The Best Medicine?

How drugs stack up against talk therapy for the treatment of depression

BY HAL ARKOWITZ AND SCOTT O. LILIENFELD

IMAGINE a treatment for depression that possesses the following properties: It is as effective as antidepressant medications but lacks their side effects. Its therapeutic results last longer than those of antidepressant medications after treatment has ended. Its benefits generalize to many domains of life. It causes changes in the brain in processes associated with depression. It usually needs to be administered only once a week. It generally costs the same or less than medications. Sound too good to be true? In fact, such a treatment has been around for decades, although many people do not know about it. It is called psychotherapy.

Why are so many people unaware of these facts? One reason is that pharmaceutical companies have huge advertising budgets to aggressively market antidepressant medications to the public and to the physicians who write prescriptions. In contrast, psychotherapists have little or no budget for marketing. In this column, we will try to level the playing field by providing a scorecard of how antidepressants compare with psychotherapies.

Antidepressants: Pros and Cons

Although a number of different classes of antidepressants exist, we will focus on the most commonly prescribed class today: SSRIs, or selective serotonin reuptake inhibitors [*see box on opposite page*].

People who take antidepressants usually do not show improvement for two to four weeks. For any given individual, some antidepressants work better than others; no one antidepressant has been shown to be more effective than any other at a group level. Many people undergoing treatment for depression try two or three SSRIs (or other antidepressants) before they find one that works and that has tolerable side effects. Studies find that about 50 to 70 percent of those who take SSRIs are responders, showing a 50 percent or greater reduction in symptoms. For some clients, depression is better but still present, whereas others become symptom-free. Residual symptoms after treatment are problematic because they signal a significant risk factor for a repeat depression.

After therapeutic effects appear, clients are usually told to continue on the drug for at least an additional six to 12 months to prevent relapse. If patients have had several previous episodes or if their depression is severe,

Imagine a treatment for depression that is as effective as antidepressant medications but **lacks their side effects**.

COURTESY OF HAL ARKOWITZ (*top*); COURTESY OF SCOTT O. LILIENFELD (*bottom*); GETTY IMAGES (*illustration*)

Some studies have shown that combining psychotherapy and medications is **more effective than either alone** for adults.

they may be told to remain on the drug longer to avoid recurrence of depression. Using antidepressants for maintenance in this way reduces the relapse rate as compared with a placebo. Save for Prozac, antidepressant therapy has *not* been shown to be effective for children and adolescents and may not be safe for a small percentage of people younger than 24 years old, as we discussed in our last column, "Can Antidepressants Cause Suicide?" [Scientific American Mind, August/September 2007]. In addition, antidepressants can cause fetal damage, so pregnant women are strongly advised not to take them.

In most drug trials, all patients receive the same antidepressant. In the real world, however, psychiatrists often try a different medication if one prescription does not work. A recent study by A. John Rush of the University of Texas Southwestern Medical Center and his colleagues more closely approximated how SSRIs are used in practice. The researchers presented depressed patients with a four-step set of options to be used if necessary. All subjects started on the same antidepressant (Celexa). At each of three subsequent steps, those who either did not respond or could not tolerate the side effects got a menu of options, which included changing medication, adding medication, or adding or switching to cognitive-behavior therapy (CBT). This study yielded an overall remission rate of 67 percent, far superior to that of most studies that show remission rates (excluding improvement rates) of closer to 33 percent.

Some studies of adults have shown that combining psychotherapy and medications is more effective than either treatment alone. Further, several studies with adults have found that drug therapy may be more effective than psychotherapy for severe depressions, although the evidence on this point is mixed.

The Scoop on Psychotherapy

Despite the voluminous research on psychotherapy as a treatment for depression, scientists have evaluated only a few types of psychotherapy. CBT has been the most extensively studied by far. Such therapies teach and encourage new behaviors and help people change excessively negative thinking. Interpersonal psychotherapy (IPT) has the second greatest amount of supporting data. Research on other therapies, such as short-term psychodynamic therapy, client-centered therapy and emotion-focused therapy, has just begun, but outcomes in these few studies have been positive [*see box below*]. In the remainder of this column, our discussion of psychotherapy refers to those practices that have been supported by research.

Antidepressants and Common Side Effects

Selective serotonin reuptake inhibitors, or SSRIs, can relieve depression but can have drawbacks.

Trade name	Chemical name
Paxil	paroxetine
Prozac	fluoxetine
Lexapro	escitalopram
Celexa	citalopram
Zoloft	sertraline

Common Side Effects of SSRIs

- **Short-term** (lasting a few weeks): nausea, diarrhea, nervousness and insomnia
- **Long-term** (lasting months or longer): low sexual desire or sexual dysfunction (in 50 to 75 percent of patients) and sedation

Research-Supported Psychotherapies

Scientists have evaluated only a few types of psychotherapy. The most supporting data exist for cognitive-behavior therapy and interpersonal psychotherapy, which have been shown to be effective in treating depression. Only a few studies have examined the performance of the other three therapies listed below, but their outcomes are encouraging.

Name	Approach
Cognitive-behavior therapy	Teaches and encourages new behaviors to help people change overly negative thinking
Interpersonal psychotherapy	Focuses on the social difficulties and conflicts associated with depression
Short-term psychodynamic therapy	Emphasizes understanding and correction of problematic interpersonal patterns
Client-centered therapy	Emphasizes the therapeutic potential of the therapist-client relationship
Emotion-focused therapy	Builds on client-centered therapy by adding a focus on increasing awareness of thoughts and feelings and resolving persistent and problematic emotional reactions

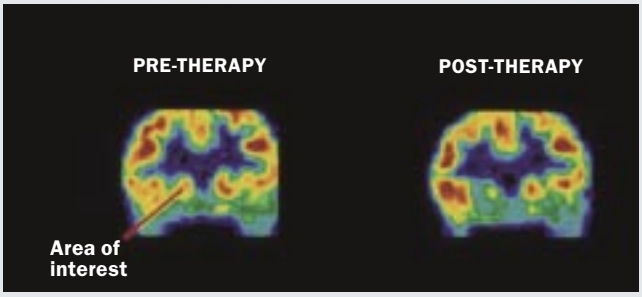
The findings regarding the efficacy of CBT are remarkably similar to those of most SSRI studies. Approximately two thirds of patients who undergo 12 to 16 sessions of CBT show improvement or remission. (The reason therapy costs the same or less than medications is largely because people are usually on antidepressants far longer than they are in psychotherapy.) So far most comparisons among different therapies have shown them to be about equally effective. As of this writing, however, no studies of psychotherapy have adopted the multistage approach used by Rush and his colleagues with antidepressants; in practice, psychotherapists often switch strategies if the one they are using is not working. Because psychotherapy studies use only one approach for purposes of experimental control, they may underestimate the efficacy of psychotherapy for depression, although that conjecture awaits formal research.

Numerous studies have demonstrated that after treatment has ended, patients treated with medication alone relapse at *twice* the rate of those treated with CBT alone. Further, dropout rates for antidepressant treatments are two to three times as high as those for CBT, with one large-scale study finding a 72 percent dropout rate for antidepressants by 90 days of use. Recovered patients who had received antidepressants and continued on them for maintenance showed relapse rates roughly equivalent to those who had completed CBT with no further treatment. These findings suggest that CBT may address some of the underlying causal processes better than medication does or that it may provide patients with coping skills that let them deal better with life events. In contrast, antidepressant treatments may be more palliative, suppressing symptoms for as long as the medications are taken. Even so, approximately half of those who respond to CBT relapse within two years, suggesting that we psychologists still have our work cut out for us. CBT researchers are working on ways to further reduce post-treatment relapse. For example, recent studies have found that an eight-session group booster treatment known as mindfulness-based cognitive therapy given to recovered depressed patients during the year after the end of initial treatment reduces relapse for those who have had three or more episodes of depression.

In depressed children and adolescents, only one of the antidepressants

Psychotherapy and the Brain

Drug company marketing suggests that depression is caused by a "chemical imbalance" in the brain. For example, an advertisement by the maker of the selective serotonin reuptake inhibitor (SSRI) Zoloft states: "While the cause is unknown, depression may be related to an imbalance of natural chemicals between nerve cells in the brain. Prescription Zoloft works to correct this imbalance." The imbalance to which the SSRI ads refer is a deficit of the neurotransmitter serotonin at receptor sites in the brain. Such advertising is misleading, however, and does *not* reflect scientific findings. There is no clear scientific evidence that neurotransmitter deficits cause depression or that there is an optimal "balance" of neurotransmitter levels in the brain. Moreover, medications that primarily affect chemical messengers other than serotonin are as effective as SSRIs.



PET images of a patient with obsessive-compulsive disorder before (*left*) and after (*right*) successful psychotherapy show decreases in glucose metabolic rates. Such brain changes have also been found in depressed patients who have received therapy.

Undoubtedly, antidepressants are helpful in alleviating depression. But there is a form of circular reasoning that goes: if SSRIs are helpful in alleviating depression, and if they do change the "chemical imbalance," then depression must be caused by that imbalance. Inferring causality from the success of a treatment is frequently a flawed endeavor: aspirin is effective for headaches, but no one would seriously claim that headaches are caused by a deficiency of aspirin.

In addition, biological treatments are not unique in their ability to cause changes in the brain. Using neuroimaging techniques, many studies have shown significant brain changes in patients treated with psychotherapy alone. One study with depressed patients demonstrated that cognitive-behavior therapy led to decreased activity in the frontal regions of the brain, some of which may be related to rumination, a common feature of depression. Some studies have found brain changes identical to those caused by antidepressant medications, whereas others have found different brain changes. These findings support the idea that psychotherapy produces measurable changes in the brain, although these modifications may sometimes differ from those produced by medication.

—H.A. and S.O.L.

SOURCE: LEWIS R. BAXTER, JR., ET AL.

(Prozac) has been shown to help, whereas several different types of psychotherapies have proved beneficial. In both cases, however, treatment effects have been only moderate. The results of studies on the combination of drug therapy and psychotherapy for these populations show either no advantage or a slight advantage for the combination over either single treatment.

Although results are somewhat mixed, most of the evidence suggests that combined psychotherapy and drug treatments are more effective for adults but not necessarily for children and adolescents. One well-designed large-scale study in chronically depressed adults compared a non-SSRI antidepressant medication, a modified form of CBT that emphasized changing interpersonal relationship patterns and negative thinking, as well as their combination. Whereas response rates for each of the single treatments were comparable to those usually obtained in depression treatment studies, the response rate for the combination treatment was a dramatic 85 percent!

Putting It Together

Antidepressant medication and certain forms of psychotherapy are reasonably effective for the treatment of adult depression, but there is considerable room for improvement in initial response rates and relapse rates. Response rates (improvement or remission) for both treatments average at around two thirds. This means that many people are helped but are left with some depressive symptoms, whereas others are not helped at all. The combination of psychotherapy and drug therapy may yield better outcomes for adults but little or no added benefits for children and adolescents. Although psychotherapy leads to half the relapse rate of drug therapy over a two-year follow-up period, relapse rates for both remain disturbingly high.

Psychotherapy, drug therapy and a combination of the two are all helpful for adult depression, but effects are weaker in children and adolescents who are depressed. Drug therapy may be better for some people, psychotherapy for others, and the combination for others still. We do not know which people will respond best to any given treatment. Moreover, many other important questions remain unanswered. Would longer psychotherapeutic treatments such as those typically used in clinical practice lead to better initial outcomes than those that result from the short-term psychotherapies that have been researched so far? Would a sequential strategy such as that used by Rush and his associates for drug therapy improve psychotherapy outcomes? What can we do to further reduce or eliminate relapse? Are some treatments better for some types of people and depression than for others?

So, to the bottom line. We have learned that psychotherapy and drug therapy are both fairly effective. We know that psychotherapy prevents relapse better than drug therapy does when treatment is discontinued, that there are few, if any, negative side effects of psychotherapy, and that psychotherapy is a safe and moderately effective treatment for depressed children and adolescents. It also can change the biology associated with depression [*see box on opposite page*]. CBT and IPT (the two best empirically supported therapies for depression) and possibly other psychotherapies with some empirical support should be seriously considered for a depressed person seeking treatment. If the response to psychotherapy is not adequate, other types of psychotherapy may be tried or a drug regimen may be added. Although the combination of psychotherapy and drug therapy may be somewhat more effective than either alone, drug side effects can be problematic.

We hope that the information we have provided will counter some of the mistaken impressions fueled by the marketing strategies of some drug companies and that it will encourage readers to think of psychotherapy as a viable treatment for depression that has several advantages over drug therapy. M

Many studies have shown significant **brain changes** in patients treated with psychotherapy alone.

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(Further Reading)

- **Psychotherapy and Medication in the Treatment of Adult and Geriatric Depression: Which Monotherapy or Combined Treatment?** S. D. Hollon, R. B. Jarrett, A. A. Nierenberg, M. E. Thase, M. Trivedi and A. J. Rush in *Journal of Clinical Psychiatry,* Vol. 66, No. 4, pages 455–468; 2005.
- **The Empirical Status of Cognitive-Behavioral Therapy: A Review of Meta-analyses.** A. C. Butler, J. E. Chapman, E. M. Forman and A. T. Beck in *Clinical Psychology Review,* Vol. 26, No. 1, pages 17–31; 2006.