

A GROUNDBREAKING COLLABORATION  
BETWEEN NEUROSCIENCE AND BUDDHISM

*Train Your*  
**MIND**  
*Change Your*  
**BRAIN**

HOW A NEW SCIENCE REVEALS  
OUR EXTRAORDINARY POTENTIAL  
TO TRANSFORM OURSELVES

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**FOREWORD BY THE DALAI LAMA**

**PREFACE BY DANIEL GOLEMAN,**  
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## Thinking Depression

Just as the UCLA scientists were discovering that a mind-based, cognitive therapy can change the brain—that thinking about your thoughts in a certain way can alter the electrical and chemical activity of a brain circuit—science was embroiled in a bitter debate over whether psychotherapy has any effect whatsoever, let alone on the physical structure and activity of the brain. The controversy centered on depression. On December 29, 1987, the U.S. Food and Drug Administration had given the pharmaceutical giant Eli Lilly and Company approval to sell fluoxetine hydrochloride as a treatment for depression. Marketed as Prozac, the drug was featured on the covers of magazines, starred in newspaper stories, inspired bestselling books, and was soon racking up \$2 billion in annual sales. Prozac was not just another drug for depression. It was hailed as a compound that specifically targeted the disease's underlying neurochemical cause, supposedly a paucity of the neurotransmitter serotonin in the brain's synapses. The rise of Prozac coincided with the continuing fall from grace of psychotherapy. Expensive, time-consuming, and the subject of more jokes than rigorous scientific studies, psychotherapy was starting to have the whiff of something as antediluvian as Freud's couch.

Which is not to say that psychotherapists were throwing in the towel. To the contrary. In 1989, scientists reported the results of the most ambitious study ever undertaken to examine the effectiveness of psychotherapy compared to medication in treating depression. Called the Treatment of Depression Collaborative Research Project, this two-year study was funded and organized by the National Institute of Mental Health. Two hundred and fifty outpatients with major depression were randomly assigned to receive one of four treatments: interpersonal psychotherapy, cognitive-behavior therapy, imipramine (a common antidepressant), or an inert pill. In the last two cases, patients also received what is called clinical management, which essentially means they saw a psychiatrist to receive their medication.

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Cognitive-behavior therapy, which was developed in the 1960s, does not dwell on causes of depression. It focuses instead on teaching patients how to handle their emotions, thoughts, and behaviors. The idea is to reappraise dysfunctional thinking, to see the fallacy of thoughts such as "The fact that I was not offered that job means I am doomed to be unemployed and homeless." Patients learn to think about their thoughts differently and not to ruminate endlessly about minor setbacks. Instead of seeing a failed date as evidence that "I am a total loser, and no one will ever love me," patients learn to view it as just one of those things that didn't work out. Instead of seeing a leaky roof as a sign that "nothing will ever go right for me," they think of it as "Stuff happens." They learn to recognize their tendency to magnify disappointments into calamities and mishaps into tragedy, and to test the accuracy of their extreme beliefs. If they are convinced that no one will ever like them, the therapist encourages them to join a social group and strike up a conversation and possibly a friendship. Such reality testing will show patients that they are unrealistically pessimistic. With their newfound cognitive skills, patients can experience sadness and setbacks without being sucked into the black hole of depression.

Interpersonal therapy, on the other hand, recognizes that although depression may not be caused by interpersonal relations or experiences, it affects them. It therefore targets interpersonal disputes and conflicts, role transitions such as becoming an empty nester, and complicated and persistent grief.

In all four groups, patients suffered fewer symptoms of depression over the sixteen weeks of the study. Imipramine produced the greatest improvement in the most severely depressed patients, placebo the least, with the two psychotherapies in between. For patients whose depression was mild to moderate, however, the two psychotherapies produced results on a par with those of the medication. "The power of the cognitive behaviour therapies in [depression] is considerable, certainly equal to the power of the standard drug treatments for depression," Gavin Andrews, professor of psychiatry at the University of New South Wales in

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Australia wrote in the *British Medical Journal* in late 1996. "If these psychological treatments had been drug treatments they would have been certified as effective and safe remedies and be an essential part of the pharmacopoeia of every doctor. As they were not developed by profit making companies, and thus are not marketed or promoted, their use often languishes." Despite this and subsequent studies validating the efficacy of psychotherapy for depression, it has been tough to shake the perception that psychotherapy is ineffective and inferior to medication.

While the NIMH study was under way, a young psychologist named Zindel Segal was studying depression. He recalls of the drugs-versus-psychotherapy debate that "the sides were drawn very sharply. There was a productive fractiousness, with psychologists saying there was good evidence for the efficacy of therapy" but many scientists convinced that psychotherapy has no place in a Prozac world. Rather than attacking the efficacy question straight on, Segal decided to study whether psychotherapy has an effect on a different, but arguably even more important, aspect of depression: the rate of relapse.

Depression is notorious for its frequent and cruel relapses. A patient may finally feel she has broken the chains of her illness, only to plunge back into the abyss of despair, as 50 percent do. Because of the high relapse rate, patients suffer an average of four major episodes of depression lasting about five months each over the course of their lives. "Many people continue to become ill," says Segal. "The typical progression, unfortunately, is that treatment brings relief, but the risk of relapse or recurrence remains high. Sustained recovery from depression is not the rule." Indeed, doctors and patients had begun noticing that antidepressants come with a dark side: unless patients continue taking the medication, they are very likely to suffer a relapse within two years of the initial treatment. Most patients, says Segal, "require treatment beyond the point when their symptoms disappear."

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That was disappointing, of course. But it was also interesting for the possibilities it suggested about the relative benefits of psychotherapy and antidepressants. "The thinking at the time was that psychotherapy, especially cognitive therapy, might produce lasting changes in people's attitudes and beliefs about themselves, which would protect them well after the end of the therapy," says Segal. "Some beliefs make people vulnerable to relapse, like the idea that asking for help is a sign of weakness or that always being right is the way to get others to respect you. If a person with these attitudes suffers a minor setback, even after successful treatment for depression, their explanations for what this means about them—they are weak, they will never be respected—make them more likely to spiral down into depression. What we proposed was that if cognitive therapy could modify these attitudes, then the risk of relapse would be reduced."

That hunch was based on the fact that cognitive therapy is, in essence, a form of mental training. It teaches patients a different way of approaching their thoughts. In the case of depression, those thoughts are, all too often, sad, glum, bleak, or otherwise "dysphoric." Everyone gets those thoughts now and then, of course. What's different in patients with depression is that the thought tips them over the emotional edge into an abyss of negative, hopeless thinking powerful and sustained enough to trigger a full-blown episode of (typically) months-long depression. A setback at work or a romantic rejection escalates to "Nothing will ever go right for me; life is hopeless, and I will always be a complete loser." As described above, cognitive therapy teaches patients to think about these triggering thoughts and feelings so they do not bring on a cascade of depression-triggering thoughts and major depression itself but instead become "short-lived and self-limiting," as John Teasdale of the University of Cambridge, England, suggested.

Here's why cognitive therapy looked as if it might be more efficacious than antidepressants in preventing relapse: the ease with which this type of dysfunctional thinking is triggered by dysphoria reliably predicts the likelihood that a patient will suffer a relapse of depression. If cognitive therapy can break the

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connection between sadness and aberrant, wildly exaggerated extrapolations, maybe it can vanquish the very mechanism that leads to relapse. It was analogous to how Schwartz taught his OCD patients to think about their obsessions as a fleeting misfire of their brain, one they had the power to keep from exploding into pointless and disruptive compulsions. But first, Segal had to see whether the basic hypothesis was right: that sad thoughts unleash beliefs that make people vulnerable to depressive relapse.

So he made people sad. By then head of the Cognitive Behaviour Therapy Clinic at the Center for Addiction and Mental Health in Toronto, he recruited thirty-four people who had been successfully treated for depression within the previous twenty-four months. To induce sadness, he had two surefire methods: asking the volunteers to think about a time when they felt sad and having them listen to Prokofiev's *Russia under the Mongolian Yoke*. Played at half-speed, Segal says, it induces five to ten minutes of deep sadness as reliably as Beth's death scene in *Little Women*.

Once the volunteers were feeling blue, Segal asked them to indicate how much they agreed or disagreed with statements such as "If I fail at my work, then I am a failure as a person," "If someone disagrees with me, it probably indicates he does not like me," "If I don't set the highest standards for myself, I am likely to end up as a second-rate person"—all known to reveal whether someone holds attitudes that make him vulnerable to depressive relapse.

Segal found that when people had been made melancholic by remembering a sad episode in their lives or listening to the brooding Slavic melody, they were much more likely to hold these attitudes. "The experience of depression can establish strong links in the mind between sad moods and ideas of hopelessness and inadequacy," he says. "Through repeated use, this becomes the default option for the mind: it's like mental kindling. Even among recovered depressed patients, the degree to which sad moods 'switch on' these attitudes is a significant predictor

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of whether the patient will relapse eighteen months later." In some people, sad thoughts unleash beliefs that put them at risk for depression.

For these unfortunate souls, successful treatment for depression helps with sleeplessness and other symptoms but leaves their gnawing personal doubt intact. As long as things go well, they can sidestep the doubt. But if they suffer a setback or reversal and become sad, this way of thinking creeps back in: "Yeah, things really are hopeless; I was stupid to believe otherwise," or "I really can't hold on to a relationship; I should just accept that." The acute setback makes them feel hopeless, worthless, unloved—exactly the state of mind that characterizes the deep despair and even paralysis of depression. Their memory works in such a way as to activate these concepts more strongly, and with greater probability, once the emotion of sadness arises. This makes it more likely that the brain's whole depression network will switch on. "The experience of depression imprints a tendency to fall back on certain patterns of thinking and to activate certain networks in working memory," Segal says.

What these patients needed, he realized, was a different way to relate to the inevitable sadness everyone experiences at one time or another, a way that would not let a passing sense of unhappiness (from schmaltzy music, no less) send them tumbling down the rabbit hole of depression. And for that, they needed to forge new neuronal connections.

## Mindfulness and Depression

In 1992, Segal met with Cambridge's John Teasdale and Mark Williams to turn his theory of depressive relapse—that people who hold despairing attitudes are more vulnerable to falling back into depression as a result of minor setbacks—into a treatment. Teasdale, who had been practicing mindfulness meditation for a number of years, had been learning about a mindfulness program developed by Jon

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Kabat-Zinn of the University of Massachusetts, a longtime participant in the Mind and Life Institute's meetings with the Dalai Lama. Although Kabat-Zinn used it mostly for stress reduction, Teasdale saw other possibilities: to harness the power of the mind to treat depression. He suspected that patients might escape repeated descents into clinical depression if they learned to regard depressive thoughts "simply as events in the mind," as he put it. The key would be to help patients become aware of their thoughts and relate to them as merely brain events rather than as absolute truths. Instead of letting a bleak experience or thought kindle another episode of depression as predictably as a spark ignites a fire in bone-dry kindling, instead of allowing their feeling to drag them down into the pit of depression, patients would learn to respond with "Thoughts are not facts" or "I can watch this thought come and go without having to respond to it." That, Teasdale suspected, might break the connection the brain made between momentary unhappy thoughts and the memories, associations, and patterns of thinking that inflate sadness into depression. It would be like putting a wall of asbestos between the spark and the kindling. It would be, literally, rewiring the brain.

The program the scientists developed, called mindfulness-based cognitive therapy, consisted of eight weekly individual sessions, each lasting two hours. Using the mindfulness training pioneered by Kabat-Zinn, the patients steered their attention to one region of the body after another, trying to focus intently on the sensations their hand, knee, foot was feeling at that moment. They then learned to focus on their breathing. If their mind wandered, they were to acknowledge it with "friendly awareness"—not frustration or anger—and focus once again on the breath, which served as a magnet pulling them back to mindful awareness of the moment. The patients also practiced at home, trying to notice their thoughts impartially rather than reacting to them, and regarding their feelings and thoughts (especially the bleak, despairing ones) as merely transient mental events that happen to "come and go through the mind" and that are no more significant than a

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butterfly floating into your field of vision. Most crucially, they kept telling themselves that the thoughts did not reflect reality.

To assess the power of mindfulness to prevent the relapse of depression, Teasdale, Segal, and Williams randomly assigned half of their 145 patients (all of whom had suffered at least one past episode of major depression in the previous five years) to receive mindfulness-based cognitive therapy and half to receive their usual care. After eight weeks of mindfulness-based treatment, the scientists followed the patients for an additional year.

Treatment as usual left 34 percent of the patients free of relapse. With mindfulness-based cognitive therapy, 66 percent remained relapse-free, Teasdale and his colleagues reported in 2000. That translates to a 44 percent reduction in the risk of relapse among those who received mindfulness-based cognitive therapy compared to those receiving usual care. Interestingly, the preventive effect of mindfulness was found only in patients who had suffered three or more past episodes of depression, who made up three-fourths of the sample. These were not easy patients. They had what is called a recurrent form of depression and suffered many, many depressive episodes. Yet mindfulness-based cognitive therapy nearly halved the rate of relapse. This was the first evidence that mental training can reduce the rate of relapse in depression.

In 2004, Teasdale and his colleague Helen Ma replicated the findings, showing again that mindfulness-based cognitive therapy reduced relapse. This time, in a study of fifty-five patients, they found that for patients with three or more episodes of major depression, the rate of relapse fell from 78 percent in the treatment-as-usual group to 36 percent in the mindfulness-based cognitive therapy group. "Mindfulness-based cognitive therapy," they concluded, "is an effective and efficient way to prevent relapse/recurrence in recovered depressed patients with three or more previous episodes." Or as Segal put it, "There are modes of thinking which are more easily triggered the more they're accessed. Mindfulness works to keep you from triggering the depression network." By monitoring their own

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thoughts, patients who practice mindfulness are able to keep the dysfunctional products of their mind from cascading into full-blown depression.

You don't have to believe in any spooky power of mind over brain to guess what might be happening in these patients. Somehow, mental training was altering brain circuits, in what we might call top-down plasticity, since it originates in the brain's cognitive processes. ("Bottom-up" plasticity is the kind that arises when plain old sensory inputs resculpt the brain, as they do when dyslexic children hear specially crafted sounds or lab monkeys carry out a repetitive finger motion.) Brain-imaging technology would show precisely how mindfulness meditation was training the mind to alter brain circuitry.

## Changing the Depressed Brain

Neuroscientist Helen Mayberg had not endeared herself to the pharmaceutical industry by discovering, in 2002, that antidepressants and inert pills—placebos—have identical effects on the brains of depressed people. In patients who recover, whether their treatment consisted of one of the widely prescribed selective serotonin reuptake inhibitors (SSRIs) such as Paxil or a placebo that they *thought* was an antidepressant, brain activity changed in the same way, she and colleagues at the University of Texas Health Science Center, San Antonio, found: according to fMRI scans, activity in the cortex increased and activity in limbic regions fell. Based on that finding, she figured that cognitive-behavior therapy would act via the same mechanism. Soon after the University of Toronto recruited her away from Texas; she therefore asked Zindel Segal to collaborate on a study to see whether there are differences between how cognitive-behavior therapy and antidepressants affect the brain.

"I definitely expected there must be a common pathway," Mayberg said. "I'd thought about doing psychotherapy while I was at Texas, but there was no one

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qualified to work with me on a study like that. But in Toronto, I met Zindel. It was like a gift."

The Toronto scientists first used PET imaging to measure activity in the brains of depressed patients. Then they had fourteen depressed adults undergo fifteen to twenty sessions of cognitive-behavior therapy. Thirteen other patients received paroxetine (the generic name of the antidepressant sold as Paxil by GlaxoSmithKline). All twenty-seven had depression of approximately equal severity and experienced comparable improvement after treatment. Then the scientists scanned the patients' brains again. "Our hypothesis was, if you do well with treatment for depression, your brain will have changed in the same way no matter which treatment you received," says Segal.

Mayberg's study showing that the brain's response to placebo and to antidepressant has the same pathway had made her expect that there is only one route through brain circuitry from depression to recovery. But no. "We were totally dead wrong," she said. Depressed brains responded differently to the two kinds of treatment. Cognitive-behavior therapy muted over-activity in the frontal cortex, the seat of reasoning, logic, analysis, and higher thought—as well as of endless rumination about that disastrous date. Paroxetine, in contrast, raised activity there. Cognitive-behavior therapy raised activity in the hippocampus of the limbic system, the brain's emotion center. Paroxetine lowered activity there.

The differences were so dramatic that Mayberg "thought we were doing something wrong in how we were analyzing the data," she said. "With cognitive-behavior therapy, activity in the frontal cortex was turned down, activity in the hippocampus was turned up—it was the opposite pattern of antidepressants. Cognitive therapy targets the cortex, the thinking brain, reshaping how you process information and changing your thinking pattern. We finally convinced ourselves that it wasn't a technical error."

Putting it in terms of mind rather than brain, cognitive-behavior therapy "decreases rumination, decreases the personal relevance of triggers that once tipped

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you into depression, increases reappraisal of thoughts," Mayberg explains. "Does a lousy date really mean that I am a failure as a human being and will never be loved? Cognitive-behavior therapy also increases new patterns of learning, as reflected in the increased activity in the hippocampus, the brain structure associated with the formation of new memories. It trains the brain to adopt different thinking circuits, to switch off ruminative modes of thinking, and to practice relating differently to negative thoughts and feeling. Cognitive-behavior therapy works from the top down, and drugs work from the bottom up," modulating different components of the depression circuit. Mindfulness-based cognitive therapy keeps the depression circuit from being completed.

It may seem surprising that mindfulness-based cognitive therapy should work so well in depression, targeting a system quite different from what a barrage of commercials and friendly media coverage have insisted is the basis for depression—namely, a shortage of the neurochemical serotonin. From the development of the first drug, Prozac, that apparently acted by keeping serotonin from being eliminated from the brain's synapses, it has been drummed into our heads that depression reflects a biochemical imbalance and that Prozac or another SSRI is the avenue to recovery. After the arrival of Prozac was greeted like the second coming of penicillin, however, reality set in. Prozac takes several weeks to work, when it works at all (some one-third of patients with depression do not respond to it). It has a high relapse rate, and many patients seem to need to stay on the drug forever.

"Massive marketing has depicted the challenge in depression as one of correcting a chemical imbalance in the brain," says Zindel Segal. "This may be true at the neural level, but we now know that there are multiple pathways to recovery, and a chemical imbalance itself can be restored in different ways."