BEATRIZ LUNA IS FINDING OUT WHY EVEN SMART KIDS DO STUPID THINGS

BY ELAINE VITONE

"WHAT POSSESSED YOU?"

Riding down a hill in a shopping cart. Racking up a $600 cell-phone bill. Cannonballing from a rooftop into a swimming pool. Totaling a car. Licking a flagpole in February. Lighting a firecracker in a bottle.

In those infamous years between ages 12 and 20, most kids pull a few stunts that they're not particularly proud of in the long run—things they just sort of find themselves doing that are… well, dumb. It's a real strain on parents. Besides being stuck with the thankless role of disciplinarians, a lot of parents' frustration stems from the way such episodes often seem to come out of nowhere. One day Johnny is behaving like the good, bright teenager he is, keeping up in school and doing well all around as he continues to grow taller, sharper, and more adultlike.

ILLUSTRATION | CATHERINE LAZURE

Then, the next day, *bam*! A blatant act of outright idiocy.

Beatriz Luna, Pitt associate professor of psychiatry and psychology and director of the Laboratory for Neurocognitive Development at Pitt's Western Psychiatric Institute and Clinic of UPMC (WPIC), says that the problem with adolescents may not be that they're prone to lapses of immaturity; it may be that every moment of every day, they're living in the big fat middle of immaturity, working harder at grown-up behavior than we will ever know.

"Adolescents kind of look like adults, but then they do really stupid things sometimes, and you're like, 'How can you do something so stupid?'" she says, speaking from experience. Luna has a 16-year-old son and a 14-year-old daughter. "But actually, those stupid things may have a real neurological basis."

KAPELEWSKI

Beatriz Luna may actually understand teenagers.

By age 10, the brain looks much like an adult's in terms of weight and size. But while the parts are pretty much all there, the wiring among them is a work in progress. These changes in circuitry are a main focus for Luna, a leader in the emerging field of developmental neuroscience—the intersection of brain-structure development and the changing behavior of adolescents.

Luna is working to establish a template for healthy brain development in teenagers. Such a template could have far-reaching implications since many disorders, including schizophrenia and depression, emerge in adolescence. In recent months she has given talks on these and other conditions in the Netherlands, England, Germany, and her native Chile. Lately, it seems, the teenage brain is all the rage. "It used to be just me and maybe three other people presenting about it," she says. "Now [at conferences] there are 10, 20 presentations a day for all three days. It's great."

At a White House ceremony last year, Luna was one of 12 National Institutes of Health–funded researchers honored with Presidential Early Career Awards for Scientists and Engineers, the U.S. government's highest honor for those professionals getting their independent careers off the ground. Long before the award, her work had already caught the attention of a broader audience outside the scientific community because it addresses an age-old question: Why do kids do stupid things?

Broadly speaking, human behaviors can be broken down into two types—the more instinctive variety, known as reactive response (lashing out when you feel angry, for example), and the more calculated behavior that requires inhibiting the reactive response and overriding it with a consciously formulated plan (stopping yourself from lashing out and going somewhere to cool off). The latter process requires executive function or cognitive control.

The ability to inhibit responses and behave more deliberately is obviously an acquired skill. Using imaging technologies and behavioral studies, Luna is tracking the gradual shifts in the brain's structure and function to illuminate how we develop this ability that separates the men from the boys, the women from the girls.

She says that as the brain reorganizes its circuitry throughout adolescence, it's vulnerable to making bad calls—which might explain why a kid would insist that, somehow, setting off fireworks in the gymnasium really did seem like a good idea at the time.

Luna has given advice to inform policy on teenage pregnancy, age limits for such activities as driving and drinking, and sentencing for minors who commit crimes. She has been published widely in academic journals and interviewed by *The New York Times Magazine*, *Discover*, *Science*, and *Scientific American Mind.* She has received letters from inmates serving life sentences: *Dear Dr. Luna, I committed a crime when I was very young. … Can you help me?*

Reporters ask her the same questions: *Can you look at a brain and tell if someone is a violent criminal or not? How old is old enough to be accountable for your own actions? What does all this mean?*

Sometimes, it's a little uncomfortable. "I don't want to stretch what we're finding," Luna says. "But I think I have a responsibility as a scientist to try to help make sense of all this."

When she responds, her eyes narrow, the furrows of her forehead rising to form a question mark in the middle as she nods. There aren't any easy answers. It's best to start small and go from there. "Our approach has always been to take these little steps."

Just before puberty, the brain has a growth spurt of its own—a disarray of new connections among parts of the brain. In order to become more efficient, the brain prunes away the connections that prove less useful. The wiring that the adolescent does end up using becomes reinforced with a white matter known as myelin—a fatty, insulative coating that protects and streamlines connections. It's a classic case of use-it-or-lose-it.

Until this process is complete, the routes that aren't fully myelinated will be slower. With too many extra forks in the roads, the adolescent brain often picks a less-than-ideal connection. Faced with this disadvantage, it's vulnerable to making mistakes.

Based on animal and cellular studies, neurobiologists have suspected as much for a while. The Luna lab has shown the effect of these developmental processes on response inhibition and cognitive control more directly and in greater depth than anyone else. The lab has demonstrated that when an adolescent completes a given task at an adult's performance level, she uses different brain systems, which are less efficient than those used by an adult.

"Sometimes the adolescent [brain] looks like a brain that's working really hard—like an adult brain doing something a lot more difficult," says Luna. "And just like an adult doing

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something very difficult, [the young brain] is vulnerable to error."

Much of Luna's research has focused on the prefrontal cortex—that package of gray matter directly behind the forehead that plays a vital part in cognitive control. The prefrontal cortex is well connected to the rest of the brain. In adulthood, it essentially uses these connections to delegate. By sharing the workload, the brain is able to complete tasks more efficiently.

The prefrontal cortex (the slowest region to mature) doesn't complete its growth until a person reaches her 20s. In the meantime, as it streamlines and fine-tunes connections, it attempts to tackle complex cognitive behaviors in-house instead of delegating.

That means it often takes on more than it can handle.

And that's why a 17-year-old talking on a cell phone in stop-and-go traffic is more likely to have an accident than a 30-year-old. For the teenager, the instinctive reaction—to freeze—is much harder to override with a cognitive response, like slamming on the brakes.

This work could have important implications for mental health research, because every single neuropsychiatric disorder has a link to the prefrontal cortex.

"It makes sense if you think about it," says Luna.

"All of them have in common the inability to have control over what's coming in and what's coming out. With schizophrenia, it's hallucinations. With mood disorders, it's emotions."

A year ago, subjects between the ages of 8 and 28 made the first of five annual trips to Luna's lab to complete what she describes as "very simple" tests as part of a longitudinal study funded by the National Institute of Mental Health.

The tests do look simple. Sitting in a dark room with a camera focused on the pupil of one eye to record its movement, the participants face a computer monitor and perform a series of tasks involving pulses of light flashing on the screen. The monitor gives them instructions: Look directly at the flash of light. Look away from it. Stare straight ahead and ignore the light as it moves around to various points.

For those study participants who don't have hindrances like braces or claustrophobia, an encore performance follows at the Brain Imaging Research Center, a facility on the South Side run jointly by Pitt and Carnegie Mellon University. Using the center's 3 Tesla scanner, the team watches which brain networks are activated.

Although other researchers investigating cognitive control have opted for video, verbal, or pencil-and-paper tasks to study decision-making, Luna's team has chosen ocular-motor tests for several reasons. For one, eye movement is a basic, well-understood function that's been thoroughly documented in animal studies. For another, the entire brain is wired to react to a flash of light by looking at it, and choosing to override that reaction is a perfect example of the executive process. This "simple" task is useful in revealing the complex circuitry of the developing brain.

Luna's team has shown that performance on these ocular-motor tests does not improve with practice, but it does with age. For example, a 12-year-old returning to the lab every day for a week won't be able to raise his score. He will score higher the following year, however, because by then the connections in his brain will be that much closer to those of an adult.

"It's very interesting, because for 8-year-olds, when you ask them not to look at that light, 50 percent of the time they're going to look at it anyway—they can't help it," says Luna. "They look immediately, say, 'Oh no, I'm sorry,' and then they look the other way, which means: 'I understand what you asked me to do. I just couldn't stop myself.'" It isn't until puberty that they're able to perform this task as well as adults—but even then, they can't do so consistently.

Near the end of the testing, a facilitator asks the subject to perform the more difficult of the tasks again, this time with a new variable: cash.

"We want to know what reward does to the brain of an adolescent, and how does it differ from an adult's," says Luna. In adolescents, Luna's preliminary results are showing immaturities and less activation in the parts of the brain that assess the meaning and value of rewards (namely the orbitofrontal cortex). But that doesn't make kids get any less wide-eyed when the dollar signs appear on the screen. She sees this excitement in the scans, too. "The part of the brain [the ventral striatum] that gets excited about a reward is like, *Whoa!*"

She has applied for further funding to look into how kids process rewards, which she expects will lend insight into addiction and the adolescent brain.

On a sunny Tuesday in early May, as Luna sits in her corner office overlooking Forbes Avenue, she talks to yet another reporter about her work. Assistant professor of pediatrics and psychiatry Miya Asato knocks at the door. "We've got some really cool brain pictures we want to show you," she says, peeking in.

"Yay!" Luna says with her characteristic almost-teenagerly zeal. (It seems that interacting with kids so much through her studies may have rubbed off on this scientist.)

Minutes later, Luna sits at a computer in an office at the opposite end of the hall, getting her first glimpses of a complex neuroimaging project more than a year in the making. Asato stands beside her, clipboard in hand, taking notes on which images they'll use in a poster they're putting together for that weekend's Cognitive Neuroscience Society conference in New York. Sitting behind Luna is Jae Kyun Woo (Class of '08), a spiky-haired electrical-engineer-turned-med-student who first put his programming expertise and interest in pediatrics to work for this project about a year ago. Woo has been coding, crunching data, and toiling away at this interface for months while MIT physics grad student Robert Terwilliger has done much of the analysis.

On the screen are three interactive images of a brain viewed from different vantage points. It's actually not the brain of any one individual, but what's known as a mean map—a sort of structural average of multiple individuals. This mean map represents more than 100 study participants. Children, adolescents, and adults are equally represented.

In each image, the gray matter is outlined (go figure) in gray; within it, a network of green lines branches throughout the brain like limbs on a tree, marking the brain's myelinated connections. A few small red, yellow, and white sections along the branches fascinate the practically giddy Luna as she zooms in and out and moves through the brain with her mouse. These "hot spots" mark areas where the brain's myelinated connections change with age, growing with time.

"Don't you love that one, Miya?" says Luna, zooming in on a hot spot near the inferior frontal gyrus, a part of the brain that influences response inhibition and executive control. "I love it so much I think I'm gonna marry it!" says Luna.

At the conference, Woo and Asato will present their poster showing the hot spots from these images, cross-referenced with results from the ocular-motor studies. The comparison reveals several interesting results. For one, the more robust the myelinated pathways, the better subjects are able to stop themselves from looking directly at the flash of light. Specific regions of the brain associated with response inhibition were more activated in these cases as well.

Watching Luna interacting with the young researchers on her team is a bit like watching your favorite high school teacher—the one who was always popular with students for her energy, humility, and dedication to sharing her passion for the subject at hand. She's a bit of a rascal, which endears her, too. In brief breaks between brain-scan swooning sessions, she turns around and taps the vertical hairs at the top of Woo's crown, instant messages a joke to the graduate student down the hall, laughs and lets her genuine joy in her work show. In the lab she keeps a light, fun atmosphere. Off-hours, she goes bowling with her team.

"She has a lot of energy and is really passionate about her work," Woo says later. "It's hard not to get infected by that."

"She's a great mentor who's really fostered the careers of young investigators," says Asato, who's in the second year of a study on epilepsy and its effects on development and behavior.

As a child neurologist with six years of clinical experience, Asato is especially attuned to what a better understanding of the brain's circuitry could mean for patients with neurological disorders. "In epilepsy and a lot of other conditions I'm interested in, the MRI scans are normal," she says. "But we know from what the child and the family are experiencing—the seizures, the developmental problems—that the brain isn't healthy."

Under Luna's guidance, Asato won a National Institutes of Health career development award, which funds the project. "Bea helped me prepare and learn about the research tools I needed to make that transition and become an investigator," she says. "This has been a big thing for me."

In the February 2007 issue of *Biological Psychiatry*, Luna published results from a study on autism, which is known to impair cognitive control. She has shown that just like people who don't have autism, those who do show dramatic improvement in cognitive control from childhood to adolescence, both in behavior and brain function. Previously, behavioral therapy for children with autism focused on the first three years of life because it is a well-recognized window of plasticity—of opportunity. This second window could be very good news for patients with autism and their families.

Ron Dahl, the Staunton Professor of Psychiatry and Pediatrics at WPIC whose research centers largely on the emotional turmoil that characterizes the teenage years, says Luna's work has been especially exciting for him and his colleagues. He likens the motivations and passions of adolescence to a ship's engine and the cognitive control to the wheel. Although cognitive control is responsible for steering the ship, it's always been a very hard thing to measure, both in the physiology of the brain and in its link to behavior.

"Bea is measuring not just the ability to inhibit behavior," he says, "but also the ability to make yourself do something that overrides an impulse—and to do it quickly, accurately, and precisely. I think that's a really unique slice that is going to leverage a whole lot of investigation that has relevance to boost clinical interventions and social policy interventions."

Yet another disorder Luna's work speaks to is attention-deficit/hyperactivity disorder, a condition that affects response inhibition. In a preliminary study led by Irene Loe, a postdoctoral research scholar at Children's Hospital of Pittsburgh of UPMC, the team has already found encouraging results. Within the ADHD subjects who've been tested so far, the researchers are beginning to identify subgroups with common circuitry that are better at cognitive control than others.

"ADHD is a serious health problem," says Asato. "A lot of these individuals don't make good choices and may not 'grow out of it.' In some cases, because of other psychiatric comorbidities, some individuals may be at higher risk of ending up in the criminal-justice system."

Last December, Luna attended a meeting in Pittsburgh's Garfield neighborhood. It looked like an ordinary PTA meeting—an informal gathering of T-shirted parents and grandparents sitting around a table and drinking coffee. They talked about their organizational newsletter, their Web site, their kids.

But this was no PTA function.

"It was the most humbling meeting I've ever been to in my life," says Luna.

She was invited to speak at the monthly board meeting for a Pittsburgh-based activist group called Fight for Lifers West. They are family and friends of prisoners sentenced to life without parole for crimes committed as adolescents in Pennsylvania. More lifers have been convicted as juveniles in Pennsylvania than in any other state in the country.

"My child was 15," one mother said. "Yes, she did something horrendous, something stupid. And now, for the rest of her life, she's going to be in a cell." Many of the group's members say this punishment is worse than dying. They call it "the living death."

None of them was crying. Luna could tell that these parents were seasoned. But as she sat listening to their stories, thinking about the cold, hard facts—sentencing at 16, life expectancy of 70-plus—it was almost too much. "I literally had to hold back the tears," she says.

Luna gave her presentation to an attentive audience. The families responded with enthusiasm, thanked her, and extended an open invitation to future meetings. "I've been so busy, I haven't been back," Luna says with a sigh.

Between working at her lab, reviewing grant proposals for an NIH study section, mentoring young researchers, answering reporters' questions, unlocking the mysteries of the adolescent brain, and raising two specimens of her own, there isn't nearly as much time for community involvement as Luna would like. She does her best, though, voicing her concerns to public-school administrators, community groups, and fellow parents. Every chance she gets, she shares what she has learned, which is, in a sentence: Adolescence is not a disease.

"Yes, it's easy to get angry when [teenagers] do something stupid, but sometimes that might be the best that they could do. Give them a break. And don't give up on them."

Luna admits that it's challenging in those I-know-everything, I-don't-care-what-you-have-to-say moments, but giving up means missing out on a valuable opportunity.

"That feedback might result in a better-developed brain," she says.

Her own son and daughter are bright, good-natured, "amazing" kids, reports Luna. Both are honors students—at 16, her son has already secured tuition awards for college. But like all adolescents, they have their trying times, especially when they're sleep deprived.

"What can I say, Mom? I'm not fully myelinated."

They can be slow to clean their rooms, quick to argue, stubborn, and unwilling to listen.

It isn't easy being one of the few parents in the world who truly knows so much about what's going on inside a teenager's brain. Your kids do eventually catch on and use the science against you.

"Just recently my son was doing it again," says Luna. "He was tired and was getting particularly moody—reactive. And I'm like, 'Have you done your homework?' We had a little fight, so the next day I was like, 'You know, that's not how we should talk to each other.' And he's like, 'What can I say, Mom? I'm not fully myelinated, and you should understand that by now.'"

"So I said, 'Yes, but part of you myelinating correctly is that I tell you when you cross the line.'" ■