Building a Better Brain

Understanding and improving the mechanisms of consciousness.

MARK WILLIAMS

I OF THE VORTEX
By Rodolfo R. Llinás
The MIT Press, 302 pages, $45

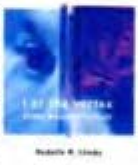
BETTER THAN PROZAC
By Samuel H. Barondes
Oxford University Press
219 pages, $26

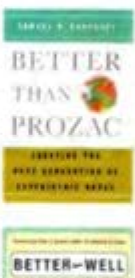
BETTER THAN WELL
By Carl Elliott
W.W. Norton, 320 pages, $27

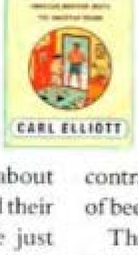
NEUROSCIENTISTS have discovered that an adult nervous system is capable of growing new neurons. Magnetic imaging has mapped how a human brain lights up when calculating sums, playing jazz, or contemplating God. New therapies, coupled with genetic diagnostics, promise to repair damaged minds. But as the press excitedly reports such things, it insists that neuroscience's greatest prize—understanding consciousness—remains as elusive as ever.

It's difficult to grasp that science may soon understand the mechanisms of consciousness; indeed, most people prefer their old assumptions about the ineffable mind. But neuroscientists have gained a much fuller picture of how the human brain works than most people—even most life scientists—realize.

One result of this is that the *scientia* (knowledge) of the human brain will inevitably become *techne* (art). Specifically, the new neuroscience will bring a revolution in psychopharmacological technology. Advocates will cast the new drugs as tools to build the souls men and women want. Opponents of the new treatments will invoke Aldous Huxley's *Brave New World*. The most thoughtful critics will attack the new drugs as a radical project to reprogram minds into something counter-evolutionary, arguing that people are remodeling the seat of human thought into an astronaut's couch. They won't be far wrong; the new drugs will radically change human thought.







But that debate is still a couple of decades away. For now, new discoveries about molecules, cells, circuits, and their roles in human brains are just beginning to lead neuroscientists toward an explanation of how single neurons communicate to create consciousness.

One way to think about this is to go to the refrigerator to get a beer. Before you reach into your fridge, and without much conscious thought, your mind will already be anticipating the weight of the bottle and the compensatory balance your hand should apply to carry it to the glass. Bending forward, most of your body's muscles will become engaged, resulting in a great many possible simultaneous muscle contractions.

How many? Any muscle contraction in any direction arises from individual muscle fibers working in groups called motor units. Each motor unit is controlled by a single motor neuron. But it isn't the number of motor units involved in any action that makes motor control difficult; it's the number of possible interactions between motor units and their sequence of activation that's problematic. Neuroscientists can calculate these things: the number of possible muscle contractions needed to get a glass of beer is astronomical.

That's because motor control must adapt to each changing moment. The optimal control method, one might think, would be to monitor muscle activation sequences continuously. For that, the brain would have to sample the body's physical state every millisecond. If so, just for the hand, arm, and shoulder's 50 or so key muscles, a person would have to choose from more than

1,015 possible combinations of muscle contractions just in reaching for that beer. If, in each millisecond, a person chooses the best of those 1,015 possible combinations, her brain would make 1,018 decisions every second; were the brain were a computer, it would need a 1-exaHz (1 billion gigaHz) processor.

But that can't be right. For one thing, the brain possesses only about 1,011 neurons. For another, just a fraction of those neurons are found in the cerebellum, the area where motor control is primarily processed. So says Rodolfo R. Llinás, author of *I of the Vortex: From Neurons to Self* and chairman of the Department of Physiology and Neuroscience at New York University's School of Medicine. He has a theory about how the human brain avoids this computational overload, and movies provide a clue: just as film shown at 24 frames per second creates the illusion of continuously moving images, so people live in a series of discontinuous pulses that only appear unbroken. Movement is a series of linked muscle twitches.

Motor physiologists have known this for more than a century. As early as 1886, scientists in the field talked of "voluntary tetanus": a discontinuity of movement, with a periodicity of 8–12 Hz, which showed in every human muscle. Later, researchers would prove that this tremor rhythm appeared even in muscles at rest; that it was human movement's upper limit of velocity, and that every voluntary motion people make begins in phase with it. Now neuroscientists have taken this further: during the 1990s, Dr. Llinás says, experiments indicated that the 8–12 Hz tremor mirrored on the musculoskeletal level a signal pulsing down from the forebrain. Such a signal provides the dual benefits of easing the brain's motor control workload and synchronizing motor neurons.

The body's movement is vital to the manner in which the brain generates consciousness, because living organisms that don't move, like plants, don't need nervous systems. Dr. Llinás points to the life cycle of an organism called the sea squirt. Free-swimming in its larval form, this marine creature has a nervous system of about 300 cells that receive basic sensory data through a light-sensitive patch of skin; an organ of balance, called the statocyst; and a rudimentary spine, known as the notochord. When the sea squirt finds an apt site, it buries its head in the sand, becomes rooted, and digests its own brain and spine, thereby assuming a more primitive form. The implication is that nervous systems evolved because any moving creature must anticipate each motion's outcome on the basis of sensory data. Prediction, Dr. Llinás writes, is both "the ultimate and most common of all brain functions."

The question thus becomes, How does the conscious mind integrate information distributed among billions of individual neurons to generate the unity of a conscious experience? From their first evolutionary appearance, individual neurons' electrical differences would have meant that some reacted faster to stimuli than others. Natural selection, scientists can postulate, would favor nervous systems with particularly sensitive neurons. Thence, explains Dr. Llinás, a "look ahead" function evolved. Some of the brain's neurons respond with hair-trigger extrapolations as sensory stimuli change, while others react at intermediate velocities, and still others measure real time. Such operations create en masse the predictive capabilities of neuronal networks. They also represent nature's general strategy for creating reliable organisms from unreliable cellular components. Yet other aspects of brain evolution seem inexplicable.

However fragmentary the result, the human brain does model the external world, and like the predictive capabilities of the brain's neuronal networks, this reality modeling evolved from simple principles. Consider the eye. In *I of the Vortex*, Dr. Llinás explains the eye's evolution from prototypes like the sea squirt's photosensitive skin patch. Over the course of more than 700 million years, photoreceptive areas enlarged, deepened into cup shapes, and developed increasingly ornate architectures and specialized neurons, until the human eye evolved: an organ that can detect a single photon of light.

This internalization of external properties like light, Dr. Llinás insists, is how life has shaped itself on every level. Just as you, the reader, internalize a photon pattern bouncing off the page in front of you and translate it into a voice in your head, he writes, so "rolling through the millennia, the system embeds, 'remembers,'" and uses simple cell-biological rules to evolve. In the case of gray matter, "neurons evolved in the space between sensing and moving. This space mushroomed to become the brain."

How does cell biology create consciousness? Dr. Llinás posits an answer by considering the phenomenon of how groups of cells fire in synchrony. Simple physical contact causes electric current to flow directly between cells, and by this process, called electrotonic coupling, every cardiac cell, for example, falls into phase and beats together, forming a heart.

Things are different in the human nervous system, yet electrotonic coupling still plays a role. Every neuron is separated from its neighbors by about 20 nanometers of fluid-filled space. Signaling between neurons is first electrical, with an "action potential" firing along a neuron's axon (its single output line), then chemical, as that action potential causes small packets (called vesicles) in the axon's terminal to release neurotransmitter molecules across the "synaptic cleft" between the neuron and its neighbor. Then the signal becomes electrical again, with the neurotransmitters binding to the receptor of each successive neuron, triggering another action potential. The whole process takes only a few milliseconds.

But this electrochemical signaling between neurons, Dr. Llinás writes, is only part of the story. During the '90s, research showed that, though neurons don't touch one another directly, electrical current flowing through the interneural fluid interconnects a large number of neurons—as well as glial cells, long thought to be just the scaffolding on which the brain anatomy is built. Moreover, this electrotonic interconnection occurs simultaneously among cells and can bind neurons that are physically separated, on opposite sides of the brain. Such electrotonic coupling between neurons amounts to "the 'roar of the masses' as many cells fire together," Dr. Llinás explains, "a choir as opposed to a solo performance."

Simultaneity is essential, because while electrochemical signaling may assemble neurons into working multicellular modules, synchronizing those modules is vital: no organism would survive if the parts of its nervous system worked at disparate speeds to generate mismatched predictions and motor commands. Electrotonic interconnection among neurons provides a medium for integrating all of their operations into one ensemble working in real time.

However, this medium of electrotonic connection is not the brain's ultimate integrating mechanism. When human subjects doing cognitive work are examined with brain-imaging techniques, Dr. Llinás reports, researchers observe 40-Hz oscillations throughout each of their brains. Neurons, like all cells, are in effect tiny batteries, and they oscillate in minute voltages across their surface membranes; neurons linked by electrotonic connection across large areas of the brain oscillate rhythmically in phase. For a metaphor, Dr. Llinás invokes cicadas on a summer night: "Imagine you hear first one cicada, then another. Soon, there are many chirping," he writes, "in rhythmic unison ... a conglomerated functional state. In the subtle fluctuations of this rhythmicity comes the transfer of information." This 40-Hz rhythmicity in electrotonically connected neurons, he proposes, is the specific control signal binding their disparate activities into one functional state, centralized in the present moment.

"We know this centralization as the abstraction we call the self," Dr. Llinás writes.

There's ample evidence for this apparently reductive view. Given the evolutionary relationship between brains and mobility, it's significant that these 40-Hz oscillations are particularly observable in a nucleus of specialized neurons, called the inferior olive, in the cerebellum, where motor control predominantly occurs. Research by Dr. Llinás and others indicates that the inferior olive not only generates the 8–12 Hz control pulse that creates mankind's innate physiological tremor, with which all active movements originate in humans, but also that during the brain's cognitive work, the inferior olive's cells become electrotonically interconnected, acting effectively as a single neuron and oscillating at 40 Hz.

In short, the signal synchronizing the body's motor control and these oscillations (the only plausible candidate to perform that function in the brain) share a physical focus. And given that solely electrochemical signaling between neurons would carry too many potential delays to provide the prompt reliability an organism needs to survive, those 40-Hz oscillations really do seem to be the only candidate for the synchronizing role in the brain. Electrotonic interconnection is the only medium that provides the necessary simultaneity.

Whether or not one buys Dr. Llinás's explanation of consciousness, it's only about a third of what *I of the Vortex* covers. The book also ranges across topics like emotions, memory, and learning, subjects that excellent volumes by other scientist-authors, like Antonio Damasio, have addressed, too. Dr. Llinás describes himself, however, as a single-cell physiologist interested in neuronal integration and thus possessing a viewpoint that is "privileged because it lies between the realms of the molecular and the systemic." His book is the only one this reviewer knows that possesses this scope, is written by one of the field's leading researchers, and is accessible to a diligent layman.

To glimpse some ways the new neuroscience will affect us, consider *Better than Prozac: Creating the Next Generation of Psychiatric Drugs*, by Samuel Barondes. He witnessed the creation of today's psychopharmacology: in 1960, having just started an apprenticeship in research at NIH, Dr. Barondes visited Julius Axelrod's lab, after the future Nobel laureate had discovered that during the brain's natural activities, the neurotransmitter norepinephrine was often spurted into a neural synapse, then sucked back into the nerve terminals from which it originated—a process called "reuptake." Thence, Axelrod found substances to inhibit reuptake, letting neurotransmitters work longer. Today's antidepressants like Prozac resulted. Yet these psychiatric drugs and others like such amphetamine-derived medications as Ritalin, used to treat attention disorders, have unwanted side effects, Dr. Barondes notes. *Better than Prozac* enthuses about the emerging possibilities of drugs that, rather than mitigating mental symptoms, target the genetic causes of these disorders, as discussed in "Better Living Through Chemistry," on page 78.

Carl Elliott argues in *Better than Well: American Medicine Meets the American Dream* that we should be more skeptical about this next-generation psychopharmacology. Dr. Elliott, a physician and a professor of bioethics and philosophy, has written a discursive account of America's ambiguous relationship with enhancement technologies. He hits the obvious stops on such a tour: drugs like Paxil that treat "social anxiety disorders," cosmetic surgery, Botox injections, skin lighteners, and transsexuality. Then he examines more radical modifications. There's the subculture of voluntary amputees, for instance—otherwise healthy people who believe their bodies are imperfect with the normal four limbs. Such individuals have chillingly specific ideas about just what they want amputated, Dr. Elliott observes, and argue, like transsexuals do, that the operation will liberate the "real person" trapped inside a disguise.

Hereabouts lies Dr. Elliott's central point: "*Brave New World* is still invoked, time and again, as a warning against the dangers awaiting us if we embark on new enhancement technologies," he writes. "It is as if we have no other metaphors." Consequently, Dr. Elliott says, we often talk about those who choose to improve their lives through drugs or surgery as if they had been forced to want to look younger, whiter, or thinner. We decide that they've internalized their oppression, arguing, for example, that Michael Jackson has undergone a hundred-odd cosmetic surgeries because he's a victim of self-directed racism. We keep repeating this story of totalitarian forces victimizing individuals, Dr. Elliott thinks, because we like tales of individuals *contra mundum*—and because we enjoy telling ourselves that we're better than the laughable dupes who've fallen for the notion of happiness in a tablet or a Botox injection. "Then we are asked to sing a solo in the church choir and can't sleep for a week, or our daughter starts getting teased at school for her buck teeth, and the joke doesn't seem so funny anymore," Dr. Elliott writes. "We all like to moralize about enhancement technologies, except for the ones we use ourselves."

Better than Well concludes by describing an amusing photograph Dr. Elliott keeps on his office door: President Richard Nixon making an obviously stoned Elvis Presley an honorary federal agent of what was then known as the Bureau of Narcotics and Dangerous Drugs. The King died at 42, face down on a bathroom floor, full of Elavil, Aventyl, codeine, morphine, Valium, ethinamate, methaqualone, ethchlorvynol, amobarbital, Nembutal, Carbrital, and

Sinutab—some in ten times their lethal dosages. No *Brave New World* totalitarianism caused his death—only, Dr. Elliott writes, "free choices made in a search for some peculiar kind of American happiness."

But abandoning reliance on illegal or prescription drugs seems unlikely. Dr. Elliott concedes this when he comments, in describing one hyperactive boy: "This child clearly worked better with Ritalin. The problem is that just about any child would. Or any adult." Or, as one middle-aged man, the son of two college professors, remarked to this reviewer, "I have attention deficit disorder. I couldn't stay in university, so now I make my living buying and selling old Volvos. Eighty thousand years ago, I'd have been a normal hunter-gatherer."

The truth is that people today, having brains that evolved on the African veld during Neolithic times, are not managing well in the technological world. Furthermore, as manufacturing jobs disappear, more people, however unsuited, will be expected to become "knowledge workers." It may be that the new neuroscience, with the psychopharmacology it brings, is society's best hope for managing better. Not only could it help the millions now suffering from confusion, depression, or debilitating mental impairment, it also might offer the means to heighten, dampen, and fine-tune human aggression, passion, and creativity. Dr. Elliott expertly sketches the dangers of such universal doping. He is unappreciative of its opportunities.

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Germs, Childbed Fever, and the Strange Story of Ignac Semmelweiss

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160 pages, $22

IN THIS SHORT volume, best-selling author and *Acumen* contributor Sherwin Nuland tells the fascinating tale of Ignac Semmelweiss, remembered for being the first, in mid-19th century Vienna, to connect "dirt" with disease, after he noticed that new mothers at the hospital where he worked were dying of fever at an alarming rate. Semmelweiss deduced that physicians themselves were unknowingly transmitting sickness through unhygienic procedures. But his challenge of the medical establishment ultimately undid the doctor himself.

THE DISCOVERY OF GLOBAL WARMING

By Spencer Weart
Harvard University Press
224 pages, $25

IN 2001, a panel of world scientists issued a definitive report announcing that the world was warming at an unprecedented rate, and that the heat up was due to greenhouse gases generated by human activity. Although environmentalists had long before shaped their opinions on the greenhouse effect, the scientific consensus was more than a century in the making. Physicist Spencer Weart portrays researchers working on discrete bits of a topic so complex that they could never achieve full certainty alone.