The Mind and the Brain: Neuroplasticity and the Power of Mental Force - Jeffrey M. Schwartz, Sharon Begley (2003)

Chapter 2. BRAIN LOCK

To refrain from an act is no less an act than to commit one.

—Sir Charles Sherrington,
"*The Brain and Its Mechanism," 1933*

The important thing in science is not so much to obtain new facts as to discover new ways of thinking about them.

—Sir William Lawrence Bragg

Dottie was a middle-aged wife and mother by the time she walked into my office at the Obsessive Compulsive Disorder (OCD) Research Group at UCLA Medical Center in Westwood, but she had been in the grip of obsessive-compulsive disorder since she was a little girl of five. Early on, it was the numbers 5 and 6 that paralyzed her with fear, she told me with some distress. I soon learned why: her obsession with the "magical" powers of numbers still consumed large portions of her life. If, while driving, Dottie glimpsed a license plate containing either a 5 or a 6, she felt compelled to pull over immediately and sit at the side of the road until a car with a "lucky" number in its license plate passed by. Without a lucky number to counteract the digits of doom, Dottie was convinced, something terrible would befall her mother. She would sometimes sit in the car for hours, waiting for the fates to bestow permission to hit the road again. When Dottie had a son of her own, her obsession shifted. Now it was eyes: Dottie was certain that if she made the slightest misstep, her son would go blind. If she walked where someone with vision problems had walked, she would throw out her shoes; if she so much as heard the word *ophthalmologist* she would cringe in terror. As she spoke, I noticed the word *vision* written four times in the palm of her hand. Oh, that, she explained, eyes downcast: while she was watching television that afternoon, a terrifying thought about eyes had popped into her head. This was her way of exorcising it. If she hadn't, there was no telling what might have befallen her son's eyesight.

Obsessive-compulsive disorder is a neuropsychiatric disease marked by distressing, intrusive, unwanted thoughts (the obsession part) that trigger intense urges to perform ritualistic behaviors (the compulsion part). Together, obsessions and compulsions can quickly become all-consuming. In Dottie's case, the obsessive thoughts centered first on her mother's safety and then on her son's eyesight; her compulsions were the suite of "magical" behaviors she engaged in to ward off disaster to the people she loved. The unremitting thoughts of OCD intrude and lay siege to the sufferer's mind (*obsession* comes from the Latin verb that means "to besiege"), insisting that the doorframe you just brushed is contaminated with excrement, or that the bump in the road you just drove over was not an uneven patch of asphalt but a body sprawled on the pavement.

One of the most striking aspects of OCD urges is that, except in the most severe cases, they are what is called ego-dystonic: they seem apart from, and at odds with, one's intrinsic sense of self. They seem to arise from a part of the mind that is not you, as if a hijacker were taking over your brain's controls, or an impostor filling the rooms of your mind. Patients with obsessive-compulsive disorder experience an urge to wash their hands, for instance, while fully cognizant of the fact that their hands are not dirty. They ritualistically count the windows they pass, knowing full well—despite the contrary message from their gut—that failing to do so will not doom their child to immediate death. They return home to check that the front door is locked so often as to render them unable to hold a job, even though part of their brain knows full well that it is securely locked. They count the steps from their car to the door of the office where they have a job interview, hoping and praying that the number will turn out to be a perfect square, a prime, a member of the Fibonacci sequence, or something else magical, since if it is not, they must do an about-face and return to the car to try again. They do this time and again, knowing that the interview time is fast approaching and that—oh, God, they've lost out on another job because of this crazy disease. OCD has a lifetime prevalence of 2 to 3 percent; in round numbers, it affects an estimated one person in forty, or more than 6 million Americans, typically striking in adolescence or early adulthood and showing no marked preference for males or females.

Excessive and ritualized hand-washing may be the best known of the OCD compulsions, but there are scores of others. They include alphabetizing the contents of a pantry, repeatedly checking to see whether a door is locked or an appliance is turned off, checking over and over to see whether you have harmed someone (peeking in on a sleeping child every minute, for instance), following rituals to ward off evil (like scrupulously avoiding sidewalk cracks), touching or tapping certain objects continuously, being unable to resist counting (totting up, every day, the traffic lights you pass en route home), or even excessively making lists. OCD can manifest itself as obsessions about order or symmetry, as expressed in an irresistible need to line up the silverware just so, or as an obsession about hoarding, as expressed in never throwing out old magazines and newspapers. Paradoxically, perhaps, giving in to the urge to wash or check or count or sort, which the patient does in the vain hope of making the dreadful feeling recede, backfires. An OCD compulsion does not dissipate like a scratched itch. Instead, giving in to the urge exacerbates the sense that something is wrong. It's like chronic poison ivy of the mind: the more you scratch it, the worse it gets.

Someone with obsessive-compulsive disorder derives no joy from the actions she takes. This puts OCD in marked contrast to, for instance, compulsive gambling or compulsive shopping. Although both compulsive shoppers and compulsive gamblers lack the impulse control to resist another trip to the mall or another game of video poker, at least they find the irresistible activity, well, kind of fun. An OCD patient, in contrast, dreads the arrival of the obsessive thought and is ashamed and embarrassed by the compulsive behavior. She carries out behaviors whose grip she

is desperate to escape, either because she hopes that doing so will prevent some imagined horror, or because resisting the impulse leaves her mind unbearably ridden with anxiety and tortured by insistent, intrusive urges. Since the obsessions cannot be silenced, the compulsions cannot be resisted. The sufferer feels like a marionette at the end of a string, manipulated and jerked around by a cruel puppeteer—her own brain.

Freud believed that OCD is a manifestation of deep emotional conflicts. As a result, patients who sought traditional psychiatric therapy for the illness were typically told that the rituals they performed or the thoughts they could not silence were rooted in sexual conflict and reflected, for instance, a repressed memory of childhood trauma. The content of the disease—why one patient can't stop thinking that she left the coffee maker on, while another is beset by a compulsion to wash doorknobs—may indeed reflect the individual's personal history. But as yet there is no biological explanation for why OCD expresses itself one way in one patient and a different way in another. Nor is it clear what the ultimate cause of obsessive-compulsive disorder is, though there is clearly a genetic contribution.

Until the mid-1960s, the psychiatric and psychological professions deemed OCD *treatment-intractable*: nothing could be done to release patients from its grip. "People didn't know what to do with OCD," says the clinical psychologist Michael Kozak, who spent nineteen years at MCP Hahnemann Hospital in Philadelphia studying the disease and its treatments. "They tried all sorts of things that didn't work very well, from electroshock and psychosurgery to any available drug and classical talk therapy." In the late 1960s and early 1970s, however, psychiatrists got a hand from serendipity: they noticed that when patients suffering from clinical depression were put on the tricyclic antidepressant clomipramine hydrochloride (Anafranil), some of them experienced relief from one or more of their OCD symptoms. Since clomipramine, among its many biochemical actions, strongly inhibits inactivation of the neurotransmitter serotonin (much as Prozac does), researchers suspected that amplifying the brain's serotonin levels might alleviate OCD.

There was at least one problem with this approach, however. Though clearly effective, clomipramine is a "dirty" drug, one with numerous pharmacological actions; as a result, it is associated with many unpleasant side effects. This problem led to the development of so-called selective serotonin reuptake inhibitors (SSRIs), such as Prozac, Paxil, Zoloft, Luvox, and Celexa, all of which specifically block the same mechanism that clomipramine acts on nonspecifically: the molecular pump that moves serotonin back into the neurons from which it was released, thus allowing more of the chemical to remain in the synapse. All of these SSRIs seem to be equally effective in treating OCD symptoms. For each of them, studies since the 1980s have shown, about 60 percent of patients respond at least somewhat, "and of those there's about a 30 to 40 percent reduction in symptoms," says Kozak. "So there's something real going on with the drugs. But when about half of the people

aren't helped significantly and those who are helped are still left with 60 percent of their symptoms, we have a ways to go."

At about the same time that researchers stumbled onto clomipramine for OCD, Victor Meyer, a psychologist at Middlesex Hospital in London, began to develop what would emerge as the first effective behavioral therapy for the disease. In 1966 he tried out, on five patients in an inpatient psychiatric ward, what would become the most widely used psychological treatment for the next twenty-five years. Called exposure and response prevention (ERP), it consisted of exposing patients to the trigger that called forth obsessional thoughts and the compulsion to engage in a distress-relieving behavior. Meyer would tell a patient to leave her house, for instance, but prevent her from returning to check whether she had left the stove on. Or he would have her touch all the doorknobs in a public building but not allow her to wash her hands afterward. Or he would tell the patient to touch dried bird droppings but not allow her to wash (at least not right away). Meyer reported significant improvement in the patients he treated with exposure and response prevention. Edna Foa, who adopted the technique and added a detailed questionnaire to allow therapists to get at the patient's so-called fear structure—the layers of emotions that underlie the obsessions—introduced it into the United States.

Typically, the first exposure during therapy uses a trigger that the patient has assigned a low score on a scale of "subjective units of distress," or SUDs. The therapist (during in-office sessions) then prevents the patient from responding as he usually does—dashing to a sink to wash, for instance. *Prevents* can mean many things, from gentle coercion to physical restraint of the patient; from carefully explaining that if the patient complies he is likely to get better, to turning off the water in the bathroom of his room in a mental hospital. Exposures are also conducted at home; the patient works at stopping himself from acting on his compulsive urges. The patient, needless to say, can become extremely anxious during this phase, which often lasts an hour or more. Ideally, however, as therapy continues, he begins to master his responses to triggers further up the distress scale, the anxiety ignited by the triggers lessens, and he gains control of his thoughts and actions.

Controversy swirls around exposure and response prevention therapy, however. The most common claim for the treatment is that three out of four patients who complete therapy do well, experiencing a 65 percent reduction in their OCD symptoms. But that little phrase "who complete" hides a land mine. "The trouble is, a lot of people won't do it at all, they're so afraid to confront their obsessions and not be allowed to carry out their compulsions," says Kozak. During his work with Edna Foa in Philadelphia, where they developed one of the best programs in the United States, some 25 percent of patients refused to undergo a single session once they learned what was involved. With less adept clinicians, refusal rates can run even higher. Some clinicians manipulate their dropout rates by fiddling with the entry criteria: by doing a little exposure and response prevention and rejecting

patients who can't take it, researchers make their results look better. Even then, 10 to 30 percent of patients who agree to start therapy drop out. And not every clinician practicing exposure and response prevention has done it well, or wisely. "There have been quite some mistakes, with therapists abusing the method or going faster than patients would have liked," says Dr. Iver Hand of the University of Hamburg in Germany, a pioneer in the field who developed a variant of ERP. "It is easy for a badly-trained therapist to abuse the method." Compared to drugs, behavioral therapy seemed to produce better results for patients who could tolerate it. But the hidden statistics made it clear: for millions of OCD patients, exposure and response prevention was not the answer.

This was the state of play when I entered the field in the mid-1980s. It wasn't so much psychology, or even physiology, that attracted me to the study of obsessive-compulsive disorder. It was philosophy. OCD, I thought, offered a wedge into the mind-brain enigma. Because symptoms are usually so clear-cut that patients can describe precisely what they feel, I realized that there should be no problem establishing the mental, experiential aspect of the disease. And since it was becoming clear even in the 1980s that psychiatric illness was rooted in the functional neuroanatomy of the brain, I was also optimistic that it would be possible to establish what was happening in the brain of people with the disease. Finally, the disease's ego-dystonic nature suggested that although the brain was acting up, an intact mind was struggling to overcome it: the events of the brain and the state of the mind were, at least partly, separable. Obsessive-compulsive disorder thus seemed to be the perfect vehicle for pursuing such profound questions as the schism between mind and brain and, in particular, the distinction between active and passive mental activity: the symptoms of OCD are no more than the products of passive brain mechanisms, but patients' attempts to resist the compulsions represent active, mental effort.

What attracted me most to the psychological treatment of OCD, however, was a tantalizing possibility. Cognitive therapy—a form of structured introspection—was already widely used for treating depression. The idea is to help patients more clearly assess the contents of their thought stream, teaching them to note and correct the conceptual errors termed "cognitive distortions" that characterize psychopathological thinking. Someone in the grips of such thinking would, for instance, regard a half-full glass not merely as half-empty but also as fatally flawed, forever useless, constitutionally incapable of ever being full, and fit only to be discarded. By the mid-1980s, cognitive therapy was being used more and more in combination with behavioral therapy for OCD, and it seemed naturally compatible with a mindfulness-based perspective. If I could show that a cognitive-behavioral approach, infused with mindful awareness, could be marshaled against the disease, and if successful therapy were accompanied by changes in brain activity, then it would represent a significant step toward demonstrating the causal efficacy of mental activity on neural circuits.

So in February 1987 I launched a group therapy session for OCD patients, meeting every Thursday afternoon, in conjunction with an ongoing study of the disease's underlying brain abnormalities that my colleagues and I at the UCLA School of Medicine had begun in 1985. One of the first patients in the group was a man who could not stop washing. His wife, driven to distraction by his compulsions, was on the verge of leaving him. Although the man felt incapable of resisting the urge to wash, at the same time he had clear insight into how pathological his behavior was. After nearly a year of group therapy, with winter approaching, he said, "That's it. I've had it. This winter I'm not doing washing compulsions. I'm not going through another winter with raw, red, cracked, chapped, painful hands. I'd rather be dead." This was a level of resolve neither I nor anyone in the group had seen before. Over the next few weeks, he actually managed to pull it off. He held his washing to normal levels and made it through the winter without chapped hands.

That case was uppermost in my mind as we delved ever deeper into the study of OCD's underlying neuroanatomy. Two years earlier we had studied depression, observing (as many other groups would later) that the brains of depressed patients are often marked by changes in cortical activity as detected on *positron emission tomography* (PET), the noninvasive imaging technique that measures metabolic activity in the brain. We had begun studying obsessions after observing that many patients with depression had intrusive, obsessional thoughts. The obvious question arose: What brain changes mark OCD itself? An advertisement that we placed in the local paper, asking, "Do you have repetitive thoughts, rituals you can't control?" brought an overwhelming response. Over the next several years, we invited about fifty of those respondents to the UCLA Neuropsychiatric Institute to undergo a full assessment for possible OCD.

In an analysis of the PET scans of twenty-four patients, published in a series of papers in the late 1980s, we pinpointed several brain structures that seemed to be consistently involved in obsessive-compulsive disorder. Compared to the brains of normal controls, the brains of our OCD volunteers showed hypermetabolic activity in the orbital frontal cortex, which is tucked into the underside of the front of the brain above and behind the eyes (hence its name) as shown in Figure 1 on Chapter 2. The scans showed, too, a trend toward hyperactivity in the caudate nucleus. Another group had found that a closely related structure, the anterior cingulate gyrus, was also pumped up in the brains of OCD patients.

By 1990, five different studies by three different research teams had all shown elevated metabolism in the orbital frontal cortex in patients with OCD, so this structure consumed our attention. We combed the literature for clues to what the orbital frontal cortex (OFC) does for a living in the normal human brain. Our first major clue came from studies by the behavioral physiologist E. T. Rolls at Oxford University in the late 1970s and early 1980s (studies whose results were later echoed by researchers elsewhere). In one key set of experiments, Rolls and his colleagues taught rhesus monkeys that every time they saw a blue signal on a monitor, licking a little tube in their cage would get them a sip of black currant

juice, one of their favorite beverages. Licking the tube in the absence of the blue light would do nothing. Good Pavlovians all, the monkeys learned quickly to lick the tube when they saw blue. Through electrodes implanted in the brains of these alert animals, Rolls observed that the orbital frontal cortex now became active as soon as blue appeared.

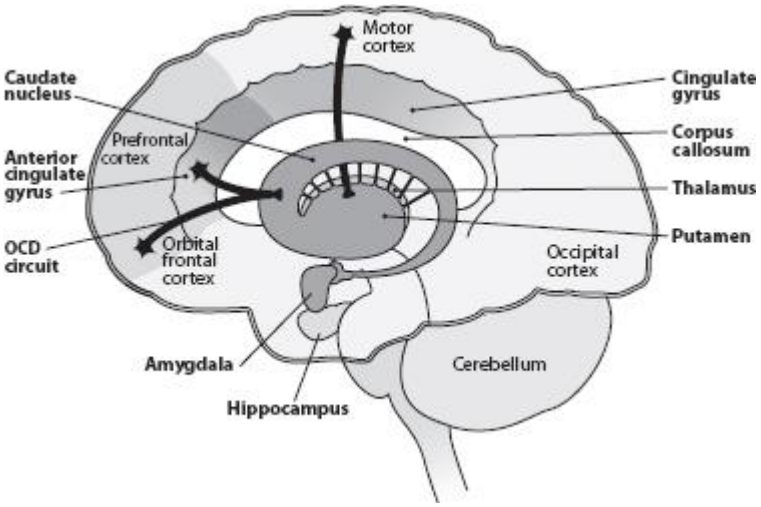


Figure 1: This side view of the brain shows some of its key structures, including those involved in OCD. In the "OCD circuit," neurons that project from the orbital frontal cortex and the anterior cingulate gyrus to the caudate nucleus are overactive, generating the persistent sense that something is amiss.

Then Rolls switched signals on his little furry subjects: now green meant juice and blue meant salt water, which monkeys (being no fools) despise. When the monkeys saw blue and licked the tube, but got brine instead of the juice they were expecting, cells in their orbital frontal cortex went ballistic, firing more intensely and in longer bursts than the cells did when the tube contained juice. Yet these cells did not respond when the monkeys sipped salt water outside the test situation. Instead, this group of cells fired only when the color previously associated with juice became associated with the delivery of something nonrewarding, or even of nothing at all. The mere absence of an expected reward, it seemed, was enough to trigger intense activity in these OFC cells. Apparently, cells in the orbital frontal cortex fire when something has gone awry, as when an actual experience (getting salt water) clashes with expectation (getting currant juice). The orbital frontal cortex, it seems, functions as an error detector, alerting you when something is amiss—if you're a rhesus monkey, getting a mouthful of brine when you're expecting currant nectar is the essence of amiss. Expectations and emotions join together here to produce a sort of neurological spellcheck.

If cells of the orbital frontal cortex do indeed function as rudimentary error detectors, then they should quiet down when expectation and reality are back in harmony. And that is what the Oxford group found. Once the monkeys learned to

associate green with juice, OFC cells quieted down, firing in shorter and less intense bursts than they did when they detected an error in the world around them. From these experiments, it seemed clear to me that error-detection responses originating in the orbital frontal cortex could generate an internal sense that something is wrong, and that something needs to be corrected by a change in behavior. They could generate, that is, the very feeling that besets OCD patients. With this realization, I got a sense of real excitement, for this was our first solid clue about the physiological meaning of the PET data showing that OCD patients have a hyperactive orbital frontal cortex: their error-detection circuitry seems to be inappropriately stimulated. As a result, they are bombarded with signals that something is amiss—if not brine subbing for fruit juice, then an iron left plugged in, a germ unscrubbed. If the error-detection system is spotting things out of whack everywhere in a person's environment, the result is like a computer's spellcheck run amok, highlighting every word in a document. Intense and persistent firing in the orbital frontal cortex, it seemed, would cause an intense visceral sensation that something is wrong, and that action of some kind—be it alphabetizing cans or checking whether appliances are turned on—is needed to make things right again. In fact, the reason for the visceral sense of dread that OCD patients suffer is that the OFC (and related structures like the anterior cingulate gyrus) is wired directly into gut-control centers of the brain. Small wonder, then, that the ERROR! ERROR! message triggers such a stomach-churning panic. Monkeys quiet their error messages by correcting their responses: they stop sipping in response to that deceptive blue signal and try other options. What about OCD patients, I wondered? How can they quiet their faulty error-detection circuit?

In 1997, some clever studies expanded the job description of the orbital frontal cortex and its neighbor, the anterior cingulate, to account even more fully for this inchoate sense of dread. Researchers led by Antoine Bechara and Antonio Damasio at the University of Iowa had volunteers play a sort of gambling game, using four decks of cards and $2,000 in play money. On each card was written a dollar amount either won or lost. All the cards in the first and second decks brought either a large payoff or a large loss, $100 either way, simulating the state of affairs that any savvy investor understands: the greater the risk, the greater the reward. Cards in decks 3 and 4 produced losses and wins of $50—small risk, small reward. But the decks were stacked: the cards were arranged so that those in decks 3 and 4 yielded, on balance, a positive payoff. That is, players who chose from decks 3 and 4 would, over time, come out ahead. The losses in decks 1 and 2 were not only twice as large, moreover, but more common, so that after a few rounds players found themselves deep in the hole. A player who chose from the first two decks more than the second two would lose his (virtual) shirt.

Normal volunteers start the game by sampling from each of the four decks. After playing a while, they began to generate what are called anticipatory skin conductance responses when they are about to select a card from the losing decks. (Skin conductance responses, assessed by a simple electronic device on the surface

of the skin, gauge when sweat glands are active. Sweat glands are controlled by the autonomic nervous system, whose level of activity is a standard measure of arousal and anxiety—and thus the basis for lie detectors.) This skin response occurred even when the player could not verbalize why decks 1 and 2 made him nervous; nevertheless, he began to avoid those decks. Patients with damage to the inferior (or *ventral*, meaning the "underside of") prefrontal cortex, however, played the game differently. They neither generated skin conductance responses in anticipation of drawing from the risky decks, nor shied away from these decks. They were instead drawn to the high-risk decks like high-rollers to the $500 baccarat table and never learned to avoid them.

Bechara and Damasio suggest that, since normal volunteers avoided the bad decks even before they had conceptualized the reason but after their skin response showed anxiety about those decks, something in the brain was acting as a sort of intuition generator. Remarkably, the normal players who were never able to figure out, or at least articulate, why two of the decks were chronic losers still began to avoid them. Intuition, or gut feeling, turned out to be a more dependable guide than reason. It was also more potent than reason: half the subjects with damage to the inferior prefrontal cortex (which includes the orbital frontal cortex) eventually figured out why, in the long run, decks 1 and 2 led to net losses and 3 and 4 led to net wins. Even so, amazingly, they still kept choosing from the bad decks.

Decision making, then, clearly has not just a rational but also an emotional component. Damage to the inferior prefrontal cortex seems to rob patients of key equipment for accessing intuition. This finding is particularly important, I realized, because it mirrors the situation in OCD patients, who have the opposite malfunction of the very same brain area. OCD patients, who have an *overactive* inferior prefrontal cortex, get an excessive, intrusive feeling that something is wrong, even when they know that nothing is. In patients in the gambling study, these areas were damaged and therefore *underactive*; these patients failed to sense that something was wrong even when they knew, rationally, that something was. The normal subjects in the gambling study felt something was wrong when it was wrong, even if they didn't know why. This all constitutes powerful evidence that the orbital frontal cortex is involved in generating the intuitive feeling "Something is wrong here."

A second overactive region we detected on the PET scans of the brains of OCD patients was the *striatum*. This structure is composed of two major information-receiving structures, the *caudate nucleus* and the *putamen*, which nestle beside each other deep in the core of the brain just in front of the ears. The entire striatum acts as a sort of automatic transmission: the putamen acts as the gear shift for motor activity, and the caudate nucleus serves a similar function for thought and emotion. The striatum as a whole receives neuronal inputs from so many other regions of the brain that it rivals, for sheer complexity, the central switching station for the busiest telecom center imaginable, with signals arriving and departing in a buzz of perpetual activity. All areas of the cortex send neural projections to the

striatum; so do parts of the thalamus and the brainstem, as shown in Figure 2 on Chapter 2.

But what particularly intrigued me was the fascinating traffic pattern connecting the striatum and the cortex. One set of neuronal projections into the striatum originates in the prefrontal cortex, especially in regions associated with planning and executing such complex behaviors as the manipulation of mental images. Small clusters of projections formed by these prefrontal arrivals are called *matrisomes*. The matrisomes are typically found near distinct microscopic patches that stipple the striatum; they are called *striosomes*. The striosomes, too, receive some input from the prefrontal cortex, in particular the areas most intimately associated with emotional expression: the orbital frontal cortex and anterior cingulate cortex. These are the very cortical structures that PET scans have shown to be overactive in OCD. But the primary inputs to these striosomes are the polar opposites of the thoughtful, rational prefrontal cortex: the striosomes are also bombarded with messages from the limbic system. The limbic system comprises the structures that play a critical role in the brain's emotional responses, particularly fear and dread. It is the limbic system's core structure, the amygdala, that seems to generate fear and dread. And it is the amygdala that projects most robustly into the striosomes' distinctive patches.

The striatum, and especially the caudate, can thus be thought of as a neuronal mosaic of reason and passion. It sits smack dab at the confluence of messages bearing cognitive content (courtesy of the matrisomes, where inputs arrive from the rational prefrontal cortex) and messages shot through with emotion (thanks to the striosomes, landing zones for inputs from the limbic system). The juxtaposition of striosomes and matrisomes therefore seems highly conducive to interactions between emotion and thought. Since the striosomes receive projections primarily from the emotional centers of the limbic system and the matrisomes receive projections from the higher cognitive centers of the prefrontal cortex, together they provide the perfect mechanism of integrating the messages of the heart with those of the mind.

In the mid-1990s researchers discovered a subset of highly specialized nerve cells that provide a key to understanding how the brain integrates reason and emotion. Called *tonically active neurons* (TANs), these cells often sit where striosomes and matrisomes meet, as Ann Graybiel and her colleagues at the Massachusetts Institute of Technology discovered. The TANs are thus perfectly positioned to integrate information from both structures and, by implication, from the intensely passionate limbic system and the eminently reasonable prefrontal cortex.

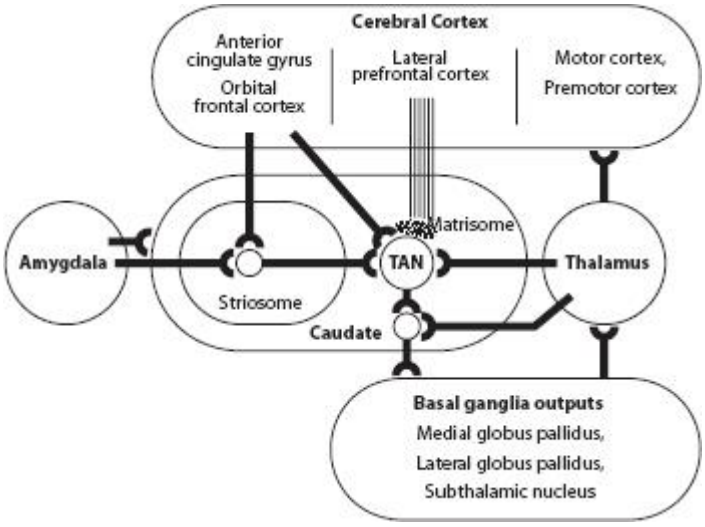


Figure 2: Cells in the caudate known as tonically active neurons (TANs) tend to be found between striosomes and matrisomes.Striosomes are areas where information from an emotion-processing part of the brain, the amygdala, reaches the caudate; matrisomes are clumps of axon terminals where information from the thinking, reasoning cerebral cortex reaches the caudate. By virtue of their position, TANs can integrate emotion and thought.They fire in a characteristic pattern when the brain senses something with positive or negative emotional meaning. Cognitive-behavioral therapy may change how TANs respond to OCD triggers.

TANs respond dramatically to visual or auditory stimuli that are linked, through behavioral conditioning, to a reward. As a result of this finding, Graybiel's team began to suspect that TANs play a central role in behavioral responses to hints of an upcoming reward. In a series of experiments on macaque monkeys, the MIT scientists found that TAN firing rates changed when a once-neutral cue became associated with a reward. Let's say, for instance, that a visual cue such as a flashing light means that the monkey will get a reward (juice) if it performs a simple behavioral response (licking a spoon). When TANs detect a potential reward, that is, they pause at first and then fire faster. But TANs do not respond to the light cue if the monkey has not learned to associate it with a reward. As the monkey's brain learns to recognize a reward, TANs fire in a characteristic pattern.

Thanks to its TAN cells, then, the striatum is able to associate rewarded behavior with particular cues. Because TANs can quickly signal a switch in behavioral response depending on the meaning of a stimulus ("That light means juice!"), they may serve as a sort of gating mechanism, redirecting information flow through the striatum during learning. As noted earlier, the entire striatum acts as an automatic transmission: the putamen shifts between motor activities, and the caudate nucleus shifts between thoughts and emotions. Different gating patterns in the striatum may thus play a critical role in establishing patterns of motor as well as cognitive and emotional responses to the environment. Such patterned responses are nothing

more than habits. Indeed, Graybiel has shown that the striatum can play a fundamental role in the development of habits. Our best guess is that the tonically active neurons underpin the gating of information through the striatum and thus its role in the formation of habits. What seems to happen is that distinct environmental cues, associated with differing emotional meanings, elicit different behavioral and cognitive responses as TANs shift the output flow of the striatum. In this way TANs may serve as the foundation for the development of new patterns of activity in the striatum.

Most important, TANs could be crucial to the acquisition of new behavioral skills in cognitive-behavioral therapy. In neurological terms, we could say that cognitive-behavioral therapy teaches people purposefully to alter the response contingencies of their own TANs. This is a crucial point. Such therapy teaches people to alter, by force of will, the response habits wired into their brains through TANs. In the case of OCD, therapy teaches patients to reinterpret their environment and apply their will to alter what had been an automatic behavioral response to disturbing feelings. If that happens often enough, then the new response—the new behavioral output—should itself become habitual. The key to a successful behavioral intervention in OCD, it seemed to me, would be to teach the striatum new gating patterns.

The gating image turns out to be particularly apt in light of what we have learned about the striatum's two output pathways: one direct and one indirect. The indirect pathway takes the scenic route, running from the striatum through the globus pallidus, to the subthalamic nucleus, back to the globus pallidus, and finally to the thalamus and cortex. The direct pathway runs through the globus pallidus, then straight to the thalamus and back to the cortex. The crucial difference is that the direct pathway provides activating input to the thalamus, but the indirect pathway provides inhibitory input. Thus the direct and indirect output pathways from the striatum have opposite effects. The direct pathway tends to activate the cortex, the indirect pathway tends to quiet the cortex.

The striatal gate determines which pathway nerve impulses will follow. Recall that the striatum receives input from the entire cortex, with the caudate specifically receiving strong input from the prefrontal areas. Prefrontal inputs include those from the orbital frontal cortex and anterior cingulate error-detection circuitry. In 1992 Lew Baxter, my longtime colleague at UCLA, dubbed the circuit containing the orbital frontal cortex and its connections to the basal ganglia the "worry circuit." It is now often called "the OCD circuit." When this circuit is working properly, the result is a finely tuned mechanism that can precisely modulate the orbital frontal cortex and anterior cingulate by adjusting the degree to which the thalamus drives these areas. When that modulation is faulty, as it is when OCD acts up, the error detector centered in the orbital frontal cortex and anterior cingulate can be overactivated and thus locked into a pattern of repetitive firing. This triggers an overpowering feeling that something is wrong, accompanied by compulsive attempts somehow to make it right. The malfunction of the OCD circuit that our UCLA group found in OCD patients therefore makes sense. If the exquisite balance

of the direct and indirect pathway outputs from the basal ganglia is impaired, it can cause the orbital frontal cortex to become stuck in the "ERROR! ERROR!" mode.

When the striatum is working normally, it gates the vast array of information about the environment that flows into it from the cortex and initiates what Ann Graybiel has termed "chunks of action repertoires." These chunks help form "coordinated, sequential motor actions" and develop "streams of thought and motivation." Thus a single bit of information, such as the feel of a stick shift in your hand, can initiate a complex behavior, for instance, a series of foot movements on the clutch and hand movements on the stick. But in OCD patients the striatum, our PET scans showed, is not even close to functioning normally. It does not gate properly, leading to serious overactivity in the orbital frontal cortex. The intrusive, persistent sense in OCD that something is wrong seems to be the result of orbital frontal cortex neurons' becoming chronically activated (or inadequately inactivated) as a result of a gating problem, which causes the direct-output pathway to overwhelm the indirect one.

In OCD, the striatum—in particular, the caudate nucleus—appears to be failing to perform its gating function properly. It has become like an automobile transmission that fails to shift. Most people have brains that shift gears automatically, but OCD patients have a sticky manual transmission. As a result, the direct pathway seems stuck in the "on" position. This is what I came to call Brain Lock: the brain can't move on to the next thought and its related behavior. Instead, such evolutionarily ancient drives as washing and checking for danger keep breaking through, creating a sense of being overwhelmed by these feelings and urges. The feeling of being "stuck in gear," which often manifests itself as the feeling of needing to get things just right, also explains why an OCD patient finds it so hard to change the compulsive behavior, and why doing so requires such focused and even heroic effort. Medications that block the neuronal reuptake of serotonin can help by at least partially decreasing the intensity of OCD urges, probably by helping to rebalance the direct and indirect pathways.

A third brain region implicated in OCD is the anterior cingulate gyrus, which also sends projections to the striosomes of the caudate nucleus. Located behind and above the orbital cortex, the cingulate also has connections to the vital brain centers that control the gut and the heart. This structure is probably responsible for generating the gut-churning sense among OCD sufferers that some cataclysm will befall them if they fail to act on their compulsion, say, to tap the steering wheel ten times (or one hundred!) before turning the ignition. The anterior cingulate seems to amplify the gut-level feeling of anxiety and dread.

Even as our UCLA group was working out the OCD circuit, a study from the other side of the country confirmed what we were finding. Researchers at a Massachusetts General Hospital (MGH) group led by Scott Rauch used both PET and functional magnetic resonance imaging (fMRI) scans to measure cerebral blood flow in the brains of eighteen OCD patients. The scientists deliberately created an

environment designed to agitate: when a patient settled into the PET scanner, the researchers placed beside him a dirty glove or other OCD-triggering object. The patient's anxiety level soared. At the same time, the MGH group reported in 1994 and 1996, the PET and fMRI scans consistently picked up significant increases in cerebral activity in the orbital frontal cortex, the anterior cingulate gyrus, and the caudate nucleus—exactly the structures found to be hypermetabolic in our PET scans at UCLA. Looking at the scans, you could almost see the brain desperately emitting "TILT! TILT" messages, signaling that something was dreadfully wrong. The conclusion was clear: when OCD urges become more intense as a result of exposure to a trigger such as a dirty object, circuitry involving these three brain structures becomes more active.

A picture of the brain abnormalities underlying OCD was emerging. The malfunctions center on circuitry within the orbital frontal cortex, containing "error alarm" circuits, and the basal ganglia, which acts as an automatic transmission or switching station. The circuit responsible for detecting when something is amiss in the environment, centered on the orbital frontal cortex, becomes inappropriately and chronically activated in OCD, probably because a malfunction in the gating function of the caudate nucleus allows the prefrontal cortex to be stimulated continuously. The result is a pattern of intrusive, persistent thoughts and feelings that something is wrong or excessively risky. Interconnections among the orbital prefrontal cortex, anterior cingulate, and caudate may allow this circuit to become self-sustaining and thus extremely difficult to break out of—as any OCD patient can attest. The result is a perseveration of the thoughts and urges that OCD creates. That these abnormalities leave the superior prefrontal regions, and thus higher cognitive function, essentially untouched seems consistent with the ego-dystonic nature of OCD's intrusive thoughts and urges—that is, with the fact that they are experienced as alien to the patient's sense of who she is, and apart from the natural flow of her stream of consciousness.

This neurobiologically based view of OCD did not exactly take psychiatry by storm. At a meeting on anxiety disorders in the early 1990s, I was presenting some recent findings, on a poster, about the brain mechanisms underlying OCD. A leading behavioral therapist strolled up to me, stopped, and glanced at the poster. Looking me up and down, she spit out, "The whole notion you have of the brain causing OCD is ridiculous!" Well, I asked, what else might be the cause, if not the brain? "I'll tell you what causes OCD. Try not to think of a pink elephant. Can you do it?" Without waiting for an answer, she continued, "There! That is what causes OCD"—and she walked away.

Fortunately, responses like this were the exception rather than the norm, and the overheated brain circuitry underlying OCD, as we and others were working out, offered a glimmer of hope for patients. Since the most evolutionarily recent (and thus sophisticated) prefrontal parts of the brain are almost entirely spared in OCD, the patient's core reasoning power and sense of identity remain largely intact. They might thus be relied on, I reasoned, to play a part in therapy. Now that science had

pretty much nailed down the brain abnormalities at the root of OCD, I was ready for the next step. I set out to find a treatment that would alter metabolic activity in the guilty triad: the orbital prefrontal cortex, the anterior cingulate gyrus, and the caudate nucleus. In particular, I had a hunch that any successful treatment would probably have to enhance the gating function of the caudate so that the worry circuit could be quieted and the patient enabled to resist OCD urges.

By mid-1987 I was leading my OCD therapy group of eight to ten patients every Thursday afternoon from 4:30 to 6:00 on the second floor of the Neuropsychiatric Institute. Though the behaviorists had pioneered an effective approach to treating what had, before 1966, been regarded as an untreatable condition (largely because psychoanalytic attempts to treat it generally yielded abysmal results), I was reluctant to adopt exposure and response prevention wholesale. I recoiled at the intense distress it caused many patients; I just couldn't see myself hauling patients to a public restroom, forcing them to wipe their hands all over the toilet seats, and then preventing them from washing. And since experienced clinicians were already estimating (at least in their more candid conversations) that at least 25 to 30 percent of OCD patients refuse, or are unable, to comply with exposure response prevention, I already knew that such therapy alone could never be the final answer to OCD. But most of all, I hated the way exposure and response prevention rendered patients almost completely passive during therapy.

The culture of behaviorism and its approach to therapy disturbed me at a philosophical level, too. Behaviorists adopted only treatment techniques that could also be used to train an animal. They were enormously proud of this, believing it somehow rendered their approach more "scientific." But I balked at it. I didn't doubt that behaviorist approaches could play a useful and even necessary role for patients who suffer from severe cases of OCD, especially in the early stages of treatment. But for patients capable of willful self-directed activity either at the outset or once the most crippling symptoms lifted, I was convinced that it was time to try a different approach. Throughout 1987, as the OCD therapy group blossomed, I decided to extract the useful parts of behaviorist practice—those that could be applied as part of self-directed treatment—and integrate them with the uniquely human characteristics that a willful, conscious person could use in treatment.

A good part of my decision reflected a change in my own life the summer before. In August 1986, I had resumed the daily practice of Buddhist mindfulness meditation, which I had begun in 1975 but fell away from in 1979. In those years, I had been deeply influenced by *The Heart of Buddhist Meditation*, by the German-born Buddhist monk Nyanaponika Thera. In this book, Nyanaponika coined the term *Bare Attention*. As I noted in the Introduction, this mental activity, he wrote, is

the clear and single-minded awareness of what actually happens to *us and in us, at the successive moments of perception. It is called "Bare" because it attends just to the bare facts of a perception as presented either through the five physical senses*

or through the mind…without reacting to them by deed, speech or by mental comment which may be one of self-reference (like, dislike, etc.), judgment or reflection. If during the time, short or long, given to the practice of Bare Attention, any such comments arise in one's mind, they themselves are made objects of Bare Attention, and are neither repudiated nor pursued, but are dismissed, after a brief mental note has been made of them.

Bare Attention, the key to Buddhist meditation, is the act of viewing one's experience as a calm, clear-minded outsider. "Mindfulness is kept to a bare registering of the facts observed," wrote Nyanaponika. A method for doing this, developed by Nyanaponika's meditation teacher, the Burmese master Mahasi Sayadaw, is called "making mental notes." This involves mindfully noting the facts as they are observed in order to enhance the mental act of bare registration.

Thus mindfulness, or mindful awareness, was very much on my mind when I began the OCD group the following February with several UCLA colleagues. We kept, at first, well within the tradition of cognitive-behavioral therapy, teaching patients to correct the cognitive distortions described earlier. But I wasn't content with that. The cognitive approach might be fine for depression, in which there are genuine cognitive distortions that need to be corrected ("It's not true that everyone hates me; those who like me include…") and the correction actually helps. But this doesn't work with OCD. To teach a patient to say "My hands are not dirty" is just to repeat something she already knows. The problem in OCD is not failure to realize that your hands are clean; it's the fact that the obsession with dirt keeps bothering you and bothering you until you capitulate and wash—yet again. Cognitive distortion is just not an intrinsic part of the disease; a patient basically knows that failing to count the cans in the pantry today won't really cause her mother to die a horrible death tonight. The problem is, she doesn't feel that way.

Because cognitive therapy alone seemed to lack what OCD patients needed, I cast about for something else. My return to meditation now convinced me that the best way to treat OCD would involve an approach informed by the concept of mindfulness. I felt that if I could help patients to experience the OCD symptom without reacting emotionally to the discomfort it caused, realizing instead that even the most visceral OCD urge is actually no more than the manifestation of a brain wiring defect, it might be tremendously therapeutic. The more patients could experience the feeling impersonally, as it were, the less they would react emotionally or take it at face value. They would not be overwhelmed by the sense that the obsession had to be acted on and could better actualize what they knew intellectually: that the obsession makes no sense. The appropriate cognitive awareness was already on board: patients generally know, with the rational, thinking part of their mind, that it makes no sense to check the oven a dozen times before leaving the house. It was now necessary for patients to engage their healthy emotions to strengthen that insight and act on it. To do this would require persistent effort, and habitual practice would be crucial.

Might the use of mindful awareness, I wondered, help an OCD patient achieve that goal? Might mindfulness practice, and systematic mental note taking (as people do during meditation), allow OCD patients to become instantly aware of the intrusion of symptoms into conscious awareness and then to redirect attention away from these persistent thoughts and feelings and onto more adaptive behaviors? It seemed worth investigating whether learning to observe your sensations and thoughts with the calm clarity of an external witness could strengthen the capacity to resist the insistent thoughts of OCD. Not that I had any illusions about how easy it would be. To register mentally the arrival of each and every OCD obsession and compulsion, and to identify each as a thought or urge with little or no basis in reality, would require significant, willful effort. It would not be sufficient just to acknowledge superficially the arrival of such a symptom. Such superficial awareness is essentially automatic, even (almost) unconscious. Mindful awareness, in contrast, comes about only with conscious effort. It is the difference between an off-handed "Ah, here's that feeling that I have to count cans again," and the insight "My brain is generating another obsessive thought. What does it feel like? How am I responding? Does the feeling make sense? Don't I in fact know it to be false?"

I began showing patients in the treatment group their PET scans, to drive home the point that an imbalance in their brains was causing their obsessive thoughts and compulsive behaviors. Initially, some were dismayed that their brain was abnormal. But generally it dawned on them, especially with therapy, that they are more than their gray matter. When one patient, Dottie (the woman with the 5s and 6s obsession), exclaimed, "It's not me; it's my OCD!" a light went off in my head: what if I could convince patients that the way they responded to the thoughts of OCD could actually change their brains? I developed a working hypothesis that making mental notes could be clinically effective and decided to introduce mindfulness into the OCD clinic. Making mental notes became, in my own mind, "Relabeling" the feeling that accompanies an OCD obsession. This would be the first step in what came to be called the Four Step method.

Having rejected standard exposure and response prevention, I instead told patients to describe their symptoms and the situations in which they arose. I then explained that the feeling that the door is unlocked, for instance, is the disorder itself, and that our brain imaging research had shown that the cause was a biochemical imbalance in the brain. I never told patients just to resist the urge and it would go away. Instead, I emphasized the importance of identifying as clearly and quickly as possible the onset of an OCD symptom—not just recognizing that an obsessive thought was intruding or a compulsive urge was demanding to be carried out, but recognizing exactly what each of these feelings was. As soon as the thought that your hands are dirty seizes your attention, I counseled them, use mindfulness to enhance awareness of the fact that you do not truly think your hands need washing; rather, tell yourself that you are merely experiencing the onslaught of an obsessive thought. The patient would start saying to herself, That's not an urge to wash; that's a bothersome thought and an unpleasant feeling caused by a brain

wiring problem. Or, if the compulsion to check a door lock intruded, the patient was to regard it as the result of a nasty compulsive urge, and not of any real need to check the lock. The feeling of doubt, I told patients repeatedly, is a false message, due to a jammed transmission in the brain. To enhance the recognition that the thoughts and urges are symptoms of OCD, I taught patients to make real-time mental notes, in effect creating a running stream of mindful commentary on what they were experiencing. This enabled them to keep a rational perspective on the intrusive thoughts and urges and not get caught up in automatic compulsive responses and thus a destructive run of compulsive rituals.

By refusing to accept obsessive thoughts and compulsive urges at face value, and instead recognizing that they are inherently false and misleading, the patients took the first step toward recovery. Done regularly, Relabeling stops the unpleasant feelings of OCD from being unpleasant in the same way: understanding their true nature gives a feeling of control, even of freedom. By Relabeling their thoughts and urges as manifestations of a medical disorder, patients make a purposeful cognitive shift away from self-identification with the experience intruding into the stream of consciousness.

The week after patients started relabeling their symptoms as manifestations of pathological brain processes, they reported that they were getting better, that the disease was no longer controlling them, and that they felt they could do something about it. I knew I was on the right track. By this time, the PET data had clearly shown that the orbital frontal cortex of OCD patients is hypermetabolic. One day, just a few months after starting the group, I happened to be carrying around some plain black-and-white PET scans. One patient asked me, "Doc, can you just tell me why the damn thing keeps bothering me—why it doesn't go away?" I looked at him. "You want to know why it doesn't go away?" I asked. "I'll show you why it doesn't go away. You see this dark spot in the brain on this scan? That is why: it means this region of the brain is hugely overactive in people with OCD. That's why the bad feeling doesn't go away."

It was as if a lightbulb went off in his head—indeed in all the patients' heads. At that moment what was to become the second of the Four Steps, Reattribute, was born. Whenever a patient told me an obsession was bothering her, I responded, This is why: I printed slides of color PET scans and showed patients the neuroanatomical basis of their symptoms. *This* is why you feel you have to wash, or check, or count, I said, photographic evidence in hand. This reattribution of OCD feelings to a brain glitch was the breakthrough that pushed us beyond simple Relabeling. Cognitive techniques that merely teach the patient to recognize OCD symptoms as false and distorted—something called *cognitive restructuring*—do not make much of a dent in OCD. Relabeling was essentially just a form of cognitive restructuring. Reattributing went further: having Relabeled an intrusive thought or insistent urge as a symptom of OCD, the patient then attributes it to aberrant messages generated by a brain disease and thus fortifies the awareness that it is not his true "self." By first making mental notes of the arrival of an OCD obsession,

and immediately attributing it to faulty brain wiring, I hoped, patients could resist that false message. "The brain's gonna do what the brain's gonna do," I told them, "but you don't have to let it push you around."

Two patients in particular picked up on this idea. One was Anna, then twenty-four, a graduate student in philosophy. She asked her boyfriend about every detail of his daily life because she was obsessed with the (baseless) suspicion that he was unfaithful. Although she never truly believed he was cheating on her, she was unable to stop obsessing about it. What had he eaten for lunch? Who were his girlfriends when he was a teenager? Did he ever look at pornographic magazines? Had he had butter or margarine on his toast? The slightest discrepancy in his accounts set Anna off, making her whole world crumble under the suspicion that he had betrayed her. The other patient was Dottie, then fifty-two, whose obsession with "magical numbers" is described at the beginning of this chapter. Both women realized that the reason they were experiencing these false thoughts was an abnormality in their brain's metabolism. "Once I learned to identify my OCD symptoms as OCD rather than as 'important' content-laden thoughts that had to be deciphered for their deep meaning," Anna explained later, as described in my 1996 book *Brain Lock*, "I was partially freed from OCD."

As I worked with Dottie and Anna as well as the other group members throughout 1988 and 1989, I began using Relabeling and Reattributing via mindfulness as a core part of their treatment. Accentuating Relabeling by Reattributing the condition to a rogue neurological circuit deepens patients' cognitive insight into the true nature of their symptoms, which in turn strengthens their belief that the thoughts and urges of OCD are separate from their will and their self. By Reattributing their symptoms to a brain glitch, the patients recognize that an obsessive thought is, in a sense, not "real" but, rather, mental noise, a barrage of false signals. This improves patients' ability not to take the OCD thoughts at face value. Reattributing is particularly effective at directing the patient's attention away from demoralizing and stressful attempts to squash the bothersome OCD feeling by engaging in compulsive behaviors. Realizing that brain biochemistry is responsible for the intensity and intrusiveness of the symptoms helps patients realize that their habitual frantic attempts to wash (or count or check) away the symptoms are futile.

Relabeling and Reattributing reinforce each other. Together, they put the difficult experience of an OCD symptom into a workable context: Relabeling clarifies what is happening, and Reattributing affirms why it's happening, with the result that patients more accurately assess their pathological thoughts and urges. The accentuation of Relabeling by Reattributing also tends to amplify mindfulness. Through mindfulness, the patient distances himself (that is, his locus of conscious awareness) from his OCD (an intrusive experience entirely determined by material forces). This puts mental space between his will and the unwanted urges that would otherwise overpower the will.

Besides Relabeling and Reattributing their OCD symptoms, I realized, patients needed to turn their attention to something else, performing an activity other than the one being urged on them by their stuck-in-gear brain. It seemed a good idea to make it a systematic part of the treatment, akin to the practice of methodically directing attention "back to the breath" when the mind wanders during meditation. So I gave it a name: Refocusing. It evolved to become the core step of the whole therapy, because this is where patients actually implement the willful change of behavior. The essence of applying mindful awareness during a bout of OCD is thus to recognize obsessive thoughts and urges as soon as they arise and willfully Refocus attention onto some adaptive behavior.

Directed mental focusing of attention becomes the mind's key action during treatment. The goal of this step is not to banish or obliterate the thought, but rather to initiate an adaptive behavior unrelated to the disturbing feeling even while the feeling is very much present. Refocusing on such a behavior, and thus resisting the false message to carry out the OCD compulsion, requires significant willpower, for the feeling that something must be washed or checked is still very much a part of the inner experience. Although the patient has Relabeled and Reattributed the obsessions and compulsions to brain pathology, the anxiety and dread still feel frighteningly real. Early in treatment, I therefore suggested to patients that they Refocus on a pleasant, familiar "good habit" kind of behavior. This is when biological reasoning became crucial: I specifically wanted patients to substitute a "good" circuit for a "bad" one. The diversion can be almost anything, although patients began telling me that physical activity—gardening, needlepoint, shooting baskets, playing computer or video games, cooking, walking—was especially effective. That is not to say it was easy. To the contrary: Refocusing attention away from the intrusive thought rather than waiting passively for the feeling to go away is the hardest aspect of treatment, requiring will and courage.

Soon after I explained the Refocus step to one patient, Jeremy, he began carrying around a small notebook in which he wrote ways to Refocus whenever a compulsive urge arose. On its cover, he had written "caudate nucleus." In what he called his "refocus diary," Jeremy told me, he recorded how he prevented himself from responding to an OCD urge and which alternative behavior he used. The diary, it turned out, not only increases a patient's repertoire of Refocus behaviors, but also boosts confidence by highlighting achievements: see, yesterday when I had a seemingly irresistible urge to count cans I did some needlepoint instead. Many patients were helped by selecting one Refocus task daily as the "play of the day," to remember and review as a form of positive feedback and self-empowerment. Over the course of treatment, patients slowly developed the sense that they could control their response to the OCD intrusions and that well-directed effort really does make a difference.

Early on, I developed a "fifteen-minute rule." The patient had to use an "active delay" of at least fifteen minutes before performing any compulsive act. Setting a finite length of time to resist giving in seems to help patients (for the same reason,

probably, that devout Catholics find it easier to give up drinking or smoking for the forty days of Lent than they do to give up bad habits for an open-ended period). The fifteen minutes should not be just a passive waiting period, however. Rather, it must be a period of mindful adaptive activity intended to activate new brain circuitry, with the goal of pursuing the alternative activity for a minimum of another fifteen minutes. This seems to be the length of time generally needed for most patients' OCD urges to diminish noticeably. When a patient's mind is invaded by obsessive thoughts, even brief periods of Refocusing help, for they demonstrate that it is not essential to squelch intrusive thoughts entirely in order to engage in healthier behaviors.

Refocusing also alleviates the overwhelming sense of being "stuck in gear." This is where Relabeling and Reattributing come in: both help keep patients' minds clear about who they are and what the disease process is. This mental clarity has tremendous therapeutic power, for it keeps the Refocusing process moving forward. It also reinforces the insight that active will is separable from passive brain processes—an awareness that forms the core of the quantum perspective on the mind-brain interface, as we shall explore later.

At the neurological level, the rationale for Refocusing is straightforward. Our PET scans had shown that the orbital frontal cortex, the caudate nucleus, and the thalamus operate in lockstep in the brain of an OCD sufferer. This brain lock in the OCD circuit is undoubtedly the source of a persistent error-detection signal that makes the patient feel that something is dreadfully wrong. By actively changing behaviors, Refocusing changes which brain circuits become activated, and thus also changes the gating through the striatum. The striatum has two output pathways, as noted earlier: direct and indirect. The direct pathway tends to activate the thalamus, increasing cortical activity. The indirect pathway inhibits cortical activity. Refocusing, I hoped, would change the balance of gating through the striatum so that the indirect, inhibitory pathway would become more traveled, and the direct, excitatory pathway would lose traffic. The result would be to damp down activity in this OCD circuit.

When patients changed the focus of their attention, in other words, the brain might change, too. I thought that if I could somehow induce the patient to initiate virtually any adaptive behavior other than whatever the compulsion was, this process would activate neuronal circuitry different from the pathways that were pathologically overactive. Then I could exploit the brain's tendency to pick up on repetitive behaviors and make them automatic—that is, to form new habits. Ideally, this alternative behavior would be one the patient already knows so well that it is almost automatic. When patients change their focus from "I have to wash again" to "I'm going to garden," I suspected, the circuit in the brain that underlies gardening becomes activated. If done regularly, that would produce a habitual association: the urge to wash would be followed automatically by the impulse to go work in the garden. I therefore began encouraging patients to plan sequences of Refocusing

behaviors that they could call on, in order to make them as automatic as possible. Refocusing is the step that, more than any other, produces changes in the brain.

In the fall of 1988 a UCLA medical student was working as my cotherapist in the OCD group sessions. We had recently begun using the group as part of a major research study on the effect of psychological interventions for OCD on brain function. Robert Liberman, who was supervising this student, asked me one day how I was conducting the group therapy. When I explained the Relabeling and Reattributing steps, and how I was teaching patients to recognize that their brain is sending them a false message, Liberman was intrigued. I had to meet a friend of his, he said: Dr. Iver Hand of the University of Hamburg in Germany. Hand had developed a technique called *exposure response management*, which is based on the insight that there is no need to make an OCD patient wait passively in an angst-ridden state for her compulsive urge to dissipate. If you instead help her to manage the anxiety caused by the exposure, Hand found, she will tolerate more exposures and improve more quickly. When I dug up some of his published papers, I saw that Hand had found that when patients acquired specific cognitive skills, they were better able to tolerate the presence of, say, a dirty washrag, and therefore more exposures. They even began to do some of the treatment on their own. I recognized a kindred spirit: Hand was finding that patients could learn to exploit their understanding of OCD to manage their anxiety.

Iver and I met in San Francisco at the American Psychiatric Association conference in 1989 and hit it off immediately. The following spring, Liberman suggested that Iver and I write the OCD chapter for a textbook on biobehavioral treatments for psychiatric disorders. We holed up at the Veterans Administration Hospital in Brentwood, a few blocks from my office. The chapter would never be written (partly because Iver and I could never quite reconcile our beliefs about whether biology or psychosocial factors caused OCD; he was convinced that OCD symptoms are the product of a patient's need to distance himself from intimate relations). But we agreed strongly on approaches to treatment. We spent hours in the coffeehouses of West L.A., debating whether exposure and response prevention was mechanistic and inhumane. Iver argued that his version of ERP was nothing of the sort: because he varied the exposures and, critically, motivated patients to resist the compulsion, he very much involved patients in their own treatment rather than treating them as a behaviorist's pet pigeons. As Iver talked, it hit me: up to that point I was explaining treatment in a sort of shoot-from-the-hip style. If I could explain things to patients more methodically, perhaps by breaking mindfulness into discrete, straightforward, teachable steps, it could become the basis for self-treatment.

I was sitting at the keyboard, typing out a case history to describe the treatment, with Iver beside me. How to explain what I was doing with patients? Okay, Relabel, Reattribute, Refocus—but what else was going on? It suddenly hit me. In 1989 I had begun reading the Austrian economist Ludwig von Mises, who defined *valuing* as "man's emotional reaction to the various states of his environment, both that of the external world and that of the physiological

conditions of his own body." This was exactly what the OCD therapy was changing. Combining Buddhist philosophy with Austrian economics, I had a name for the last of the Four Steps: Revalue. "This might actually be important," I thought, for I now had, in a simple and usable form, a strategy for treating OCD: Relabel, Reattribute, Refocus, Revalue.

Revaluing is a deep form of Relabeling. Anyone whose grasp of reality is reasonably intact can learn to blame OCD symptoms on a medical condition. But such Relabeling is superficial, leading to no diminution of symptoms or improved ability to cope. This is why classical cognitive therapy (which aims primarily to correct cognitive distortions) seldom helps OCD patients. Revaluing went deeper. Like Relabeling, Reattributing, and Refocusing, Revaluing was intended to enhance patients' use of mindful awareness, the foundation of Theravada Buddhist philosophy. I therefore began teaching Revaluing by reference to what Buddhist philosophy calls wise (as opposed to unwise) attention. Wise attention means seeing matters as they really are or, literally, "in accordance with the truth." In the case of OCD, wise attention means quickly recognizing the disturbing thoughts as senseless, as false, as errant brain signals not even worth the gray matter they rode in on, let alone worth acting on. By refusing to take the symptoms at face value, patients come to view them "as toxic waste from my brain," as the man with chapped hands put it.

In both my individual and my group practice, I was getting encouraging results with the Four Steps by the early 1990s. With continued self-treatment—for I always intended that patients be able to follow the treatment regimen on their own—the intensity of their OCD symptoms kept falling. As it did, the patients found they needed to expend less effort to dismiss OCD symptoms through Relabeling, and less effort to Refocus on another behavior.

Some of the OCD patients, especially those willing to be treated without drugs, were recruited into the brain imaging study that Lew Baxter and I were starting, with the goal of measuring whether the positive behavioral changes we were seeing in patients were accompanied by brain changes. Our UCLA group therefore performed PET scans on eighteen drug-free OCD patients before and after they underwent ten weeks of the Four Steps, with individual sessions once or twice a week in addition to regular group attendance. The patients who signed on exhibited moderate to quite severe symptoms. What they all had in common was a willingness to be PET-scanned twice and to try a largely self-directed, drug-free treatment. Twelve of the patients improved significantly during the ten-week study period. In these, PET scans after treatment showed significantly diminished metabolic activity in both the right and the left caudate, with the right-side decrease particularly striking. (See Figure 3.) There was also a significant decrease in the abnormally high, and pathological, correlations among activities in the caudate, the orbital frontal cortex, and the thalamus in the right hemisphere. No longer were these structures functioning in lockstep. The interpretation was clear:

therapy had altered the metabolism of the OCD circuit. Our patients' brain lock had been broken.

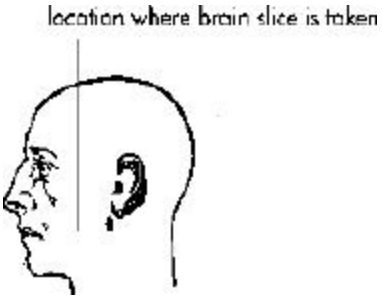
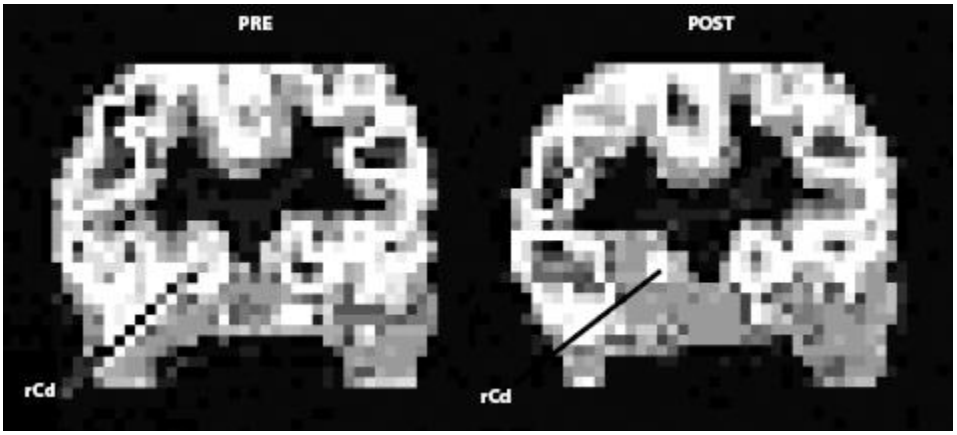
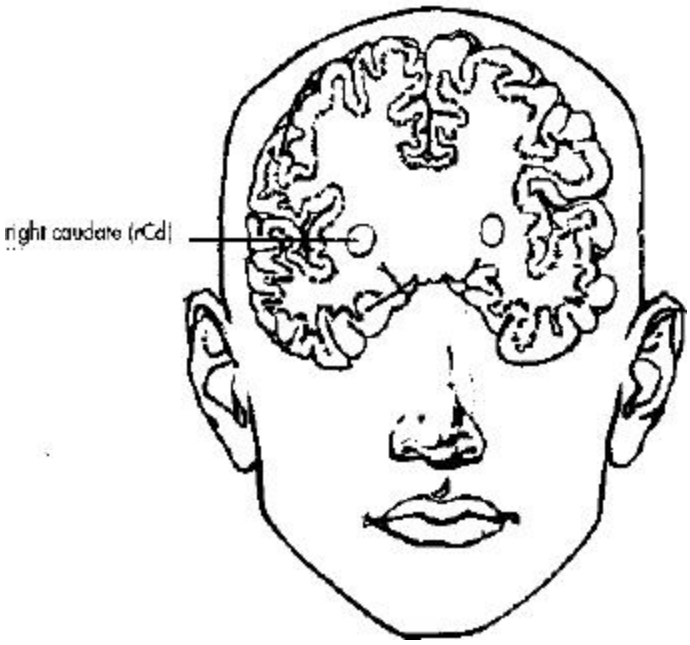


Figure 3. PET scan showing decreased energy use in the right caudate nucleus (which appears on the left side in a PET scan) in a person with OCD after successful treatment with the Four-Step Method. PRE shows the brain before and POST ten weeks after behavioral therapy with no medication. Note the decrease in "size," which signifies decrease in energy use, in the right caudate (rCd) after doing the Four-Step Method. The drawings show where the caudate nucleus is located inside the head. (All illustrations reprinted from *Brain Lock* © 1996 by Jeffrey M. Schwartz)





This was the first study ever to show that cognitive-behavior therapy—or, indeed, any psychiatric treatment that did not rely on drugs—has the power to change faulty brain chemistry in a well-identified brain circuit. What's more, the therapy had been self-directed, something that was and to a great extent remains anathema to psychology and psychiatry. The changes we detected on PET scans were the kind that neuropsychiatrists might see in patients being treated with powerful mind-altering drugs. We had demonstrated such changes in patients who had, not to put too fine a point on it, changed the way they thought about their thoughts. Self-directed therapy had dramatically and significantly altered brain function. There are now a wealth of brain imaging data supporting the notion that the sort of willful cognitive shift achieved during Refocusing through mindful awareness brings about important changes in brain circuitry as we will see in later chapters.

With this evidence in hand, my group therapy sessions increasingly took on the air of an informal neuroscience seminar. In addition to showing PET scans, I began to lecture patients on the OCD circuit. If the basal ganglia is like a car's transmission—which in OCD patients can stick like the gear shift in an old Plymouth Valiant—what I was showing them was that simply by practicing, they could learn how to shift behavioral gears themselves, changing the functioning of the brain's transmissions. As a result, their OCD symptoms would become less intense, and shifting to an alternative, adaptive behavior would become more automatic. Done regularly, Refocusing strengthens a new automatic circuit and weakens the old, pathological one—training the brain, in effect, to replace old bad habits programmed into the caudate nucleus and basal ganglia with healthy new ones. When the focus of attention shifts, so do patterns of brain activity. (Quantum physics, as we'll see later, is consistent with this.) Regular Refocusing helps patients resist giving in to OCD thoughts and urges because engaging in intentional rather than automatic

behavior—gardening rather than counting cans—puts in play different brain circuitry. Just as the more one performs a compulsive behavior, the more the urge to do it intensifies, so if a patient resists the urge and substitutes an adaptive behavior, the metabolic activity of the caudate, anterior cingulate, orbital frontal cortex, and thalamus changes in beneficial ways. The bottom line, I told my patients, is that Refocusing holds out the tantalizing promise of systematically substituting healthy circuitry for pathological circuitry—of literally reprogramming your brain.

In the winter of 1995–1996, Eda Gorbis began work as cotherapist in my OCD group. Gorbis came by her interest in fears honestly: born and raised in what was then the Soviet Union, she grew up in an atmosphere poisoned by very real threats, yet one where imagined threats thrived, too. Even as a child Gorbis was acutely aware that some of her parents' friends were riddled with anxiety over the dangers inherent in their world, while others seemed immune to them. The question of why—what enabled one person to shrug off real and ever-present threats while another became psychologically crippled by them?—lingered in her mind for years, even after she and her family fled the Soviet Union when Gorbis was a young teenager. She hopscotched to five different countries, before she arrived in the United States and earned the degree in clinical psychology that would let her pursue an answer to the question of her childhood. Baxter and I had just opened the OCD treatment center, and Gorbis signed on as a volunteer.

As had virtually everyone else in the field, she had pored over *Stop Obsessing*, by Edna Foa and Reid Wilson, which laid out the standard behaviorist approach to OCD: expose patients to the "triggers" that cause them distress (have them touch a doorknob if they are obsessed with germs, for instance), but prevent them from engaging in the ritualistic behavior that ordinarily dissipates that distress (prohibit them from running to a sink to wash, in this case). "I had the book like a Bible on my night table," Gorbis said. But even as she practiced what Foa preached, Gorbis had her doubts. "The strict behaviorist approach seemed, to me, a bit too mechanical," she recalls. "It was treating patients as if they had no humanity; it was not recognizing that they had a thinking, feeling mind inside." Despite her doubts, in the autumn of 1995 Gorbis left her family and spent several months with a group of leading behaviorists, including Foa. When she returned to UCLA that winter, she began coleading my OCD group, integrating the Four Steps with her own approach to behavior therapy.

As its reputation grew, the UCLA Four Steps approach began to draw intractable OCD cases from around the United States, people so enslaved by their obsessions and compulsions that they could hardly get through a day, much less hold a job. Yet by blending the Four Steps with standard behavioral therapy methods, Gorbis was achieving a success rate of over 80 percent with no relapse to anything close to pretreatment severity. That compares to Foa's 65 to 75 percent initial success rate (that is, excluding relapse rates, which are significant), and 60 percent or less at other centers toeing the strict behaviorist line. "We were changing the lives of

people who before had been almost totally paralyzed by their OCD," Gorbis says. And she was not removing the rearview mirrors from patients' cars. "Mindfulness became an empowering tool for the patients, giving them—finally—control over their lives," she says. By the late 1990s, the UCLA group was treating hundreds of patients a year, and the Four Steps was at the center of the group practice. It was gratifying to get independent confirmation of the power of this approach in 2002, when Dr. Nili Benazon of Wayne State University published a major study showing that a mindfulness-based cognitive-behavioral method closely related to ours is very effective at treating children with OCD.

As I thought about the therapy sessions, and of how the patients' mental effort and acts of will had the power to regate the circuitry of their brain, a simple but deeply important question arose. What happens at the instant a person decides not to wash her hands, after decades of doing so in response to the false signals from the orbital cortex and despite her anterior cingulate's making her heart race and her gut churn? Why and how does this person switch gears, activating circuits in the dorsal prefrontal cortex connecting to adaptive basal ganglia circuits, rather than the OCD circuits connecting the orbital frontal cortex to the anterior cingulate and caudate? (See Figure 4.) At the instant of activation, both circuits—one encoding your walk to the garden to prune roses, the other a rush to the sink to wash—are ready to go. Yet something in the mind is choosing one brain circuit over another. Something is causing one circuit to become activated and one to remain quiescent. What is that something? William James posed the question this way: "We reach the heart of our inquiry into volition when we ask, by what process is it that the thought of any given action comes to prevail stably in the mind?"

The demonstration that OCD patients can systematically alter their brain chemistry through cognitive-behavioral therapy such as the Four Steps regimen has inescapable implications for theories trying to explain the relationship between mind and brain. As I began to consider how best to make the OCD work relevant to questions of how the mind can change the brain, I became more and more intrigued by the idea that there must be a force to account for the observed brain changes. The willful effort OCD patients generate during treatment, I suspected, was the most reasonable way to account for the generation of this force. The results achieved with OCD supported the notion that the conscious and willful mind differs from the brain and cannot be explained solely and completely by the matter, by the material substance, of the brain. For the first time, hard science—for what could be "harder" than the metabolic activity measured by PET scans?—had weighed in on the side of mind-matter theories that, as explained in the previous chapter, question whether mind is nothing but matter. The changes the Four Steps can produce in the brain offered strong evidence that willful, mindful effort can alter brain function, and that such self-directed brain changes—*neuroplasticity*—are a genuine reality. Let me repeat this: the Four Steps is not merely a self-directed therapy; it is also an avenue to self-directed neuroplasticity.

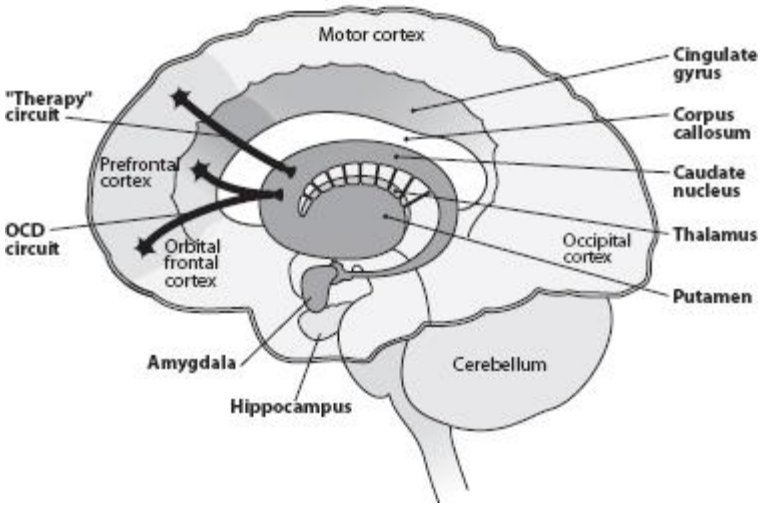


Figure 4: The exertion of willful effort during cognitive-behavioral therapy can activate a "therapy" circuit in the dorsal prefrontal cortex.This can help to override the effects of the OCD circuit.

I anticipated the objections that materialist reductionists would raise. Surely what is happening here, they would say, is that one part of the brain is changing another. The brain is changing itself; there is no need to invoke a separate, nonmaterial entity called mind to account for the changes documented by the PET scans. But a materialist explanation simply cannot account for these findings. To train people suffering from OCD requires tapping into their natural belief in the efficacy of their own willful actions. Explanations based exclusively on materialist causation are both infeasible and inappropriate for conveying to OCD patients the steps they must follow to change their own brain circuitry systematically. In order to work, behavioral medicine (of which the Four Steps is an example) absolutely requires the use of the patient's inner experience, including the directly perceived reality of the causal efficacy of volition. The clinical and physiological results achieved with OCD support the notion that the conscious and willful mind cannot be explained solely and completely by matter, by the material substance of the brain. In other words, the arrow of causation relating brain and mind must be bidirectional. Conscious, volitional decisions and changes in behavior alter the brain. And as we will see, modern quantum physics provides an empirically validated mathematical formalism that can account for the effects of mental processes on brain function.

The demonstrated success of mindfulness-based cognitive-behavioral therapy for OCD led me to posit a new kind of studyable force. I called it directed mental force. It would arise, I thought, from willful effort. What mental force does is activate a neuronal circuit. Once that new circuit begins to fire regularly, an OCD patient does not need as much effort to activate it subsequently; the basal ganglia, responsible for habitual behaviors, take care of that. My still-nascent thesis held that directed mental force is the physical aspect of the willful effort to bring healthy circuitry on line. With regular use of the frontal cortex, changes occur in the gating function of

the caudate, and mental function improves. Relabeling and Refocusing attention begin to be automatic. In this way, frontal cortex thought processes begin to be wired directly into the caudate. As the brain takes over, less mental force is needed.

Mental force needs the brain to express itself. But it is more than brain, and not reducible to brainstuff. In the fractions of a second when the brain might activate either the pathological circuit underlying a dash to the sink to wash or the healthy circuit underlying a stroll to the garden to prune, mental force amplifies activity in the healthy circuit. You can generate a mental force that activates one circuit rather than another. In a more innocent age, we called that will. But the very idea that the brain can change at all, much less that it can change in response to mind, first had to overcome a century-old dogma.