NEWS**FOCUS**

Talking Back to Madness

As the search for genes and new drugs for schizophrenia stalls, psychotherapies are getting new attention

NEW YORK CITY AND NEWCASTLE, U.K.— Terry was 13, a lonely African-American boy growing up in a troubled home in Detroit, when he first heard the voices. They were ugly and mean. The voices said he was no good, that no one loved him, and that he should kill himself. So he tried his best: When he was 15, he took 30 Valium pills and had to have his stomach pumped. Then the voices commanded him to kill his father. They told him exactly how to do it put rat poison in his food. Fortunately, some other, gentler voices intervened and told him not to.

After high school, Terry began attending university in Detroit, but that didn't last long. Still haunted by the voices, he was soon addicted to heroin, and his marriage ended in divorce. In 1980, he moved to New York, looking for a new start. He got a job at a doughnut shop, then at a community center, but eventually the voices got worse and so did his drug habit. He found another woman to be with, but she

Waking nightmare. People suffering from schizophrenia often have hallucinations, delusions, and severe emotional problems.

was also taking drugs, and eventually abandoned Terry and their two daughters.

Terry (not his real name), now 60, is telling me his story over lunch at a restaurant on 42nd Street, across from Grand Central Terminal. He's tall and stocky, with kind eyes and a gentle sense of humor that mask his tortured soul. But things are better for Terry now. About 14 years ago, he met the psychotherapist he credits with saving his life. During a drug-fueled crisis, with the ugly voices raging in his head, his eldest daughter checked him into New York Methodist Hospital in Brooklyn, where psychologist Jessica Arenella was working. "I was there 6 weeks," Terry says. "She would sit by my bedside, listening to me rambling on."

Four years later he was hospitalized again, just when Arenella was about to go into private practice. She suggested that he start seeing her. "I said, 'You're a white bitch, how the hell can you help me?"" Terry recalls. "She said, 'I may be a white bitch, but I can back my play with you.' She was tough."

Terry has been seeing Arenella for psychotherapy sessions for the past decade. The voices haven't entirely gone away, he says, but she has taught him how to live with them, and how to follow the gentle voices and ignore the nasty ones. "Without Jessica, I wouldn't have made it," Terry says.

Terry is suffering from schizoaffective disorder, one of a number of so-called schizophrenia spectrum disorders. By treating his psychosis with "talk" psychotherapy, Arenella, along with a small number of other psychologists and psychiatrists, is bucking a decades-old trend, in which antipsychotic drugs have long been seen as the first line of defense against the illnesses. In a radical departure, Arenella and other advocates of psychological approaches are engaging with patients' symptoms, such as hearing voices or experiencing hallucinations or paranoid fantasies, and taking them seriously rather than dismissing them or relying on medication to stamp them out.

A number of clinical trials of these techniques have shown modest but measurable effects on symptoms such as hallucinations and delusions. One of these, a short-term approach called cognitive service approa approach called cognitive behavioral ther-

A Sample of Recent Clinical Trials

Year and authors	Subjects	Treatment type	Results
2010 Lynch <i>et al.</i>	Meta-analysis of nine trials with schizophrenia patients	CBT vs. counseling, "befriending," psycho-education, and other psychological interventions	CBT not more effective in reducing symptoms or preventing relapse
2011 Seikkula <i>et al.</i>	117 patients having first episode of psychosis	Family therapy and intense community support	81% recovery rate after 24 months
2011 Wykes <i>et al.</i>	Meta-analysis of 40 studies of remediation for cognitive problems	Cognitive remediation therapy	Moderate effectiveness
2012 Van der Gaag <i>et al.</i>	201 people at high risk of psychosis	CBT + TAU vs. TAU	Significant reduction in transition to psychosis after 18 months
2012 Grant <i>et al.</i>	60 "low-functioning" schizophrenia patients with severe social/emotional problems	CBT + TAU vs. TAU	Moderate to strong improvement after 18 months
2012 Rosenbaum et al.	269 patients having first episode of schizophrenia	Psychodynamic therapy + TAU vs. TAU	Significant improve- ment in symptoms after 24 months
2012 Jones <i>et al.</i>	Cochrane review of 20 previous trials	CBT vs. other "talking" therapy treatments	CBT not better on symptoms but better on relieving distress
2014 Jauhar <i>et al.</i>	Meta-analysis of 52 previous studies	CBT	CBT has "small" effect on symptoms
2014 Turner <i>et al.</i>	Meta-analysis of 48 previous studies	CBT, "befriending," cognitive remediation, etc.	CBT significantly more effective
2014 Morrison <i>et al.</i>	74 people with psychotic symptoms but not taking medication	CBT + TAU vs. TAU	Moderate reduction of symptoms after 18 months
CBT = cognitive behavioral therapy		TAU = treatment as usual	

Jury still out. Psychological treatments for psychosis have shown moderately positive results in many, but by no means all, published studies.

nia, and long-term psychotherapy has been adopted as standard treatment in a number of Scandinavian communities. It's generally combined with traditional drug treatment, but one study, published earlier this year, suggests that CBT could substitute for antipsychotic drugs in some cases. "There is a strong possibility that psychological treatments are likely to be at least as effective as drugs, and they are certainly preferred by patients," says Peter Tyrer, a psychiatrist at Imperial College London.

Nevertheless, the idea that schizophrenia, long regarded as a disease of the brain, can be treated psychologically remains very controversial, and some are not swayed by the recent clinical trials. "These studies have no more credibility than studies of homeopathy," says Keith Laws, a psychologist at the University of Hertfordshire in Hatfield, U.K., and

co-author of a recent meta-analysis concluding that CBT has only a very small effect on psychotic symptoms.

Stress and vulnerability

About 1% of people worldwide fall victim to schizophrenia or a related disorder over their lifetimes. They may suffer both "positive" symptoms, such as hallucinations and delusions, and "negative" symptoms, such as emotional withdrawal and severe inability to focus on daily tasks.

Most schizophrenia experts subscribe to the stress-vulnerability model of the disorder, in which some individuals have a greater predisposition-either because of genes, childhood trauma, or environmental factors-to psychosis than others. In vulnerable people, psychotic episodes are often set off by some sort of stressful event, usually in the late teens or early adulthood.

But past psychological approaches, such as psychoanalysis, have shown limited success in treating the disease. Sigmund Freud, the founder of psychoanalysis, eventually gave up on using it to treat psychotic patients, although a number of later post-Freudian psychiatrists continued to use it with sporadic success. When antipsychotic drugs arrived

in the 1950s, with their clear ability to dampen the worst psychotic symptoms, psychotherapy became increasingly marginalized.

Drugs have serious side effects, however, and at least 50% of patients either refuse or fail to take them, according to recent studies. Moreover, the search for genes behind schizophrenia and other mental illnesses, which might lead to new drug therapies, has failed to produce any smoking guns and has led only to the discovery of a large number of genetic variants, each conferring a

very small additional risk. "We're trying to fix something, but we don't know what's broken," says Brian Koehler, a psychologist at New York University in New York City who also sees schizophrenia patients in private practice.

Now, psychological treatments are gaining ground again. Most advocates of psychotherapies insist they are not claiming that schizophrenia is purely a psychological malady caused by a dysfunctional family background. "We're looking for a much more nuanced form of psychiatry that doesn't reject biology, but that is able to situate the biology within the realm of lived human experience, which is socially and culturally determined," says psychiatrist Pat Bracken, director of mental health at Bantry General Hospital in Ireland.

Today's psychotherapists use two main approaches to treat schizophrenia. The first, called psychodynamic therapy, is derived from earlier psychoanalytic techniques but discards older Freudian ideas that sexual repression is behind psychosis. Instead, it focuses on both childhood experiences and the way that psychotic symptoms unconsciously serve a useful function for the patient, for example, by masking unbearably painful thoughts and feelings.

Psychodynamic sessions typically go on for many years, as in Terry's case, and scientific evidence for their benefits is limited. Although anecdotal stories of success abound, advocates of psychodynamic therapy increasingly recognize the importance of rigorous trials. "We live in an evidence-based era, we can't duck out of that," says Brian Martindale, a U.K.-based psychiatrist and chair of the International Society for Psychological and Social Approaches to Psychosis.

The gold standard for medical evidence

is the randomized controlled trial, and

these have been difficult to design for psycho-

dynamic treatment. For one, the treatment is

lengthy and costly, and few patients receive

it—thus making adequate sample sizes difficult to assemble. But one influ-

ential study, led by psychiatrist Bent

Rosenbaum of the University of Copenha-

gen and published in the journal Psychiatry

in 2012, did find signs that it is effective.

Rosenbaum's study compared 150 patients

receiving what is often called treatment as

usual (TAU)-including meetings, edu-

cation about their condition, and low

doses of antipsychotic medication-with

119 patients who also received intense

psychodynamic therapy. After 2 years,

both groups had improved, but the psycho-

dynamic cohort achieved markedly greater

such improvements last after the treat-

ment ends, and whether they are really

due to the treatment or, as psychiatrist

Richard Warner of the University of

Colorado, Boulder, puts it, "because they had

contact with a human being who was kind

shorter, more pragmatic method that

takes patients through a series of guided

steps designed to explore alternative inter-

pretations of what he or she is experi-

The second approach, CBT, is a

Still, questions remain about whether

reductions in psychotic symptoms.

and interested in them."

encing, with the goal of changing both outlook and behavior. CBT, which has proven effective for depression and anxiety disorders, typically takes months rather than years, and it has shown more clearcut effectiveness.

"There's always a little bit of truth at the heart of the delusion," explains

Douglas Turkington, a CBT pioneer at Newcastle University in the United Kingdom. "If someone has a funny idea we call a delusion, you have to talk about it and put it on the table." says Ross Tappen, a psychologist at the Manhattan Psychiatric Center in New York City.

And if delusions are taken seriously, Tappen adds, they can often be treated. "A delusion is the



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-DOUGLAS TURKINGTON, **NEWCASTLE UNIVERSITY**

psychological equivalent of an inoperable tumor that is out of control and takes over your normal functioning," he says. "What therapy does, at its best, is to shrink the psychological tumor."

Sandy's CBT

An invisible companion, named John, had been tormenting Sandy (a pseudonym) since he was 10. John would talk and sing loudly, often during the night, keeping him awake. Once, John told Sandy to put the wrong answer on a school exam, and he obeyed. When Sandy, who lives in Britain's Greater Manchester area, was 18, doctors referred him to the Psychosis Research Unit in Manchester, a joint program of the University of Manchester and local mental health services. There he came under the care of psychologist Paul Hutton.

Sandy was convinced that John was real and had nearly complete control over his life. He declined to take medication, but did agree to undergo a series of CBT sessions. Hutton, now at the University of Edin-burgh, was able to figure out that John made Sandy feel less lonely, and also that John was helpful in some situations, taking his side during Sandy's frequent arguments with his parents. But having John in his life convinced Sandy that he was "weird."

Hutton encouraged Sandy to avoid trying to push John away and instead let him 븝 come and go as he pleased. Sandy was also 5

14 MARCH 2014 VOL 343 SCIENCE www.sciencemag.org

taught to test how much control John really had over him with so-called mindfulness exercises in which he remained detached during John's exhortations. Meanwhile, Hutton gave Sandy educational materials indicating that having invisible friends was normal, and that he was not really weird at all. Each week, Sandy was asked to rate how convinced he was that John was real, how often John appeared, and for how long.

With these numbers steadily dropping, by week 4 Sandy agreed to get rid of John entirely. After week 11, he had done so, and the psychotic episode seemed to be over—at least for the time being, as Hutton described in a case study first published online in 2011 in *Behavioural and Cognitive Psychotherapy*.

Hutton concedes that Sandy is "at the positive end of the spectrum" of CBT successes, because he was fairly young and his hallucinations were "very amenable ... to the sort of well-tested approaches we use." But he adds that he often sees "fairly dramatic responses" to CBT.

As early as 2000, Turkington and others published a study of 90 patients in the *Archives of General Psychiatry* showing that while 9 months of either CBT or a sym-

pathetic support technique called befriending could improve both positive and negative schizophrenia symptoms, only the CBT group maintained its improvement 9 months after the trial had ended.

In 2012, another team confirmed that CBT could be effective for so-called negative symptoms of schizophrenia, such as emotional distance, apathy, and social withdrawal, which are usually much harder to treat.

And the most recent CBT trial, published last month in *The Lancet*, concludes that CBT might serve as a substitute for antipsychotic drugs in some cases, rather than just an adjunct to them as in most clinical studies (see *Science*NOW, http://scim.ag/schizCBT). In this study,

74 schizophrenia spectrum patients who were being treated in Manchester and Newcastle, and who had declined to take drugs, were randomized by computer into two groups, one receiving TAU and the other TAU plus CBT.

After 18 months, the CBT group showed

moderately better scores on various tests for psychotic symptoms; indeed, CBT performed about as well as antipsychotic drugs do when compared with placebos, meaning that CBT could substitute for drugs in some situations—especially those in which patients are refusing to take them anyway.

Clinical psychologist Anthony Morrison of the University of Manchester, who led the study, stresses that a drug-free approach might be appropriate only for patients who are relatively high-functioning and have not shown any risk to themselves or others. Nevertheless, the results are "utterly convincing," says Max Birchwood, a psychologist at the University of Warwick in Coventry, U.K.

Other researchers, however, are deeply skeptical of the claims for CBT. In January, a team led by Laws and psychiatrist Peter McKenna, now at the University of Barcelona, concluded in a meta-analysis in *The British Journal of Psychiatry* that past trials of CBT for schizophrenia were seriously flawed. The study found that the differences between treatment and control groups were very small, and that these were reduced further when sources of bias—such as inadequate blinding or masking—were controlled for. "The UK

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> > -JESSICA ARENELLA, PSYCHOLOGIST

government's continued vigorous advocacy of this form of treatment ... might be considered puzzling," the authors wrote, adding that "claims that CBT is effective against these symptoms of the disorder are no longer tenable."

Arenella, who treats Terry and some of her other patients with a combination of psychodynamic and CBT approaches, says that in the end it doesn't matter whether talk therapies work because of the theory behind them or just because someone is taking the patient and their symptoms seriously. "It may be a placebo effect, but I will go for all the placebo effect I can get," she says. "I'll take it."

In the end, the spread of talk therapies for psychosis could be limited by a scarcity of resources, and of therapists willing to try them. Treating such clients is very stressful and seldom financially rewarding. "A lot of people don't want to take these patients," Arenella says. "Working with them is scary. People get violent, people get hurt, computers get thrown to the ground, ceiling tiles get pulled out." And Martindale says that "contact with madness is very disturbing; it conjures up all sorts of feelings."

Government agencies and insurance companies can help by covering such treatments, even though they are more expensive in the long run than drugs, say Arenella and others. They are worth trying, Bracken says. "I have a lot of patients whom I would say recovered from psychosis. I see people who move on with their lives, get their quality of life back, are able to live independently." Indeed, the popular notion that a schizophrenia diagnosis is a life sentence of mental illness is not borne out by the statistics: In one typical study, published in the *American Journal of Psychiatry* in 2004, researchers found

that nearly 50% of firstepisode schizophrenia or schizoaffective disorder patients were symptomfree after 5 years.

"But many people don't get there no matter what we do," Bracken says, "until that spark in them finally says, 'I want my life back.""

My lunch with Terry was coming to an end, so I pulled out my American Express card to pay the bill. Terry was still smiling, although he

looked very tired from telling me his story over the previous 2 hours. As I paid up, I told him about a meeting I had just attended in San Francisco on psychological approaches to psychosis, as part of my reporting for this story.

"I'd like to fly to San Francisco and take people out to lunch with my own American Express card," Terry said. "I'd like to get married again, or have a girlfriend. I'm going to get all that. It's going to happen because, like I told Jessica, I'm not going to settle for anything less."

-MICHAEL BALTER

www.sciencemag.org SCIENCE VOL 343 14 MARCH 2014

