ON THE BRAIN

THE HARVARD MAHONEY NEUROSCIENCE INSTITUTE LETTER



Growing the Brain through Meditation

OR MORE THAN 2,500 years, Buddhist monks have known that practicing meditation leads to increased inner strength, calmness and selfawareness, strengthened contact with subconscious feelings and thoughts, and greater spiritual growth. Now, Harvard Medical School scientists have found that regular meditation can also alter the structure of our brains.

A team led by Sara Lazar, Ph.D., a neuroscientist at Massachusetts General Hospital and an instructor in psychology at HMS, found that meditation increased thickness in the regions of the brain associated with attention and processing sensory input. Using magnetic resonance imaging (MRI), Dr. Lazar's group assessed the thickness of the cerebral cortex in 20 participants with extensive experience in insight meditation, a form of meditation that focuses attention on internal experiences.

While previous research with monks has demonstrated that long-term meditation may lead to altered brain wave patterns, Dr. Lazar's team hypothesized that long-term meditation practice might also result in changes in the brain's physical structure, possibly reflecting increased use of specific brain regions. In fact, they found that brain regions associated with attention, interoception (sensitivity to stimuli originating inside the body), and sensory processing were thicker in the meditation participants than they were in matched controls. These areas included the prefrontal cortex, which is responsible for planning complex cognitive behaviors, and the right anterior insula, which is associated with bodily sensations and emotions.

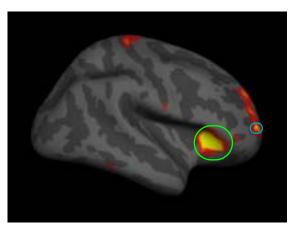
"As predicted," says Dr. Lazar, "the brain regions associated with attention and sensory processing were thicker in meditators than in the controls. These findings provide the first evidence that alterations in brain structure are associated with meditation practice." In addition, the researchers found that, in the region of the cortex thought to be involved in integrating emotional and cognitive processes, the differences in cortical thickness were more pronounced in older subjects, suggesting that regular meditation might reduce normal age-related cortical thinning.

Unlike Tibetan Buddhist monks, whose lives are devoted to the practice of meditation, practitioners in the United States typically meditate just 30 to 40 minutes daily, incorporating the practice into their busy work and family lives. The participants in Dr. Lazar's study were practitioners of Buddhist "insight" meditation, which focuses, she says, on a trait called mindfulness, a non-judgmental awareness of present-moment sensory stimuli. Two of the study subjects were full-time meditation instructors, two were part-time yoga or meditation teachers, and the remainder were professionals with varied careers. On average, they had nine years of meditation practice, averaging six hours of meditation Fall 2006 Vol. 12, No. 3

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The insula, circled in green on the left, and the prefrontal areas, circled in blue on the right, were thicker in meditators.

The Creative Muse

Science fiction writer Isaac Asimov, who wrote nearly 500 books, reportedly suffered from it. So, too, did such noted authors as Fyodor Dostoyevsky, Herman Melville, Virginia Woolf and Charles Dickens. What these authors all had in common, in addition to incredible talent, is a neurological condition called hypergraphia, the overpowering desire to write. A surprising number of them also suffered from mood disorders, including manic depression or temporal lobe epilepsy, both of which are associated with hypergraphia.

What goes on in the mind of a creative genius that turns a fairly commonplace task – writing – into such a driven compulsion? Alice W. Flaherty, M.D., Ph.D., a neurologist at Massachusetts General Hospital and an assistant professor at Harvard Medical School, has spent the past eight years studying human creativity, as well as dealing with her own episodes of hypergraphia.

Push-pull in the brain

For years, popular culture has considered creativity to be a right brain/left brain phenomenon, but there is evidence that it is much more than that. Creativity involves interaction among the brain's limbic system, which controls emotions, the temporal lobe, which is responsible for language and idea generation, and the frontal lobe, which is the brain's organizational center.

"Writing and other creative work seem to involve a push-pull interaction between the frontal and temporal lobes," says Dr. Flaherty.

Relatively defined brain disorders that involve the temporal and frontal lobes can trigger hypergraphia and writer's block, a crushing inability to write, respectively. These include temporal lobe epilepsy (a neurological condition in which an individual has seizures during which he may experience heightened senses and emotions), bipolar disorder and depression. When there is too little activity in the temporal lobe, it can lead to hypergraphia; when there is too little activity in the frontal lobe, it can lead to writer's block.

The author William Styron suffers from profound depression, as well as severe bouts of writer's block. Some studies show that nearly 70 percent of poets have a mood disorder. Dostoyevsky, a prolific writer, had temporal lobe epilepsy and vividly described the disorder in his novel "The Idiot." Temporal lobe epilepsy can produce mood instability, and that may be what drives the hypergraphia.

Drive vs. talent

From a psychological perspective, says Dr. Flaherty, the drive to write is more important than talent in producing creative work. Researchers have argued that composers like Beethoven and Mozart have produced the greatest works because they constantly composed music. But, she adds, the source of an individual's motivation is also important. Teresa Amabile of the Harvard Business School found that intrinsic motivation (e.g., the personal satisfaction of writing) is more likely to produce creative work than extrinsic motivation (e.g., monetary rewards), which can actually hurt the creative process. Drive and motivation are regulated by the limbic system and are more related to the temporal lobe than is talent.

"Hypergraphics tend to be internally driven," Dr. Flaherty says. "They write for their own pleasure, or to deal with their own demons. Being paid a dollar a word can make you prolific, but it's not the same thing as being hypergraphic. You have to ask what the motivation is."

Other artistic genres

"There are equivalents [to hypergraphia] in other genres and it is generally the same brain mechanism at work," says Dr. Flaherty. "A lot of people who are hyper in one field are hyper in another."

Perhaps more interesting, she notes, is that the rate of mental illness for artists – musicians, poets, writers, performers – is about 70 percent, but only 25 percent for other professionals seen as creative in other fields such as government or the military.

Drugs, alcohol and creativity

Many creative people believe that drugs and alcohol have opened their hypergraphic floodgates. Robert Louis Stevenson reportedly wrote the 6,000-word "The Strange Case of Dr. Jekyll and Mr. Hyde" in six, cocaine-fueled days. While writing "In Cold Blood," Truman Capote was said to drink double martinis – before, during and after lunch. Ernest Hemingway and William Faulkner, arguably two of the greatest 20th century authors, were also prodigious drinkers.

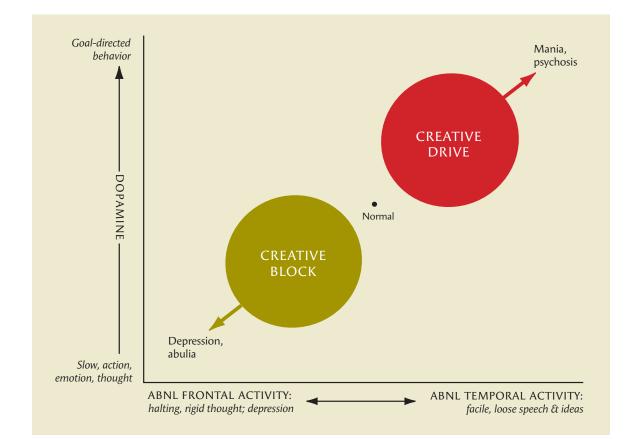
One small study of creative writers (including such luminaries as Philip Roth, Kurt Vonnegut and Robert Lowell) found that 80 percent had episodes of affective disorders such as bipolar disorder. Many also were alcoholics, giving credence to the popular notion of creative artists as "mad."

While many writers claim that alcohol and drugs help them write and that self-medication helps ease their anxiety, substance abuse probably has a deleterious effect on creativity. "The truth is," says Dr. Flaherty, "the more one drinks, the less likely he is to be a good writer. Look at [F. Scott] Fitzgerald. Early in his career, he was a great writer, but his writing failed the deeper he sunk into alcoholism."

Miracle and disease

While there are educational, psychotherapeutic and medication treatments for hypergraphia, many people don't want to be "cured." In her book "The Midnight Disease: The Drive to Write, Writer's Block and the Creative Brain" (Houghton Mifflin, 2004), which reveals the science behind hypergraphia and details her own bouts with the disorder after the death of her twin infants, Dr. Flaherty says hypergraphia can be both a miracle and a disease.

"People who didn't know me when I was hypergraphic ask why I call it a disease, especially since I also think of it as a miracle," she says. "In part, it is because of the way my writing sucked me away from everything else. Also, because of how strange it felt to be suddenly propelled into a creative state by what were probably postpartum biochemical changes. I hated to think that writing – one of the most refined, even transcendent talents – should be so influenced by biology. On the other hand, as a neuroscientist, I realized that if we can get a handle on fluctuations in creativity, we might be able to find ways to enhance it."



Reversing the Habits of Tourette Syndrome

RENCH PHYSICIAN Georges Gilles de la Tourette first described the disorder that bears his name in 1885. This neurological disorder, which usually begins in early childhood or adolescence, is characterized by both multiple motor tics and at least one or more vocal tics, though not necessarily at the same time. Simple motor tics include eye blinking, grimacing and shoulder shrugging, while simple vocal tics include throat clearing, sniffing, coughing and humming. Some TS patients have more complex tics such as pulling at clothing and touching other people or objects. Though rare, some TS patients repeat others' words (echolalia) or swear involuntarily (coprolalia).

The first symptom of TS is usually a facial tic, which is often replaced by or added to tics involving other parts of the body. While most tics are mild, TS is a chronic condition. Symptoms typically wax and wane. TS is often also associated with attention deficit hyperactivity disorder, obsessive-compulsive behaviors and depression.

While some tics occur without warning, many TS patients report phenomena called "premonitory urges," impulses to perform a tic, which are followed by momentary relief when the tic is performed.



French physician Georges Gilles de la Tourette

The cause of Tourette syndrome (TS) remains unclear, but scientists have known for years that the disease is due to a disorder of the brain's frontalsubcortical circuits (one of the many neural circuits in the brain that mediate behavioral responses) and inappropriate regulation of the chemical messenger dopamine in the brain. Traditionally, TS patients have been treated with a variety of neuroleptic, antidepressant or antianxiety medications to quell the motor and vocal tics commonly associated with the disorder. These, however, often provide only partial relief.

Faculty members at Harvard Medical School are among only a handful of clinicians using a behavioral therapy called habit reversal (HR) that teaches TS patients to implement movements that are incompatible with tics to reduce their occurrence. Though not a new approach, habit reversal has become an effective therapeutic tool for decreasing the severity and intensity of tics and for improving patients' self-esteem.

"Our research," writes Thilo Deckersbach, Ph.D., staff psychologist at the Tic Disorders Clinic at Massachusetts General Hospital (MGH) and an assistant professor of psychology at HMS, in *Behaviour Research and Therapy* (August 2005), "suggests that HR appears to be effective for pharmacotherapy failures, partialresponders, patients who relapse after pharmacotherapy, and may be a behavioral treatment alternative to pharmacotherapy." In other words, HR may be an effective treatment for Tourette syndrome on its own or as part of a multi-prong approach using both behavioral and medication therapy.

Awareness training and competing responses

In the 1970s, psychologists Nathan Azrin and R. Gregory Nunn developed a technique for treating nervous habits such as tics, stammering and skin picking. They called this technique habit reversal. The therapy focuses on increasing a patient's awareness of their nervous habit (where, when and under what circumstances it occurs) and developing responses to it.

"Most people with TS tend to have a repertoire of tics. Certain tics are active; others are latent. Some go away and come back," says Dr. Deckersbach. "We develop a list of a person's active tics and develop a tic hierarchy that tells us which are the most frequent and bothersome. We start addressing these with habit reversal."

The two primary components of HR are awareness training and competing responses. During awareness training, patients are taught to recognize the initial sensation, or premonitory urge, that leads to a tic. If a TS patient does not have premonitory urges, clinicians use the first tic encountered as the initial sensation. Then, the patient and clinician develop a competing response, a behavior opposite that of the tic.

A competing response works in the following way: Say a patient with TS has a motor tic in which he needs to rotate his arm inward in order to find relief. Through habit reversal, the patient would be taught a slight outward rotation of his arm as a competing response and to hold that competing response until the tic urge is gone.

"The goal," says Dr. Deckersbach, "is to come up with a movement that is not noticeable to others, but one that prevents recurrence of the tic. The frequency and intensity of tics decreases with the consistent implementation of the competing response."

In addition to awareness training and habit reversal, clinicians also use control techniques to prevent or eliminate the recurrence of tics and their consequences. They also examine situational antecedents that don't cause tics but increase their likelihood. Psychological education about tics and relaxation and exercise techniques are also used to treat TS.

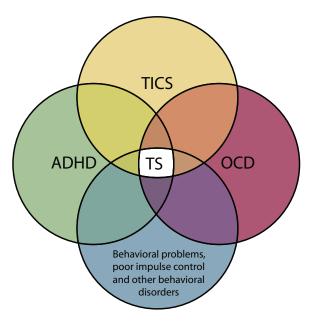
HR vs. supportive psychotherapy

In a study published in 2005, Dr. Deckersbach and his colleagues at MGH compared the efficacy of habit reversal therapy in reducing tics and improving self-esteem and psychosocial functioning to supportive psychotherapy, which includes support around a variety of issues, including anger/stress management, disruptive behaviors and social issues. The researchers found that patients who were treated with HR showed greater reductions in tic severity than those who underwent supportive psychotherapy. Further, this reduction in tic severity remained relatively stable in these patients during a six-month follow-up. "In our study, we found that supportive psychotherapy doesn't do anything about tics," says Dr. Deckersbach, "but it was effective in increasing self-esteem. It's not an ineffective treatment; it is just less effective for tics than habit reversal."

The MGH researchers are currently part of a four-year, multi-site trial (with Yale University and Wilford Hall Medical Center in San Antonio) called CBITS – Comprehensive Behavioral Intervention for Tics, a behavioral therapeutic approach that includes the elements of habit reversal and relaxation training. One hundred twenty adults participating in the study are assigned to CBIT or a structured supportive psychotherapy program. Following several therapy sessions and follow-up assessments, the researchers will measure the change in tic severity in the patients. Other collaborating sites are conducting a similar study in children with TS.

"Habit reversal has been around for 30 years," says Dr. Deckersbach, "but only in the past five or six years have researchers started to investigate its efficacy for TS and tics disorders."

While only a few controlled studies of habit reversal therapy have been conducted, the work being done by Dr. Deckersbach and others is leading to greater understanding of the effectiveness of HR in treating and controlling chronic tics and Tourette syndrome – and giving patients an alternative to often ineffective medications.



Economic Choice: Assigning Value Based on Neuronal Activity

HEN WE GO to the supermarket to buy our groceries, we don't often think about how we make decisions about what products to purchase. We buy foods that satisfy our tastes or are healthy for our bodies. Researchers at Harvard Medical School, however, have identified neurons that might play a role in how we select the goods we purchase.

"We have long known that different neurons in various parts of the brain respond to separate attributes, such as quantity, color and taste," says Camillo Padoa–Schioppa, Ph.D., a research fellow in neurobiology at HMS. "But when we make a choice, for example, between different foods, we combine all these attributes. We assign a value to each available item."

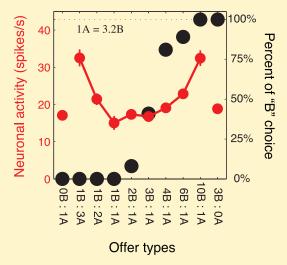
Dr. Padoa–Schioppa and John Assad, Ph.D., HMS associate professor of neurobiology, identified neurons in the orbitofrontal cortex (OFC) that encode the value individuals assign to available items when they make choices based on subjective preferences. This behavior is called "economic choice."

The HMS researchers chose to study neurons in the OFC because previous studies indicated that damage to this area can lead to abnormal gambling behavior, eating disorders, drug addiction, and asocial behavior, all of which can be considered "choice deficits."

In their study, published in the May 11 issue of *Nature*, the HMS researchers had macaque monkeys choose between two types of juice offered in different quantities and observed the monkeys' decisionmaking behavior. In one trial, the monkeys chose between one drop of grape juice (which they prefer) and one drop of peppermint tea; in another, they chose between one drop of grape juice and two drops of peppermint tea, and so on. Dr. Padoa-Schioppa says there was a trade-off that indicates the value the monkeys assign to the juice type and quantity.

Based on the choices the monkeys made, the researchers correlated the activity of neurons in the OFC directly with the value assigned to the two types of juice. The study identified several classes of neurons. Neurons of one class encode the variable *chosen value*.

"Different quantities of juice had different values," says Dr. Padoa–Schioppa, "so that the value chosen by the monkey varied from trial to trial. The



Figure

Activity of one OFC neuron encoding the chosen value. In this session, the monkey chose between variable quantities of grape juice (juice A) and peppermint tea (juice B). The xaxis represents different offer types. Black dots represent the percentage of trials in which the monkey chose juice B. When offered 1B or 2B against 1A, the monkey nearly always chose juice A. In contrast, the monkey nearly always chose juice B when offered 4B, 6B or 10B against 1A. Finally, when offered 3B against 1A, the monkey was roughly indifferent (i.e., it chose juice B half of the time). Hence, the value of 1A was roughly equal to the value of 3B. Red dots represent the activity of the neuron. The firing rate was low when the monkey chose 1A and 3B; it was medium-high when it chose 2A and 6B; and it was highest when the monkey chose 3A and 10B. The activity of the neuron did not depend on the movement with which the monkey indicated its choice.

activity of neurons encoding the *chosen value* is correlated with the value chosen by the monkey, independently of the juice type." [see figure]

Other neurons encode the variable *offer* value (the value of one particular juice offered to the monkey). Their activity is correlated with the value of that particular juice only. The researchers determined the encoding of value by the firing rate of the neurons, or the frequency at which the nerve cells generate spikes. In general, low value equals a low firing rate, while high value equals a high firing rate.

They also found that neurons in the OFC encode economic value independent of the specific action the monkeys used to signal their choices. That is, the OFC neurons encode the value of the goods regardless of whether the goods are offered on the monkeys' right or left.

Human economic choice

How does this equate to the choices humans make?

Imagine that you are at your local supermarket wanting to buy yogurt, says Dr. Padoa–Schioppa. Before you are an intimidating number of options: different brands, different flavors, different sizes, different fat content, different unit prices. You quickly narrow your decision to a couple of options, say, strawberry yogurt and peach yogurt. Your brain assigns values to the available options – in this case, the two flavors of yogurt – and then decides by maximizing the value.

"Some of the neurons we found in the OFC represent precisely the value of the various options the monkeys chose between. Had we recorded from the brain of this consumer while they chose between yogurts, we presumably would have found some neurons that encode the value of the strawberry yogurt and other neurons that encode the value of the peach yogurt. We suggest that the choice is based upon the activity of these neurons."

Behavioral decision making

The Harvard research is part of a growing field called neuroeconomics, the study of the neural bases of behaviors that are traditionally the focus of economic theory. Standard economics, says Dr. Padoa– Schioppa, describes reasonably well a great deal about human choice behavior; however, there is a

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per week. None of the control subjects had any experience with meditation or yoga.

"Our findings are consistent with other reports, which demonstrated that practices such as playing a musical instrument or learning to juggle, are also associated with increases in cortical volume," says Dr. Lazar. "Our data suggest that meditation practice can promote cortical plasticity in adults in areas important for cognitive and emotional processing and well-being."

Meditation and cognitive ability

The cerebral cortex, made up of four lobes (occipital, parietal, frontal and temporal), is involved in many higher–order cognitive functions, including memory, attention, perceptual awareness and language. Dr. Lazar says it is not clear what her findings mean in terms of the relationship between cortical thickening and cognitive ability. Past studies have shown cortical thickening to be associated with an increased ability to perform specific cognitive tasks, depending on the area of the cortex that gets thicker. Additional studies show that relaxation (a manifestation of meditation) facilitates the learning–based processes that underlie such cortical plasticity.

Supporting the researchers' hypothesis is the fact that the pattern of cortical thickening corresponds well to the specific activities that practitioners of insight meditation repeatedly engage in over time: paying attention to breathing sensation and sensory stimuli. The more one meditates, the thicker the cortex grows. She likens this to weight lifting to build bigger, stronger muscles.

While Dr. Lazar's study examined one specific form of meditation, she and her colleagues suspect that other types of meditation may have a similar effect on the cortex, though the pattern of thickening may be somewhat different.

Aging, meditation and the brain

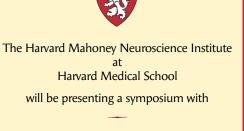
Perhaps one of the more intriguing aspects of Dr. Lazar's research is the finding that cortical thickness was more pronounced in the older subjects. A number of factors, including age, sex and genetics, influence the thickness of the human cortex, with age being the leading factor. Despite the affects of aging on the prefrontal cortex, Dr. Lazar and her team found that the average cortical thickness in two regions of the cortex of the 40- to 50-year-old meditators was similar to the average thickness of the 20- to 30-year-old meditators and control subjects. This suggests that meditation may slow the rate of neural degeneration in specific locations of the cortex.

"It [the effects of meditation on cortical thinning] is certainly tantalizing," says Dr. Lazar, "and an angle we are pursuing. However, it is a very small region which is preserved, not the whole cortex."

ON THE BRAIN

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growing body of empirical evidence, referred to as behavioral economics, that shows that in a variety of contexts people's choices violate one or more standard economic axioms.

"If preferences were always rational, economists would be happy to ignore the mental and brain processes that take place when people choose, as they have for a long time," he adds. "But, it turns out that we are not so rational after all. Then the question becomes: what are the underlying mental processes, which ultimately means brain processes? That's when economists want to know more about the brain."

While his research has no direct application for consumers, Dr. Padoa–Schioppa says his study focuses on the very question of what brain processes take place even for very simple and rational choices.

"Our results have broad implications for possible psychological models of economic choice," he says. "They suggest that economic choice is, at its essence, a choice between goods as opposed to a choice between actions."

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