

Efficacy of antidepression drugs challenged

A controversial new report challenges the view of many psychiatrists that antidepressant drugs act as powerful depression-busters. Standard antidepressants, as well as the new generation of antidepressants such as fluoxetine (Prozac), ease depression only about as well as or slightly better than placebo pills, contend psychologist Roger P. Greenberg of the State University of New York Health Science Center at Syracuse and his colleagues.

"The efficacy of antidepressants and other psychoactive drugs has been inflated because of problems with study designs," asserts SUNY psychiatrist Seymour Fisher, a collaborator on the project. Critics, however, say the new study is itself flawed by design problems.

Since psychological factors generate noticeable improvements among many depressed individuals given placebos, similar factors must also contribute to the comparable effectiveness of antidepressants, Greenberg's group argues in the October *JOURNAL OF CONSULTING AND CLINICAL PSYCHOLOGY*.

The fatal flaw in most antidepressant studies concerns the inability to keep participants and clinicians truly "blind" to who gets an active drug and who gets a placebo, the researchers hold. Physical reactions and side effects induced by antidepressants often stand in stark contrast to placebo treatment, they note.

More informative, but much rarer studies compare the effectiveness of a newer antidepressant with two control groups, one receiving a standard antidepressant and the other receiving a placebo, according to Greenberg and his associates. With this strategy, it becomes harder to identify recipients of active drugs based on side effects (which occur less often with newer antidepressants), and the experimenters' vested interest in establishing the efficacy of the standard drugs lessens, they maintain.

Greenberg's group used a statistical technique known as meta-analysis to combine the results of 22 independent antidepressant studies that included dual control groups. Participants in the studies suffered from moderate to severe depression. For both standard and newer antidepressants, clinicians reported modest patient improvement beyond that obtained with placebos, while patient ratings revealed roughly equal effectiveness for drugs and placebos.

This finding held steady when the researchers controlled statistically for the ratio of men to women in the sample, drug dosage, age of participants, and severity of depression.

Until larger studies with appropriate controls appear, claims that antidepressant drugs quell depression "need to be conservative," Greenberg's group asserts.

Several studies suggest that cases of severe depression with no clear external cause and featuring disturbances of sleep and endocrine function prove highly responsive to antidepressants, writes psychologist Michael Feinberg of Hahnemann University in Philadelphia in a comment accompanying the new report.

However, such patients did not derive any special benefits from antidepressants in the meta-analysis, responds Fisher.

Psychiatrist David J. Kupfer of the University of Pittsburgh disputes the methods used by Greenberg and his co-work-

ers. Their analysis relied on studies ranging from three to six weeks long, but researchers must track patients for at least eight weeks to gauge accurately the effectiveness of antidepressants, Kupfer argues. Moreover, Greenberg's group chose studies that examined the least effective of the newer antidepressants rather than the widely prescribed Prozac, he adds.

No evidence suggests that longer antidepressant studies would yield different results, Fisher contends. And Prozac proves about as effective as other antidepressants, according to an unpublished meta-analysis by Greenberg and Fisher of more than a dozen fluoxetine studies.

— B. Bower

Trickling grains, sandpiles, and avalanches

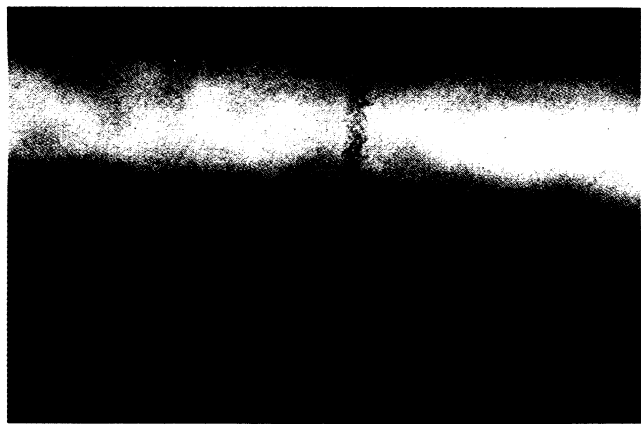
The slow trickle of sand through an hourglass produces more than just a neat, conical sandpile. Close observation reveals a rich array of phenomena, among them the occurrence of miniature avalanches triggered by newly fallen grains and the seemingly automatic settling of particles into a pile with a characteristic slope.

To help illuminate the details of sandpile formation, physicist Franco M. Nori and his co-workers at the University of Michigan in Ann Arbor devised an apparatus that considerably reduces the speed at which grains of sand arrive at a pile's surface. Such a deposition strategy allows the researchers to concentrate on the subtle rearrangements and tiny avalanches that occur when grains arrive at very low speeds.

The apparatus they use to demonstrate "two-dimensional" sandpile formation consists of a strip of sand at the top, a layer of air bubbles in the middle, and a liquid at the bottom, all sandwiched between two parallel, vertical glass plates. The air bubbles act as a valve, trapping the sand so that only a few grains at a time can escape through a small gap among the bubbles into the liquid layer. The released grains then drift slowly down through the liquid and gradually build up into a sandpile.

As shown in the photograph, the deposited sand grains (of two different colors) rearrange themselves and settle so that the angle of the sandpile slope maintains a characteristic value.

To track avalanches, Nori's group used another apparatus, consisting of a high-walled acrylic tray containing a thick layer of tiny beads, that operates somewhat like the back of a dump truck. By



Formation of a sandpile by slow deposition of grains.

electronically recording any changes in the appearance of the bead surface, the researchers could monitor the movement of even one or two beads as the tray's tilt angle slowly increased and the beads rearranged themselves.

As reported in a paper scheduled for the Oct. 12 *PHYSICAL REVIEW LETTERS*, Nori and his colleagues obtained clear evidence that grain rearrangements occur via avalanches of varying sizes. Large slides involving most or all of the upper grain layer periodically "reset" the bead bed to its characteristic slope. But a sequence of smaller, "precursor" avalanches—most of which take place on the slope's upper half—also occurs between these large slides.

Previous experiments by other groups had produced contradictory or inconclusive results on the distribution and size of avalanches in the formation of sandpiles (*SN*: 7/15/89, p.40). However, such factors as humidity, the types of grains used, and the speed and rate of deposition apparently influenced the findings. Moreover, most earlier experiments measured only those avalanches in which grains moved all the way down and off a slope.

"Results are often hard to reproduce because there are so many different variables involved," Nori says. "There's nothing simple about a sandpile." — I. Peterson