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Family Medicine Residency Program

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Why do people with mental illness have good days and bad ones?

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But Halpern isn't baffled by such experiences; she's prepared. She asks herself: Is that really a skull or will it turn into a soccer ball when I glance back at it? Is the person in the grocery aisle someone I should avoid or just a shadow on the floor?

Halpern, who has undergraduate and graduate degrees in public policy from Duke and Harvard universities, knows her brain plays tricks on her. She has schizophrenia. And she's learned that monitoring her reactions can tell her if she's getting worse.

"It's my way of trying to piece together a barometer of my health," she says. "If it takes me a half an hour to notice that the skull is really a soccer ball, then my brain health is not doing that well. If it takes a split second, my brain health is doing pretty well."

She pauses and adds thoughtfully, "After all, everyone mistakes what they see every now and then."

It's true, everyone has good days and bad. But new research is explaining why people with conditions such as schizophrenia, traumatic brain injury, attention-deficit hyperactivity disorder and dementia may have more extreme inconsistencies. The explanation is rooted in the fact that all these disorders are linked to damage in the frontal lobe. Psychologists are discovering what Halpern already knows intuitively: Wide swings in thought and perception may foreshadow worsening symptoms or even a psychotic episode.

"What's interesting about this field is that it's looking at errors or lapses of attention as predictive of other adverse outcomes," says Kaarin Anstey, PhD, who directs the Ageing Research Unit at the Centre for Mental Health Research of Australian National University in Canberra. In the past, evidence for such errors and lapses was blamed on methodological flaws or measurement errors in the studies.

Now, they're the main event.

Possible causes

Relatives of people with diseases such as Alzheimer's disease or schizophrenia have noticed that people with neurological disorders can be clear one day and foggy the next, or calm one minute and then explode with rage.

Preliminary research suggests that such extremes may result from damage to the frontal lobes, home to such executive functions as impulse control, multitasking, judgment and attention, according to a literature review by University of Victoria psychology professor Stuart MacDonald, PhD, published in *Trends in Neurosciences* (Vol. 29, No. 8). That damage includes frontal lobe lesions and reduced gray-matter density. "We need to help people with these conditions and their family members understand that variability is part of these disease states."

BARRY JACOBS

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Because the frontal lobes regulate attention, mood and concentration through their connections with other brain regions, any damage to them can throw the whole brain off, says Barry Jacobs, PsyD, director of behavioral sciences at Crozer-Keystone Family Medicine Residency Program in Springfield, Pa.

But these executive function errors don't just arise directly from damage to the frontal lobe: They may be the result of problems along the way in brain processes that rely on several parts of the brain, says Harvard University researcher Trey Hedden, PhD, who studies brain function, memory and attention in aging adults. In preliminary results from a study he's conducting, he's found that people with memory problems — a function that depends on the medial temporal lobe also have frontal lobe difficulties that may be the result of the brain's weakening ability to cull useful information from the cacophony of stimuli bombarding it at every second.

The signal, in other words, becomes "less precise" in people with greater moment-to-moment fluctuations, says Ulman Lindenberger, PhD, director of the Max Planck Institute for Human Development in Berlin. This lack of precision may reflect changes in physiology: In a 2007 study in *Neuropsychologia* (Vol. 45, No. 8), Anstey found that older people with mild cognitive disorders who exhibited greater variability in cognition and behavior also had a smaller and probably less efficient corpus callosum, the thick band of white matter that helps relay information from one brain hemisphere to the other.

"Greater variability in [frontal lobe] tasks may be due initially to very small inefficiencies in the transmission of information or lapses of attention," she says. "These inefficiencies accumulate as pathology accumulates."

In other words, those inefficiencies — and inconsistencies — may build up over time and slowly worsen until they become clinical-level disorders. But, cautions David F. Hultsch, PhD, director of the University of Victoria Centre on Aging, "the research is not absolutely conclusive yet."

That's because researchers must first track the cognitive and behavioral inconsistency of healthy people over a long period of time to see if that inconsistency predicts who develops disorders such as Alzheimer's.

Armed with such research, says Hultsch, "then we can determine: Could we have predicted with efficient accuracy who is going to end up with Alzheimer's disease years prior using these inconsistency measures — and would those measures be better than the ones we more typically use?"

Preliminary findings

Such research is now under way. In Australia, Anstey is overseeing a longitudinal study of 7,500 people that monitors behavioral, psychological and neurological changes. So far, research on inconsistency has found associated white matter changes in the frontal lobe — and that the inconsistency predicts mild cognitive disorders, even adjusting for behavioral choices, such as alcohol abuse, that can change brain function.

Hultsch's colleague Allison Bielak, PhD, analyzed data from Hultsch's prospective study of older adults and found that the more inconsistent a participant's response time was at the start of the study, the more impaired his or her memory was six years later. Although few participants have developed clinical dementia, the study has found that cognitive inconsistency reliably indicated a participant's decision to leave the study. Such attrition has been shown in other studies to be an indicator of impending health and memory impairments, says Bielak.

Similarly, Martin Lovden and Lindenberger found in a study in *Neuropsychologia* (Vol. 45, No. 12) that inconsistent response times precede and predict long-term cognitive decline in processing speed.

The promise of this research is that some day, adults may be able to train to keep their brains strong as they age. After all, developmental psychologists have known for years that increased variability in the thinking strategies of young children signals those children's readiness to shift to a new level of learning. So why shouldn't changes in behavior and cognition in people with specific conditions be an indicator of another type of change?

"Intraindividual variability is the youngest kid on the block when it comes to this type of training, but it's developing at a fast rate," Lindenberger says. "And it may prove to be a key to future improvements in brain health."

Meanwhile, the same inconsistent behavior that fascinates researchers often leaves caregivers baffled, says Jacobs, author of "The Emotional Survival Guide for Caregivers" (Guilford Press, 2006.) He must frequently tell family members that occasional lucidity among people with dementia or improved mood in someone with traumatic brain injury doesn't mean recovery.

"We need to help people with these conditions and their family members understand that variability is part of these disease states, and those inconsistencies need to be predicted in a way that doesn't catch them off guard."

Heather Boerner is a medical writer in San Francisco.