Gray Matters—The Really Big Picture

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*"Welcome to the only town in the world where you can wake up in the morning and listen to the birds coughing in the trees."**
—*Joe Frisco*

Because I was born in Hollywood, I feel it is my birthright to rewrite the Academy Awards. So, let's do three hours in 30 minutes!

And the **Oscar for Best Picture** goes to *Gray Matters—The Really Big Picture*. Why does this gray matter matter to us hand therapists? Because that is where *executive function* resides and rehabilitation research has identified executive function as the most critical factor in a successful outcome.[1] Last year the *Journal of Hand Therapy* published a paper entitled "A Research Agenda for Hand Therapy," which identified outcome studies to be the second most commonly required research.[2] We are not alone in this quest. Even the cash-strapped federal government is funding qualitative research in the outcome arena—studying self-advocacy, self-efficacy, and strong work ethic versus dependency, co-dependency, and entitlement.[1,3]

So how can we wring the performance of a lifetime from our patients' inscrutable and sometimes recalcitrant brains? Like any four-star flick, *Gray Matters—The Really Big Picture* should generate more questions than answers and stir meaningful and controversial post-movie discussions. How do we engage executive function? Why was this picture made and who cares about outcomes? Here's the scoop.

Functional outcomes have been a documented concern of hand surgeons at least since 1868 when Weir Mitchell created a special ward for Civil War nerve injuries. There he prescribed group exercises and games to restore power and movement to the upper limb after injury.

Wynn Parry, in his guest editorial in the *Journal of Hand Therapy*, addressed outcome as the major concern after WWII. 25,000 patients were treated in their units and 70% returned to their companies fully fit, 20% went back to modified duties, and only 5% were invalided. Their treatment included progressive exercise programs, cycling, games, and recreational activities.[4]

Moving to the present, Lundborg states: "The clinical outcome from nerve repair and reconstruction today is not much different from 25 years ago." Even with the advent of growth factors introduced to the surgical repair site and improved biogradable neural tubes seeded with cultured adult Schwann cells, complete recovery of all sensory functions in an adult patient is still rare after nerve repair.

Lundborg believes the future for nerve repair is in tissue engineering, neurotrophic factors, immunosuppression, bioimplants, and mechanisms for cortical remodeling of the central nervous system. Together, he believes, these can result in improved postoperative rehabilitation programs for nerve injuries. His research suggests that a positive environment during sensory reeducation appears to have a strong influence on cortical remodeling in humans. By comparison, unattended, passive exercise seems to have limited capacity to drive central representation changes in the brain.[5]

This summer the journal of *Science* published a report by German scientist Dinse and his colleagues on the study of amphetamines administered in conjunction with fingertip pressure. Subtle fingertip pressure, sustained for three hours, triggered co-activation in which additional neurons were recruited to the somatosensory cortex to process the increased amount of tactile information. This approach increased fingertip two-point discrimination sensitivity by 23%. The enhanced sense of touch lasted only about 24 hours, but additional stimulation raised its level again. This study is another step in the recognition of the importance of cortical engagement in a tactile process.

Even in the absence of nerve laceration or central nervous system lesion, some of us are having functional outcome challenges with the "future present patient" so aptly described by Mark Walsh in his 1998 Nathalie Barr Lecture, "Clinical Reasoning: The Passion of Practice."[6] Mark's future present patient had:

- Obscure diagnosis
- Diminished treatment time
- Fewer protocols
- Increased support staff
- Outcomes-driven
- Less trauma–more soft tissue

Five years later, I would add to Mark's original list:

- Pain-focused
- Deconditioned
- Overweight/obese (64% of the adult population)

This article is an edited version of the Eighteenth Nathalie Barr Lecture presented at the Annual Meeting of the ASHT, October 2003 in Hollywood, California.

*Frank LR. Quotationary. New York: Random House Webster's, 2001.

doi:10.1197/j.jht.2003.10.023

Nathan and colleagues determined that overweight and obesity contribute to carpal tunnel syndrome, the most prevalent of the cumulative trauma disorders.[7] Multiple factors are probably involved, such as:

- Pre-diabetes
- Subclinical traction on the brachial plexus by a fatty, dependent upper extremity
- Awkward carrying angles or postures related to adipose tissue
- Two to three additional miles of vessels laid down to arborize added fat and skin

The highly vascularized peripheral nerves, especially those located furthest from the heart, may not be well served in the presence of overweight or obesity.

Let's cut to the chase and see who is responsible for this national obesity and pain epidemic and why.[8] And the **Oscar for Best Actor** goes to—a mass of electrochemical tissue that is 50% fat and awash in a sea of hormones. Sounds like the villain, but it's really our complicated and conflicted hero, the 3-pound *brain*.

The human brain has been called the most complex object in the known universe. In fact, the only simple thing about our Oscar winner is its life goal: *survival*. Nature programmed the brain for autopreservation. Quite simply—it's all about me. We can't help it. Ninety-three percent of the time we think about ourselves. I'm not nervous. I'm lucky if I have 7% of your attention.

Now for some clips of the Oscar winner as seen in the Really Big Picture: Brain is the hungriest organ, consuming 25% of all glucose and oxygen we absorb. Glucose is the brain's sole fuel, but it is stored elsewhere in the body. The energy the brain absorbs is 16 times as much as muscle tissue per unit weight. Species with the largest brains dine on the choicest foods.

When the brain is under stress it craves foods full of fat and sugar. They blunt the body's response to chronic stress. The National Academy of Sciences confirmed eating calorie-rich food seems to calm nerves. Scientific evidence shows that a tendency to overeat in the presence of chronic stress is biologically driven. By comparison, acutely stressed animals stop eating, lie low, and pull fat and protein from their bodies. After a few days they need a fix from high-energy foods, like a slab of bacon or a dozen Krispy Kreme donuts. Saccharin won't help. The real thing is needed to balance the system.

Once the brain knows it is surviving, its interest turns to maintaining a sense of well-being and pursuit of pleasure.[9] The brain becomes easily bored, craving novelty. Questing after the unknown, flirting with mortality—from mountain climbing to consuming fugu, in which the most accomplished chefs leave just enough of the poison in the fish flesh to make the diners' lips tingle so they know how close they came to death.[10]

The brain influences personal risk factors such as lifestyle, obesity, smoking, and hobbies. Ultra-low-anxiety ancestors were bitten by snakes, were gored by tusks, and fell out of trees. Those premature deaths shifted the gene pool toward humans with higher levels of trepidation.[11] Like the Academy Awards, natural selection awards no prize for second place.

The brain not only survived, but also advanced the species. Rewards are great for the pursuit of new or unusual activities that activate large areas of the cerebral cortex, firing lots of pleasure cells. Pleasure cells, the opiates, grow more numerous as information proceeds through higher processing levels where shape, pattern, and texture are perceived. Opiates are sparse in the primary sensory areas where we perceive lines, edges, and simple tones. Pleasure cells are densest in the so-called association areas, where faces, voices, and meaningful objects are represented and where our perceptions become associated with past experience.[12] The take-home message: to obtain the maximum effort from your patients, reward them with legal "opiates." Treat them with complex, interesting functional activities that are associated with past experience, be it work or play. Humans are defined by their occupations or by what occupies them and their time.

The human brain has approximately 100 billion neurons, the fundamental building blocks of the nervous system. They generate enough electricity to illuminate a light bulb. Each neuron has from 1,000 to 100,000 connections, all of which are constantly changing.[11] Sophisticated noninvasive imaging techniques such as the fMRI and the diffusion sensor magnetic resonance imaging help us to understand how and where information flows in the brain. The graphically enhanced PET scan displays increased activity in parts of the prefrontal cortex and in the amygdala in depressed patients. These techniques are beginning to enable prescription of the specific medication, activity, and/or exercise to improve the individual's function or mental state.

Cajal, in the late nineteenth century, discovered how nerve cells interact with one another in the adult brain, and he deduced that learning might be explained by the changes in the strength of the synapses, "in a way analogous to how muscle cells become stronger with use or exercise."[9] This demonstrates the "use it or lose it" principle as applied to neurons and neural networks.

Neurons fire together once, and then repeatedly become bound together in neural networks or neural maps, reinforcing cortical representation and behaviors. Cells that are never on simultaneously start to suppress one another. Can we change or modify what happens at the synapse? Yes. Not only the strength of the synaptic transmission, but also the shape of the synapse and the synaptic densities. The strength of the synapse changes and modifies with use. Neuroplasticity lives or dies at the synapse both through the neurotransmitters and through use. **The crucial chemical players** are the neurotransmitters: *dopamine, serotonin, opiates, and oxytocin*. Dopamine and serotonin in particular are essential neurotransmitters that help sustain attention and concentration.

To coax the neurotransmitters to span the synaptic space and strengthen the synapses, we need active patient participation, especially in interesting, meaningful activities. This can maximize executive function and can be accomplished through behavioral reinforcement.

Two basic classes of learning, the associative and the non-associative, can assist us in synaptic modeling. Habituation is an example of non-associative learning. The stimulus is presented over and over again so the magnitude of the stereotyped response to the stimuli progressively decreases. Amoebas are conditioned in this manner. Associative learning requires a nervous system.[13]

There are two basic types of associative learning: The *classical* type used by Pavlov with his dogs, and *instrumental* learning, which requires active participation. B. F. Skinner's work in reinforcement learning is an example of instrumental learning. The consequence of instrumental learning is either pleasure or pain. Because instrumental learning requires voluntary initiation of behavior, it appears the critical site of synaptic plasticity is in the cerebrum rather than the cerebellum as previously considered.

And the **Oscar for Best Supporting Actress** goes to *The Hand.* The homunculus shows the hand's 30% representation on the cortex and confirms the extent to which they are dependent upon one another. Brains are more individual than fingerprints. Recent studies look not only at changes in brain anatomy, architecture, and chemistry with mental illness, but also at the subtle differences between the brains of shy children and their more outgoing peers.

Ackerman describes the brain as blind, deaf, dumb, and unfeeling. Despite this poor review, the brain is hardly a wooden actor in the Really Big Picture. The sensations we crave are perceived only indirectly by the brain. The body is the transducer taking mechanical energy and converting it to electrical energy.[10]

The *neocortex* or the *forebrain* is the most complex area of the brain. It sports four special sensory systems that have a role, if not star power, in contributing to this level of complexity. Of the four (olfactory, visual, humoral, and osmotic), olfactory and optic are the major cranial nerves.[9,11] Both deserving of Oscars. The other two, in the blood and guts category, will be passed over tonight.

And the **Oscar for Visual Effects**, or more precisely, appreciation of them, goes to *Vision*. There is an enormous body of literature on the visual system and its processing is exceptionally complicated. Color does not occur in the eye or the world, but in the mind. This explains why some painters use color so differently. Oliver Sacks in the *Island of the Color Blind*, discovered that the inhabitants of Pinglelap Island are achromatopes with congenital absence of cones who see all colors and all grays as only differing luminances, yet they can perceive shading in black and white that we cannot appreciate, particularly after dark.[14]

The use of sign language by native deaf signers, also of Pinglelap Island, results in heightened powers of visual perception and analysis. This in turn leads to enlarged cortical representation of the peripheral fields.[14]

Not only is the visual system responsible for vision, but it is also the circadian rhythm generator. The circadian rhythm plays a critical role in self-preservation. Consider the state of consciousness or wakefulness. Wakefulness consists of three phases. The initiation phase involves the *search* for an object or goal—such as obtaining food or coffee driven by low levels of blood glucose or caffeine withdrawal. The second phase is the *foraging or procurement* phase, consisting of exploratory strategy to find the goal or object. Finally, there is the *consummatory* phase, where the goal or object is used resulting in pleasant or unpleasant sensations. Behavior then comes to an end because of satiation or exquisite pain.[9]

Our next **Oscar for Life Time Achievement** goes to *Olfaction*. Early medicine used odor to detect illness and infection. Helen Keller could identify children from adults, men from women, by smell. Because it is the simplest of the neo-cortex's four sensory systems in terms of network organization, let's take a moment for a more in-depth exposé of our award winner.

The cell body of an olfactory neuron is located in the olfactory mucosa of the nose. Its axon extends directly into the cerebral cortex where it synapses with mitral cell dendrites in the olfactory bulbs.[9] The stimulus then goes straight to the limbic system. Relay through the thalamus is unnecessary. Smell needs no interpreter.

Here's the buzz. Smell, considered by some to be the first of our senses, was so successful that in time the small lump of olfactory tissue grew into a brain. Our cerebral hemispheres were originally buds from olfactory stalks. Ackerman calls smell the mute sense because we have so little language to describe the myriad odors around us. As compared with vision, the physiological links between language and smell centers in the brain are pitifully weak. But with smell, the memory link is absolute.[10]

The hardware of memory is the *hippocampus*, that horseshoe-shaped structure in the limbic system. Smells stimulate learning and retention. Olfactory cues given along with word lists improve retention and recall. Use of odor in aromatherapy does work with some individuals to decrease stress and increase alertness.

Although the olfactory nerve is the first cranial nerve, neuroanatomists have uncovered other unnumbered nerves in the olfactory bulb and the vomeronasal system. So the traditional classification of the 12 cranial nerves has begun to break down. The vomeronasal nerve arises from a pit in the olfactory mucosa. The vomeronasal system is very prominent in mice for reproduction. This system develops in the human embryo, as it would in rodents, but degenerates for reasons not yet known.[9,15]

What is known is that in the adult brain newborn neurons are found in the olfactory bulbs and in the hippocampus. Neural stem cells divide in two main areas, the ventricles and the hippocampus. As they proliferate they create other neural stem cells and neural precursors that can become either glial cells or neurons. The newborn neural stem cells must move away from their progenitors before differentiation occur. An average of 50% migrate successfully; the others perish. Neuroscientists are researching ways to entice the neural stem cells to divide and migrate to where they are needed, especially after central nervous system lesions.[15]

Our next **Oscar for Costume Design**, which is a matter of *Taste*, is joined at the hip with olfaction. In fact, NASA offered a challenge for nutritionists in space food design. Weightlessness makes astronauts lose taste and smell in space. Molecules are not volatile in the absence of gravity, so few of them get into the nose deeply enough to register as odors. Brain pathways for smell and taste intermingle and they both project signals to the same parts of the frontal cortex during sensory processing.[11]

The Honorary Oscar goes to *Touch*. Language deftly describes touch. Problems are described as "thorny," "sticky," "ticklish," or "must be handled with kid gloves." We will not dwell on this sense because it is so well known by hand therapists it would be like preaching to the choir.

No surprise, the **Oscar for Sound Editing** goes to *Hearing*. As you all know, the organs of hearing and balance are interconnected. But did you know hearing music has a healing quality? When we hear music our pupils dilate and our endorphin level rises. Endorphins are not only painkillers but also a class of hormones that appear to be important in social bonding. Music helps synchronize group actions such as those you see with a choir or a marching band. This might explain the chanting and singing during social activities that are pervasive not only in ancient cultures but in modern ones as well. Music engages the whole body from tapping feet to rising hair follicles.

Lundborg, the consummate acting coach, looked at hearing as a substitute for sensibility for irreversible sensory loss. He used the hand, incased in a tactile glove with condenser microphones on the glove fingers, for sensory feedback.[16]

Our next **Oscar for Best Foreign Language Film** goes to *Synesthesia*—-which is pretty much Greek to most of us. Synesthesia is described in the scientific literature as a blending of the senses. People with intense synesthesia respond in predictable ways to the colors they assigned to numbers, sounds, and other stimuli presented in laboratory settings. Such people are rare—only about one in every 500,000 people.[17]

Neurologist Richard Cytowic traces the phenomenon to the limbic system. He calls these folks "living cognitive fossils" because they may be people whose limbic systems are not entirely governed by the sophisticated neo-cortex. Synesthesia may be the memory of how the early mammals perceived the world. Many famous artists, writers, and composers are synesthetes.[10]

We say there are five senses but know there are more. Butterflies, birds, and whales navigate in part by reading the Earth's electromagnetic field. Could people who dose for water have an electromagnetic sense that we too may share?[10] Praying mantises use ultrasonics to communicate. Elephants and alligators use infrasonics. Bats and dolphins use echolocation to navigate. Spiders, fish, and bees have highly developed vibratory senses that are being studied for their relationship to humans. In fact, a new and controversial theory has emerged that humans might smell through molecular vibrations rather than the long accepted molecular shape recognition theory. All molecules pulse with vibrations, not unlike musical instruments that create an endless variety of sounds. Olfaction is recognition of an unending symphony of odors.[18]

Last but far from least, the **Oscar for Best Director** goes to *the limbic brain*, aka the emotional brain. Paul MacLean, an evolutionary neuroanatomist and senior research scientist at the National Institute of Mental Health, proposed that the human brain is a *Triune*, composed of three distinct subbrains: the prefrontal or neocortex, the limbic brain, and the brain stem or the reptilian brain. Each brain section is the product of a separate age in evolutionary history. According to MacLean, the subunits of this triune brain are different from one another in functions, properties, and even chemistries. Although they communicate with one another, some information is lost through their differences.[11] The result is a need for multiple learning systems. The "see it, hear it, do it" principle. Multi-tiered approaches have more opportunity to modify or change the synapses.

The reptilian brain, also known as the brain stem, programs the body's appliances, the heart, lungs, and kidneys, to name a few. The appliance with profound influence on brain function is the heart. The first is through a neurological communication. The heart has its own intrinsic nervous system. The heart produces the strongest electrical signal in the body—60% stronger than the electrical output of the brain. The second pathway is a biochemical communication, a kind of hormonal gland. Neurochemicals such as epinephrine, norepinephrine, and oxytocin are also manufactured in the heart. Oxytocin is a neurotransmitter that directs attachment; it gushes at birth for the mother and baby bonding and then again at puberty.[9,11] (Perhaps one of nature's mistakes?)

Located in the brain as well as the heart, oxytocin is an example of a magnocellular neuroendocrine neuron. It is a peptide hormone and as such is also a gland cell, secreting hormones into the blood in concentrations high enough to reach and influence distant body parts.[9,11]

For a final look at the appliances, we turn to the adrenal glands and their part in the flight-or-fight response. This response is evolutionary in nature and designed to increase blood flow to muscles through release of epinephrine and norepinepherine. As part of the flight-or-fight response another stress related hormone, cortisol, is released into the blood stream. Cortisol is a type of glucocorticoid that affects glucose metabolism. Its release process is regulated by neurons in the hypothalamus. Hippocampal damage occurs with long-term exposure to excessive levels of glucocorticoids. This results in neurotoxicity that kills off groups of neurons and shrinks the hippocampus.[19] Yes, given the right circumstances, stress can make you stupid and, as we learned earlier, fat.

Back to our award-winning director, the limbic brain, not about to be upstaged by plumbing and electricity. Anatomically situated between the reptilian brain and the neocortex, the limbic brain has a profound influence on us. Mammals attach and care for one another and bond with a sense of community because of the limbic brain. It has *more opiate receptors* than any other area in the brain. Let's take a close look at dopamine and its receptors in particular. This is a BBC remake of the 1960's flick, *Sex, Drugs and Rock'n Roll*. Forty years ago we intuited that they might be connected, and new technology proves they are. Sex, drugs, music, and food share common neural pathways. And if you don't get any one of them when you want them, the result is pretty much the same: irritability, frustration, and anger.

Opiates not only extinguish physical pain but also ease emotional pain. On the other side of the limbic sword is *limbic pain*—isolation, sorrow, bitterness, anxiety, loneliness, and despair. It helps explain our losing the war on drugs, both street and prescribed. The cause of addiction remains obscure. Of all humans who try cocaine, thought to be the most powerfully addictive substance known, less than 1% become regular users.[11]

At last we have reached the highest branches of the brain's evolutionary tree. At the base we have the reptilian brain with its control and maintenance of reflexes and metabolic systems. The trunk and lower branches of our tree contain the limbic brain with its basic behaviors, drives, and motivations. In the highest and most tangled branches we have emotions and feelings.

Emotions and feelings are the human spirit's greatest creation in neurologist Damasio's tree-like hierarchy.[20] Nerve cells are not impartial bystanders or innocent conveyances waiting to transmit. Damasio states that our brains do not begin as a *tabula rasa.* Neural mappings are in place to ensure our survival—especially the primary or basic emotions: fear, anger, disgust, sadness, surprise, and happiness.

Social emotions are more complex in the feelings they elicit: sympathy/empathy, embarrassment, shame, guilt, pride, and jealousy. Still they are making a comeback in the, pardon the pun, heady neuroscientific communities. Secondary to new technology and the experimental data produced, visceral sensations, synonymous with emotion, can now be trusted. We have it on the best neuroscientific authority.[9,11,20] You can listen to and believe your body. That "from the heart" or that "gut level" feeling is intuition.

Intuition is as mysterious as the neocortex itself. The year 1997 ushered in the first studies of intuition using the new technologies, but they are still in their infancy. Intuition is the most sophisticated means of achieving knowledge. But intuition occurs only after amassing knowledge and then examining it with reason. Intuition is linked to memory. It endures and accrues. People don't forget a capacity that depends on feel rather than fact.[14] Future studies on intuition could eventually lead to so-far-unimagined means of recognizing depression or even subterfuge in our patients.

Despite the renewed interest by scientists in motivation, emotion, and intuition, the 1990s replaced mammalian care health care with reptilian managed care. Corporate takeovers injured the emotional heart. Corporations have fiscal relationships, not limbic ones.[11] But health care is also ailing in part because of the very same dazzling technologies that have advanced it.

Intellect has become western medicine's agency of cure, and therein lies the disconnect. Emotions reach back 100 million years, while cognition is a few hundred thousand years at best. Patients are mammals that sensed the growing limbic void. They voted with their feet and wallets, seeking alternative treatment in varying forms including laying on of hands, listening, and Eastern or integrated approaches.[11]

Research sometimes takes you where you didn't expect to go and leads you to things you did not expect to find. Among other things in my quest to get my arms around this huge subject, I discovered there has been very little scientific research on what gives us pleasure, but there are libraries full of research on pain. Yet you cannot experience pain at the same time you are experiencing pleasure. Perhaps we should look into being proactive rather than reactive, especially in our approach to chronic pain.

The dénouement: For positive functional outcomes, gray matter must be recruited and engaged on both sides of the treatment table. The power of you as a placebo is not to be underestimated. Hand therapists acting not only as superior neocortex clinicians but also as cheerleaders and limbic directors can enlist the patient's executive function and make successful outcomes a reality, even in difficult soft-tissue cases.

The brain is infinitely modifiable and adaptable; in fact, it is rewarded by innovative behavior through release of pleasure cells and increased discharge of nerve growth factor. It really is mind over matter. Even down to some basic reflexes. Note the sword swallower.

There are four functional systems of the brain: motor, sensory, cognitive, and behavioral state control.[9] We are becoming experts at the first two. The creative and emotional energy requisite to spur motivation and recruit executive function from the last two can be a challenge, but we must persevere. To quote Lewis from *A General Theory of Love,* "The brain's dense thicket of interrelationships, like those of history or art, does not yield to the reductivist's bright blade."[11] For the best outcomes avoid the reflex reaction of the quick fix, by the latest and greatest technology, because, frankly, our patients don't have the brains for it.

REFERENCES

1. Stineman MG. *Maximizing Health Environmental Integration through Occupational Science.* Keynote Address, The Spheres of Rehabilitation: Body, Mind and Social Structures. USC 15th Annual Occupational Science Symposium, January 2003.
2. MacDermid JC, Fess EF, Bell-Krotoski J, et al. A research agenda for hand therapy. J Hand Ther. 2002; 15:3–15.
3. Bowler DF. It's all in your mind: the final common pathway. Work. 2001; 17:167–73.
4. Wynn Parry CB. Some aspects of the history of rehabilitation of the hand. J Hand Ther. 1997;10:199–205.
5. Lundborg G. A 25-year perspective of peripheral nerve surgery: evolving neuroscientific concepts and clinical significance. J Hand Surg Am. 2000; 25:391–407.

6. Walsh M. Clinical reasoning: the passion of practice. 13th Nathalie Barr Lecture. J Hand Ther. 1998;11:244–50.
7. Nathan P, Meadows K, Istvan J. Predictors of carpal tunnel syndrome: an 11-year study of industrial workers. J Hand Surg. 2002;4:644–51.
8. Brand P. Pain—it's all in your head: a philosophical essay. J Hand Ther. 1997;10:59–63.
9. Swanson LW. Brain Architecture. New York: Oxford University Press, 2003.
10. Ackerman D. A Natural History of the Senses. New York: Vintage Books, Random House, 1990.
11. Lewis T, Amini F, Lannon R. A General Theory of Love. New York: Vintage Books, Random House, 2000.
12. Blakelee M. A simple theory: beauty is in the ping of the pleasure cells. *USC News*. 2002;3(3).
13. Byl N, Melnick M. The neural consequences of repetition: clinical implications of a learning hypothesis. J Hand Ther. 1997;10:160–74.
14. Sacks O. The Island of the Colorblind. New York: Vintage Books, Random House, 1996.
15. Gage BF. Repair yourself. Sci Am. 2003;Sept (special issue):47–53.
16. Lundborg G, Rosen B, Lindberg S. Hearing as substitution for sensation: a new principle for artificial sensibility. J Hand Surg [Am]. 1999;2:219–24.
17. Ramachandran VS, Hubbard EM. More common questions about synesthesia. Sci Am. (online edition). 2003; Apr 14.
18. Burr C. The Emperor of Scent. New York: Random House, 2002.
19. Sapolsky R. Taming stress. Sci Am. 2003;Sept (special issue):87–95.
20. Damasio A. Looking for Spinoza-Joy, Sorrow and the Feeling Brain. Orlando: Harcourt, Inc., 2003.