2 Thinking About Thinking

I will not be reviewing thinking from psychological or philosophical points of view, but rather from the mechanistic view of how the brain accomplishes thinking. That is, I will consider how external and internal "information" is encoded, processed, and acted upon in terms of neural circuitry. In the process, I hope to show that thought is a physical reality, not something that is necessarily mystical or unknowable.

Brain researchers have learned a lot, especially in recent years, about how brains in general think. One thing is clear: thinking comes from brains. So before we can explain how people think we have to know a little about brains. Don't worry. We are not going to make you go through a lot of tedious anatomy and physiology. But a couple of things are fundamental. So let's begin with those.

Scientists who study the nervous system ("neuroscientists") typically approach "biology of thought" issues from the perspective of brain structures and functions that give rise to thought. Some neuroscientists (called cognitive neuroscientists) are more focused on how the brain produces thought in the context of stimuli, goals, and tasks. But few neuroscientists study thought *per se*, because we don't have good theories or tools, or even vocabulary, for doing that.

Defining Thought Biologically

Before we can get much further, we must try to define "thought," which confronts us with the vocabulary problem just mentioned. I hate it when an author starts out with a definition. But here I am doing just that. Thinking can mean different things to different people. For example, a minority believe it is fallacious to think the brain thinks. They call this the mereological fallacy (Bennett and Hacker 2003, 480p). The point is that brains can only think if they function as only one part of a whole body. While this view is fashionable among some philosophers, many neuroscientists consider the position a contrived provocation, especially when extended to the point that the firing of neurons cannot constitute "thought." A neuroscientist only wants an operational definition of "thought" and can find it in a petri dish where a

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brain slice thinks in the sense that it can process information and deliver an output from electrical stimulation of an input pathway, for example. Anyway, the mereological argument is not central to the argument of this book.

For convenience, this book assumes that thinking is what brains do, and is most evident when brains generate a conscious state. I consider thinking to mean what the brain does to analyze, process, decide, and remember. Thinking includes both conscious working of the brain and the workings that go on beneath the radar of consciousness.

Webster's dictionary defines thought as "the process of thinking," which is a circular definition. Other definitions include words such as "reasoning," "imagination," "conception," and "consideration" – all of these are abstract nouns. None of these definitions treat "thought" as a real or tangible object. In this book, I shall attempt to present my ideas about thought in ways that are not abstract and philosophical but rather as tangible biology.

What matters most here is the process of thinking. By the end of this book, I hope to have shown what neuroscientists think this process entails, that is, how thoughts are generated and sustained, and how well thoughts govern not only bodily action but also mentalistic processes such as beliefs, ideas, choices, decisions, and even consciousness. Many people tend to think of mind as "something out there" rather than something going on "in here," in the brain. Most neuroscientists consider that notion to be nonsense.

A conventional way to think biologically about thought derives from experiments in which one records the nerve impulse discharge response to excitatory sensory input. The source of the input, such as the features of an object seen by the eyes, is represented by the train of spikes, pulses of electricity. *Representation* is a key word, one that has implications throughout this book. Different neurons may represent, that is, be selectively responsive to, only one feature of the stimulus, such as its color, contour, or motion, as I discuss later in my summary of the work of Hubel and Wiesel. Getting the whole stimulus represented in brain requires the information in each participating neuron to become functionally bound together. How binding occurs is not known, but is an active area of widespread interest.

So you might say, as many do, that "thought" emerges from the constellation of neurons in particular circuits in the brain. A thought is not possessed by a single nerve impulse nor even a train of impulses. However, the *pattern* of impulses in a network of neurons is possessed by the network and is a property of the network. The brain is a collection of intimately interacting networks, and the properties of these networks make up the system property, a thinking system in this case.

Alternatively, we can think of brain representing information in spatially coherent oscillation patterns that engage large areas of brain. But this view is not mutually exclusive with the one just mentioned. In both cases, information is represented and processed by patterns of nerve impulses flowing through distributed and interacting circuits. Neurons in many brain areas connect with each other to form multiple circuit loops in which many connections are reciprocal. According to the latest thinking of Walter Freeman (2009), this functional anatomy produces brain function in the form of state variables. The ongoing succession of changing state variables in the brain is produced by dynamical interaction between body, brain, and environmental stimuli (I would include brain-generated thought that acts like “stimuli”). Rather than brain being a passive receptacle for receipt of information in the world, brain dynamics support purposive action in which the brain directs its sense organs as needed to detect, abstract, interpret, and learn from sensory experience. Such a system can generate goals and intent (I add also even free will – see Chap. 7 on Free Will Debates). Each perception is the outcome of a preceding action and at the same time serves as the condition for a following action. This serves to remind statisticians that brain function is highly governed by Markovian serial dependencies (see later coverage on such dependencies in trains of nerve impulses in Chap. 4).

I will argue that “thoughts” are abstractions, represented as patterns of nerve impulses coursing through various paths and networks, that can represent certain physical entities. They certainly have a physical basis. They emanate from anatomy, biochemistry, and physiology of the brain. Thoughts *must* have a physical “carrier,” that is some physical representation of the thought. Can we regard “thoughts” as patterns of activity within certain groupings of neurons? Why not? Whether or not this is altogether appealing, this definition may be as close as we can get to a non-circular definition.

Actually, the idea of patterns of neural activity needs considerable refinement, which is a major purpose of this book. One fundamental extension is clarification of time and space. Thoughts, i.e. patterns of impulse activity, are distributed spatially and across time. Different parts of the brain generate different patterns of activity, yet these parts are all more or less connected and capable of influencing each other. The timing interactions among these various patterns of activity are, I believe, central to understanding the nature of thought.

Scientists typically think of “mind” as something that emerges from brain operations, yet remains “in here.” This view applies to each of the three kinds of mind I consider in this book: conscious, subconscious, and non-conscious. I will explain the differences in some detail later.

Maybe we should think of mind as the collective processes of brain operation. Admittedly, this is not a very satisfactory definition of mind, but at least it does not limit the idea of thought to conscious mind only. Many brain operations proceed just below the surface of consciousness, and the results of that subconscious thinking even pop in and out of consciousness.

If you think thought is intangible, how do you explain away the clear signs that thought comes from biology? The brain origin of mind and its thoughts seem indisputable. If you change the brain, you change the mind. If you damage the brain, you damage the mind. If you shut down the brain, you shut down the mind.

Animals think too, especially higher animals, like primates. Even our pets give clear signs of the ability to think (although my dog sometimes acts as if it only has three neurons).

Whatever “mind” is, it begins in the womb from a brain serving as a “blank slate.” The thoughts the brain generates and the increasing capacity for generation of new thought, derive from the senses and experience that begin in the womb. As Thomas Aquinas said around 700 years ago, “There is nothing in the intellect that was not first in the senses." This notion is not totally true, given the brain's amazing ability to generate quite abstract and unique thought. But the brain does not operate in a mentalistic vacuum. It builds on what it has experienced and learned. Brains imagine and create thoughts that have not been directly experienced.

In addition to individual experience, most scientists (Gangestad and Simpson 2007, 448p) would say that the human brain has evolved since it first appeared in primordial form perhaps some two million years ago from natural forces that selected the genes that have been passed on to us. Thus, human brain of today has inherited neural processes for generating certain kinds of thought (such as fear of snakes, predator avoidance, sexual attraction, aversion to incest, ability to infer the mind of others, desire to forage and hoard, and socialization and cooperation). Most importantly, human brain has evolved intelligence. The neural processes supporting such thought categories are more or less built into circuitry that generates nerve impulse patterns more or less biased to produce the corresponding kind of thought.

Brains operate with propagating pulses of electricity (nerve impulses), modified by chemicals (neurotransmitters) in the junctions between neurons. A few impulses and squirts of neurotransmitter do not constitute much of a thought. They are just impulses and squirts, though the neurotransmitter systems in neuronal junctions are thought to be the repository for long-term memory. When orchestrated through the circuitry of neuronal assemblies, the mundane takes on the life of mind. Explaining how the impulse patterns yield conscious awareness of thought is the real challenge.

First Principles

Physicists think the "Holy Grail" of science is to unify general relativity theory and Quantum Mechanics (QM). But life scientists think that the Grail is to explain the human mind. I suspect that the general public would vote for the latter, because everybody has a personal stake in understanding who we are and why and what we do. Moreover, many people are perturbed by the thought that materialistic explanations for thought conflict with their religious beliefs.

I think there is not one mind, but three highly integrated minds (Fig. 2.1). The lowest form of mind is non-conscious and occurs in the spinal cord and brainstem to mediate simple reflexes, visceral control, and regulate hormone systems. Non-conscious mind is that which governs our simple body functions, such as regulating heart rate, blood pressure, and spinal reflexes. These operations all operate at the brainstem and spinal cord levels. This mind is clearly a physical phenomenon and has been abundantly explained by science. This mind is readily explained in terms of anatomy, physiology, and biochemistry. No one speaks of this mind as "emerging" from brain function. It IS brain function. Keep this "in mind" as we later ponder the functions of subconscious and conscious minds.

The representations in non-conscious mind take the form of patterns of propagated nerve impulses, flowing in designated pathways (i.e., hardwired circuits) that have evolved to provide servo-system regulation of certain basic functions necessary to sustain life. These representations are not accessible to conscious mind. For example, one is not aware of his own blood pressure or state of hormone release.

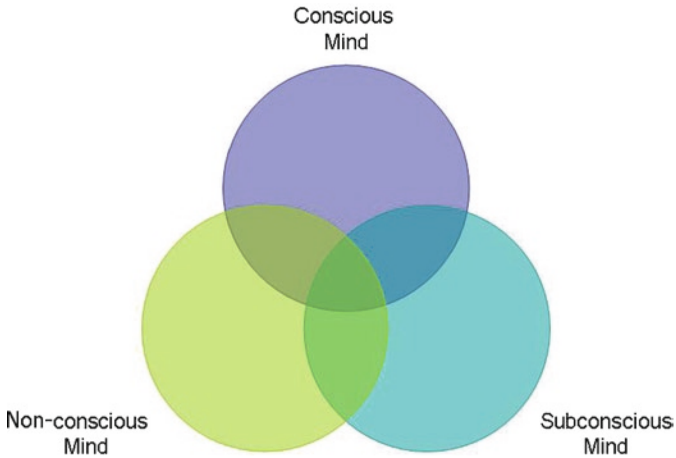

Fig. 2.1 The brain has "three minds," each overlapping and interacting with the other. All objective evidence indicates that all these minds arise from anatomical, physiological, and biochemical processes of the brain

Much of what scientists have learned about the brain has come from research on the non-conscious mind. I assert that this information must be fundamentally relevant to whatever processes create conscious mind.

The Brain's Three Minds

Ever since the discovery a little over 100 years ago that neurons exist as distinct units, scientists have been trying to figure out how brains work. Scientists have learned about nerve impulses, the architecture of neural networks, and what happens biochemically and electrically at the junctions ("synapses") between neurons. We can now say with good assurance that thinking *involves* impulses, neurotransmitters, post-synaptic membrane receptors and biochemical signaling amplifiers, and post-synaptic ionic currents in multiple, parallel and recursive circuits. But it is not enough to say that these things are involved in or mediate thought. Such words are too glib and have little explanatory power. The knowledge accumulated over the last 100 years has, however, made it possible to hope that a true theory of thought is at hand.

Whatever theory of thought emerges, it must explain and unify at least five major categories of thought:

Non-conscious thought
Subconscious thought
Conscious thought
Hallucinatory thought
Dream thought

One reason it is so difficult to unravel the mind-brain enigma is that theorists tend to approach the problem from the wrong end. By trying to explain consciousness, theorists immediately get caught up in philosophical or religious, not scientific, issues and become trapped by their premises.

Rather than starting by explaining conscious mind, I find it more fruitful to take an opposite approach, beginning with operations of the simplest levels, first non-conscious mind and then subconscious mind, eventually leading to an attempt to explain conscious mind (which I do in the last chapter).

At this point, I need to establish some ground rules for how we should use language to describe "awareness." This term carries a lot of anthropomorphic baggage, usually inferring that awareness is a conscious operation. We speak, for example, of ants being aware that there is food in the kitchen. Ant brains can do many impressive things, including detecting food in the kitchen, but they are not "aware" of such a fact. When describing non-conscious and subconscious operations, we are safer saying that the brain "detects" stimuli and situations. To say that someone is "consciously aware" is redundant. If one must refer to some subconscious detection, it is more correct to say that the subconscious detects or "is informed" of certain events or situations.

To illustrate the point, the non-conscious processing of the solitary tract nucleus enables those neurons to *detect* sensations from the vagus nerve with which it connects. The nucleus should not described as "aware" of vagus nerve input. Likewise, the deep nucleus of the cerebellum detects influence from the cerebellar cortex, but cannot be "aware" of it.

A higher level of detection can be illustrated with fear, of snakes for example. The amygdala generates a sense of fear upon being notified that snakes are near. Even animals can be afraid of snakes; in that sense they detect the snake stimuli. But we have to ask, "Are they aware that they have detected a snake?" That is, do they have a sense of self, and do they know that they know about snakes and why they are to be avoided?

Level of awareness no doubt depends on which species of animal is involved. A human, for example, surely has a different level of awareness about snakes than does a chicken.

Let us now consider subconscious mind. This is the mind with buried memories, unrecognized desires, compulsions and assorted emotions. This mind operates when we sleep and operates without conscious recognition throughout our wakefulness. This mind, like non-consciousness mind, can be explained by anatomy, physiology, and biochemistry, though such understanding is far from complete. Again, no one speaks of subconscious mind as emerging from brain function. It too IS brain function.

Why then should conscious mind be any different? Yet most theorists seem to think that conscious mind is fundamentally different. Conscious mind is said to "emerge" from brain function but not be equivalent to it. The problem is that nobody knows what is really meant by saying that conscious mind is an emergent property of brain. Most brain scientists do, however, accept that conscious mind comes from the brain. But some seem to have difficulty in accepting that this mind also IS brain function.

Conscious mind cannot describe its processes, but it does know that those processes are going on and that they have consequences that can be altered – by conscious mind itself. The most fundamental aspect of conscious mind is the "sense of self." That is, conscious mind knows it exists, residing separate from subconscious mind and able to be aware of at least some of what it knows and thinks. Such awareness extends across time, from past to future, integrating the present. Some theorists like to emphasize its autobiographical nature, but that just refers to memory of things that happened to oneself in the past. I think other primates, even dogs and cats, do that. Animals like these also seem to have a sense of self, but certainly not in the same way humans do. Most do not recognize themselves in a mirror.

Throughout this book I will operate from the premise that conscious mind IS brain function. I will lobby my colleagues to think of it that way in the hopes that experiments will be developed that can explain just what brain functions produce conscious mind and how those functions create consciousness.

For now, let me assert that a whole mind consists of three interacting "minds," each of which IS brain function – albeit different manifestations of brain function.

Brains as Liquid-State Electronic Devices

The processing unit in the brain is the neuron, and in a typical case, the neuron's cell membrane branches out into multiple projections like limbs on a tree. These branches are typically polarized electrically in the sense that some of the branches can generate ionic current that flows into the other branches of the neuron. Details can be found in any general biology or physiology book.

What needs emphasis here is that the brain is a liquid-state electronic device. Unlike solid-state computer chips, where electric current is carried by electrons flowing through metal conductors, the brain's currents are in the form of charged atoms (ions) flowing through water. The important ions in brains (sodium, potassium, and calcium) are atoms that have lost one or more electrons, giving them a positive charge.

The "Atoms of Mind" are, of course, all the atoms that make up neurons. But the atoms most directly responsible for thought are the ionized forms of sodium and potassium. When atoms like sodium and potassium dissolve in water, they give up electrons. Where do the released electrons go? Few people ask that question, but it seems clear that they do not flow from neuron to neuron like electrons in copper wire. Most likely, electrons in tissue are not free to flow, because they become captured by organic molecules, especially by intracellular proteins (which account for much of the net negative charge inside of resting cells).

Calcium ions need to be mentioned, because they help to promote neurotransmitter release and certain "second messenger" systems inside of neurons. But the thought content of mind, as it operates in real time, is contained in patterns of nerve impulses, and these are created by flow of sodium and potassium ions.

Some of the greatest research of all time, in my opinion, is the Nobel Prize winning work of Alan Hodgkin and Andrew Huxley. They did not stumble on discovery of how nerve impulses where created, but rather they systematically set out to identify the mechanisms. Based on the work of Adrian (see sidebar in Chap. 4) and others, Hodgkin and Huxley developed a complex plan to determine the ionic carriers that created nerve impulses. Based on electronic instrumentation innovations, which were pretty clever for the time, they impaled giant squid axons with electrodes arranged to detect the various currents that appeared during an impulse. Salts were suspected for a variety of reasons, not the least of which was that they ionize when placed in water and thus could constitute an electric current.

What the two demonstrated was that the initial phase of an impulse was generated by flow of sodium ions into a neuron, followed by a termination phase involving the flow of potassium ions out of the neuron. They also explained why this happens, which you can find in a textbook. They developed equations to quantify this flow. These findings might seem counter-intuitive, but they are abundantly documented. The important point for our purposes here is that a nerve impulse is created by flow of sodium and potassium ions into and out of an activated neuron.

As these ions move through tissue fluid, they are in fact carriers of electric current and generators of voltage from the ionic currents that flow through the resistance of tissue and its fluids. Ohm's law (voltage = current x resistance) applies. Under typical electrical recording procedures used experimentally, it is the voltage aspect of impulses that are recorded.

This flow of ions creates voltage fields around a neuron, and the voltage associated with impulses destabilizes adjacent neuronal membrane. This serves to trigger changes in the permeability of the neuron's membrane, and when this change occurs in certain terminals of the neuron, chemicals can be released into the gaps (synapses) between one cell and another, serving either to stimulate or inhibit the target neuron. Positively charged calcium ions are important to the process for releasing transmitter and also to the biochemical reactions in synaptic targets. This need not concern us here.

Neurons are organized into distinct circuits, where ionic currents flow in specific spatial patterns. Some circuits in brain are markedly malleable, selectively changing in response to the kinds of input they receive. Also, a given neuron is not always exclusively tied to a given circuit. It may be recruited into multiple circuits, again depending on inputs and ongoing activity in other circuits with which it is in contact.

Thus, thinking is an electro-chemical process in the central processing units (neurons) of the brain and their associated circuitry. Neurons are to brain as transistors are to integrated circuits. Beyond this point, however, the comparison of neurons to transistors becomes fallacious.

Brains vs. Computers

I once team taught a graduate electrical engineering course with a group of engineers and a mathematician who worked with electronic "neural networks." They had hoped that my expertise on how the brain works would help teach their students how to design better computers. It did not take long for all of us to realize this was a pretty naïve idea. Although "neural network" technology can emulate some of what brains do, such as rudimentary learning, there are just far too many differences between brains and computers. The differences are qualitative, not just a matter of speed and memory capacity.

Nowhere is the difference more clear than in the ways computers and brains "think." As stated, a computer thinks with a steady stream of electrons flowing through conductive wires and semi-conductor material. Computer circuits are "hardwired," that is, built into the system and not reconfigurable unless there is preplanning with programmed instructions. How, when, and where information flows is predetermined by the hard-wired circuitry or by programmed instructions. This is only partially the case in brain. Some circuits there are also hard-wired by in-born anatomical connections among neurons, but many are reconfigurable by experience and can even self-organize. Most significantly, brains can program themselves through learning. Even more astonishing is that this learning by brains can actually change some of their structure and connecting pathways, creating new capabilities.

A brain thinks with pulses of ionic flow ("spikes") that are separated from each other by variable intervals that are electrically silent. "Information" content of a spike train is represented by when spikes start and stop, how many spikes there are per unit of time, and the sequence of intervals, or equivalently the sequential appearance of spikes in successive adjacent time periods. How, when, and where spike trains flow may or may not be predetermined by the brain's hard-wired circuitry. As with computer networks, information may be gated to flow or not flow in various networks and their sub-circuits.

Both kinds of systems can learn to develop preferential pathways for information flow. Learning in computers results only when nodes in a circuit are programmed with certain weighting factors for certain kinds of input. Brain circuit pathways are built-in by genetics by some circuits are constructed directly by input, without third-party mediation.

A most basic difference is that neurons are not digital. They are analog devices that generate their own electrical current that flows into, through, and outside their cell membranes through micropores (ion gates) that allow flow of the charged atoms that constitute the current. These nerve impulses are quasi-digital in that they occur as isolated pulses. But the forces that generate these pulses are analog and non-linear.

Impulses are triggered by slow and graded changes in membrane current in and nearby the cell body of neurons. These can summate algebraically, from multiple inputs to a given neuron. If these currents are depolarizing, like shorting a battery, and of sufficient magnitude, the neuronal membrane becomes unstable and responds by blasting off impulses.

Slow, graded changes in membrane current occur prominently in the synaptic junctions. Electrical inputs into a given synapse may be depolarizing or hyperpolarizing, and the algebraic summation of opposing synaptic currents should be regarded as a fundamental kind of cell-level thinking. The net summed current, if depolarizing, can trigger output, whereas hyperpolarizing current blocks output, or in other words is inhibitory.

The Currency of Thought

If there is no impulse flow, there is no on-going thought. For example, one can inject an anesthetic into a carotid artery and stop all impulse traffic – and the corresponding thoughts – in the area of cerebral cortex supplied by that artery.

There is *latent* thought however. In the above example, those anesthetized cortical circuits still have a capacity for thought stored in their synapses and connection pathways. However, thought itself is not expressed.

The relationship of synaptic anatomy and biochemistry to human mind, compared with nerve impulses, can be likened to the relationship of potential energy to kinetic energy. The one represents the capacity for mind while the other reflects mind in action. Thoughts, for example, can reside in latent form in the microanatomy of neural circuits and their associated synaptic biochemistry or they may be expressed and on-going in the form of the circuit impulse patterns (CIPs). When a person is awake, the CIPs constitute an actively deployed, "on-line" mind that interacts with the world. This is also the mind that programs what goes into storage (memory) for later deployment as "up-dated" on-line mind.

Once triggered into being, impulses spread throughout a neuron like a burning fuse and extend into all the cell terminals, which provides a way for one neuron to communicate with many others at roughly the same time. Actually, because a given neuron has numerous terminals, its impulses may reach hundreds of target neurons.

Brains have two basic kinds of cells: neurons and cell types that support them called "glia." As far as we know, the primary cause of brain function and mind comes from neurons. Neurons are organized into circuits, formed either under genetic control or under influence of environmental stimuli and learning. Some of these circuits are in constant state of flux, turning off and on, becoming more or less active, and changing their constituent neurons, impulse firing patterns, and routing pathways. A given neuron can be recruited into more than one circuit, as shown for the center neuron in Fig. 2.2, which participates in all four circuits shown. Activity may be going on in parallel in all the circuits shown above and the circuits may interact with each other via feedback. This constellation of these multiple processes underlie what I call thinking.

Some circuits are hard-wired, and perform a predictable behavior when activated. An obvious example is the knee jerk reflex. Most people have had a physician tap on a knee tendon to observe the magnitude of knee jerk. Other neuronal circuits are malleable and can be constructed on the fly, so to speak, depending on the needs of the moment. Such circuits also are a repository for learning and memory.

Scientists have traditionally studied neurons in their live state by using small electrodes to record voltage changes, both the graded synaptic changes and the pulsatile nerve impulses. If a relatively large electrode, about a third the diameter of a dime, for example, is placed on the scalp, it will sense the voltage changes of thousands of neurons in the region of brain closest to the scalp. This is what we call the electroencephalogram or EEG. The EEG thus can monitor thinking states of large populations of neurons in the outer mantle of brain, the neocortex, which is the part

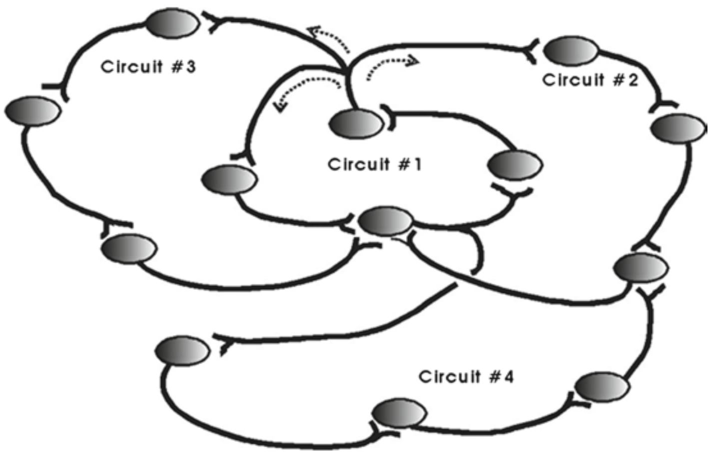

Fig. 2.2 Simplified neural network. This figure is central to all that follows in this book. The key ideas are that neurons are organized into circuits in which information is propagated in the form of temporal patterns of impulses. At any given instant, the impulse coding may be combinatorial, that is, contained as the impulse patterns in all the neurons of the circuit at a given moment. Neurons have cell bodies (*circles* in drawing) and membranous processes that project to other neurons. Note that these processes may branch so that a given neuron can act on multiple targets in multiple circuits. Impulses (direction of impulse flow shown in *line arrows* above) propagate outward from cell bodies to act on target neurons. Such circuitry illustrates parallel distributed processing with feedback. The contact-point gaps, known as synapses, are regions where neurochemical transmitters are released to bind with receptor molecules on target cell bodies and their small membranous process known as spines (not shown). Such binding facilitates or inhibits information flow, depending on the nature of the transmitter and its molecular receptors

of the brain that provides most of the electrical signal at the scalp, does the most sophisticated thinking, and gives rise to conscious awareness.

If the electrode is very small, like a micro version of the tip of a sharpened pencil, and is thrust directly into the brain, it will detect the net electrical activity of a dozen or more neurons in the immediate vicinity. Scientists call this "multiple-unit activity," because the activity comes from multiple neurons. If you insert into the brain an electrode that is less than the diameter of a human hair, the electrode may detect only the voltage of the nearest neighbor, a single neuron. If you impale a single neuron with such a microelectrode, the electrode will detect not only the impulses from that neuron but also reveal slow graded excitatory and inhibitory modulations of the voltage across that neuron's cell membrane. If in addition, you use a glass capillary microelectrode and suck a small patch of membrane into the tip, you can even detect ionic currents as they flow through ion channels as they open and close in response to input to the neuron.

These micro-methods take us further away from understanding the larger matter of thinking. In that sense, such methods teach us more and more about less and less.

This is important to emphasize, because nerve impulses are the only things that are propagated throughout circuitry. Neurotransmitters (see below) operate in the junctions between adjacent neurons, but they do not propagate their signal over more than a few microns. Post-synaptic receptors and biochemical amplifier systems are also confined to synapses. Post-synaptic voltage changes do propagate for a few microns of space, but do not move the many millimeters, even meters, that can be accomplished by impulses as they self-generate along the axons of neurons.

The idea of nerve impulse patterns as information representation is key to developing expanded understanding of mind. Detecting and quantifying impulses in a single neurons is not sufficient. Thought is represented by the spike trains from all the neurons in a given circuit at roughly the same time. Thus, whatever code neurons use for thinking, it must be some kind of combinatorial code (more about this later in Chap. 4; for now, see Fig. 2.2).

Such nerve impulse patterns are the currency of thought, presumably at all levels of mind. Is it not conceivable that both subconscious and conscious minds include impulse pattern representations that extend beyond the fixed circuitry of spinal cord and brainstem to include dynamic assemblies of neurons whose functional connections come and go in the course of neural processing? No doubt, the richness of combinatorial coding in dynamic assemblies would be greatest in conscious mind.

Sub-conscious mind can also include certain servo-system operations, such as regulating emotions and their influence on brainstem neuroendocrine controls and on the neurons regulating such visceral functions as heart rate, blood pressure, and digestive functions. Subconscious operations also include a wide range of movements that have become so well-learned by neural circuitry that the controls are automatic and can be performed in zombie-like fashion without consciousness. But in all subconscious operations, it seems reasonable to assume that the representation for information and operating on it to generate responses or actions occurs in the form of combinatorially coded circuit impulse.

Impulses can be triggered by stimulation or certain chemicals. A neuron at rest, like all cells, is an electrical battery, polarized, with the inside of the cell electrically negative relative to the outside. The "battery" of neurons, however, can be discharged (depolarized), which is manifest as a brief reversal of the voltage on the order of about 1 ms. Neurons propagate their spike discharges of electricity through circuits such as those shown above. As impulses reach the junctions between neurons (synapses), they generate voltage fields in the synapses, causing chemicals (neurotransmitters) to be released to modify information flow. The circuits are embedded in the extracellular voltage fields that they generate, although many regions of the circuitry may be electrically insulated by surrounding glia cells. The layout of a given circuit may change as it receives particular input from other circuits in the brain and spinal cord: some neurons may drop out of the circuit, while others may be recruited. Many neurons are shared by multiple circuits.

How do all these impulses, voltage fields, chemical releases into synapses, and dynamically changing circuitry give rise to thinking? Well, they *are* the process of thinking. I like to say that thinking is equivalent to the CIPs. Why CIPs instead of what is happening in the synapses? First, thinking is a dynamic process and its "messages" are carried and distributed in real time through CIPs. What happens in the synapses becomes manifest in the CIPs. The chemical and microanatomical changes that occur in synapses represent the memory storage and processing of thought. The expression of thought is most evident in CIPs.

In any given neuron, the impulse patterns take the form of rate and rate change in firing, onset and offset of firing, and sequential order of intervals. I think of CIPs as instruction sets for performing such brain operations as detection, integration, decision-making, and commands. The ideas that I develop in this book are abundantly supported by the research of others and bolstered in my own experiments, both at the cell level and at the "mind" level.

Research in the last several years is exploding with evidence for the above view. For example, I realized in the early 1980s that nerve impulses did not occur randomly, that they contain a code, not only in the rate of firing, but also in their interval patterns. At that time a few other scientists had arrived at the same conclusion. More recently, I realized that oscillation and synchrony of the more global electrical voltage fields were important. These new insights are not mine alone. In the last 10 years, numerous researchers have been providing experimental data to support both ideas. Now the time is right to make these thoughts explicit and simply explain how they are supported by experiment. These ideas of CIPs and oscillation of circuit activity (see Fig. 2.3) are central to much of which follows in this book and to my idea about consciousness that is developed in the last chapter.

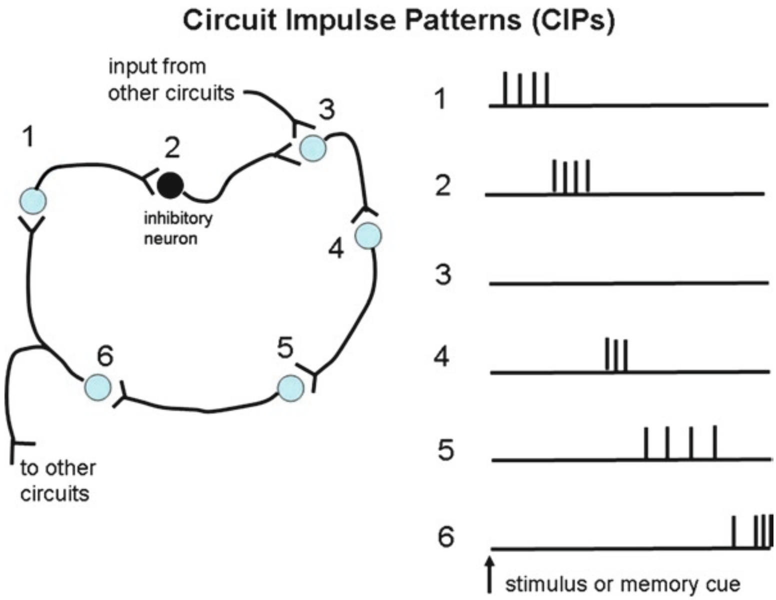

Fig. 2.3 Illustration of the idea of CIPs. In this example small circuit, each neuron generates a certain temporal pattern of spikes that affects what happens in the target neuron. For example, the inhibitory neuron #2 shuts down activity in #3, which nonetheless may reactivate when the inhibition wears off or when excitation comes from another circuit with which it interfaces. Collectively, all the neurons in the circuit constitute a CIP for a time epoch. When embedded within a network of interfacing circuits, such a CIP may become part of a more global set of CIPs. Such CIPs are regarded as a representation of specific mental states. The meaning of this representation may lie in the combination of spikes in all the circuit members, contained in the form of some kind of combinatorial code

Why and how should “information” be captured, processed, and propagated as a *combinatorial* feature of CIPs? First, a real nervous-system circuit does not operate in isolation. Many neurons in a given circuit have reciprocal connections with neurons in *other* circuits. Thus, the spike train of a given neuron embodies within the time distribution of its impulses the influence of other neurons in its parent circuit and the inputs from other circuits.

The CIPs most relevant to conscious thinking come from neurons in the cerebral cortex, and the circuits of these neurons are closely packed in small columns oriented more or less perpendicular to the brain surface. With such close packing, the electrical currents resulting from impulses in each column’s circuitry readily summate as a collective consequence of the impulse activity in all members of the circuit. Often, this collective combinatorial effect drives frequency-specific oscillations of the whole circuit and neighboring circuits. These ideas underlie a recurrent theme in this book that will culminate in the last chapter’s discussion of the nature of consciousness.

Neurons come with a wide variety of firing patterns. Even in a single brain area, intrinsic properties vary widely. In the hippocampus, for example, one cell type produces a short train of spikes that habituates after stimulation with a short depolarizing pulse but a single spike in response to a superthreshold pulse of current. Another type fires bursts of pulses in response to long and strong current pulses, but only a single spike in response to weak stimulation. Another type also fires bursts in response to weak but long stimulus pulses. Another type is similar but its bursts are very stereotyped. Yet another type fires rhythmic bursts of spikes spontaneously without stimulation (Izhikevich 2007).

CIP representations are undoubtedly the stuff of non-conscious and subconscious minds. But what about conscious mind? Numerous tomes over the centuries have attempted to explain conscious mind from arcane and esoteric perspectives. Herein I propose another way of thinking about consciousness that may prove helpful. These patterns are the primary representation of the information, the processing, and the instructions set that we can collectively call non-conscious or subconscious mind. This mind is strictly physical, not too unlike a computer chip except in the nature of the current carriers.

So what then is conscious mind? Is it generated as a combinatorial code of electrochemical CIP processes operating in multiple, dynamically changing circuit patterns? Probably. But nobody knows how this mind has an awareness process that is so different from subconscious mind.

Brain circuits are arranged not only in series but also in parallel. Multiple operations can go on simultaneously in multiple parallel circuits. This kind of processing is especially prominent in the cerebral cortex, the outer mantle of cells that surrounds the rest of the brain. The various regions of cortex highly interconnect between and among other cortical areas. Many of these areas are mapped for both sensations and motor output. Moreover, the mapped regions are reciprocally connected to each other, so that input into one region can be fed back into the region that supplied the input. The upshot of such arrangements is

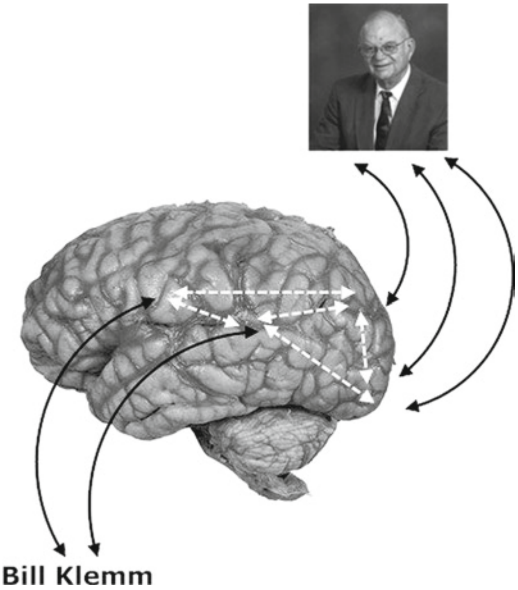

Fig. 2.4 When the brain receives stimuli, such as images and sound, it extracts key features and distributes nerve impulse representations in parallel to different parts of brain that specialize in processing the respective types of information. In this case, sensory information about name and face are "deconstructed" and contained as CIP representations in different parts of cortex (especially speech centers and visual cortex). These areas exchange information with each other, as well as with other parts of brain (not indicated here) that might participate in supporting roles involving movement, emotion, memory, etc. When that information is consciously recalled CIP representations are again activated simultaneously to reconstruct the original stimuli

that any given mapped region of cortex can get near-instantaneous feedback on the effect of its operations.

Let me illustrate what happens to sensory input. Suppose you see a picture of a person and at the same time hear someone say the name of the person in the picture. That information registers as neural CIPs widely distributed in the respective parts of the cerebral cortex that are hard-wired for sound and vision. Figure 2.4 shows that during recall of such information, information about my name, for example, is retrieved from the speech centers, as well as to multiple areas in the cerebral cortex (in the illustration, I only show a few arrows in order to keep the diagram simple). Likewise, visual information of my face is resurrected from multiple areas of the visual cortex. In short, sensory input is deconstructed, distributed and stored widely, and retrieved in a way that binds it all together to reconstruct the original stimuli.

Such deconstruction and re-construction of information do doubt occurs at all levels of mind. But, of course, what intrigues us most is what happens when brain becomes aware of the results of the re-construction, as in consciousness.

Brain Creation of Consciousness

These deconstruction/reconstruction processes can occur subconsciously or consciously. How the brain creates its conscious mind is not entirely understood. "Consciousness" is often equated with "mind," and for centuries philosophers and scientists have grappled with what has been called mind-brain problem. In the nineteenth century, people thought of mind as a "ghost in the machine," and perhaps most people regard it that way today. That is, people accept that mind seems to come from brain, but mind has a ghost-like quality and may not seem to be a physical entity. Mind seems inextricably linked with vague notions of spirit or soul. By the twentieth century, science began to show that conscious mind might have a material basis. In the twenty-first century, science may be able to explain that material basis.

My stance is that by studying CIPs and oscillatory circuitry, we will come to see that mind is not a ghost, but is matter. In this regard, what we know about non-conscious mind is very well established. Much of the non-conscious mind emanates from the brainstem and its peripheral connections (Klemm and Vertes 1990). If we accept evolutionary theory, this knowledge is surely relevant to explaining subconscious mind and conscious mind.

Non-conscious mind governs our simple body functions, such as regulating heart rate, blood pressure, and spinal reflexes. These operations all operate at the brainstem and spinal cord levels. This mind is clearly a physical phenomenon and has been abundantly explained by science. This mind is readily explained in terms of anatomy, physiology, and biochemistry. No one speaks of this mind as "emerging" from brain function.

Next we come to subconscious mind. This is the mind with buried memories, unrecognized desires, compulsions, assorted emotions, and even a great deal of subconscious decision making. This mind operates when we sleep and operates without conscious recognition throughout our wakefulness. This mind, like non-consciousness mind, can be explained by anatomy, physiology, and biochemistry. Again, no one speaks of subconscious mind as emerging from brain function. It too IS brain function.

For now, let me assert that a *whole* mind consists of three interacting "minds," each of which IS brain function, as is whole mind.

I contend that the same principles apply to the brain's creation of conscious mind.

Hallucinatory Consciousness

Conscious thought is sometimes hallucinatory. Hallucination is unreal thought, as when we imagine hearing voices or seeing sights that are not there. Though erroneous, such thought is nonetheless consciously realized. People who hallucinate are consciously aware of such thoughts but may not be aware of their unreality.

Is there a subconscious counterpart? I don't think anybody knows. What we do know is that hallucinations are characteristic of insanity, particularly the hearing of voices and seeing of non-existent images that occur in schizophrenia. One has to be schizophrenic to know what these conscious experiences are like, but we can surmise the imaginary nature from self reports from schizophrenics.

Science cannot explain schizophrenia. Only a few clues are provided by the silent self-talk and imagined scenes that we all experience.

Normal people hallucinate when they dream. Often, the dreamer knows at the time of the dream that the dream is just that, a dream and not real. So dreaming, and perhaps schizophrenia, are the brain's way of staying busy inventing events and story lines. In Chap. 8, I present a new theory that I think explains dreaming.

Another important shared function in normal people and schizophrenics is that they both hear voices. Of course, the voices heard by normal people are usually their own self-talk, whereas schizophrenics hear voices other than their own.

Schizophrenic hallucinations are especially problematic because the patient believes the alien hallucinations are real and may cause the person to engage in destructive behaviors. Back in the 1970s, Princeton psychologist Julian Jaynes caused quite a stir with his book that proposed that the human brain, as it evolved the capacity for consciousness, first began with hallucinations (Jaynes 1972). Imaginary sounds and sights began to be perceived in consciousness, and later consciousness evolved to the point where hallucinations could be seen to be unreal. Proof for such conjecture is not possible, and I don't think his arguments are compelling. He even went so far as to claim that all religions began from founding prophets whose claims of hearing God or angels were hallucinations. That could be the case, but it does not support the notion that everybody in the time of the prophets hallucinated. Today, people would say that hearing God speak to them is crazy. One wonders why this was less suspect in the days of the prophets.

Jaynes' notion has several problems. One is the unlikely possibility that in the short span of a couple thousand years of recent history, humans switched from schizophrenic-like to conscious beings. Worse yet for Jaynes' argument is the fact that billions of today's evolved humans who do not hallucinate still hold religious beliefs of one sort or another. Mentally normal people still believe at least some of what their prophets may have hallucinated about.

This line of thought could lead us elsewhere into the topic of the biology of beliefs, religious and otherwise, that arise as a complex consequence of experience, memory, and reason. Books on the biology of belief exist, (Lipton 2005; Shermer 2000) though the understanding is quite incomplete and beyond the scope of this book.

According to Jaynes, schizophrenia is the prototype of normal human mental function, and remains as a vestige in modern humans. He claims that in the first human cultures, no one was considered insane because everyone was insane. While this idea seems bizarre, it does seem likely that one function of normal consciousness is to prevent and correct hallucinogenic tendencies that may be inherent in primitive brains. As human brains evolved to become bigger with more neocortex, conscious thinking became effective and powerful, and more capable of constraining and teaching subconscious operations.

Jaynes postulates that hallucinations arise in the right hemisphere and in normal humans are suppressed by the dominance of the left hemisphere (and vice versa in left-handed people). He cites a few EEG studies that show a difference of electrical activity in the two hemispheres, but there are few modern studies using sophisticated quantitative EEG that address this question.

Of special interest is time-locked activity (coherence) among various regions. Since schizophrenics hear voices, hallucinate, and have disordered logic, it would suggest that various parts of brain are not coordinating well. Schizophrenic patients do have abnormal EEG coherence in both resting and stimulus conditions, suggesting more diffuse, undifferentiated functional organization within hemispheres (Wada et al. 1998).

I think that consciousness, as a state of mind, is not what is at issue here. People who hallucinate, whether because of brain abnormality such as schizophrenia or because they are having normal dreams, are still consciously aware of their hallucinations. We should also bear in mind that mentally normal people can be consciously aware of hearing voices, particularly self-talk chatter, and music in their "mind's ear." The line separating normalcy and insanity may be finer than we like to think.

Dream Consciousness

Dream thought falls into a similar category. Dreams may be total hallucinations or grounded in reality. Common experience teaches that dreams are a special form of consciousness. Though we are behaviorally asleep, the dream content is a conscious experience, though we may not remember it after awakening. Such forgetting is a memory consolidation problem, not a consciousness issue. Many people have dreams where they not only are aware of the dream experience but are also aware that the events are not real but part of a dream. Dreams have to be a special form of consciousness, maybe not too different from ordinary consciousness.

Let us consider animal dreaming. Anybody who has ever watched a sleeping dog bark and paddle its feet can have little doubt that they are chasing a critter in their dreams. Sleeping dogs will even sometimes twitch their nose, suggesting that they even have olfactory hallucinations. All higher mammals, and to a lesser extent birds and higher reptiles, show multiple sleep episodes where bodily signs are identical to those of human dreaming: an EEG of low voltage, high-frequency activity, rapid eye movements, irregular heart and respiratory rates, and spastic twitches of muscle.

Are higher animals thinking consciously when they are awake? No one can know (except the animals), but there are many books that argue both sides of the possibility. Given that animals have less developed brains than humans, according to the Jaynes' view, we might think that the waking state of higher animals would be perpetual hallucination. I doubt it, but don't know how to disprove it. Their dreaming indicates that their brains have the capacity for non-linguistic hallucination, but that is not proof that hallucination is the default mode of operation in the awake state. Since higher animals, especially performance-trained animals, can exhibit a great deal of adaptive, purposive awake behavior, it would suggest that they are not hallucinating.

Physiologically, we know that dreaming is the hallmark of advanced animal evolution. It is fully developed only in mammals, whose brains have a well-developed neocortex capable of "higher thought." Paradoxically, babies spend more of their sleep time in dreams than do adults, yet their neocortex and fiber-tract connections are poorly developed compared to adults. I have an explanation for that in Chap. 8.

Why do we dream? Books have been written on the subject, and we still don't know. We do know that dreaming is a necessity. Many animal and human experiments show that the brain does not function normally if it is not allowed to enter the physiological state that enables dreaming. A whole array of reasons for dreaming have been suggested, and they are not necessarily mutually exclusive: (1) to ensure psychic stability, (2) to perform off-line memory consolidation of events of the preceding day, or (3) to restore the balance of neurotransmitters that has been disrupted by ordinary non-dream sleep. Dreaming may also just be an inevitable a side effect of re-organization of subconscious mental processes.

Maybe, like our dogs and cats, human dreams reflect an inevitable physiological drive state that is just the brain's way of entertaining itself. In any case, dreams can be very good indicators of what is on our minds, though the pronounced symbolism in dreams may require a good deal of introspection and analysis to interpret. Why are dreams so often symbolic rather than literal, though both types occur? Nobody knows, but maybe symbolism is a result of subconscious thinking trying to become manifest in the special consciousness of the dream state.

Human Mind Is in the Brain

As far as contemporary science can determine, there is no evidence that minds are floating around in space. Each mind is confined to and not separable from brain. The brain is the vessel that not only contains mind but also generates it.

Of course, the products of mind, its ideas, feelings, and thoughts, can be shared to the world outside a given brain through speech, writing, and observable deeds. In that way, many minds can contribute to the evolving nature of any given single mind as that mind experiences and learns from worldly encounters.

What troubles many scholars is the question of how consciousness can affect brain. However, that is only a problem if you think of conscious mind as some sort of out-of-body "ghost in the machine." The problem goes away when you realize that conscious mind IS matter. That is, mind affects matter, because mind is itself matter, expressed in processes to be fully elaborated in this book. Once a given thought, for example, is initiated in material process of brain, those same processes can change the brain so it can regenerate the thought and integrate it with other thoughts, past, present, and future.

One question cannot be answered by today's science. Is there such a thing as an individual soul, embedded or otherwise entangled with mind? Most people in the world believe there is, and this is the basis for the world's religions. The soul, by most people's definition, is not a material thing, so it makes no sense to try to explain "soul" via what science has revealed about the material nature of mind. This book has a focus on explaining the material basis for mind, as scientists understand it today. But recall the earlier comments about known material realities, such as dark energy and dark matter, that scientists do not understand.

If we accept the brain's central role in all thought, the next issue is how do brains make decisions? At the cell level, decisions are made in the synapse, the junctions between neurons where chemical communication occurs.

Circuits and Networks

Less obvious is the answer to how brains make decisions at the circuit level. First, it is helpful to review the basic kinds of circuits in brains. There are only four basic kinds (Fig. 2.5).

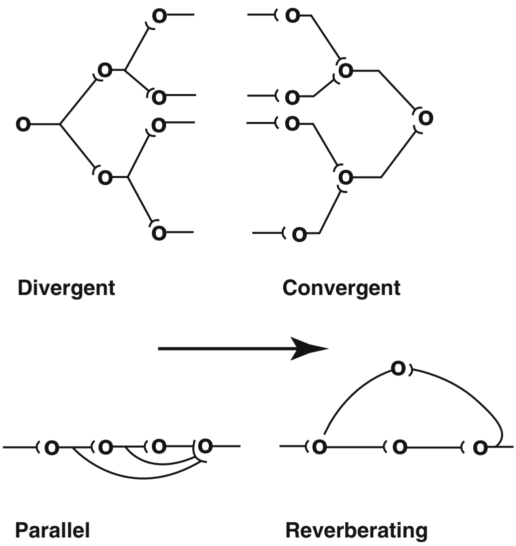

Fig. 2.5 Four basic types of brain circuits, shown in simplest form. *Open circles* represent the cell body of a neuron. *Lines* indicate their fibers that propagate nerve impulses, and terminal branches indicate the synaptic junction with a target neuron

These circuits interface with each other in various ways. They often operate in parallel, sharing with each other the “information” going on in each respective circuit. One way to illustrate inter-circuit interactions with a Venn diagram, showing the overlap of different circuits to represent those features of processing that are shared among all the circuits. Each circuit has an output of some type, either to glands and muscles or to other circuits. Each circuit’s “decisions” are thus influenced by other circuits and likewise influence the decision-making of those circuits with which it has an interface.

Note that the circuit diagrams above suggest how single neurons connect with each other. Most action in the brain is based on large populations of neurons. Thus, we should extend our view of these elementary circuit designs as applying to many neurons in a network in which the nodes of the network can be laid out in such patterns of divergence, convergence, etc.

Many factors further complicate our understanding of neuronal networks. First, the influence of one node in the network to another is not a simple “on/off” or “yes/no” signal. Rather, what is transmitted from one node to another is a temporal pattern of nerve impulses. Moreover, not all the fibers in the “cable” that connects one node to another are sending the same temporal pattern of impulses. Further, the pattern of connecting activity dynamically changes.

Finally, the brain should be thought of as a network of networks, wherein a given network (or for simplicity, one circuit) typically connects with other networks (or circuits). There may be multiple points of egress and access within a given network. A given “target” circuit may be simultaneously supplying input to the circuit from which it is receiving input. Reciprocal connections among networks are common in brain. They provide a way for one circuit to be informed of what another network is doing. Reciprocity also allows feedback, so that consequences of a decision made by one network can be used to inform an ongoing decision-making process. A classic example is how decisions made in “motor cortex” are modulated by feedback from cerebellar circuits.

The upshot of all this is that the brain is so complex that its neural networks may not be realistically amenable to adequate scientific exploration. Many very smart people in computer science, bioinformatics, mathematics, and engineering work in the area of neural network analysis. Yet their work is severely constrained by the complexity of the network processes in brain and by the insufficiency of their analytical tools.

Manifestations of Thought

Thoughts, as we commonly generate and experience them, are complex mixtures of more basic elements. If we can identify what the elements of thought are, we have at least some chance of developing an all-encompassing theory of thought. Some of these elements are found in the latent or stored form of mind, such as microanatomy and biochemistry.

Biochemistry

Biochemists like to grind up brain, from sacrificed animals of course, and examine its chemistry as an index of what the animal had been thinking. This approach has led to many major discoveries, such as the existence of about 100 biochemicals, called neurotransmitters, that mediate synaptic communication among nerve cells. However, this cannot tell us much about what brains are thinking at any given moment. That information is carried, in real-time as people say, by patterns of nerve impulses.

But the thinking represented by impulses causes biochemical changes, especially in the synapses. In turn, these biochemical changes may serve as a repository of the "information" signaled by the impulses and may affect subsequent discharge patterns of impulses.

Related approaches include collecting neurotransmitters from localized regions of brain in a live animal while it is performing a given behavior. This is done with implanted double cannulae, in which perfusion fluid is pushed through one cannula and pulled out in the other, picking up along the way chemicals that have been released by nerve cells in the vicinity of the cannula tip. This approach can tell us a lot about the biochemical processes that are supporting thinking in real time, but obviously only a minute region of brain can be monitored this way.

There are many other biochemical techniques too complicated and beyond the scope of this book. In general, biochemical analyses are not direct indicators of thinking, but rather indicators of the activity of biochemical dynamics in neurons as they participate in "thinking." Certain biochemicals in synapses are the storage reservoir of thought – that is, memory.

A metaphor for comparing relative roles of impulses and biochemicals in the function of mind could be 18-wheeler trucks and the Inter-state highways system. The highways link various cities together, serving as a communication network, much like the axons and dendrites that connect neurons constitute the networks of the brain. Each truck represents stored information. No communication or exchange of goods occurs if the 18 wheelers sit parked at the various warehouses around the country. The trucks are a reservoir, having the potential for distribution. Only when the trucks start moving in the highway network does communication occur. In the nervous system, what moves – that is, what is propagated throughout the networks – are nerve impulses.

Electroencephalogram (EEG)

The EEG is a voltage waveform reflecting underlying impulse activity summed over many neurons. This kind of signal was first discovered by coupling electrodes on the scalp to high-magnification amplifiers that drove pen-and-ink displays. Similar signals can be seen from electrodes implanted within the brain, but these are called "field potentials" because they are not obtained from on top of the head. Think of such a signal as a plot of voltage (in microvolts) as a function of time. The waveform

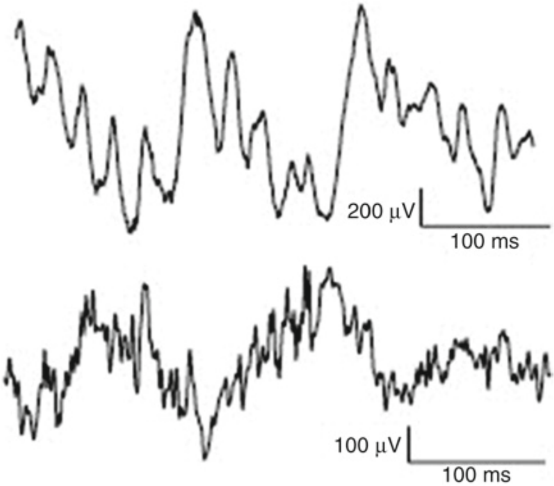

Fig. 2.6 Illustration of the compounded nature of the EEG, as recorded from the hippocampus. Small waves seen "riding on top of" larger and slower ones. *Top*: small, slow frequency "theta" waves (about 6 waves per second, but not so obvious here because the total time shown is less than 0.4 s). *Bottom*: high frequency "gamma" waves (about 4 per 100 ms) (From Colgin et al. 2009; Note: EEG frequencies are usually designated in engineering Hertz units (Hz), as if their frequency were constant. In reality, a given EEG frequency "jiggles;" the cycle time is not absolutely uniform, and this is evident in the signals shown in this figure. "Waves per second" is the better term)

is generated from the voltage generated by ionic current flowing through the resistance of tissue, body fluids, and, in the case of scalp recordings, the skin.

Tissue resistance has a capacitance component that shunts some of the high-frequency amplitude so that higher voltage frequencies are not fully represented in what is seen under typical recording conditions (see Fig. 2.6). As you will see later, this is not a trivial point, because higher thought processes are associated with higher frequencies in the EEG.

The EEG provides a near-instantaneous index of the brain's electrical activity in the region of the sensing electrode. However, that activity is hard to interpret because the signal seen is a composite of all sources of current in the region: postsynaptic and action potentials of multiple neurons and membrane potentials of supporting (glial) cells. As a result, the EEG is not a pure waveform but is rather compounded from voltages of different frequencies. Think of the EEG as a wiggly line that is a mixture of large slow wiggles with intermingled and superimposed faster-changing wiggles.

A similar mixing of frequencies is seen everywhere in the brain, but is most conspicuous in areas, such as the cortex, where oscillation at several frequencies in the same general area is prominent. It is evident that time resolution is excellent, to the level of a few milliseconds. This time resolution is not possible with the other popular way of studying brain function non-invasively: brain scans.

Brain Scans

The original brain scan technique, called positron emission tomography (PET) involved injecting a radioactive substance into the blood. Since brain areas that are more active get more blood flow, the radioactivity level there can be greater and thus indicate "hot spots" of activity in response to stimuli or mental task performance, for example.

The radioactive feature of the technique has caused it to fall out of favor for routine brain scans and is being supplanted by magnetic resonance imaging (MRI) which poses no health hazard (that we know of). With MRI, a giant magnet surrounds the subject's head and forces hydrogen atoms to align. When the brain is hit with a strong radio signal, the atoms are knocked out of alignment, and the rate at which they return to the aligned state provides a detectable signal. These signals increase when the level of blood oxygen goes up, indicating which parts of the brain are most active. Because MRI is much safer than PET scans, it is used for repeated scans on the same subjects under different cognitive conditions.

A more recent refinement, called functional MRI (fMRI) uses special computers to increase the speed at which scanning is done. Even so, compared with EEG, the scan is slow. The value for research purposes is just the opposite of that for the EEG: the spatial resolution is excellent (on the order of millimeters), but the speed is slow (on the order of seconds).

Brain scanning, especially with fMRI is THE hot area of neuroscience. The instrumentation is extremely expensive, but every brain research center wants to have one. All this popularity is misplaced in my view. Aside from the time resolution problem, fMRI scanning has numerous other problems. The first is the misuse of statistics (Vul et al. 2009). This kind of scanning is usually used to identify correlations between a specific cognitive task with increased activity in certain brain areas. But a survey of 54 randomly selected fMRI studies revealed that many had grossly inflated correlations between brain "hot spots" and the cognitive task. The process by which one determines the subset of voxels in an image to use in correlation calculations is often suspect. The matrices can consist of hundreds of thousands of numbers derived from specific brain areas or areas seeming to show activation. Then these pre-selected numbers are used to calculate a pair-wise correlation coefficient across subjects, often from the average response across trials on the average activity of X-number of adjacent voxels or the peak activity in the population of voxels. Then a separate correlation may be calculated for the cognitive task and those voxels whose activity exceeds a certain arbitrary statistical threshold (some of which will qualify for use in the analysis just by chance). With huge numbers of voxels involved, it is easy to generate inflated correlation values. Over half of the 54 fMRI publications had such flawed methods. The authors of the meta-analysis of the 54 papers used such procedures on a simulated analysis of pure noise and found a correlation coefficient of 0.9 (1.0 is perfect correlation).

The basic cause of such misleading correlations is that the data selected for analysis are inter-dependent. Multiple t-tests are performed to compare voxel activity in one task with another or the control state. Many MRI researchers do not properly correct for this kind of statistical error.

Another problem is reliability of the numbers. Test and re-test reliability between repeated trials can be as low as zero, even for voxels which on the average seem to show an association with the cognitive task.

But the most serious limitations are the ones typically glossed over. Even if and when we can believe the reported correlations of seeing areas of increased activity ("hot spots") in certain brain areas during specific cognitive tasks, serious physiological interpretive problems arise. The fMRI scans measure blood flow change, which is also parallel with oxygen consumption. But even with "significant" effects, the magnitude of blood flow change is small, often less than 5%. We infer that this is caused by increased electrical activity. But what kind of activity? …. graded postsynaptic potentials or nerve impulses? … or the ultraslow electrical changes in glial cells? Recent fMRI studies that included acquiring neuronal activity data at the same time revealed that nerve impulses used only a small proportion of the total oxygen consumption (Alle et al. 2009). The vast bulk of fMRI signal therefore comes from postsynaptic potentials, not impulses. Of course that is also true of EEG signals. But how can fMRI signals tells us much if messaging and the results of information processing are expressed in nerve impulses?

It does seem that fMRI correlates with EEG-like field potentials more than with nerve impulses. The reason that fMRI correlates better with field potentials than impulses is that both are "average" measures of activity of large populations of neurons. At any given instant, many individual neurons may be functioning as exceptions to the over-all population activity.

Note that EEG is summed activity, mostly from postsynaptic potentials. With visual cortex responses in cats, increasing stimulus intensity increased high frequency field potentials, impulse activity, and fMRI signals (Niessing et al. 2005). Similar studies in two human neurosurgical patients showed correlations between field potentials, neuronal firing, and fMRI signal in the auditory cortex (Mukamel et al. 2005).

We might wonder why major changes in cognitive task demands don't produce more robust fMRI responses. As mentioned above, I believe that active cognition is achieved mostly by impulse patterns, which are under-represented in a brain scan. One reason is that patterns of inter-spike intervals can undergo major change without a change in total number of impulses, and therefore presumably no change in total oxygen demand would occur. Patterning of impulses can be more important than the number of impulses (see Chap. 4), and thus brain scans are not capturing the neural events most directly relevant to thinking.

It should also be obvious that hot spots only indicate the possible location of neurons that support a given mental process but is not likely to show *how* they do it. Most brain researchers realize this, which is probably the reason they term hot spots "regions of interest." That is an admission that they must be restrained in drawing conclusions about what hot spots mean.

Brain-scan hot spots don't indicate whether the activated neurons exert excitatory or inhibitory influences on their targets. We don't know if increased MRI activity is coming from synaptic processes in inhibitory or excitatory neurons, which produce opposite effects.

There is also the problem that any change in activity is a correlate of a given thought, but not necessarily a part of the cause of a cognitive process. For example, during a mental task, several areas may show as hot spots, and researchers typically regard these as indicating a system of connections responsible for a given mental function. A recent advance in fMRI is the technique of "functional connectivity" analysis (Rogers et al. 2007). These statistical methods test for correlations of activity in brain areas under various mental performance conditions. The focus is on brain areas that show increased activity at the same time (testing for correlations of increased and decreased activity might also be useful, but not commonly done). Such analysis might identify brain areas that are necessary for a various function, and longitudinal analysis (also not commonly done) could indicate changes over time from learning, disease, age, etc. could alter the degree of needed connectivity.

However, showing that several areas are activity at the same time can be misleading. There is no way to if one area is driving the others, or if the others mutually facilitate each other. One or more of these hot spots may be incidental to the process being studied with scanning. The activity could have been released from inhibition by one or more of the other hot spots which were actually causally related to the mental process. Thus, some of the hot spots may have nothing to do with causing the mental process under study.

Even when increased activity may be part of the cause, the role played is not self-evident. The same part of the brain may be activated under a variety of conditions. The amygdala, for example, is activated by the sight of snakes, intense odors, or erotic stimuli. Another example is the hippocampus, which is activated by a wide range of emotional stimuli as well as participating in the formation of memories regardless of the content of those memories.

Still other problems exist. While some areas of brain increase activity during a cognitive task, other areas show a decrease. Most scientists ignore areas of decreased activity. Yet those should not be dismissed, because if the decreased activity is in a pool of inhibitory neurons, the result is likely to be a disinhibition that might ultimately be the release activity in a remote site that is attributed to be the cause of the cognitive process when the real cause came from the area of diminished activity.

Another issue told to me by an fMRI expert I visited in Houston is that an area of increased activity, regardless of task, is often preceded by diminished activity in that same area. Almost no one pays attention to such data, because everyone seems fixated on finding areas and conditions of increased activity.

Behavior

Most of us judge what other people are thinking by their behavior. If someone yells at me, I assume that he is thinking about his reasons to be mad at me. If a crook robs a store, he is probably thinking about getting money, how to get away, and how he wants to spend it.

Anyway, scientists like to call this ability to “read one’s mind” from observing behavior as a special human ability called “theory of mind.” We presume that others have a mind, based on what they do and how our own mind would be operating in similar circumstances. Actually, a theory of mind has been attributed to many species of animals, though obviously their capacity for imputing mind to other animals is far more limited than our own.

There is also the issue that you cannot always know for certain what other people are thinking from what they do. Even their speech, which is a behavior, can be misleading. They may mean one thing while saying another. They may even lie, even to themselves.

I won’t pursue this further here, because behavior is mostly beyond the scope of *how* brains think. I will, however, come back to behavior later when I explore how behavior is a feedback device for brain, and brain uses the feedback from behavior and its consequences in altering the brain’s thinking.

The simplest element of thought is so simple we would not ordinarily think of it as a “thought.” Let us begin, for example, with the idea that many thoughts arise from sensory experience, and the first stage of such thought is the way that nerve cells create an impulse-based representation of an environmental stimulus. For example, if you touch a hot stove, nerve fibers in the finger generate impulses that are sent into the spinal cord and brain. This initial registration of the stimulus can be thought of as “tagging” the stimulus in the form of the impulse pattern, in this case in a pathway that goes from the fingers directly to the spinal cord. This tag pattern is one fundamental element of thought, and in this case the element will be a building block for subsequent elements that lead to the brain’s response that we can more clearly classify as the thought: “Damn! That hurts.”

As thought grows from the thought elements that are activated by touching a hot stove, we now have impulses spreading into the divergent circuits in the spinal cord, thalamus, and sensory cortex. As the thought of “Damn! That Hurts” grows, the representational tag now becomes one of circuit impulse patterns (CIP). It is the CIP that represent the thought. More than that, I would argue, the CIP *is* the thought.

Thinking of CIPs as thoughts is somewhat of a stretch if we limit our view to *conscious* thought. I will get to that later, but for now I want us to view non-conscious and subconscious thoughts as CIPs. That should be more intuitive and easier to accept.

The CIPs are an abstract representation of a complex thought. If they *represent* the thought, is it not possible that they *are* the thought?

The Brain as a System

A brain is an information-processing system. While there are a few maverick scientists who don’t believe this, the vast majority of neuroscientists think the evidence for information processing is overwhelming. Thoughts, whether conscious or subconscious, arise from this system and can be remembered by it. Neuronal information is moved around in multiple, parallel pathways, the circuits of which are juxtaposed and commonly overlapping. A given neuron may be recruited into more than one circuit.

Neurons and their clusters, called nuclei, are typically connected reciprocally, so that output from one place to another in the brain can be processed and fed back to the source of input.

While it is tempting to think of a hierarchical organization in “top-down” terms, wherein the cerebral cortex “supervises” the hierarchy of subsystems within the nervous system, the matter is not that simple. For instance, neurons in the spinal cord can carry out mundane control functions for their respective body segment while the cortical neurons are “free to think higher thoughts.”

But the assignment of rank order to subsystems in the brain and the spinal cord is not as obvious as it may seem. Although the part of the brain that provides intelligence, the neocortex, ranks above the reflex systems in the brainstem and spinal cord, there are practical limits on the degree of control exerted by the neocortex. If neocortex control were absolute, for example, people would not succumb to the dizziness and ataxia associated with motion sickness and the vestibular system of the brainstem. If cortical control were absolute, people would be able to suppress the pain that is mediated in the thalamus. They could stave off sleep indefinitely by keeping the reticular activating system active. This is clearly not the case.

Thus, rather than relying on a permanent “supervisor” neuron or population of neurons, the nervous system functions as a hierarchy of semiautonomous subsystems whose rank order varies with situational stimuli. Any subsystem may take part in many types of interrelationships. Whichever subsystem happens to dominate a situation, each subsystem is independent only to a certain extent, being subordinate to the subsystem above it and modulated by the inputs from its own subordinate subsystems and from other subsystems whose position in the hierarchy is ill-determined. This design feature of the mammalian nervous system provides maximum flexibility and is probably the basis for the brain’s marvelous effectiveness.

Even for a function that we habitually think of as top-down, such as attention, the actual process may be bottom up. György Buzsáki (2006) points out that the effect can be produced by gain control from primitive subcortical structures. The neurotransmitters acetylcholine and norepinephrine are released from brainstem sources, and these enhance sensitivity of cortical circuits to sensory input. This becomes manifest in enhancing cortical gamma rhythms, which are strongly associated with attentiveness and complex thinking. What excites these brainstem structures? For one, intense sensory input suffices (see my comments about the Readiness Response later in this chapter). But because the cortex and these brainstem structures are reciprocally connected, thought processes emanating from the cerebral cortex can accomplish the same thing, as for example happens when we think about some idea that really excites us or some intense phobia.

Cerebral circuits can maintain an autonomous, self-organized activity independent of input. Buzsáki explains that the activity and thinking processes of brain are a “synthesis of self-generated, circuit-maintained activity and environmental perturbation.”

If different brain areas and systems can be autonomous, how can they interact with each other? First, they are connected via fiber tracts that convey information from one area to another. Thus, information in one area becomes shared with other brain areas. The sharing comes not only because the anatomy of the circuits overlaps, but also because the impulse activity in the various areas may become time-locked (coherent). Such coherence seems to be achieved through oscillations that become entrained to certain frequencies (see Chap. 6).

Nonlinearity Matters

A linear response or linear system is one wherein a steady increase in input leads to a proportional change in output. A graph of such output produces a straight-line curve, making it easy to predict the output for given levels of input.

In the instance of a nonlinear response, there is no direct proportion between input and output. Responses may be discontinuous or non-related, or may relate in non-proportional, non-linear ways (Fig. 2.7).

Cell-Level Consequences of Nonlinearity

The inherent definition of nonlinearity precludes the possibility of *directly* predicting the amount of response exhibited by a nonlinear process during a given passage of time.

Aside from some unpredictability, additional consequences of nonlinearity exist. In the case of second messengers, for example, nonlinearity allows for much more

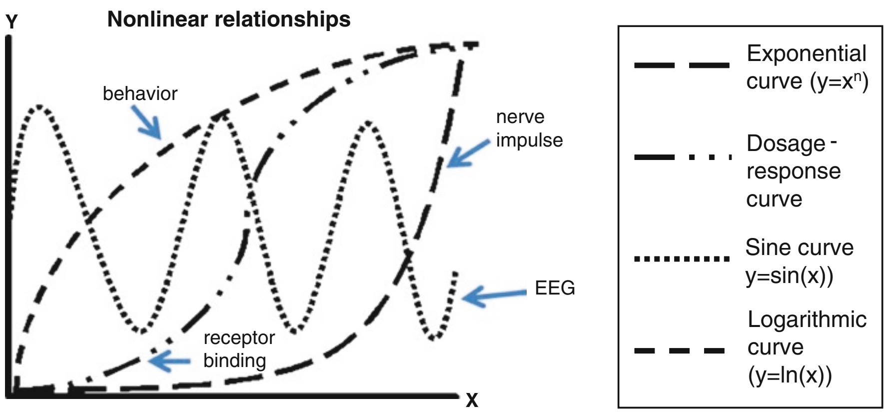

Fig. 2.7 Different kinds of non-linearity seen in the nervous system

effective and efficient operation of the nervous system. One second messenger can activate many other molecules in the course of a signal transduction pathway, and each of these molecules can activate many more molecules. The result is an exponential relation between second messenger concentration and cellular response, so that just a few second messengers can be used to educe a greatly magnified cellular response. Amplifying a response across time in turn increases the speed at which it is elicited, which is vital considering how central response time is to effective nervous system functioning.

There are other practical benefits to nonlinearity. Consider the release and binding of neurotransmitter, which takes the form of an S-shaped curve. Once neurotransmitter concentrations reach the saturation point where all stereospecific binding sites are filled, the body would be squandering valuable resources if it released neurotransmitter in a linear manner. As such, once binding sites are filled and neurotransmitter concentration reaches a level of excess, the body may begin a pathway of feedback inhibition where the neurotransmitter "left over" from the filled binding sites serves to inhibit ("down regulate") the molecules that initiate its production.

Cognitive Consequences of Nonlinearity

Nonlinear consequences at the cell level show up in thinking. For example, an S-shaped curve that holds great implications is the learning curve, depicted below (Fig. 2.8).

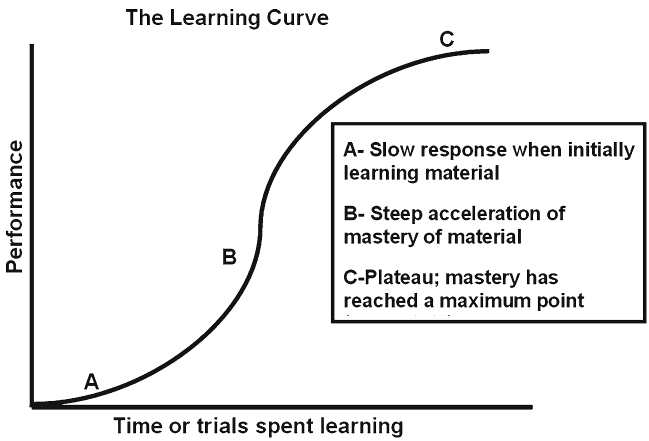

Fig. 2.8 This curve indicates that when initially exposed to material to learn, an individual's mastery of it is somewhat gradual, until a certain point is reached and the pace at which material is mastered accelerates. However, eventually an asymptote is reached where more time spent learning has no effect on performance tests for mastery, meaning that maximum mastery has been attained. Further attempts at learning a certain material become, at this point, relatively futile

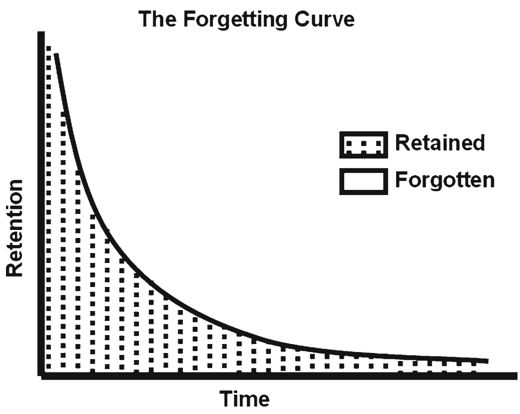

Fig. 2.9 This curve, which models retention of material over time, approximately depicts Hermann Ebbinghaus's formula for forgetting, given by $R=e^{(-t/S)}$ where R is memory retention, S is the relative strength of memory, and *t* is time. Material is forgotten at a predictable, albeit nonlinear rate over time, although a number of variables including the difficulty of the material and physiological fluctuations of an individual may affect the exact depiction of this curve. Interestingly, though, studies have shown that retention in each material-specific curve can be improved over time by conscious review. This observation holds many implications, especially in the realm of the education system, but outside of it as well. For instance, it might be used to support the concept of "refresher courses" as a means of augmenting knowledge for individuals in a professional career

A graph of forgetting, as opposed to learning, is also non-linear, but the shape is quite different (Fig. 2.9).

Inhibition Matters

Some neurons are inhibitory. That is, their only effect on their targets is to produce inhibition by driving the resting potential of target neurons away from firing threshold. When a neural pathway contains inhibitory elements, non-linearity is introduced (Fig. 2.10).

If an inhibitory neuron acts to suppress activity in an excitatory chain, it is said to "disfacilitate" it. If an inhibitory neuron inhibits an inhibitory neuron that acts in an excitatory chain, it is said to "disinhibit" the target and may thus lead to increased output activity.

Another thing inhibitory neurons do is serve as crucial nodal points in feedback circuits (Fig. 2.11). The inhibition may be a negative feedback on the target, a feed-forward inhibition of the target or a lateral inhibition on neurons in parallel pathways.

Inhibition not only selects pathways of neuronal chains, but can also select whole assemblies of neurons. Slight differences in synaptic strengths between the inputs to an inhibitory neuron can determine what happens in whole populations of related neurons.

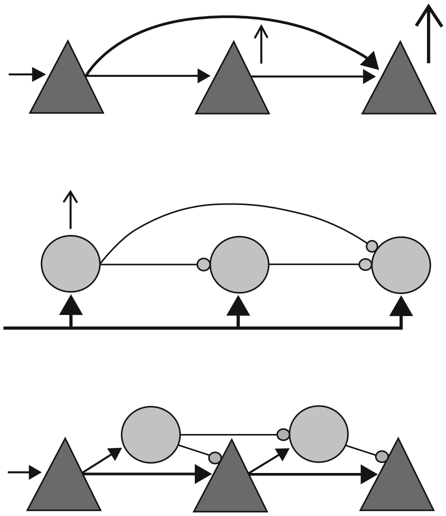

Fig. 2.10 Inhibitory neurons introduce non-linearity. *Top*: chain of excitatory neurons (*black*) produces steady increase in excitation. *Middle*: and *bottom*: presence of inhibitory neurons (*gray*) introduces unpredictable effects on output that vary with the details of connections and strength of connections (Reproduced with permission from Buzsáki (2006))

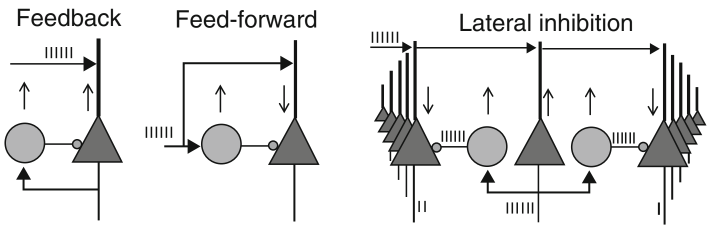

Fig. 2.11 *Left*, feedback inhibition: activation of an excitatory cell (*triangular shaped*) activates an inhibitory neuron that feeds back inhibitory influence to suppress activity in the cell that excited it. *Middle*, feed-forward inhibition: Activation of an excitatory cell is damped when a parallel input path includes an inhibitory neuron. *Right*, lateral inhibition: activity in parallel pathways can be suppressed or shut off when an excitatory neuron activates inhibitory neurons that supply input to the parallel pathways. The superimposed triangles representing principal cells in the parallel pathways indicate neurons that excite each other or are simultaneously excited by the same input (Reproduced with permission from Buzsáki (2006))

Whole competing assemblies can be isolated, and the same network can produce different output patterns at different times, depending on the time-and-space distribution of inhibitory influences. Inhibitory influences also modulate the firing pattern of impulses to determine whether target neurons fire in bursts or in more or less steady streams of impulses.

Variable flexibility in inhibitory influences is of special importance in the highest levels of neuron function in the cerebral cortex. These neurons will not normally get locked into excitatory overdrive (epilepsy is a notable exception). Likewise, these neurons will not get frozen into a state of unresponsiveness.

Bodies Think Too

Thinking is not de-contextualized. Brain is embodied. If "thought" is the neural activity within certain circuitry associated with a body part, then one could argue that a simple knee-jerk reflex is a thought.

What I really want to emphasize is that most of the brain's thinking occurs from the reference point of the body and its relationship to its inner parts and to the outside world. Biologically speaking, the brain exists primarily to help make the body work right and to make behavior appropriate and successful in the context of the real world in which bodies operate.

We can have subconscious thought, as for example emotional kinds of thought that affect our body and behavior. Our heart may race or palpitate, cold sweat may appear, we may blush, we may become sexually aroused – all can occur subconsciously. We can even have subconscious responses in our dreams that affect our body (recall the earlier example of foot paddling and barking in sleeping dogs).

In the simple case of spinal reflexes, "thought" inevitably is mediated through the body, in which a train of nerve impulses arising from a nerve fiber in the patellar tendon travel up the nerve to the spinal cord, where they activate nerve cells that project back to that muscle to which the tendon was attached. Thus, you might say that the spinal cord thinks, non-consciously of course, the equivalent of: "My tendon has been stretched and to get my leg back to normal position, I must contract the thigh muscles." Such thought is obviously embodied.

Physiological and Behavioral Readiness

Many of us have been embarrassed by friends teasingly sneaking up behind us and startling us into jumping or letting out a little scream of surprise. All of us react similarly to such startling stimuli – our head turns toward the stimulus, our heart rate picks up, our muscles tense, and our mind assumes a heightened sense of awareness. These reflexive reactions allow us to quickly make appropriate behavioral responses to environmental contingencies.

I fondly remember the pioneer researcher in the study of this "orienting reflex," Andre Grastyán, in Pécs, Hungary in the 1970s. It was there I met his student, György Buzsáki, who was later to become a research pioneer more famous than his mentor.

Neurons in the central core of the brainstem govern the orienting reflex. This system engages a constellation of sensory, integrative, and motor responses to novel or intense stimuli.

The brainstem core is ideally situated to monitor and respond to a variety of stimuli, because its cells receive inputs from all levels of the spinal cord. When brainstem core neurons are stimulated by sensory input of any kind, they relay excitation through numerous reticular synapses and finally activate widespread zones of the cerebral cortex, enhancing consciousness and arousal level. If this stimulation occurs during sleep, it can disrupt sleep and trigger consciousness. Concurrently with cortical activation, muscle tone is enhanced, preparing the body for forthcoming movement instructions. At the same time, the limbic system is activated, which allows new stimuli to be evaluated in the context of memories, and neurons of the hypothalamus and the autonomic nervous system mobilize the heart and other visceral organs for the so-called fight-or-flight situations. This conglomeration of responses makes an animal or person ready to respond rapidly and vigorously to biologically significant stimuli, including the pranks of mischievous friends (Fig. 2.12).

The central core of the brainstem produces what I call a "Readiness Response" (Klemm 1990). Such readiness creates the capacity for conscious thought by awakening the brain, mobilizing and making it alert. It is the brain's way of saying to itself "wake up brain, you have some incoming information you need to deal with." Without it, the brain remains in a comatose state, even if the primary sensory pathways are functioning normally (Ropper 2008).

Other scientists have used more restrictive terms, such as "arousal response" and, as mentioned earlier, "orienting response," but these terms don't capture the full

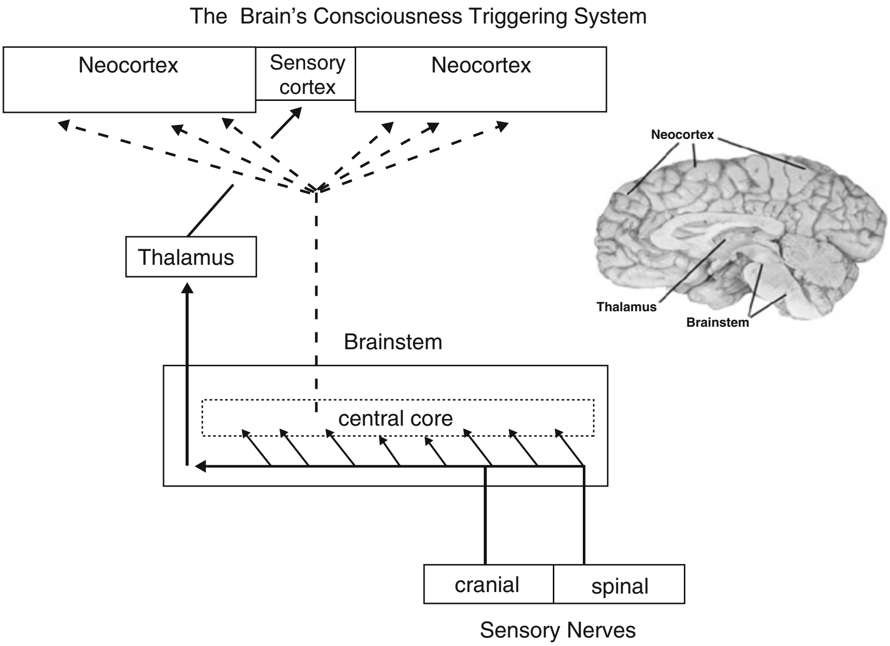

Fig. 2.12 The major pathways in the brain that are crucially involved in the genesis of consciousness: neocortex, thalamus, and the central core of the brainstem. Sensory inputs enter specific thalamic nuclei, which project the information into the small strip of the sensory cortex part of the neocortex. All the rest of the neocortex gets diffuse input from sensory nerve collaterals that activate the central core of the brainstem which in turn provides widely distributed excitatory drive to all parts of the neocortex. This brainstem influence is the essential part of the consciousness triggering system

range and significance of the response. In fact, it was during my visit with Grastyán that I realized his "orienting response" ideas did not capture the full range of associated activities.

It is well established that consciousness, however it "emerges," arises from the interaction of the cerebral cortex and the brainstem core. When the core is active, it provides an excitatory drive for the whole cortex. In a sense, the reticular formation can be said to "arouse" cortical cells to be more receptive to sensory information arriving over the primary sensory pathways. That same arousal effect operates on internally generated images, memories, and thoughts. Conversely, depression of reticular activity leads to behavioral sedation. Destruction of the reticular formation causes permanent subconsciousness and coma.

No more fundamental relationship among the three kinds of mind can be found than in the functions of the brainstem, because it is the seat of the non-conscious mind and links intimately with the other two kinds of mind. The brainstem and spinal cord enable the other two kinds of mind. This idea was popularly captured in Paul MacLean's idea of the "Triune Brain", (Fig. 2.13) (MacLean 1990) although he did not explicitly apply the idea to the three kinds of mind as I have done earlier in this book.

MacLean's triune brain was originally intended to be a model for the evolutionary development of the brain. It holds that there are three distinct brains, each of which has a unique set of functions that become increasingly more complex with progression along the hierarchy of brains and evolution. First is the "reptilian brain." It carries out autonomic processes as well as instincts and is involved in survival functions, such as eating, escaping predators, reproduction, and territorial defense. Reptilian structures are those deepest in the brain, including the brainstem and cerebellum. The next brain is the limbic system, or the paleomammalian brain, which wraps around the reptilian brain and includes such structures as the hippocampus, amygdala, thalamus, and hypothalamus. Emotions, memories, and the subconscious value judgments stemming from emotion and memory fall within the domain of

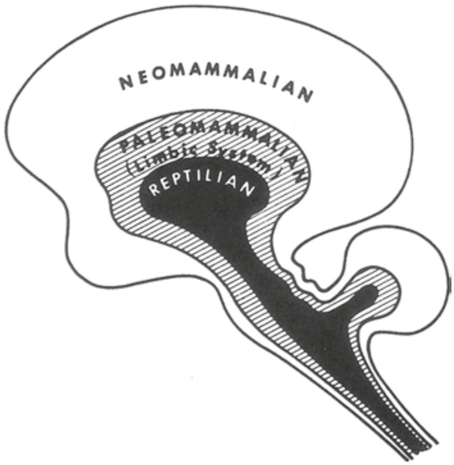

Fig. 2.13 Paul MacLean's triune brain concept, showing gross structural changes at different evolutionary stages of brain development

limbic system control. Most evolved is the third brain, the neocortex, which is evident in higher mammals- especially primates. Attributable to the neocortex are the complex functions that distinguish primates and especially humans from other animals: language, logical and rational analysis, thought and abstraction, and advanced learning and memory. Its anatomical domain includes the two cerebral hemispheres that envelop the two other brains, and especially the prefrontal cortex.

Application of the “triune *brain*” concept to the three *minds* leads to some interesting comparisons. The Reptilian Brain, for instance, because it controls autonomic functions and instinctual urges, is comparable to the non-conscious mind. The subconscious mind certainly includes the limbic system, which creates motivational drives and emotions that in turn regulate judgments just below the level of consciousness. Subconscious mind also includes basal ganglia, those multiple clusters of neurons that create a complex network for subconscious controls over movement. Finally, the neocortex is the seat of the conscious mind, though it only operates in concert with arousal drives from the brainstem. In MacLean’s triune brain theory, he explicitly attributes consciousness to the neocortex.

In MacLean’s theory, it is easy to see that as essential as the neocortex and limbic system are to life as we experience it, it is the Reptilian Brain that is essential to life itself, since it controls vital functions. The Reptilian Brain’s non-conscious mind is also responsible for the function of the upper two levels of mind in other ways. For instance, the brainstem contains many neurons that activate the cortex, and in the process triggers consciousness. We know this from several lines of evidence, but the classic study of Moruzzi and Magoun stands out as landmark in the history of neuroscience (Moruzzi and Magoun 1949). Their paper, by the way, inspired my own interest in pursuing a career in neuroscience. What they did was to discover that mild electrical stimulation of the core of the brainstem of experimental animals created behavioral alertness and “activation” of the EEG, as is seen when an animal is awake and alert.

Ascending Reticular Arousal System Guiseppe Moruzzi (1910–1986) and Horace Magoun (1928–1942)

As a student of such renowned neuroscientists as Lord Adrian (see sidebar in Chap. 5) and Frederic Bremer, discoverer of the electroencephalogram, Giuseppe Moruzzi had the pedigree for great discovery. So when the Rockefeller Foundation sponsored a visiting professorship that united Moruzzi’s skills, namely his expertise on the use and interpretations of EEGs, with Horace Magoun’s knowledge on states of sleep and wakefulness and his interest in the brain’s “waking center,” it is not surprising that the result was a paper of great insight that is now a citation classic.

Giuseppe Moruzzi

Horace Magoun

(continued)

Ascending Reticular Arousal System Guiseppe Moruzzi (1910–1986) and Horace Magoun (1928 –1942) (continued)

Moruzzi, an Italian professor from the University of Pisa, and Magoun, an American professor from Northwestern University, began their collaboration in 1948. Originally, their intention was to study inhibition pathways of motor-cortex discharges in the cerebellum of anesthetized cats using stimulating electrodes placed in the cerebellum and the brainstem reticular formation, with the EEG used to measure provoked discharges. However, when they stimulated the reticular formation, they unexpectedly observed what appeared to be flattening of the cortical wave. However, when they used more amplification, they saw the waveforms were high frequency, low amplitude waves that are typically seen during waking states. This led them to consider the reticular formation as part of a pathway that activated the entire cortex, which in turn provoked them to conduct stimulation experiments testing the role of the reticular formation in arousal.

Several important conclusions were drawn from their experiments. Foremost is the existence of a so-called "ascending reticular activating system," (ARAS) also known as the "wakefulness center," that generates an arousal reaction upon stimulation that is analogous to the arousal reaction generated by sensory stimulation. Magoun and Moruzzi also pointed out that the reticular formation receives many messages of sensory input from the main sensory pathways and weights these messages before projecting them to thalamic neurons and the cortex. Another conclusion noted that wakefulness appears to result from background activity in the ARAS.

The existence of the ARAS proved that wakefulness was an internally-regulated property of the brain that results cumulatively from such control functions as the regulation of neurotransmitter activity and synaptic inhibition, and the activation of excitatory systems.

Knowledge of the ARAS holds important clinical implications. For example, in their experiments, Magoun and Moruzzi were able to induce waking states or comas from, respectively, stimulation and inhibition or destruction of the reticular formation. It follows that when someone is put under anesthesia, the activity of the ARAS is suppressed. Over-arousal stemming from ARAS activity has been implicated in ADD and ADHD, and behavior states and internal clock regulation both appear to stem from ARAS activity. These are just a few instances of the expansive possibilities of ARAS influence; as research continues, we will inevitably continue to see just how broadly ARAS activity affects our minds and bodies.

Many scientists today think Moruzzi and Magoun should have gotten the Nobel Prize for this work. They were passed over, it is felt, because their discovery now seems so obvious. But it wasn't obvious to anybody else until they demonstrated it.

Their discovery excited most neuroscientists of their era. I know they excited and inspired me to become a neuroscientist.

Sources:

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The ADD/ADHD Support Site. (2008). *Reticular activating system: The ADHD brain and behavior*. Retrieved June 30, 2008, from http://www.attentiondeficit-add-adhd.com/reticular-activating-system.htm
Neylan, T. C. (1995). Physiology of arousal: Moruzzi and Magoun's ascending reticular activating system [Electronic version]. *Neuropsychiatry Clinical Neuroscience*, *7*(2), 250.
Moruzzi, G., & Magoun, H. W. (1981). Citation classic – Brain-stem reticular-formation and activation of the EEG [Electronic version]. *Current Content/Life Sciences*, (40), 21–21.

Donald Lindsley and colleagues provided the corroborating evidence that lesions of the central core of the brainstem caused coma, while lesions of the surrounding fiber tracts did not.

These key ARAS experiments were performed over 50 years ago seem to have been forgotten by today's neuroscientists. Many modern textbooks don't even mention it.

The brainstem's scope of functions extends still further. Various populations of neurons in the brainstem are nodal points between sensory input and motor output. These populations govern consciousness and alertness, as mentioned, but they also govern the responsiveness to sensory input, activation of many visceral and emotive systems, the tone of postural muscles, and the orchestration of primitive and locomotor reflexes. Particularly important to this constellation of responses is activation of the reticular formation and the periaqueductal grey region. Also engaged during activation are brainstem nuclei whose neurons release specific neurotransmitters: raphe (serotonin), locus coeruleus (norepinephrine), and substantia nigra (dopamine).

We can think of a readiness response as including behavioral and mental arousal (Fig. 2.14). When the animal is aroused by sensory input, all relevant systems are activated by reflex action. More than that, the brainstem also mediates most of the other components of readiness by generating a global mobilization that can include enhanced capability for selective attention, cognition, affect, learning and memory, defense, flight, attack, pain control, sensory perception, autonomic "fight or flight," neuroendocrine stress responses, visuomotor and vestibular reflexes, muscle and postural tone, and locomotion. Each of the changes associated with a readiness response prepares us to face our environments in different ways. When the cerebral cortex is excited, the resultant enhancement of consciousness and arousal level allows us to better observe our environment. Muscle tone enhancement prepares the

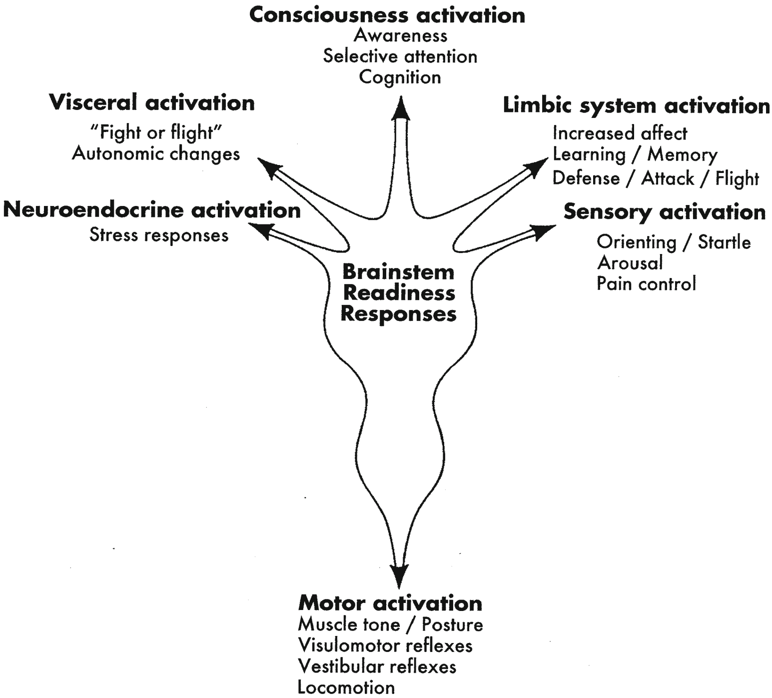

Fig. 2.14 Diagram of the physiological components of the readiness response

body for forthcoming movement instructions. Activation of the limbic system allows new stimuli to be evaluated in the context of memories, and activation of neurons in the hypothalamus and autonomic nervous system mobilizes the heart and other organs for so-called fight of flight situations. This conglomeration of responses makes an animal ready to respond rapidly and vigorously to biologically significant stimuli.

These multiple reflex-like responses are for the most part very obvious during startle and orienting reactions of either animals or humans. For example, consider orienting. If you hear a sudden, loud noise, most likely you will reflexively turn your head toward the sound and become tense. Other, less evident responses may occur, including visceral changes, such as an immediate rise in pulse rate and blood pressure. Less intense stimuli may not evoke a full-blown readiness response because the brain can quickly determine whether or not a response of great intensity is appropriate to the stimuli.

Another good example to which most people can relate is found in a sleeping cat that is suddenly startled into arousal by a dog barking nearby. The cat leaps to its feet, orients to the dog, becomes extremely tense (including arching of the back and extension of the limbs). The hair will rise and the cat will hiss and prepare to lash out its claws toward the dog. Clearly, the cat is mobilized for total body response to the threat.

How can the brainstem accomplish all of these responses? It was mentioned earlier that various neurons in the brainstem are nodal points between sensory input and motor output. This is mainly evidenced in the brainstem reticular formation neurons that receive collateral sensory inputs from all levels of the spinal cord, including such diverse sources as skin receptors of the body and head, Golgi tendon organs, aortic and carotid sinuses, several cranial nerves, olfactory organs, eyes, and ears, in addition to extensive inputs from various other brain regions, particularly the neocortex and limbic system (Starzl et al. 1951). Such input can be a major influence on behavior, which makes the brainstem core neurons ideally situated to monitor and respond to a variety of stimuli that can be biologically significant. For example, the cortical and limbic-system activities that are associated with the distress of a newly weaned puppy probably supply a continuous barrage of impulses to the brainstem, which in turn continually excites the cortex to keep the pup awake and howling all night.

The role of the brainstem core in these arousing responses can be demonstrated by direct electrical stimulation at many points within the brainstem reticulum. Such stimulation activates the neocortex (indicated by low-voltage, fast activity [LVFA] in the EEG), the limbic system (rhythmic 4–10/s [theta] activity in the hippocampus), and postural tone (increased electrical activity of muscles). Additionally, many visceral activities are activated via spread of brainstem core excitation into the hypothalamus.

All readiness response components seem to be triggered from the brainstem core and some of its embedded nuclei (Hobson and Brazier 1980, 564p; Steriade and McCarley 1990). Evidence that the ARAS performs an important function in readiness includes: (1) humans with lesions in the brainstem core are lethargic or even comatose, (2) surgical isolation of the forebrain of experimental animals causes the cortex to generate an EEG resembling that seen in sleep, (3) Direct electrical stimulation of the brainstem core has unique abilities to awaken sleeping animals and to cause hyperarousal in awake animals, and (4) brainstem core neurons develop a sustained increase in discharge just before behavioral and EEG signs of arousal.

Some recent studies have implicated cholinergic neurons in the pons in the EEG arousal component of the readiness response. These neurons appear to be under tonic inhibitory control of adenosine, a neuromodulator that is released during brain metabolism. This may relate to the mental stimulating properties of caffeine and theophylline, which act by blocking adenosine receptors.

Note that in addition to the bodily activation, if one is asleep at the time of stimulus, the brain will be jolted into conscious awareness and prodded to be more aware, more attentive, and to think more effectively.

Triggering Consciousness

The consciousness that such anatomy can generate has to be switched on. Otherwise, we would remain in perpetual sleep or coma. Once triggered, consciousness is dynamic, bobbing up and down like a raft in an ocean of ideas and feelings. The processes by which consciousness is sustained are distinct from those that trigger it.

As in waking from sleep or from anesthesia, consciousness can just “pop up.” Surely, something must trigger this. The suddenness may be an illusion, in that the activation process could have taken longer than we think, but we are too groggy to remember what happens in the groggy state. It may be akin to the problem of remembering dreams. Physiological monitoring can show you had them, but often can’t remember what they were about.

What triggers consciousness, whether from waking in the morning or from emerging from anesthesia? As I just explained, increased activity from the brainstem triggers behavioral readiness *and* consciousness. What increases activity in the brainstem core? Sensory input certainly does. That is why it is hard to go to sleep in a noisy and bright environment. Or when you wake up in the middle of the night worrying about a personal problem or thinking about a work task, all the conscious mental activity keeps you awake because the neocortex is reciprocally connected to the brainstem and keeps re-exciting it.

In general, there is a barrage of brainstem activity immediately prior to any form of arousal. I have recorded during stimulus-induced behavioral arousal such antecedent barrages of multiple-unit activity in the reticular formation of rats and rabbits, species that presumably don’t have robust consciousness because of their poorly developed cortex. Reduction of brainstem activity, in turn, correlates with decreased levels of arousal that may lapse into coma.

Consider the possibility that conscious mind is not so much triggered as it is released. Arousal seems to be produced by activation of the ARAS in an indirect way. Though the original idea was that consciousness results from a global excitation of the neocortex, there is clear evidence that the excitation is indirect and results from a release from inhibition (Yingling and Skinner 1977).

Where Consciousness Comes from

I still haven’t said exactly where consciousness comes from. Presumably, in lower mammals at least, the ARAS may trigger arousal and the readiness response without much accompanying consciousness. How does an activated brainstem-cortex call up its conscious mind? Is it automatic? We certainly don’t seem to have voluntary control over this. We can’t just say: “I want my conscious mind to go away for a while.” The closest thing we can say is, “Now I lay me down to sleep.” By definition, when we do go to sleep, we lose consciousness (dreaming is an exception that I will explore later in Chap. 8).

Associated with the loss of consciousness is a decline in brain metabolism. A common interpretation for why we sleep is that it provides rest for the brain. In other words, consciousness makes demands on the brain. Direct measures of glucose consumption by whole brain of humans has shown that over-all brain metabolism decreases some 25% and oxygen consumption decline by about 16% during sleep. The exception is during dream sleep, when metabolism increases (Boyle et al. 1994).

I would say that calling up conscious mind is automatic. When we wake up after a night's sleep, conscious mind just appears. The same is true when you come out of anesthesia. It is an amazing thing. We go from oblivion to suddenly being aware – and aware that we are aware.

If either the brainstem core or neocortex is non-functional, as during anesthesia or brain damage, there will be no conscious mind. If your body is alive in such situations, that in itself is proof that your non-conscious mind that controls your heart and breathing is still operational. We can only assume that the subconscious mind is also still operating, but perhaps at an impaired level varying with the amount of brain damage.

Other relevant "ancient" experiments from the Moruzzi/Magoun era include studies revealing that sensory pathways are still intact in anesthetized brain and in fact the propagation of sensory information may even be greater than in the conscious state (French and King 1955). Recording electrodes were implanted into various points along the sensory pathways and the thalamus. Responses to stimulus showed that the sensory activation not only could still activate brain responses, but that the magnitude of response was often larger than could be obtained without anesthesia. In other words, the sensory information was *re*ceived, but obviously not *per*ceived. This, by the way is a key point often missed even by scientists: pain occurs only in the consciousness. A species that cannot generate consciousness can respond to noxious stimuli, but such animals cannot feel pain.

Modern research has made it abundantly clear that consciousness emerges from distributed processes within multiple regions of the cortex. This has been confirmed by brain imaging and by brainwave coherence during consciously performed tasks (see Synchronization in Chap. 4 and EEG Coherence and Consciousness in Chap. 6). A consensus is starting to build among many neuroscientists that synchronization of electrical activity among widely distributed parts of the cortex is central to the conscious state, though in ways that are by no means understood. Currently, the idea is that neurons in shared oscillatory circuits have an impact that stands out from the unsynchronized activity of other neurons. Whatever is being held in consciousness at the time persists only so long as the linked oscillation persists.

Most recently, emphasis is being placed on high-frequency oscillations in cortex, in the beta and gamma range as the index and probable cause of the enhanced thinking capabilities that occur as part of the readiness response (Uhlhaas et al. 2009). Synchrony among multiple oscillatory circuits also seems to be a core operation of higher-level thinking.

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