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## Staying Sane May Be Easier Than You Think

By John Cloud

We tend to view the brain like an alien that happens to reside in the skull. We see it as unpredictable, ungovernable in ways that other organs aren't. Proper diet, exercise, no smoking — these will help prevent heart and lung disease. But diseases of the mind? They strike at will, right? You just can't keep yourself from going crazy.

And yet — what if you can? The most exciting research in mental health today involves not how to treat mental illness but how to prevent it in the first place. Hundreds of studies that have appeared in just the past decade collectively suggest that the brain isn't so different from, say, the arm: it doesn't simply break on its own. In fact, many mental illnesses — even those like schizophrenia that have demonstrable genetic origins — can be stopped or at least contained before they start.

This isn't wishful thinking but hard science. Earlier this year, the National Academies — an organization of experts who investigate science for the Federal Government — released a 500-page report, nearly two years in the making, on how to prevent mental, emotional and behavioral disorders. The report concludes that pre-empting such disorders requires two kinds of interventions: first, because genes play so important a role in mental illness, we need to ensure that close relatives (particularly children) of those with mental disorders have access to rigorous screening programs. Second, we must offer treatment to people who have already shown symptoms of illness (say, a tendency to brood and see the world without optimism) but don't meet the diagnostic criteria for a full-scale mental illness (in this case, depression).

Neither approach is without controversy. Early-detection programs will identify as candidates for mental illness some people who are merely persnickety or shy or eccentric. Some prevention programs even prescribe psychiatric medications, including antipsychotics and antidepressants, to people who aren't technically psychotic or depressed. "This is a big concern," says Joseph Rogers, founder of the Philadelphia-based National Mental Health Consumers' Self-Help Clearinghouse. "Because, gee, if you miss, you can really do more harm with some of these drugs than good."

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But those who contributed to the National Academies report say preventing the suffering of people with mental illness is worth the risk of some false positives, partly because of the enormous cost of treating mental illness after it's struck. The National Academies estimates that the total economic cost of mental disorders just among Americans under 25 was \$247 billion in 2007. (There are no such recent figures for all adults, but one 2000 study estimated that in 1992, the total cost of adult mental illness was \$161 billion.) Another 2007 study found that more than a quarter of the costs for young people are incurred in the education and juvenile-justice systems, which must deal with illnesses that, in many cases, could have been prevented.

But how do you predict and stop disorders as capricious and varied as depression and schizophrenia? Though treatment of mental illness is far more costly over time, prevention isn't without up-front costs. In a health-care system already overburdened, who pays? More fundamentally, what kind of country will we have if we attempt to "cure" various odd behaviors and quirky traits — qualities that can sometimes look like symptoms of a coming illness and other times look like evidence of a lively mind?

### **Prevention Pioneer**

In the early 1970s, before Dr. William McFarlane was one of the world's top authorities on preventing mental illness, before his hair had thinned and receded to a salt-and-pepper pouf, back when he was a student at the Albert Einstein College of Medicine in New York City, few psychiatrists talked about prevention. At the time, the U.S. had half a million psychiatric beds (there are 200,000 today), and psychiatrists faced less financial pressure to move inpatients quickly to outpatient care. Many people spent years on locked wards, their brains slowly gelatinizing from the combination of underlying illness and the blunt-instrument antipsychotic drugs of the day.

After he finished school and began seeing patients and teaching, McFarlane, like a few other pioneers, started to wonder if you could do something to stop the cycle before it began. But there was little research at the time on the early stages of mental illness. A key break came in the late 1970s, when a UCLA team began to publish the results of an influential long-term study called the UCLA Family Project. The study found that you could predict, with remarkable accuracy, which 16-year-olds would develop schizophrenia later in life based on only a few characteristics. The teenagers whom the Family Project tracked had already sought treatment for a psychological problem, although the study excluded actively psychotic teens, since it would not have been a surprise if they had developed schizophrenia.

Studying such kids for more than a decade, the researchers discovered that those who became schizophrenic were most often from families that, when first interviewed, displayed "communication deviance" (unclear, unintelligible or fragmented speech) and highly critical and intrusive parenting. These weren't merely families that argued with difficult sons and daughters; they were families that had lost all ability to cope.

McFarlane and others began working with some of the families to address their interactions and teach them how to communicate better — more slowly, with less anger and intrusion. Even after they are on medication, people with schizophrenia have a difficult time tracking rapid, highly emotional speech, yet that's the kind they often hear from frustrated family members. These patients would improve in hospitals but relapse once they got home,

even when they continued to take antipsychotics.

For several years, McFarlane developed and tested the Multi-Family Group approach, which brought several families together at a time to learn from one another how they sounded to outsiders. In twice-monthly sessions, the families modeled greater clarity and compassion and troubleshoot daily-living problems like kids' marijuana use or sexual activity. It was a simple intervention that, when combined with antipsychotic drugs, worked to reduce schizophrenic relapse rates significantly more than the drugs alone.

McFarlane wondered if the treatment could work even earlier, to help prevent the illness in largely asymptomatic kids who were at risk for schizophrenia. Such prediagnosis would not be easy, but McFarlane knew that once a patient's perception of reality has cracked for the first time, it becomes exceedingly hard to walk back to normality. Indeed, a major study just published in the journal *Neuropsychology* shows that the signature cognitive problems of schizophrenia — deficits in verbal learning and memory along with processing speed — actually begin days or weeks before a first psychotic episode, making the earliest possible detection all the more urgent.

And so in the 1980s, McFarlane began canvassing schools in the New York City area to try to get the staffs excited about preventing schizophrenia among their students. A number of the superintendents "practically threw us out the window," he says. "They just kept saying, 'We don't have mental illness in our high school.'" It was dispiriting: based on the epidemiological data, McFarlane knew that each year about 12 in 10,000 young people suffered a first episode of psychosis. Some of the kids were clearly in those schools, but if he couldn't get through the door to screen them, he couldn't prevent any illness.

### **A Theory Goes Wide**

Even as McFarlane was exploring his schizophrenia-prevention idea, other researchers were having similar what-if moments with respect to other, more routine conditions. Suppose irritable infants who become fearful toddlers who become shy children somehow could be stopped from becoming adults with anxiety disorders. Suppose men and women who go to war or become cops in inner cities could be helped before developing posttraumatic stress disorder. Could you, similarly, identify the children of depressed parents early and give them skills to prevent their own first depressive episode?

In any given year, approximately 17% of Americans under 25 have a mental, emotional or behavioral disorder. (Over our lifetime, 46% of us will receive such a diagnosis.) If we reduce the proportion of young people who become mentally ill by even one-quarter, that would mean about 3.8 million saved each year from what can turn into a lifelong struggle.

But if most mental illnesses have a genetic origin, isn't even that modest 25%-reduction goal unlikely? The science can get tricky here, but the simple answer is that genes aren't destiny. You can't do anything to change your genome, but your environment and experiences have powerful effects on the way those genes are expressed. A susceptibility to cancer may remain just a susceptibility — until you start smoking and kick the disease process

into motion. Similarly, change a child's emotional experiences for the worse and you can trigger mental illness; change them for the better and you may hush the problem genes. One concrete example of this: in 2003, a study in *Science* found that the larger the number of copies an individual carries of a serotonin-transporter gene called 5-HTTLPR the greater the risk of developing major depressive disorder and suicidality — but only if the individual suffers stressful early-life experiences like abuse.

How long is the window between first symptoms and actual diagnosis? The National Academies report says that across several mental illnesses — including obsessive-compulsive disorder, depression and substance dependence — we have about two to three years to intervene and keep short-term symptoms from becoming long-term afflictions.

Depression offers particularly good evidence of this idea at work. Currently, about 5% of adolescents experience an episode of clinical depression in any given year. Rates of depression are three to four times as high among the children of depressed parents as among those whose parents aren't depressed. Dr. William Beardslee of Children's Hospital Boston, one of the authors of the National Academies report, has spent more than 25 years studying how some kids of depressed parents avoid the illness, and he has found that resilience is key. The kids who don't develop depression are "activists and doers," Beardslee says. Even growing up in the darkness of a depressed home, they muster the capacity to engage deeply in relationships. They also are likelier than other kids to understand that they aren't to blame for their parents' disorder — and that they are free to chart their own course.

How do you foster resilience in order to prevent depression? Over the past 17 years, Beardslee's team has developed an early intervention that targets kids from families in which at least one parent is depressed. Like McFarlane, he uses a family-based approach because a bad home environment tends to be more predictive of adolescent mental illness than dysfunctional peer relationships are. Beardslee's Family Talk Intervention includes both separate meetings with parents and kids as well as family meetings with social workers or psychologists that focus in part on demystifying depression — explaining that it is a treatable illness, not a beast that will necessarily crush a family. In a randomized trial, Beardslee found that just seven sessions of this intervention decreased predepression symptoms among the kids and improved the parents' behavior and attitudes. All this makes kids more resilient.

### **Tackling Schizophrenia**

McFarlane hadn't gotten far with the New York City schools in the 1980s, and his prevention work waned for a few years as he taught at Columbia University and wrote articles on his Multi-Family Group approach to treating psychosis. Eventually, he moved to Portland, Maine, where he had been offered the chairmanship of Maine Medical Center's psychiatry department. There, he settled into quieter, less paradigm-changing work.

It wasn't until 1996 that his prevention work resumed. That year, a team of researchers in Norway — one that included Dr. Thomas McGlashan of Yale — approached McFarlane about training therapists to use the Multi-Family Group approach with patients who had just suffered a first psychotic episode. These patients already had the illness, so it was too late for prevention. But the Norwegians had succeeded where McFarlane had failed in

New York: they had connected with schools and other local institutions to identify the first signs of psychosis and refer patients to the team immediately.

In October 1998, the picture grew still more promising when NATO sponsored a major psychotic-disorders conference in Prague, where McFarlane learned that several groups around the world, including one in Australia, had also been trying to prevent first episodes of psychosis. He returned from Prague and tried again to set up an early-detection system with schools, this time in Portland. By now, the stigma against mental illness had eased a bit; schools had seen a dramatic rise in emotional and behavioral problems during the '90s. Unlike their New York counterparts, Portland school superintendents welcomed McFarlane.

At about the same time, McGlashan's team at Yale was working on a screening interview that might distinguish kids who would become psychotic from those who wouldn't. McGlashan tested his questions at various sites in North America, including with teens who sought treatment in McFarlane's department in Portland. By 2001, McGlashan and his team had completed their "Structured Interview for Prodromal [pre-disease] Symptoms" (SIPS) — a two-hour assessment involving various oral tests and a family history. Those who meet SIPS criteria for risk are about 30 times as likely as the general population to develop a diagnosable psychotic disorder. SIPS allows for the careful scoring of warning signs, some of which are obvious (hearing mumbling that isn't there) and some of which are less so (changing your behavior because of a superstition).

McFarlane and his team connected with most of Portland's principals and pediatricians. The message was simple: If you encounter kids who seem slightly off — prone to jumbled thoughts, maybe even hearing voices — send them our way. Among those referred to him, McFarlane found that 80% of those who met SIPS criteria for prodromal psychosis would receive a diagnosis of schizophrenia within 30 months. He put kids who met a certain SIPS threshold into Multi-Family Group psychoeducation. At first, he intended not to use drugs with these prediagnosis kids, particularly since the meds can cause side effects like weight gain, acne and uncontrollably shaky legs. But McFarlane found that once symptoms like auditory hallucinations started, he couldn't correct them with only psychosocial interventions. (Today, virtually everyone enrolled in his Portland Identification and Early Referral prevention program is prescribed psychiatric medication.)

The combination of the family approach and drug support seems to be working well. The National Institute of Mental Health is funding a trial of McFarlane's work, and while he is still writing up his data for publication, his anecdotal results are promising: most of the kids are so far avoiding a first psychotic episode. Even those who have heard voices and nearly dropped out of high school are going to college and getting jobs.

But this approach doesn't come cheap. The kids who are enrolled are bombarded with care: social workers help them at school or work; therapists guide them and their families in individual and group sessions; a psychiatrist or nurse practitioner carefully calibrates their medication based on response rates and side effects.

When members of McFarlane's clinical team gather each day to discuss cases, they know virtually everything about their kids: they know about boyfriends, girlfriends and summer plans. They know the kids' grades in

English class, how much pot they smoke, what they did on a recent trip to Disneyland. They know whether Dad just lost his job and if Mom's grandmother killed herself. This is what prevention of mental illness looks like: unwavering, sweeping, complicated. But it works.


### **One Family at a Time**

The Robert Wood Johnson foundation is so impressed with McFarlane's program that it has devoted \$15 million to its national expansion. It is the foundation's single largest mental-health initiative. McFarlane's approach costs about \$3,500 per patient per year, but compare that with the \$150,000 a year to care for a hospitalized schizophrenic or severely bipolar patient.

Still, not all the kids McFarlane sees can be helped. Patti White is a plainspoken 47-year-old Mainer who works for McFarlane as an administrative coordinator. She has a son who began experiencing psychotic symptoms a few years ago, and he might have seemed like a perfect fit for her boss's program. He wasn't; prevention isn't that easy. Instead, White's son Tyler, who turns 20 this month, was too far along in his illness — eventually diagnosed as schizoaffective disorder, a relative of schizophrenia — to benefit from prevention therapy. A social worker on McFarlane's team helped Tyler get into treatment, and he is doing better and holding down a job in food service.

But White has another son, Jacob, who causes her to worry. A few months ago, Jacob, 10, started to withdraw. He was getting paranoid. At school, he started seeing complicated machinations where none existed. And even though White works for one of the world's leading prevention experts, she at first resisted having Jacob take the SIPS test. "If his brother had had diabetes, I wouldn't have thought twice about having Jacob screened for diabetes," she says. "But I just couldn't deal with the idea that another one of my kids would have" — she pauses — "this enormous thing."

Three weeks ago, Jacob took SIPS. The good news: he showed no red flags for psychosis. He does have depressive symptoms and is now taking a low dose of Prozac to help prevent a full-blown depression. But for Jacob — and millions of other Americans with all manner of mental ills — intervention can now come in time. ▣

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