman primates. The simpler organisms provide huge practical advantages for developmental studies, not the least of which are their relatively simple nervous systems and the short time span during which key developmental events occur. There is the tacit assumption in the neuroscience community that what applies

to one species also applies to others. There is undoubtedly a substantial degree of commonality across a wide range of species in terms of the developmental events and the underlying mechanisms that govern different aspects of brain development. For instance, apoptosis (programmed cell death) is a ubiquitous phenomenon that occurs during the development of all nervous systems. Indeed, the genetic basis of apoptosis was first worked out by H. Robert Horwitz and his colleagues at MIT, for which be was awarded the Nobel Prize in 2002. No one can question the fact that general principles of nervous system development apply across diverse species. But that certainly does not rule out the possibility that genuine differences in molecular and cellular events could have evolved in the evolutionary process of building the brains of different animals.

Visual System Organization Differs among Species

Let's consider the topic on which I have spent a good portion of my working life, the formation of connections in the mammalian visual system. Over the years my laboratory has utilized different animals, including cats, ferrets, hamsters, rats, mice, and monkeys, depending on the particular problem we were studying. The visual systems of all mammals share some common feature: The neural retina of mouse and primates contains five layers (three cellular and two synaptic) and the cell types found in the cellular layers are also of the same type. Ganglion cells in both species innervate the dorsal lateral geniculate, and in turn geniculate neurons project to the primary visual cortex. So the flow of information, from the time that light activates the photoreceptors to the processing of visual information in the cortex follows the same general plan in all mammalian species. At the same time there are some pronounced differences in the organization of the visual systems of different mammalian species. For instance, the retinal decussation pattern, which refers to the ratio of retinal ganglion cells that project to the contralateral or ipsilateral hemisphere, varies markedly. In the macaque monkey as in the human the ratio is nearly 50:50, with about an equal number of ganglion cells projecting to one or the other hemisphere. By contrast, in the mouse about 95 percent of the neurons project contralaterally, with only about 5 percent forming the ipsilateral contingent. Moreover, the

major target structure of these retinal ganglion cells, the dorsal lateral geniculate nucleus (dLGN), displays marked variations across species. In the macaque monkey the dLGN comprises six distinct layers of cells, each layer separated by a clear-cut cell-sparse zone. The retinal projection to the monkey dLGN is highly stereotypic, with each cell layer receiving a functionally unique input. Thus, the largest retinal ganglion cells, making up what has been termed the magnocellular pathway, innervate the two ventral layers, one layer receiving input from the contralateral and the other from the ipsilateral eye. The other four cellular layers of the dLGN are innervated by smaller ganglion cells that form the parvocellular pathway, each of these innervated by either the contralateral or ipsilateral eye. Thus, input to the six layers of the monkey dlGN is segregated by eye of origin as well as ganglion cell type. Notably, the lamination pattern of the human dLGN can be more complex and variable than in the monkey (Jones, 2007).

The situation is very different with respect to the organization of the mouse dLGN, where there are no cell layers whatsoever. Although retinal ganglion cells of the mouse are composed of many different types (Coombs & Chalupa, 2008), there is no evidence that these selectively innervate different regions of the geniculate. The projections of the two eyes are segregated in the mouse, as is the case in all mammals that have been studied to date, with the contingent of cells that stem from the ipsilateral retina localized to a small region in the ventromedial aspect of the dLGN that is devoid of a contralateral input.

At the level of the visual cortex the mouse and monkey organization is also markedly different. Both species contain binocular cells, but these are distributed in a dissimilar manner. In the monkey the visual cortex is characterized by repeating ocular-dominance columns, where cells in all layers of a given column respond preferentially to stimulation of one eye. In the small binocular segment of the mouse visual cortex there are no ocular-dominance columns and the preference of binocular cells for one eye or the other appears to be randomly distributed.

In spite of these fundamental differences in the organization of the mature visual system between mouse and primate, the mouse visual system is increasingly being used as a model for visual-system development and plasticity (MIT Press recently published a book on this topic, *Eye, Retina, and Visual System of the Mouse*, that I edited with Rob

Williams; see Chalupa & Williams, 2008). It remains to be seen what the boom in mouse studies will tell us about the human visual system or that of other primates.

Species Differences in Visual System Development

In the spirit of Mike's recent book, I would like to focus on what I believe to be some rather remarkable differences in the development of the visual system of primates and that of other species. To this end I will consider four fundamental features of the mammalian visual system: the retinal decussation pattern, formation of retinogeniculate projections, retinotopic organization, and corpus callosal connections. In each case, I will summarize evidence showing that the developmental events occurring in the primate are more precise than what has been noted in rodents or carnivores. The evidence summarized here led Bogdan Dreher and me to write an article for *The Journal of Cognitive Neuroscience* (Chalupa & Dreher, 1991) in which we suggested that systems that require a high level of precision to function effectively at maturity are characterized by a high level of developmental precision. Although for the most part, developmental neurobiologists have paid scant attention to the idea of species- or even system- related differences in developmental events, I believe that this idea continues to have merit. Only time will tell whether the differences in developmental events that I discuss here relate to the yet to be discovered properties of human brain development.

Retinal Decussation Patterns

As summarized, in all mammalian species some retinal ganglion cells cross to the opposite side of the brain, while the projections of other cells remain uncrossed. Ganglion cells with crossed and uncrossed projections are located in selective regions of each retina, with the crossed cells localized to a portion of the nasal retinal, while the uncrossed cells are found in a region within the temporal retina. The location of the crossed and uncrossed population of cells can be readily identified by making a large deposit of a retrograde anatomical tracer into the retinorecipient targets of one hemisphere. After such tracer deposits, one can see the distinct and highly localized distribution patterns of crossed and uncrossed ganglion cells in each retina. In contrast to this mature pattern,

if one makes an equivalent deposit of a retrograde tracer into one hemisphere of a developing brain, the situation is found to be rather different. In rodents, many retinal ganglion cells will be labeled in retinal regions outside the mature zone. The proportion of such ectopic ganglion cells can be rather substantial, as much as 5 percent of the total population, depending on species and the age of the animal. This means that a significant contingent of retinal ganglion cells makes an incorrect decision at the optic chiasm, by projecting to the wrong hemisphere. As development proceeds these ectopic neurons are eliminated by a wave of cell death.

When we examined the retinal decussation pattern in the fetal monkey, we were much surprised to find that at all stages of development the location of crossed and uncrossed retinal ganglion cells was remarkably precise (Chalupa & Lia, 1991). With very few exceptions, the ganglion cells projecting to the contralateral hemisphere were all confined to the nasal retina, and those projecting to the ipsilateral hemisphere were in the temporal retina. To be sure, there were some ectopic neurons at a very early stage of development, but the percentage of such cells was very low. Thus, in the fetal monkey, when there is a total of some 3 million ganglion cells, only a few thousand project to the wrong hemisphere. At a comparable stage of development, rodents (rat or mouse) have a ganglion cell population of around 100,000, and the absolute number of ectopic cells is greater than in the fetal monkey. Our current understanding of the molecular cues that guide ganglion cells at the optic chiasm is far from complete, although considerable progress has been made in recent years in studies of the embryonic mouse (Petros & Mason, 2008). Nevertheless, the striking differences in the magnitude of the decussation errors exhibited by the primate visual system in comparison to that of rodents suggests that the events guiding the decussation process must be different either qualitatively (more signal expressed) or quantitatively (a different combination of signals). Currently nothing is known about molecular cues guiding retinal decussations at the primate optic chiasm, so this issue remains to be resolved.

Targeting of the Dorsal Lateral Geniculate Nucleus

More than thirty years ago Pasko Rakic (1977) discovered that in the fetal monkey, the projections of the two eyes overlap extensively when

the retinal fibers first innervate the dLGN before the eye-specific layers characteristic of the adult monkey become established. This developmental phenomenon has been documented in a wide variety of other mammalian species, indicating that the initial overlap followed by gradual segregation of the projections of the two eyes is a general mammalian developmental plan. This naturally raises a whole host of questions: one obvious issue concerns the cellular events underlying this process. Two nonmutual possibilities could account for the initial exuberance and later segregation of developing retinogeniculate projections. One factor may be that the arbors of early retinal fibers are more widespread, spanning territories that will be later innervated by the other eye. The other possibility is that ganglion cells that initially innervate the inappropriate region of the dLGN become eliminated through a process of cell death. In all species, a large proportion of retinal ganglion cells are gradually lost in the course of normal development, and some of this cell loss occurs when segregated eye-specific projections are being formed. To assess when developing retinal arbors are exuberant, it is necessary to label single fibers shortly after these have innervated the dLGN. This has been done in fetal cats and in the macaque monkey (Snider, Dehay, Kennedy, Berland, & Chalupa, 1999), and the results show clearly that the two species have evolved an entirely different strategy with respect to the development of retinogeniculate projections. In the fetal cat, as was first shown by Carla Shatz and her colleagues, retinal arbors are initially exuberant, and during the course of development these become more compact as their terminals become localized to a single layer of the dLGN (Sretavan & Shatz, 1984). By contrast, we found that in the fetal monkey individual retinal axons show no sign of exuberance throughout the developmental period when eye-specific inputs are being formed. Instead, terminal arbors grew progressively and became more complex. Since Rakic's initial observation were confirmed and extended using modern axoplasma-based tracing methods (Huberman, Dehay, Berland, Chalupa, & Kennedy, 2005), the fact that individual axon arbors are not exuberant leads to the conclusion that the withdrawal of retinal projections in the fetal monkey reflects the loss of these axons through ganglion cell death. So here is a prime example of how a given developmental event, the formation of eye-specific retinal projections to the dLGN, reflects two distinct cellular mechanisms.

Retinotopic Errors

For the visual system to function effectively, neurons at every level must be interconnected in a precise manner, giving rise to the multiple maps that characterize the visual brain at maturity. There is now compelling evidence, as postulated by Roger Sperry's chemoaffinity hypotheses (Sperry, 1963), that molecular cues play a crucial role in the formation of retinotopic projections. At the same time, there is evidence for topographic errors, since a certain proportion of retinal ganglion cells initially innervate incorrect regions of the target structure. Such ectopic errors are subsequently eliminated through an activity-mediated mechanism thought to follow the Hebbian rule whereby cells that fire together wire together. Thus, it is now well established that the formation of topographically correct connections is a two-step process requiring both molecular cues and activity-mediated refinements. This general scenario appears to apply to all systems. What is less apparent is the fact that a given system exhibits different degrees of developmental specificity in different species. In my laboratory we focused on the retinocollicular pathway, which studies by Dennis O'Leary and colleagues showed, in the rat, to be initially highly imprecise with respect to retinotopic order (Simon & O'Leary, 1992). By contrast, our experiments on the developing carnivore showed a remarkably precise projection pattern even at very early stages of development (Chalupa & Wefers, 2000), and in the fetal monkey we found that the degree of specificity exhibited by the developing geniculo-cortical projection was even more precise, since the fetal pattern was essentially the same as that found in the mature monkey (Chalupa and Lia, unpublished). Thus, with respect to topographic errors, it appears that the more advanced the system, the more precise the projection pattern throughout ontogeny. This implies that molecular cues play a bigger role and activity-mediated refinements a lesser role in setting up retinotopic order in primates than is the case in lower species. By contrast, in systems that are vitally important for the survival of lower species, such as the barrel cortex of rodents, relating to their whiskers, activity-related events might be less of a factor than molecular cues in specifying precise patterns of connections.

Formation of Corpus Callosal Connections

The corpus callosum is a structure that Mike made famous in his seminal studies of split-brain patients. Here I want to briefly consider what is

known about the development of callosal projections and how this work impacts the main theme of this chapter. In all species callosal projection neurons are distributed in a nonhomogeneous pattern, with certain regions of a given cortical area being richly endowed with such cells while other region are sparsely populated by callosal neurons. The termination pattern of callosal projections is also nonuniform within a given cortical region. A number of years ago, Giorgio Innocenti discovered that in the visual cortex of the postnatal cat the distribution of callosal projection neurons was initially essentially uniform and that the mature delimited pattern was gradually attained as development progressed (Innocenti et al., 1977). Herb Killackey and I showed that this ontogenetic change from a widespread to a delimited pattern occurs during the development of callosal projections in the somatosensory cortex of the fetal monkey (Killackey & Chalupa, 1986). Thus, it appeared as if callosal exuberance was a common feature of mammalian brain development. But this turned out not to be the case, since Henry Kennedy and his colleagues in Lyon, France, discovered that the primary visual cortex of the fetal monkey shows no such exuberance in callosal projection neurons (Dehay, Kennedy, & Bullier, 1988). This exception to the rule was subsequently confirmed in my laboratory (Chalupa, Killackey, Snider, & Lia, 1989). It provides another example that the visual system of the fetal primate shows more precision in the formation of specific projections patterns than is the case in lower species.

Concluding Remarks

The fact that humans possess higher cognitive functions, including language and related abilities, not found in even our closest evolutionary relatives would seem to argue for unique brain circuitries underlying these higher functions. So it would surprise no one to find that the development of frontal cortex and the language areas of the temporal lobe occur in a specialized manner as compared to the homologous cortical areas of other species. The evidence summarized here, that the formation of fundamental attributes of the primate visual system is characterized by cellular events not evident in nonprimate species, is rather unexpected. The primate visual system exhibits a greater degree of specificity than that found in carnivores and rodents. It may well be the case that, as we originally suggested (Chalupa & Dreher, 1991), a high degree of

developmental precision evolved because of the high survival value of a functional visual system in a newborn primate.

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14

Why Methods Matter in the Study of the Biological Basis of the Mind: A Behavioral Neurologist's Perspective

Mark D'Esposito

Six years ago I edited a book entitled *Neurological Foundations of Cognitive Neuroscience* (D'Esposito, 2002), in which each chapter was written by a behavioral neurologist who also "practiced" cognitive neuroscience, and highlighted the interface between the study of patients with cognitive deficits and the study of cognition in normal individuals. Each chapter began with a description of a case report, often a patient seen by the author, and described the symptoms seen in this patient, laying the foundation for the cognitive processes to be explored. After a clinical description, the authors provided a historical background about what we have learned about these particular neurobehavioral syndromes through clinical observation and neuropsychological investigation. Each chapter also explored investigations using a variety of methods—electrophysiological recording in awake-behaving monkeys, behavioral studies of normal healthy individuals, event-related potentials, and functional neuroimaging of both normal individuals and neurological patients—all aimed at understanding the neural mechanisms underlying the cognitive functions perturbed in each particular clinical syndrome. After completion of this book, I was convinced that the collection of chapters presented—although not intended to be all-encompassing—had captured the essence of cognitive neuroscience, a discipline aimed at studying the biological basis of the mind.

The idea for the book was launched at a MIT Press booth at the annual meeting of the Cognitive Neuroscience Society after one of the book editors asked me about my professional and research background. I told him I was a behavioral neurologist interested in understanding the relationship between the brain and behavior. As I talked, I could tell that he was perplexed about something, and when I finished he asked

me, "Why would a neurologist come to a meeting like this?" That question perplexed me. It never occurred to me that someone would ask me that. As I thought about this exchange during the rest of the day, I realized that although the discipline of cognitive neuroscience was being "practiced" by many different individuals with many different backgrounds, we had not yet begun to fully engage in conversations with each other.

About the time I had just finished my neurology residency, someone told me their definition of cognitive neuroscience: the study of the biological basis of the mind. It sounded very much like my definition of "behavioral neurology." And when I attended my first Cognitive Neuroscience Society meeting, I noticed that the poster sessions looked very similar to those I had been visiting at the behavioral neurology sessions at the American Academy of Neurology in past years. Today, in classrooms across the country, we teach our students that the phrase "cognitive neuroscience" was coined in the late 1970s in the backseat of a New York taxi when Mike Gazzaniga was riding with the eminent cognitive psychologist George Miller to a meeting to gather scientists to join forces to study how the brain enables the mind. On neurology wards across the country, we teach our medical students and residents that the emergence of "behavioral neurology" as a subspecialty of neurology began in the 1960s, prompted by the work of the eminent neurologist Norman Geschwind. But we all know that the roots of both these disciplines are to be found deep in the nineteenth century and the work of psychologists such as Williams James and neurologists and psychiatrists such as Jean-Martin Charcot, Paul Broca, Hughlings Jackson, James Papez, and Carl Wernicke. Actually, to be more historically accurate, we should recognize Hippocrates, who in the fifth century B.C. set forth the notion that it was the brain—not the heart—that was the seat of behavior. To my mind, modern behavioral neurology and cognitive neuroscience began in 1861 at the meeting of the Anthropological Society of Paris, when Dr. Paul Broca presented the history and autopsy findings of a patient who suffered an impairment in speech production such that he was capable of producing only the monosyllable "tan," which the patient repeated over and over (Broca, 1861). Broca showed this patient's brain to his colleagues and set forth the hypothesis that this patient's deficit in speech production was due to damage of the left inferior frontal gyrus. In this

way, the "human lesion method"—establishing the function of various parts of the brain by correlating a cognitive deficit with the location of a brain injury—provided a foundation for all other approaches that are used today aimed at the study of the relationship between brain and behavior.

The roots of cognitive psychologists who turned to the study of the brain (especially those newly trained in brain imaging techniques) lay within the discipline of psychology, the study of the mind. The roots of neuroscientists who study cognition lie within the discipline of neuroscience, the study of the nervous system. Many others engaged in the study of the biological basis of the mind are grounded in psychiatry, neurology, computer science, mathematics, economics, and other disciplines. As an act of unity and purpose, all of us have agreed to call what we do "cognitive neuroscience," despite our markedly different approaches. In my opinion, the major step forward that we have made in the thirty years since the phrase was coined is that we are all having more conversations with each other.

We are having these conversations in large part due to the contributions of the greatest ambassador of cognitive neuroscience, Michael Gazzaniga, to whom we dedicate this book. Undoubtedly the neuronal networks that store the meaning of "cognitive neuroscience" light up in our brains when we hear his name. In 1989 Mike launched the *Journal of Cognitive Neuroscience* with himself as the first editor-in-chief and five years later created the Cognitive Neuroscience Society. He edited the first comprehensive treatise on this discipline, "The Cognitive Neurosciences" (Gazzaniga & Bizzi, 1995), and the first cognitive neuroscience textbook for undergraduates and graduate students (Gazzaniga, Ivry, & Mangun, 2002). Each of these efforts was critical for defining as well as moving our discipline forward, both scientifically and socially. With the creation of the Summer Institute for Cognitive Neuroscience, Mike has created a forum for training generations of future cognitive neuroscientists. During this summer meeting, Mike always hosts dinner parties for the speakers, bringing together cognitive neuroscientists for provocative conversations that often stimulate new ideas and collaborations. In my opinion, cognitive neuroscience will grow stronger as the number of such conversations grows. I believe that Mike recognized this from the start by, in effect, organizing one very large

"dinner party" that has lasted roughly thirty years and should last for many more years to come.

Methods Used to Study the Relationship between Brain and Behavior

Early in my career I was attending a study section meeting at the National Institutes of Health when each of the panel members was asked to introduce him- or herself briefly and state their research interests. I said that I investigated "prefrontal function." My colleague, who was a psychologist, said he investigated "cognitive control." Clearly, we investigated the same phenomenon, but from different perspectives. As I have mentioned, those who practice cognitive neuroscience come from numerous backgrounds (psychology, cognitive science, neuroscience) and take numerous approaches. It is not surprising that the number of approaches has increased as rapidly as the number of questions that are being asked. To me, this is what generates the excitement in this discipline. However, despite my excitement, I offered this cautionary tale in the preface of *Neurological Foundations of Cognitive Neuroscience*:

> It is an exciting time for the discipline of cognitive neuroscience. In the past 10 years we have witnessed an explosion in the development and advancement of methods that allow us to precisely examine the neural mechanisms underlying cognitive processes. Functional MRI, for example, has provided markedly improved spatial and temporal resolution of brain structure and function, which has led to answers to new questions, and reexamination of old questions. However, in my opinion, the explosive impact that functional neuroimaging has had on cognitive neuroscience may in some ways be responsible for moving us away from our roots—the study of patients with brain damage as a window into the functioning of the normal brain.

What prompted this cautionary tale? Functional magnetic resonance imaging (fMRI) emerged on the scene in the early 1990s, and around the time of the publication of my book, journals and meetings were being filled to the brim with fMRI studies. For example, a PubMed and Ovid search revealed 3,426 unique fMRI articles published across 498 journals from the years 1991 to 2001. In only three years, from 1998 to 2001, the number of published articles on fMRI doubled (Illes, Kirschen, & Gabrieli, 2003). The tables of contents of journals dedicated to studies using functional imaging, such as *NeuroImage* and *Human Brain*

Mapping, were increasing in size each month, and attendance at the meetings of the Organization for Human Brain Mapping began rising exponentially. A simple walk down the aisle of a poster session at the annual meeting of the Cognitive Neuroscience Society mirrored what could be seen in the explosion of writing. During this time it was alarming to me that a walk through a cognitive neuroscience poster session rarely led to a poster using patients with focal lesions to study the relationship between brain and behavior. In fact, at the 2005 Cognitive Neuroscience Society meeting, studies using patient populations made up only 16 percent of all posters, and only half of these were focused on studying brain-behavior relationships (Chatterjee, 2005). Had studying patients with brain lesions taken a backseat to newer methods? To further explore this historical circumstance, as well as make an attempt to gaze into the future, let us take a very critical look at these two prominent cognitive neuroscience methods.

General Considerations Regarding Cognitive Neuroscience Methods

Lesion studies and functional neuroimaging studies of normal, healthy subjects provide complementary but different types of information regarding brain-behavior relationships. Clearly, both of these kinds of studies are necessary to provide an inferentially sound basis for drawing conclusions about the neural basis of cognition. Converging evidence from both types of studies is necessary because of inferential limitations of each method when performed in isolation.

The nature of functional neuroimaging studies is that they support inferences about the association of a particular brain system with a cognitive process. However, functional neuroimaging is unable to prove that the observed activity is necessary for a putatively isolated cognitive process. This is because one never has perfect control over the cognitive processes in which a subject engages. An experiment may control the conditions or tasks to which a subject is exposed, but it cannot conclusively demonstrate that a subject is differentially engaging a single, identified cognitive process. It should be noted that "a more sensitive cognitive task" (as sometimes suggested by reviewers of publications) might not solve this problem, as it is always possible that the subject engages in unnecessary cognitive processes that either have no overt,

measurable effects or are perfectly confounded with the process of interest. As a result, observed neural activity may be the result of some confounding neural computation that is not itself necessary for the execution of the cognitive process seemingly under study. In other words, functional neuroimaging is a *correlative* method (Sarter, Bernston, & Cacioppo, 1996).

It is important to note, however, that the limitations on the inferences that can be drawn from functional neuroimaging studies applies to all methods of physiological measurement, including microelectrode recording of neurons, scalp evoked-related potentials, magnetoencephalography, hemodynamic measures, and measures of glucose metabolism. The inference that some brain region, system, or process is "necessary" cannot be drawn absent a demonstration that its inactivation disrupts the cognitive process in question.

To illustrate these issues consider the types of inferences that can be drawn from lesion versus neurophysiology studies. Single-unit recordings in awake-behaving monkeys have revealed neurons in the lateral prefrontal cortex (PFC) that increase their firing during a delay between the presentation of information and its later use in behavior (Funahashi, Bruce, & Goldman-Rakic, 1989; Fuster & Alexander, 1971). These studies have been taken as evidence that the lateral prefrontal cortex represents a neural correlate of working memory, the temporary retention of information that was just experienced or just retrieved from long-term memory but no longer exists in the external environment (D'Esposito, 2007). The necessity of this region for working memory was demonstrated in monkey studies that have shown that lateral prefrontal cortex lesions impair performance on delayed-response tasks, but not on tasks that require visual discrimination and saccades (rapid intermittent eye movement) without the requirement of holding information online (Funahashi, Bruce, & Goldman-Rakic, 1993). However, delay-specific neurons have also been found in the hippocampus (Cahusac, Miyashita, & Rolls, 1989; Watanabe & Niki, 1985), a region thought to be involved in long-term memory, as opposed to working memory. Lesions of the hippocampus, however, were originally found not to impair performance on delayed-response tasks (with short delay periods) suggesting that the hippocampus may be involved in maintaining information over short periods of time but is not necessary for this cognitive

operation (Alvarez, Zola-Morgan, & Squire, 1994). These findings in monkeys were consistent with observations in humans. For example, the well-studied patient H.M., with complete bilateral damage to the hippocampus, had the severe inability to learn new information, but could nevertheless perform normally on working-memory tasks (Corkin, 1984). More recent studies have been able to further characterize the precise role of the hippocampus in working memory. For example, based on complementary functional magnetic resonance imaging (Ranganath & D'Esposito, 2001) and lesion studies (Hannula, Tranel, & Cohen, 2006), the hippocampus is implicated in long-term memory especially when relations between multiple items or multiple features of a complex, novel item must be retained. Thus, the hippocampus may only be engaged during working-memory tasks that require someone to subsequently remember novel information.

As can be seen by this example of working memory, a stronger level of inference results from combining lesion studies and those with physiological measurements. That is, it was observed that a lesion to a cortical area impaired a given cognitive process and that the cognitive process, when engaged by intact monkeys or humans, evoked neural activity in the same cortical area. Thus, the inference that the neuroanatomical area is computationally necessary for the cognitive process is now rendered less vulnerable to the faulty assumptions noted previously for each method performed in isolation. As a result, lesion and functional neuroimaging studies are complementary, in that each provides inferential support that the other lacks.

No Cognitive Neuroscience Method Is Perfect

The perfect cognitive neuroscience method would allow noninvasive simultaneous recording of all neurons in the brain on a millisecond timescale. Obviously, the methods available at this time differ in their spatial and temporal resolution, and none of them achieve the highest resolution in both domains (see figure 14.1). However, in addition to limitations of these methods imposed by their technical specifications, the interpretation of data derived from each method is bound by a number of conceptual constraints, many of which are inherent in the method and not fixable by technological advances.

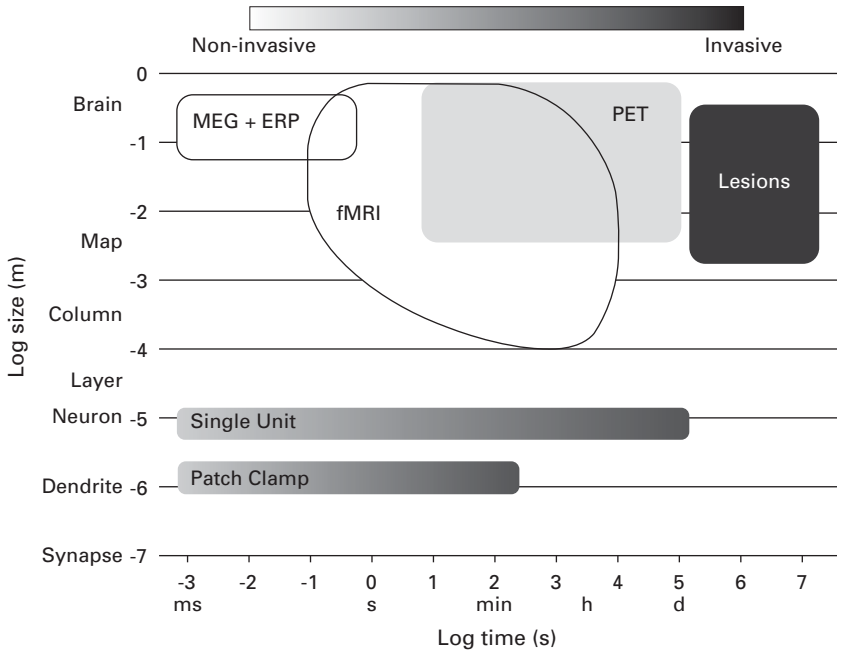

Figure 14.1
Temporal and spatial resolution of various cognitive neuroscience methods.

The Lesion Method

Unlike the lesions produced in animal models, which can be created with surgical precision, lesions in human patients are often extensive, and even if they are quite focal they will follow the boundaries of the brain's blood supply. Also, certain locations in the brain are more likely to be damaged by a stroke, the most common cause of focal brain lesions in humans. For instance, the middle cerebral artery is more commonly affected by strokes than other arteries, leading to damage in the lateral frontal, parietal, and temporal cortex. Also, it is not possible to study a group of patients each with the same exact lesion location and extent. For this reason, studies have often adopted a "lesion-overlap" approach (Chao & Knight, 1998), where a behavioral deficit is correlated with the location of the lesion that is found in all individuals. However, as Rorden and Karnath (2004) have elegantly pointed out, the conclusions drawn from such an approach are prone to error. These researchers present as an example an attempt to identify where primary vision is processed in

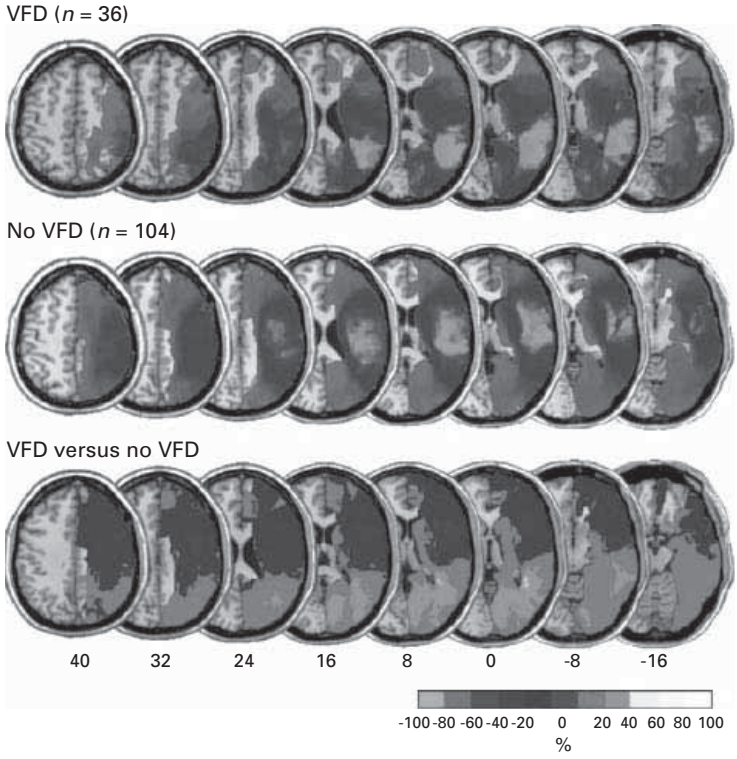

Figure 14.2 (plate 4)
The data in this figure illustrate lesion-overlap analysis of 140 patients with right-hemisphere damage due to stroke. The top panel shows the distribution of lesion frequency of patients with visual-field deficits showing maximal overlap of lesions within the temporoparietal cortex. The middle panel is patients without visual-field deficits (control group). The bottom panel is the subtraction image of patients showing visual-field deficits minus those without such deficits. It demonstrates that visual field deficits are actually due to damage in primary visual cortex within the occipital lobe.

the brain by studying patients with visual-field deficits as a result of stroke (see figure 14.2, plate 4). The lesion-overlap analysis was first performed in patients with visual-field deficits, the researchers observing that the area of maximal overlap of their lesion was in the temporoparietal cortex. However, if one subtracts the lesion overlap of a control group, a second group of stroke patients without visual-field deficits, it is observed that the primary visual cortex within the occipital lobe is the area most commonly damaged in patients with visual-field deficits. This example illustrates how the failure to include a control group in such

lesion-overlap analyses could have led to the conclusion that primary vision is a function of the temporoparietal cortex rather than of the primary visual cortex.

Another important issue is that lesions may damage not only local neurons but also "fibers of passage." It is also possible that connections from region A support the continued metabolic function of region B, but that region A is not computationally involved in certain processes undertaken by region B. Mechanisms that may produce such an effect include diaschisis (Feeney & Baron, 1986) or retrograde trans-synaptic degeneration. The concept of diaschisis is that damage to the brain deprives other intact regions of normal afferent inflows from the injured area. Thus, a lesion can cause dysfunction of a remote area because of its strong connections with that other area. For example, a PET study of a patient with amnesia demonstrated that a stroke damaging the septum, within the basal forebrain, resulted in decreased activity remotely in the hippocampus (Abe, Inokawa, Kashiwagi, & Yanagihara, 1998). Even though the hippocampus was not damaged directly, decreased activity resulted because it is anatomically connected to the septum via the fornix. Determination of the neural substrate of the patient's memory loss in this case would be difficult. Thus, patients who are tested in the acute stage are problematic for studies attempting to link structure and function. However, new imaging techniques such as perfusion and diffusion-weighted MRI may allow one to overcome these potential limitations by identifying decreased brain function remote to the infarct observed by structural imaging. Moreover, these MRI techniques can also distinguish between infarcted brain tissue and tissue that may be rescued from permanent damage (see Hillis et al., 2008).

When tested later after injury, patients' recovery of function may have plateaued and brain plasticity and reorganization may have occurred. At this point in time it cannot be assumed that intact regions of the brain will function in the same way after injury as before (for further discussion of this idea see Farah, 1994). A relatively new lesion-based method, transcranial magnetic stimulation (TMS), overcomes confounds due to potential brain reorganization because it causes a transient lesion, and behavioral performance is assessed before this type of brain reorganization can occur. Other potential benefits of transcranial magnetic stimulation include (1) the ability to study healthy subjects who do not have

additional potential pathologies; (2) the ability to be performed repeatedly in the same subject; (3) the potential to study a larger number of subjects than in a patient study; and (4) the ability to target different locations in the brain of one subject (Pascual-Leone, Bartres-Faz, & Keenan, 1999). Of course, transcranial magnetic stimulation has its own limitations. For instance, it is not currently possible to accurately determine the spatial and neuroanatomical extent of the disruption produced by the procedure. Moreover, TMS's possible disruptive effects on distant cortical and subcortical areas cannot be ruled out, and the precise physiological mechanisms of action of TMS are unclear. Nevertheless, it is a powerful method for studying brain-behavior relationships (for a review of the types of empirical applications that are possible with TMS, see Sack, 2006).

Functional Neuroimaging

Numerous options exist for designing experiments using fMRI. The prototypical fMRI experimental design consists of two behavioral tasks presented in blocks of trials alternating over the course of a scanning session, during which the fMRI signal between the two tasks is compared. This is known as a blocked design. For example, a given block might present a series of faces to be viewed passively, which evokes a particular cognitive process, such as face perception. The "experimental" block alternates with a "control" block, which is designed to evoke all of the cognitive processes present in the experimental block except for the cognitive process of interest. In this experiment, the control block may be a series of objects. In this way, the stimuli used in experimental and control tasks have similar visual attributes, but differ in the attribute of interest—faces. The inferential framework of "cognitive subtraction" (Posner, Petersen, Fox, & Raichle, 1988) attributes differences in neural activity between the two tasks to the specific cognitive process, that is, face perception. Cognitive subtraction was originally conceived by Donders in the late 1800s for studying the chronometric substrates of cognitive processes (see Sternberg, 1969) and was a major innovation in imaging (Petersen, Fox, Posner, Mintun, & Raichle, 1988).

The assumptions required for cognitive subtraction may not always hold and could produce erroneous interpretation of functional neuroimaging data. Cognitive subtraction relies on two assumptions: "pure insertion" and linearity. Pure insertion implies that a cognitive process can

be added to a preexisting set of cognitive processes without affecting them. This assumption is difficult to prove because one needs an independent measure of the preexisting processes in the absence and presence of the new process. If pure insertion fails as an assumption, a difference in the neuroimaging signal between the two tasks might be observed, not because a specific cognitive process was engaged in one task and not the other but because the added cognitive process and the preexisting cognitive processes interact.

An example of this point is illustrated in working memory studies using delayed-response tasks. These tasks (for an example, see Jonides et al., 1993) typically present information that the subject must remember (engaging an encoding process, followed by a delay period during which the subject must hold the information in memory over a short period of time (engaging a memory process), followed by a probe that requires the subject to make a decision based on the stored information (engaging a retrieval process). The brain regions engaged by evoking the memory process theoretically are revealed by subtracting the blood oxygenation-level dependent (BOLD) signal measured by fMRI during a block of trials that the subject performs that do not have a delay period (engaging only the encoding and retrieval processes) from a block of trials with a delay period (engaging the encoding, memory, and retrieval processes). In this example, if the addition or "insertion" of a delay period between the encoding and retrieval processes affects these other behavioral processes in the task, the result is failure to meet the assumptions of cognitive subtraction. That is, these "nonmemory" processes may differ in delay trials and no-delay trials, resulting in a failure to cancel each other out in the two types of trials that are being compared. In fact, this has been shown to occur in a fMRI study using a delayed-response task (Zarahn, Aguirre, & D'Esposito, 1997).

Other types of inferential failure should also be considered when interpreting functional neuroimaging studies. For example, there are two main inferences that can drawn from functional neuroimaging data. A "forward inference," which is typical for most imaging experiments, derives from the assumption that if a particular brain region is activated by a cognitive process (evoked by a particular task), then the neural activity in that brain region must depend on engagement of that particular cognitive process. For example, a brain region that responds with

a greater magnitude of fMRI signal to face stimuli than to other stimuli (such as cars, buildings, and so forth) would be considered to be activated by face perception. This type of inference was already discussed. In contrast, a "reverse inference" derives from the assumption that if a particular brain region is activated then a cognitive process must have been engaged by the subject during the study. This type of inference is highly prevalent within discussion sections of functional neuroimaging papers. For example, activation within the prefrontal cortex during a mental rotation task (Cohen et al., 1996) might be taken as evidence that subjects were using working memory to remember the identity of the rotated target (this assumption was derived from previous imaging studies that have shown activation of PFC during working memory tasks). It can be shown in general that "reverse inferences" of this type are logically incompatible with simultaneous forward inferences. In our previous example, one cannot be sure that the working memory was engaged to evoke prefrontal cortex activation, since some other cognitive process could have activated this region (D'Esposito, Ballard, Aguirre, & Zarahn, 1998). For a discussion of potential ways to improve one's confidence in making a reverse inference, the reader is referred to a discussion by Poldrack (2006).

The Impact of Cognitive Neuroscience Methods

In 2005, Lesley Fellows and colleagues (2005) published a paper that asked the question: What is the comparative impact of the two most common methods employed for studying structure-function relationships in the human brain: lesion and functional imaging? They examined this question by performing a systematic literature review of cognitive neuroscience articles that employed either functional imaging or lesion techniques, published at one of two time points in the 1990s, and assessed the effect of the method used on each article's impact across the decade. They hypothesized that lesion studies would have a greater scientific impact, even though the relative proportion of such studies in the cognitive neuroscience literature had declined since the advent of functional neuroimaging. This is because lesion studies can establish a causal role for a brain region in behavior and thus provide a stronger inference (despite the caveats regarding diaschisis in acute lesions and reorganiza-

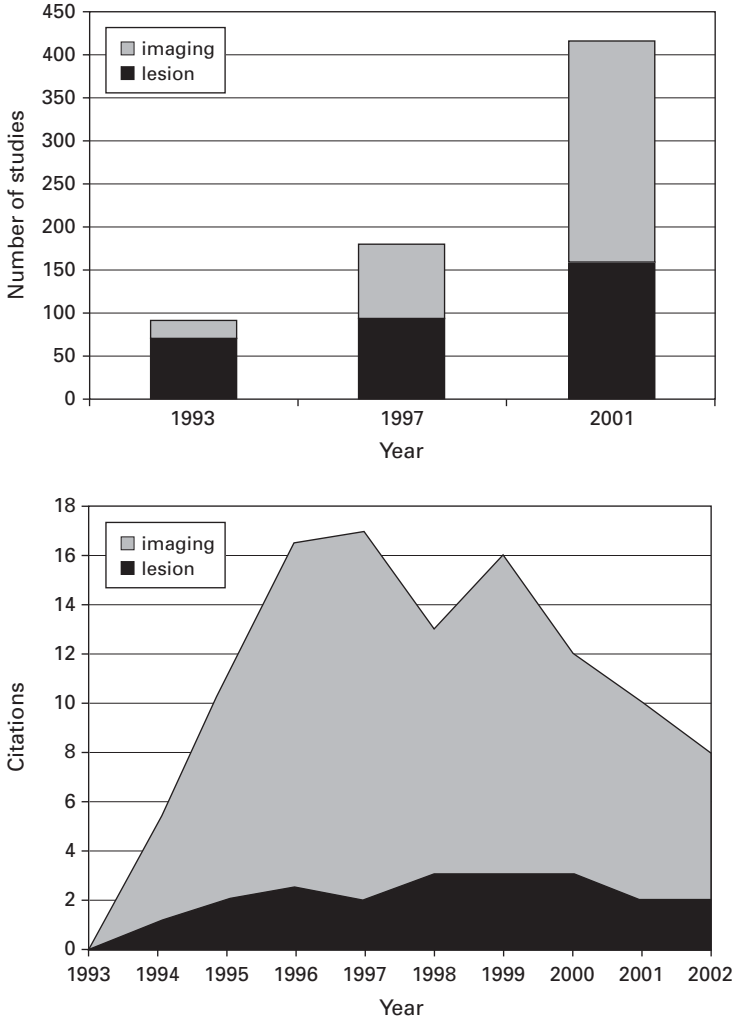

Figure 14.3
The top panel shows the number of functional imaging or lesion studies published in 1993, 1997, and 2001. The bottom panel shows the median number of citations per year from the date of publication in September 1993 for articles published in 1993.

tion in function in chronic lesions), whereas functional imaging studies cannot. It was assumed that citation counts would "bear some relationship to the inferential strengths of the cited studies." Contrary to this hypothesis, functional neuroimaging studies were cited three times more often than lesion studies (see figure 14.3). This finding was primarily due to the fact that functional imaging studies were more likely to appear in high-impact journals and functional imaging studies were less likely to cite studies utilizing other methods.

Anjan Chatterjee offers three potential factors that drive the findings reported by Fellows and colleagues (Chatterjee, 2005). First, "Novelty is intrinsically appealing." We all believe that newer things are generally better, and functional neuroimaging is the newer thing. Second, conducting research with patients is not easy because the access to such patients is much more difficult than the access to MRI scanners. Third, lesion and functional imaging studies, respectively, tend to test different types of hypotheses. A study of "function" that is typical of imaging studies is to test whether a specific cognitive function is supported by a particular brain region; a study of "structure" that is typical of lesion studies is to test whether a particular brain region is necessary for a specific cognitive function. Chatterjee argues that even though lesion studies have great inferential strengths in understanding "structure," in practice their great strength has been in probing "function." Much of our knowledge about mechanisms of reading, for example, has derived from studies of patients with lesions. As Chatterjee puts it, "Herein lies the great paradox about lesion studies."

Final Thoughts

This exposition of my thoughts on the history of cognitive neuroscience and the approaches we have taken toward studying the biological basis of the mind brings me back to the contributions of Mike Gazzaniga. It is apparent to me that many newly trained cognitive neuroscientists lack exposure to the rich history of patient-based approaches for studying brain-behavior relationships. However, I am optimistic that the astonishing infrastructure that Mike has built over the years will remind cognitive neuroscience trainees that research aimed at understanding the function of the normal brain can be guided by studying the abnormal brain. After

all, this is how Mike himself got started with his landmark studies of split-brain patients—people with complete sections of their corpus callosum—which led to enormous insight regarding hemispheric asymmetries (Gazzaniga, 1967). If Mike had had only functional imaging available to him at the time, he likely would have had a difficult time reaching the conclusions he derived from the observations of his patients. For example, it is well established that many language tasks exhibit bilateral hemisphere activation (Binder et al., 1996). The incredible insight derived from patients with neurological and psychiatric disorders still provides a foundation for our discipline, and should continue to be an important methodological tool in future studies. It is now one of many tools available to us, and although numerous other writings have paid lip service to the value of the convergence of methods, published studies that actually combine methods remain few and far between. No doubt there are numerous reasons for this, but whatever they are, the time has come for funding agencies and journals to insist on studies that combine methods.

When I took over from Mike as the editor-in-chief of the *Journal of Cognitive Neuroscience*, the editors and I asked him a series of questions so that we could learn more about his thoughts regarding the discipline of cognitive neuroscience (Gazzaniga, 2004), one of which was the following:

Has the conduct of brain/mind research changed since you entered the field in the 1960s, or is the process the same, merely the methods different?

His response:

It is funny you should ask. I recently had the pleasure of being the "wildcard" speaker at the Stanford Neuroscience Retreat in Monterey. The assignment was to reflect on what the future of neuroscience might look like. After the proper caveats that only fools spoke about the future I took my shot at it.

One of the first things I discussed was the fact that scientific enquiry is much less direct and personal and much more interdisciplinary and communal. When I started my graduate studies with Roger Sperry and stumbled into doing the first human split-brain studies at Cal Tech, it was relatively easy and very personal. Everything from calling the patient to conceiving, designing and implementing the experiments were done by me. Nothing was between the scientist and his topic. There were not 6 technicians, complex devices, and a hierarchy of staff to deal with. It was you and the patient. There was no networking and the artificial relationships that arise from that kind of thing. It was all deeply personal and almost private.

Of course, all of this was enhanced in immeasurable ways with daily conversations that sometimes went on for hours with Sperry. He and I had a very personal relationship during my time at Caltech. He was every much a part of the work as I was and his wisdom was all over the place. Sperry was a truly great scientist. That goes without saying. Yet, the actual ability to do the work was much simpler.

So I think the process has changed dramatically. Adding to the process is the content of the questions asked. In the early 1960s the full impact of cognitive science on neuroscience had not yet occurred. Moving out of Stimulus-Response psychology and into the realm of "representations" was a process that took time and to some extent continues until this day.

We may differ in the questions we ask and the approaches we take to study the biological basis of the mind. We may differ in whether we believe what we do should be called cognitive neuroscience, behavioral neurology, or neuropsychology. Nevertheless, I believe that Mike's subtle message in his answer to this question is that we should not forget where we came from as we attempt to move forward.

Acknowledgments

I would like to thank Brad Buchsbaum and Andy Kayser for their helpful comments regarding this chapter.

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15

Ethics and the Ethical Brain

Steven Pinker

For ingenious studies of split-brain patients which illuminated the functions of the cerebral hemispheres. His discovery that the right hemisphere can act without the awareness of the left, which then invents an interpretation about what the whole person did, is a classic of psychology, rich with implications for consciousness, free will, and the self. He created the field of cognitive neuroscience, and his accessible writings inserted it into the national conversation. His wit and joie de vivre showed generations of students and colleagues the human face of science.

—Citation for the American Psychological Association's Distinguished Scientific Award to Michael Gazzaniga, 2008

When the American Psychological Association asked me to sum up Michael Gazzaniga's contributions to psychology in less than a hundred words, I had to compress a significant chunk of these contributions into the phrase "inserted [cognitive neuroscience] into the national conversation." For in addition to his scientific and institutional impact, Mike has done more than any scientist to point out that cognitive neuroscience, and modern scientific psychology more generally, has profound moral implications. These implications, moreover, don't just concern practical issues in the applications of cognitive neuroscience, such as in the diagnosis of psychiatric disorders, innovations in lie detection technology, or pharmaceuticals that enhance memory and cognition. They also involve deep, existential concerns: the core of political and moral theory, and the meaning that people ascribe to their lives. Gazzaniga has not flinched from pointing out these implications to a wide national audience, and doing his best to make sense of them. My own efforts to explore the political and moral implications of the cognitive neuroscience revolution (Pinker, 2002) have been deeply influenced by his writings, and I think that they are in broad sympathy with them.

A standard view in Western culture, developed under the influence of Judeo-Christian doctrines, is that every person has a soul (alternatively, that every person *is* a soul). As a consequence, everyone is equal, and equally precious. Everyone has free will, which allows us to try to perfect society and ourselves, if we so choose, and makes us responsible for our actions. The soul also gives us a higher purpose, above and beyond biological imperatives, including love, worship, and the pursuit of knowledge, beauty, and morality. As I documented in *The Blank Slate*, this general view is not confined to nonscientists or devout theists. In a famous book attempting to reconcile science and religion, the paleontologist Stephen Jay Gould (1999) argued that the two correspond to "non-overlapping magisteria," science being concerned with fact and explanation, religion's purview being meaning and morality.

Though few scientifically literate people would connect their beliefs about meaning and morality to a literal commitment to the existence of a soul, I think that many still tacitly subscribe to the metaphor that the brain is a kind of personal digital assistant (PDA), which stores information and does calculations at the behest of a user, the soul in disguise (Bloom, 2003). We see this tacit belief in the brain-as-PDA in the widespread perception that freedom, dignity, and responsibility are incompatible with a biological understanding of the mind, which is often denounced as "reductionist" or "determinist." We see it in the stem-cell debate, where some of the theologians who've weighed in on this issue have framed it in terms of when "ensoulment" takes place in embryonic development, which means that perhaps the most promising medical technology of the twenty-first century is being debated in terms of when the ghost first enters the machine (Gazzaniga himself has published emphatic editorials in national media arguing for the humanity of stem-cell research and so-called therapeutic cloning). And we see a tacit belief in the brain-as-PDA theory in everyday thinking and speech; it's hard to get away from. We talk about "John's body" or "John's brain," which presupposes some entity, John, that's separate from the brain that it somehow owns. And we see it when journalists speculate about "brain transplants," which they really should call "body transplants," because as Dan Dennett once pointed out, this is the one transplant operation where you really want to be the donor rather than the recipient.

Gazzaniga has made it clear that none of this can survive the cognitive neuroscience revolution—the realization that it's "PDA all the way up." All of our thoughts, feelings, and decisions consist of physiological activity in the tissues of the brain. Indeed, Gazzaniga's research is largely responsible for showing that not just low-level mechanical functions such as memory and pattern recognition are instantiated in the brain but also our highest and most distinctively human mental activities, including the emotions, social life, conscience and morality, consciousness, and the self of self.

Gazzaniga not only made these discoveries, but vigorously promoted the development of the field of cognitive neuroscience, which extended the biology to higher levels of mental function. And in several books, most recently *Human: The Science Behind What Makes Us Unique* (Gazzaniga, 2008), he popularized all of the sciences of human nature (cognitive neuroscience, cognitive science, evolutionary psychology, behavioral genetics) and their applicability to every aspect of mental life. Gazzaniga was also an early appreciator of the ethical and philosophical implications of the cognitive neuroscience revolution. He explored these implications in his book *The Ethical Brain* (Gazzaniga, 2005), midwifed the new fields of "neuroethics" and "neurolaw," and served on George W. Bush's President's Council on Bioethics—often courageously defying the antiscience, "theoconservative" slant of that panel (Pinker, 2008). An underlying message of Gazzaniga's writings is that we ignore the moral and political implications of cognitive neuroscience at our peril. If scientists and secular thinkers don't address these implications, politicians, theologians, and reactionary pundits will do it for us.

Like Gazzaniga, I believe that it is essential to look at the connection between the politics and the sciences of human nature with care: to explore the emotional reactions and moral inferences that people draw from cognitive neuroscience, and the best ways to respond to them and their consequences.

It seems to me that four issues are at stake here: the fear of inequality, the fear of imperfectability, the fear of determinism, and the fear of nihilism. My own view (Pinker, 2002) is that all four fears are in fact baseless: they don't logically follow from recent discoveries or theories,

but have arisen because the discoveries and theories are so novel, and people haven't had a chance to digest their implications.

Let me begin with the fear of inequality—a fear made acute by findings from behavioral genetics (in particular, studies of twins and adopted children) that have shown that much of the variation in cognitive and personality traits within a society has genetic causes. Gazzaniga himself contributed to this literature with an important finding, that the brains of monozygotic twins are more similar in morphology than the brains of dizygotic twins (Thompson et al., 2001; Tramo et al. 1995)—a signature of genetic influence. Many people find such discoveries troubling, for they refute the idea that the mind at birth is a blank slate—and if we're blank slates, we must be equal. That follows from the mathematical truism that zero equals zero equals zero. But if the mind has any innate organization, according to this fear, then different races, sexes, or individuals could be biologically different, and that might seem to justify discrimination and oppression.

I think it's easy to see the confusion here: the conflation of the value of *fairness* with the claim of *sameness*. The lines in the Declaration of Independence, "We hold these truths to be self-evident, that all men are created equal," surely do not mean, "We hold these truths to be self-evident, that all men are *clones*." Rather, a commitment to political equality means two things. First, it rests on a theory of universal human nature, in particular, universal human interests, as when the Declaration states that "people are endowed … with certain inalienable rights, and that among these are life, liberty, and the pursuit of happiness." It's also a commitment to prohibit public discrimination against individuals based on the average of certain groups they belong to, such as their race, ethnicity, or sex. And as long as we have that policy, it doesn't matter what the average statistics of different groups turns out to be.

The second fear is the fear of imperfectability: the dashing of the ancient dream of the perfectibility of humankind. This is the fear that Gazzaniga examined in his book *Nature's Mind* (Gazzaniga, 1992), as well as more recently in *Human*. The thinking behind this fear runs more or less as follows: if ignoble traits such as selfishness, violence, prejudice, or, lust are innate, that means they are unchangeable, so attempts at social reform and human improvement are a waste of time. Why try to make the world a better place if people are rotten to the core and will just foul it up no matter what you do?

But this thinking, too, is unsound. Even if people do harbor ignoble motives, they don't automatically lead to ignoble behavior. For example, most people report having homicidal fantasies, but needless to say very few act on them. That disconnect is possible precisely because the human mind is a complex system of many parts, some of which can counteract others—among them a moral sense, cognitive faculties that allow us to learn lessons from history, and the executive system of the frontal lobes of the brain, which can apply knowledge about consequences and moral values to inhibit behaviors.

Indeed, the undeniable social progress that *has* taken place in the last few centuries did not occur because human nature was reprogrammed from scratch, but because one part of human nature was mobilized against other parts. The argument comes from the philosopher Peter Singer in his book *The Expanding Circle* (Singer, 1981). Singer argued that one can find in all cultures the glimmerings of an emotion of empathy, an ability to treat other people's interests and perspective on a par with one's own. The problem is that the default setting for the empathy circle is to extend it only to the members of one's own clan or village, while those outside the circle are treated as subhuman and can be exploited with impunity. But over the course of history, one can see signs of the circle expanding to embrace other villages, other clans within the tribe, other tribes, other nations, other races, and most recently, as in the Universal Declaration of Human Rights, all members of *Homo sapiens*. This change in sensibility didn't come from reengineering human nature de novo, but rather from enlarging the circle that embraces the entities whose interests we treat as comparable to and as valid as our own.

The third fear of human nature is the fear of determinism: if behavior is caused by people's biology, they can't be held responsible for it. It's not an idle fear; about ten years ago the *Wall Street Journal* ran the headline "Man's Genes Made Him Kill, His Lawyers Claim." This issue of responsibility versus genetic determinism has been a main concern of "neurolaw," the application of neuroscience to legal scholarship and practice, which Gazzaniga has recently encouraged.

What is the suitable response to the fear of determinism? First we have to think about what we mean when we say we "hold someone responsible." Ultimately what it means is that we impose *contingencies*—reward, punishment, credit, blame—on the person's behavior. For

example: "If you rob the liquor store, we'll put you in jail." These contingencies are *themselves* causes of behavior—environmental causes, to be sure, but causes nonetheless—and we impose them because we think that they will change behavior in the future. For example, they will lead to fewer people robbing liquor stores. This logic does not appeal to an immaterial soul or a capricious ghost or some strange entity called free will, but rather to parts of the brain that can anticipate the consequences of behavior and inhibit it accordingly. Legal and judicial policies that hold people responsible are ways of engaging these brain systems for inhibition; they can do this even while neuroscience is coming to understand the separate brain systems for temptation (the ones that would be shaped by the "genes that made man kill," should they exist).

In any case, most of the bogus defenses for bad behavior that have been concocted by ingenious defense lawyers are in fact more likely to be environmental than biological in the first place. Examples are the "abuse excuse" offered during the 1993 murder trial of the Menendez brothers, in which the brothers' lawyer claimed that they killed their parents because they had suffered a history of emotional abuse in childhood; the so-called "black rage syndrome" that was cited to exculpate the Long Island Railroad gunman, who supposedly exploded one day under the pressure of living in a racist society and started to shoot white passengers in the train at random; and the "patriarchy-made-me-do-it" defense offered by some defenders of rapists, who supposedly were inflamed by misogynistic images from pornography and advertising.

Finally, there's the fear of nihilism, the fear that biology strips life of meaning and purpose. To deal with this uncomfortable emotion, one first has to distinguish between religious and secular versions of the fear of nihilism. The religious version is that people need to believe in a soul, which seeks to fulfill God's purpose and is rewarded or punished in an afterlife. According to this fear, the day that people stop believing in a soul we will have, in Nietzsche's words, "the total eclipse of all values."

The answer to the religious version of the fear of nihilism is that a belief in a life to come is not such an uplifting idea, because it necessarily devalues life on Earth. Think about why you sometimes mutter the cliché "Life is short." That realization is an impetus to extend a gesture

of affection to a loved one, to bury the hatchet in some pointless dispute, to vow to use your time productively instead of squandering it. I would argue that nothing makes life more meaningful than a realization that every moment of consciousness is a precious gift.

Also, there is a problem in appealing to God's purpose. Have you ever noticed that in practice, God's purpose is always conveyed by *other human beings*? This opens the door to a certain amount of mischief or worse. Many of you are familiar with the satirical newspaper *The Onion*. Four years ago, they ran the following notorious headline: "Hijackers Surprised to Find Selves in Hell. 'We Expected Eternal Paradise for This,' say Suicide Bombers.'" It may be in dubious taste, but it makes an important point. Even if there might be some people who can't be deterred from mass murder by anything short of the threat of spending eternity in hell, we know that there are people who are attracted to mass murder by the promise of spending eternity in heaven.

What about the fear of nihilism that has secular roots? People who believe in an afterlife are not the only ones who are troubled by the idea that we're just products of evolution. This fear of nihilism felt by non-believers is often triggered by the kind of research that Gazzaniga reviewed in *The Mind' s Past* (Gazzaniga, 1998), which shows that the left hemisphere of the brain constantly weaves a fictitious narrative that makes the person's goals and behavior *appear* coherent and moral—to others, and to the person himself or herself. In light of this deconstruction of "the self" and its meaning and purpose, people naturally worry about whether their *own* sense of self, and their higher goals in life, are meaningful concepts. The alternative would seem to be that that love, beauty, morality, the self, and all that we hold precious, are just figments of a brain pursuing selfish evolutionary strategies.

My favorite response to the secular fear of human nature comes from the opening scene of the Woody Allen movie *Annie Hall*, in which the five-year-old Woody Allen character is taken to the family doctor by his mother because he's depressed, leading to the following dialog:

Doctor: Why are you depressed, Alvy?

Mother: It's something he read.

Doctor: Something he read, huh?

Alvy: The universe is expanding.

Doctor: The universe is expanding?

Alvy: Well, the universe is everything, and if it's expanding, someday it will break apart and that will be the end of everything!

Mother: What's that your business? [To the doctor:] He's stopped doing his homework.

Alvy: What's the point?

The appropriate response came from Alvy's mother: "What has the universe got to do with it? You're here in Brooklyn. *Brooklyn is not expanding*."

We laugh at Alvy because he has confused two different time scales. He's confused the scale of human time—what is meaningful to us, how we want to live our lives today with the brains we have—and evolutionary time, which is the process that determines how and why our brain causes us to have those thoughts in the first place. Another way of putting it is that even if in some metaphorical sense our genes are selfish, and evolution is amoral and without purpose, that doesn't mean that the products of evolution, namely ourselves, are selfish, or that *we* are amoral and without purpose.

But even after one differentiates one's own goals from the metaphorical goals of the genes and the evolutionary process, *The Mind's Past* and similar accounts could still make one wonder whether one's own goals are mere figments of our wiring and devoid of meaning or objective content. This fear, too, can be countered. There is a strong argument that morality, far from being a hallucination of our neural constitution, has an inherent logic that the human moral sense *implements*. The simplest explanation of this idea that I know if comes from the late lamented cartoon strip *Calvin and Hobbes*. One day Calvin announces to his tiger companion, Hobbes, "I don't believe in ethics anymore. As far as I'm concerned, the ends justify the means. Get what you can while the getting's good, that's what I say. Might makes right. The winners write the history books. It's a dog-eat-dog world, so I'll do whatever I have to and let others argue about whether it's 'right' or not." Whereupon Hobbes pushes him into the mud, and he exclaims, "Hey! Why'd you do that?!" Hobbes explains, "You were in my way. Now you're not. The ends justify the means." Calvin says, "I didn't mean for everyone, you dolt. *Just me*."

This sequence shows the logical untenability of a morality based on the ethic of "just me." As soon as your fate depends on the behavior of other people and you engage them in dialog, you can't maintain that your interests are privileged simply because you're the one who has them and you expect others to take you seriously, any more than you can say that the point that you happen to be standing on is a privileged spot in the universe because you happened to be standing on it at that very moment. It's this core idea of the interchangeability of perspectives, or the recognition of other people's interests, that's the true basis of morality, as we see in numerous moral precepts and moral codes, such as the Golden Rule, Singer's expanding circle, Kant's categorical imperative, and Rawls's veil of ignorance.

Throughout his career, Michael Gazzaniga has not only illuminated the neural bases of the self, the moral sense, and the higher mental functions, but also has raised questions about how these discoveries bear on meaning, ethics, politics, and law. He has done so not because he claims to have the answers but because the issues cannot be escaped, and if scientists don't frame these issues in a way that is friendly to the enterprise of scientific inquiry, others will do it for us, and not necessarily on such favorable terms.

I've suggested that traditional ethical convictions in our culture have been grounded in a belief (often tacit) in an immaterial soul that somehow *uses* the brain, but reserves for itself the powers of moral reasoning, decision making, and an appreciation of meaning and purpose. The cognitive neuroscience revolution challenges that belief, and increasingly forces us to recognize that all mental life is a product of the evolved, genetically influenced structure of the brain. This challenge has also been seen to threaten sacred moral values, but I would argue (and like to think that Gazzaniga agrees) that in fact that is not a logical consequence. On the contrary, I think a better understanding of what makes us tick, and of our place in nature, can clarify those values. This understanding shows that political equality does not require sameness, but rather policies that treat people as individuals with rights; that moral progress does not require that the mind is free of selfish motives, only that it has other motives to counteract them; that responsibility does not require that behavior is uncaused, only that it responds to contingencies of credit and blame; and that finding meaning in life does not require that the process

that shaped the brain have a purpose, only that the brain itself have a purpose.

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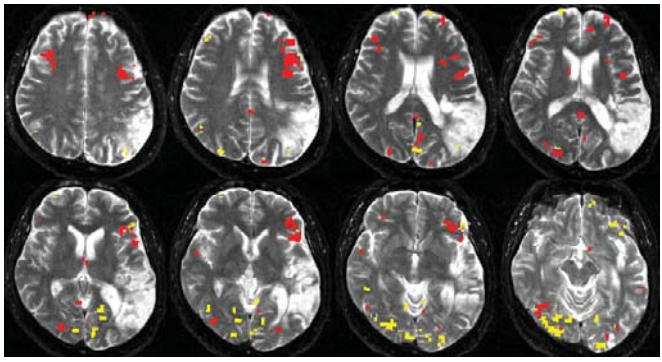

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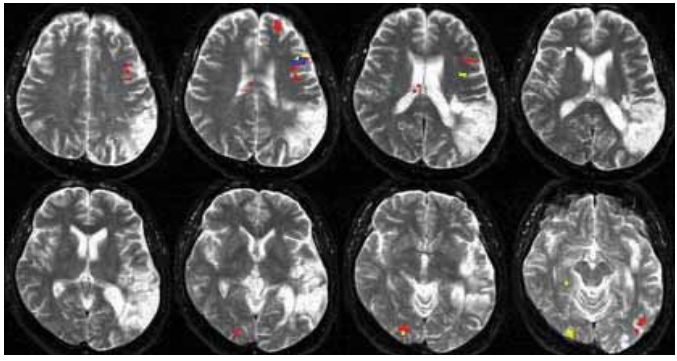

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Plate 1 (figure 4.1)
Comparison of activation between pre- and post-therapy sessions for the Verb-Generation Task (a) and Lexical Decision Task (b). Images are in radiological view (left is right). Key: yellow = pre-therapy; red = post-therapy; blue = overlap between pre- and post-therapy.

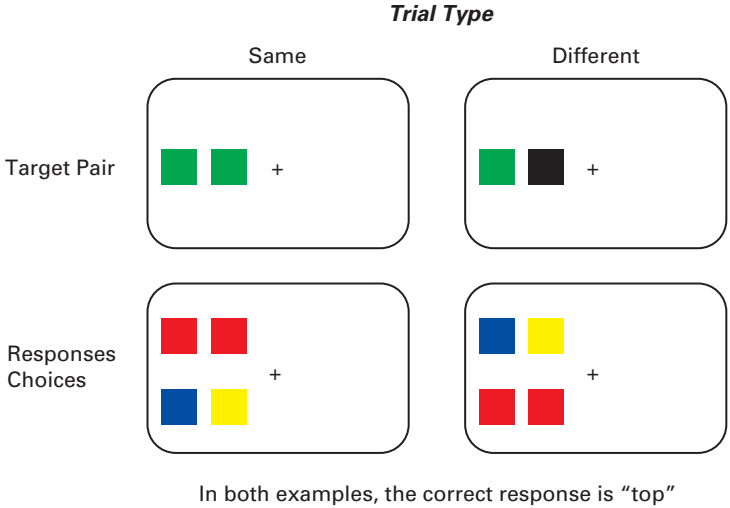
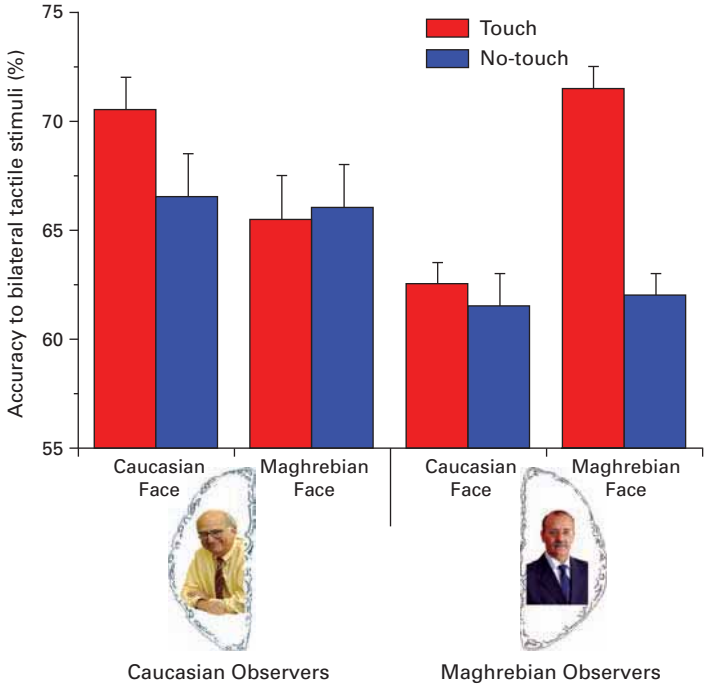
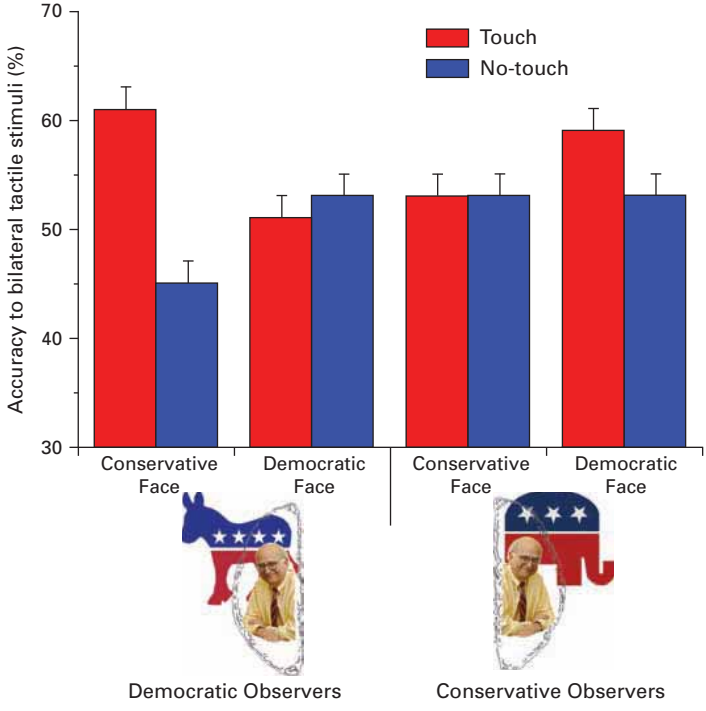


Plate 2 (figure 5.1)
Example of the stimuli for the relational category-matching task. The left-hand panel depicts a trial in which the squares in the target pair were the same color, and the right-hand panel depicts a trial in which the target squares were different colors. In both types of trials, the correct response is "top," as the two squares on the top are related to each other in the same way that the two target squares are related to each other.

Plate 3 (figure 11.3) (opposite)
Visual remapping of touch varies as a function of the similarity between the observer's and observed face: an effect of ethnic (upper panel) and political (lower panel) similarity. Modified from Serino, Giovagnoli, & Làdavas (2009)


Accuracy to bilateral tactile stimuli (%)
75
70
65
60
55
Touch
No-touch
Caucasian Face
Maghrebian Face
Caucasian Face
Maghrebian Face
Caucasian Observers
Maghrebian Observers


Accuracy to bilateral tactile stimuli (%)
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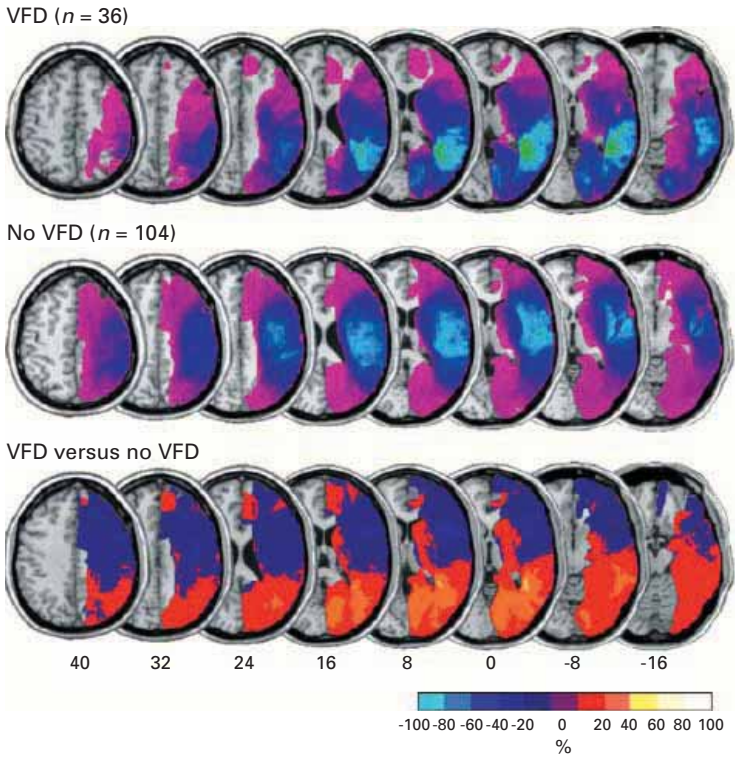

Plate 4 (figure 14.2)
The data in this figure illustrate lesion-overlap analysis of 140 patients with right-hemisphere damage due to stroke. The top panels show the distribution of lesion frequency of patients with visual-field deficits showing maximal overlap of lesions within the temporo-parietal cortex. The middle panel is patients without visual-field deficits (control group). The bottom panel is the subtraction image of patients showing visual-field deficits minus those without such deficits. It demonstrates that visual field deficits are actually due to damage in primary visual cortex within the occipital lobe.