

Pulling out the stops for autism

A toddler sits at a table at home, a red, shiny ball the size of his fist in front of him. As he repeatedly hears *touch ball*, a parent's or health worker's hands move his finger to the ball. At some point—not right away, since the child has an autism spectrum disorder (ASD)—*touch ball* connects. A small hand, on its own, reaches out at the prompt.

Since one in 110 children has some degree of ASD—the umbrella term for autism, Asperger syndrome and a more general type of developmental disability—the odds are high that a similar scene plays out daily worldwide.

But as helpful as this common approach to therapy is, the focused, one-on-one in a home setting might benefit kids even more as part of a program that features social interaction, according to new research. Work reported by **Rebecca Landa** and Hopkins colleagues in a recent issue of *Journal of Child Psychology and Psychiatry* suggests that as early as possible, children with ASD are helped by training them to ease the skills they learn into everyday social life. The idea is to appear natural and spontaneous in dealings with others.

Landa's "integrated development" approach heavily targets the abnormal social behavior that, along with communicating, is a key problem in autism. Social inabilities, she says, possibly sidestep hardwired brain programs that cement the ability to communicate or carry out abstract social thought—brain activity that relies on interactions with people.



For two decades Rebecca Landa has worked to pry open autism's black box. Her early research helped map ASD's first signs in young, at-risk children. All of her studies shout out the need for early, aggressive therapy that's affordable.

But how to improve those interactions? Landa's recent study pulled out the stops. The researchers offered a group of 25 young toddlers with ASD an established curriculum—Landa laughingly calls it "gorgeous"—in a nursery school setting. For six months, four times a week, 2.5 hours a day, each child had direct face time, literally, with a mentor, plus encouragement to interact with four other tots. Through play—toys weren't in short supply—children were taught to notice and understand meaning in others' faces and actions. They learned the behavioral signs of sharing an interest with someone and how to imitate those signs. The results were what she'd hoped,

Landa says. Children improved significantly, especially in developing language.

But the study revealed more.

A second, matched group of toddlers received an extra helping of social practice. The benefits there, in becoming more socially engaged, were dramatic. "Extra gains," says Landa, "at no extra expense." When a teacher uses a toy car to coach a child to share attention and feelings, that's one thing. To see that child, on his own, offer the car to another? That's the happiest sort of ending. ■

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Dr. Landa directs the Center for Autism and Related Disorders at the Kennedy Krieger Institute.

Adults and ASD

What happens to adults with autism spectrum disorder? Do their problems in communicating ease? How do they cope with the aging process? Do most get along in life or barely get by? If they need help, what's best to do?

In 1943, when America's—and Hopkins'—first child psychiatrist, Leo Kanner, published the monograph that established autism as a childhood psychiatric illness, the idea of adults with the disorder wasn't in mind. Children Kanner studied were so severely ill that concern was channeled into doing anything to make their young lives better.

But change has come in the last decade, says **Peter Rabins**, a professor and specialist in geriatric psychiatry. "That's partly because of autism's newer place as part of a spectrum of disorders. Now we see more adult patients with milder illness," he says. Also, with the growing idea that therapies can help children (article, left), and that adult brains may be plastic enough to benefit from therapy, the need to look into that is stronger.

And that's what's beginning at Hopkins. Because adults with ASD are presently in health care's cloud of unknowing, that group first needs better defining, says Rabins. Recently, he, **Kostas Lyketskis** and **Eric Samstad** surveyed patients at a unique clinic that for some 25 years has treated the psychiatric problems of those with "intellectual disabilities." About 10 percent, they found, have autism disorders. "Patients have been sent to us with the old label of 'mentally retarded' whose primary problem is really ASD," says Rabins. "Their intellect isn't impaired."

And in looking into those patients' situations, the researchers saw, for example, that either illiteracy or psychiatric disorders or both appear to hamper an otherwise independent life. "We can target those problems," says Rabins. ■



"Patients have been sent to us with the old label of 'mentally retarded' whose primary problem is really ASD."

—PETER RABINS

Parkinson's possibility

Does early anxiety point the way?

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Could early anxiety flag Parkinson's? Greg Pontone wants to find out.

Parkinson's anxiety is likely more than plain vanilla

Ask most anyone about Parkinson's disease (PD), and you'll hear about the motor symptoms: the tremor, the unsteadiness, the freezing in place. Ask psychiatrists, and it's depression and anxiety that come to mind. The latter disorders are *rampant* in PD. More than half of patients report depression. Some 40 percent experience anxiety.

But geriatric psychiatrist **Gregory Pontone's** focus is even finer. His time as a clinician and as director of Hopkins' Movement Disorder Psychiatry Clinic has honed his feel for the anxiety that PD patients suffer. And his sense is that it's more nuanced than most suspect: Subtle but important differences in biology likely separate the anxiety his patients experience from the garden variety, he says.

Depression is common within five years of Parkinson's onset, "but the anxiety tied to it could occur far earlier," Pontone says, "as much as 20 years before you see motor symptoms." And like recent Alzheimer's studies that now confirm that disease's long approach, knowing what happens before PD takes hold brings hope of changing its course.

Now Pontone is putting his ideas to the test. As a start, a just-out paper describes an anxiety subtype unique to PD patients. What Parkinson's patients experience covers a spectrum of anxiety types, often PD-tinged: Some have phobias related to fear of falling, for example, or of "freezing" in the midst of a crowd. Others have anticipatory anxiety tied, say, to facing an upcoming trip. Generalized worry or anxiety attacks—with or without panic—are common.

But "fluctuation-associated anxiety," Pontone says, "is likely Parkinson's-unique." In a cruel irony, it stems from the therapy. Patients typically take levodopa—a drug that

boosts much-needed dopamine—and symptoms fade. But after the body metabolizes levodopa they return in force. So patients well into the disease, who need more frequent doses, can ride a roller coaster multiple times a day. And that may bring psychological symptoms ranging from "a sense of discomfort and worry," Pontone says, "to physical feelings of restlessness and agitation that turn panic-like for some patients. They can last minutes to hours, depending on time until the next dose."

To help, he and clinic colleagues, including Hopkins neurologists, fine-tune levodopa dosage or add drugs made to pull every shred of benefit from the drug. Then they turn to standard antianxiety agents (except for benzodiazepines, which are risky here). Behavioral therapy is also useful, he says.

But Pontone's goal is a far earlier approach. Parkinson's runs a route that begins in the gut, current ideas say, and that spreads to the brain's motor areas and higher. The movement problems surface with the motor takeover, but earlier stages are supposedly symptom-free. "Many of us, however, think that's when PD's psychiatric disorders start," Pontone says, and he's singled out panic disturbances, which his work suggests might be a flag.

"That certainly doesn't mean every middle-aged person with panic gets Parkinson's!" he says. It could be just that the early disease affects the same fight-or-flight pathways as classic anxiety disorders. "So we need to research those stages more carefully." Even now, Pontone's mapping studies to reveal which is which. ■

For information: 410-502-0477

CLINICIAN UPDATE

Huntington's, through a glass rosily

"Nobody gets cured of emphysema. It's a progressive, misery-inducing ailment," psychiatrist **Adam Rosenblatt** begins, "but you don't see pulmonologists broken up about their patients when they come to clinic." The same is true, he adds, when you treat congestive heart failure or severe osteoporosis: "Any physician's job, to the best of their abilities, is to make life as good as possible for patients, no matter how serious the disorder."

Rosenblatt takes a dim view of clinical crepe-hanging around patients with progressive diseases. It's natural to do, he says, but even the suggestion of pity or—worse—hard-heartedness can have catastrophic results for patients and their families. "We were taught to be aware of such things in medical school, but that can fade," he says.

As clinical head of Hopkins' Baltimore Huntington's Disease Center, Rosenblatt knows in particular the workings of that illness. Unlike Parkinson's or Alzheimer's, which usually strike later in life, HD typically starts during prime working and family-raising years, before patients have financial security or a satisfying bank of life experiences. "It's a cruel disease that way," he says. Moreover, most patients and those who know they carry HD's dominant gene have seen family members struggle with the disease. They're aware that uncontrolled movements and dementia lie ahead.

Still, Rosenblatt says, an unhelpful mythology dogs Huntington's. He once bought into it himself: "I believed all the stereotypes about HD: You can't do anything to help these patients with a horrible, progressive illness. You have to be a saint to work in this field." Not true, he says. "The saints burn out in about two years and are gone, and patients with Huntington's can enjoy a good quality of life for quite some time."

Rosenblatt advocates putting on the armor of a helping attitude. "The physician that patients need has a positive outlook and a sense of humor," he explains, "someone who's pragmatic and points out victories where they

come, who actively seeks to make life better in the time that remains." He mentions a need for professional detachment. "That doesn't mean you're humorless or cold, but you must find some way to separate the clinic from the rest of your life."

Help also comes from knowing the disease. One new patient of Rosenblatt's, for example, was admitted because of severe insomnia and inertia. He wouldn't talk or leave the bed. It wasn't depression, says Rosenblatt. But neither was it totally apathy—part of the executive function syndrome that's an HD hallmark. A look at medications showed that several he was taking could worsen the man's symptoms. "They were tapered off and we put him on a 'take no prisoners' approach," says Rosenblatt. That meant a regular schedule with mandated activities. Now the patient is active by day and sleeps well at night. His family calls his improvement remarkable.

The optimum for psychiatry, Rosenblatt suggests, blends being aggressive, providing relief where you can, and having *aequanimitas*—calmly accepting what comes. ■

For information: 410-955-2398.



"An unhelpful mythology dogs Huntington's," says psychiatrist Adam Rosenblatt.

Grand delusions—anything but grand

At a recent Grand Rounds, world-class author, researcher and teacher **Kay Jamison** offered a scholarly, humane take on the delusions of grandiosity that affect a third of adult patients who experience bipolar mania. We've shaped this Q&A from her talk. A professor of psychiatry, Jamison is coauthor of a definitive text, *Manic-Depressive Illness: Bipolar Disorders and Recurrent Depression*. With her writing, she's made considerable impact in lessening the stigma of that disease.

People with schizophrenia (SZ) also have grandiose delusions, right?

Yes, but studies show us they're more common in bipolar mania. You also see qualitative differences. In SZ, they are more fixed over time, more flavored by paranoia. In bipolar disorder, they're ephemeral, often tinged with a great sense of unity with the universe.

Is grandiosity always delusional?

I would say someone could be grandiose without being delusional, though others might disagree. I'm struck by

how little we know about this. The relationship, say, between depressed mood and thinking is well-studied, but there's hardly anything that looks at expansive, elevated moods and thought. Is there a short period when grandiose people are lucid? Are we in a similar state when we're creative?

I'm interested—clinically and as someone who writes about this—in the long-term impact of having grandiose delusions. They can be terrifying. The assumption is that, frightened or embarrassed, you'd just as soon never think about them again, but I'm not convinced that's the only reaction. People vary and we need to study this. If you've once genuinely believed you're able to do anything, mightn't that affect your mental "territory" when you're well?

That's not to give this too positive a spin. This is a terrible illness. And it's perverse: People with grandiose mania are the most likely to be helped by lithium, but they're the least likely to take it because grandiosity can be intoxicating. Then they suffer when their manias and depressions overwhelm them.



Kay Jamison shared her expertise at Grand Rounds

How much do delusions reflect someone's life experiences?

Some. Certain common themes exist and reappear from episode to episode: being a prophet on a divine mission, being Christ, the president, having supernatural powers, having secret adventures. But you also see idiosyncracies based on a person's life.

Research tells us delusions are a sign of worsening disease. They're also among the first things to improve when mania begins to clear.

Isn't this way of thinking marked by more than unrealistic, expansive topics?

Yes. It's not just that thought is delusional but it's scattered and incredibly fast in manic delusions. There's the notion of a *flight* of ideas. That's not the case, typically, in delusions that come with schizophrenia.

Couldn't we capture that, quantify it with neuroimaging? What can MRI or even PET scans tell us about grandiose delusions?

Very little, simply because they don't exist. Even if someone with manic delusions has the most interesting brain in the universe, the odds of that person holding still in a scanner are zero. It's odd how remarkably little we know about this intrinsically interesting phenomenon which has been observed for thousands of years.

You've been a dedicated student of poet Robert Lowell's life and the effects of his bipolar illness. There's an especially moving bit you read ...

Toward the end of his life, Lowell responded well to lithium. When he didn't take it, he was very sick indeed. A friend wrote: *No one predicts*

Mr. M,* an international sales rep who manned his company's Libya office before his hospitalization, was described at a Grand Rounds. A patient with bipolar disorder and especially grandiose delusions, he's responded well to therapy and is on a good path.

The mania Mr. M developed in Libya came on suddenly, with his desire to see Muammar Gaddafi. Mr. M's hallucinations, wherein God touched him with fire, convinced him he could reform the leader by reading the New Testament to him. With that start, Mr. M believed a grateful world would elect him U.S. president. That, in turn, would be his platform to bring peace to the entire cosmos. His conviction that he could heal people "by opening their skulls and touching their brains" extended to his own family and led his wife to seek help.

In his first days at Hopkins, Mr. M expanded his plan, adding the idea to convert military bases to psychiatric wards, thus decreasing the world suicide rate. He was so sure his call to the White House would come shortly that he brought his suit and very best shoes to Meyer 4.

*We've changed key details to protect privacy.

how long it will be before the drugs take hold and Lowell begins to be himself again. Meanwhile he writes and revises translations furiously and with a kind of crooked brilliance and talks about himself in connection with Achilles, Alexander... and Christ. It breaks your heart."

SUPPORTING THE CAUSE

A Huntington's story

Follow your mother into the supermarket. See if you notice anything unusual. Maureen Collins felt wary about her father's request but complied. She found her mom standing in the soup aisle, staring straight ahead. The moment passed, but Collins began to see a pattern in the spells and what followed: two fenderbenders because her mother could no longer drive defensively; a broken hip when balance went awry; behavior changes even more subtle.

Even before the testing, Collins felt sure that, like a cousin in the family, her mother had Huntington's disease. Collins brought her mom to Hopkins for gene analysis. She herself joined a clinical trial that included the test—

a terrifying step, Collins says, "but one I felt obligated to take for the sake of my three adult children." As suspected, her mother was positive. But Collins was not.

And so began more than a decade of challenges for Maureen Collins and her husband, George, underscoring Huntington's as very much The Family Disease.

Hopkins became the Collins' medical base. But George's duties as a corporate captain and world-class sailor—Google him under the Whitbread races—often divided them between other homes in Florida and Connecticut. That meant care for the mother, now living with them, was spread out. "We came to depend on Adam

Rosenblatt (article, left) as our advisor and advocate through some tough situations," says Maureen Collins.

The need for that hit home when Collins' mother began telling "little fabrications." Early dementia and loss of inhibition in an articulate woman were an unhappy mix. "My mother had people believing terrible things about our family," says Collins. When Rosenblatt suggested a new medication and reduced others she'd been taking, "it turned my mother around," Collins says.

Collins' mother lived to be 87. Today George and Maureen Collins remain effective, committed advocates for better Huntington's care and research. ■



When Huntington's overtook Dorothy Sullivan (left), daughter Maureen Collins was there for her mom.

Sickle cell psychiatry: don't give up

In medical school, the feedback other doctors gave **Patrick Carroll** about his wanting to work with sickle cell patients wasn't favorable. "If you'd say sickle cell," he remembers, "their eyes would roll back in their heads. The impression that's out there is that these patients are very tough, that there's lots of bad behavior, that they're too interested in opiates."

Sickle cell disease (SCD) is marked by pain crises—times when misshapen red blood cells turn blood to syrup.

The resulting oxygen starvation brings searing pain that only IV opiates and fluids can relieve. So, yes, many of these patients are more than a little interested in opiates. And, yes, the crises' unpredictability and what that does to a career or raising a family makes the disease a sieve for depression or other psychiatric illness.

Carroll came to Hopkins as "an addictions doc," he says. But asked to see some troubled patients who came to its new Sickle Cell Infusion Center for medical therapy, the psychiatrist found "an assortment of psychiatric illnesses, as well as problems in relating to doctors and the very occasional genuine case of addiction." He signed on right away.

Rather than viewing SCD as a crisis-based disease, Carroll sees it as a chronic condition that requires treating the whole person. His work begins when clinicians notice something going on with an infusion patient—maybe it's missed appointments or someone just looking burned out. Then Carroll meets with the person, separating demoralization from depression, checking for anxiety or other psychiatric ills. He draws up a comprehensive plan to address



Patrick Carroll: in for the long haul.

problems and settles in for what may be the long haul.

It's the rare sickle cell patient who has everything going for him except the disease itself, Carroll explains. Many people he sees are like a current patient—a young man who had dropped out of high school and who remains unemployed due to his sickle cell pain. His family—many members crammed into a tiny, drafty house—relies on his meager disability check to pay the bills. He doesn't have a car, so he has to walk to his appointments, a journey that could take two

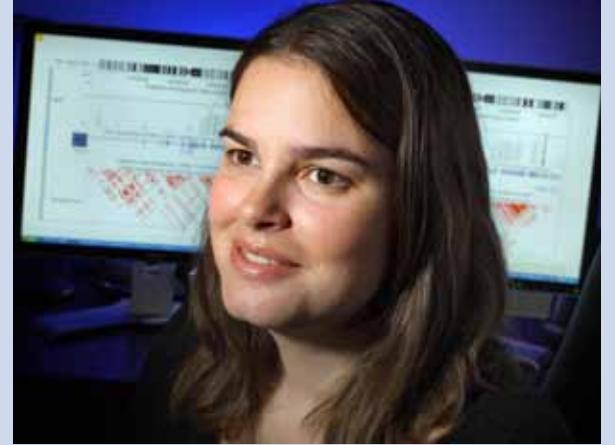
hours because of his chronic pain. The patient's previous doctors complained that he frequently missed appointments. But from the patient's point of view, the situation was hopeless—he was in chronic pain and no one was helping.

"He was depressed out of his mind, but he had never been diagnosed with depression," says Carroll. "We started working on that."

Carroll sees patients take better care of themselves and their sickle cell disease once their underlying medical and/or psychiatric issues are addressed—a process that can take months, rather than a few hours or days. "At a really pragmatic level, it's just irrational to give up," he says. "If you do something, there is some chance it will work—maybe it's slim, but if you give up, you've decided on certain failure."

The young man has made significant progress, Carroll adds. He's now coming to more appointments—for him, a sure step in the right direction. ■

For information: 410-955-6792.



Pamela Mahon asks "Who does best on lithium?"

Lithium in the picture

The amygdala is hit hard in bipolar disorder. The small, almond-shaped structure that nestles in each temporal lobe assumes a major role in quality of life. It's a crossroads for fear, anger and emotional learning. It also affects mental state. But something happens to the organ in bipolar disease. Blood flow increases and MRIs don't look the same; there's a clear loss of volume.

Enter lithium. Although the mood-stabilizing mineral doesn't help everyone with bipolar disorder, for many, results are remarkable. Functionally, the amygdala acts healed.

But what happens to it physically? Can lithium actually reverse the organ's structural damage? **Pamela Mahon**, whose specialty combines neuroimaging and genetics, aims to find out. As part of Project Match, a broad effort to help people with bipolar disorder find the best medication as quickly as possible, Mahon is surveying brain MRIs from each new patient who joins the study. "We'll be comparing the images of those who respond well to lithium with those who don't," she says. The hypothesis is that the amygdala will plump out to normal size in people helped by the drug.

At the same time, Mahon's colleagues are doing animal studies and analyzing patients' DNA sequences, combing for genetic clues that signal who'll be a lithium responder.

The next step, she says, will be to match the genetic variations with any physical differences the images reveal. "If things work out, that will let us connect the genes, ultimately, to the mechanism of bipolar disorder itself. You're linking gene to brain to understanding disease."

But a clinical benefit could come sooner. With positive results—a leap, at this point—and more medications tested, comes a prize: a set of genetic markers packaged as a routine lab test. A blood sample could tell physicians if lithium or Depakote is better to even out a patient's moods. More studies could tailor antidepressants—Prozac? Effexor? Wellbutrin?—to a person's brain chemistry. Hitting that goal would change the face of mental illness worldwide, and Mahon knows that well. ■

For information: 410-550-0019.

Hopkins BrainWise

This newsletter is published for the Department of Psychiatry and Behavioral Sciences by Johns Hopkins Medicine Marketing and Communications, 901 South Bond Street, Suite 550 Baltimore, MD 21231

Some of the research in this newsletter has corporate ties. For full disclosure information, call the Office of Policy Coordination at 410-223-1608.

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