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## What Makes Teens Tick

By Claudia Wallis; Kristina Dell

Five young men in sneakers and jeans troop into a waiting room at the National Institutes of Health Clinical Center in Bethesda, Md., and drape themselves all over the chairs in classic collapsed-teenager mode, trailing backpacks, a CD player and a laptop loaded with computer games. It's midafternoon, and they are, of course, tired, but even so their presence adds a jangly, hormonal buzz to the bland, institutional setting. Fair-haired twins Corey and Skyler Mann, 16, and their burlier big brothers Anthony and Brandon, 18, who are also twins, plus eldest brother Christopher, 22, are here to have their heads examined. Literally. The five brothers from Orem, Utah, are the latest recruits to giant study that's been going on in this building since 1991. Its goal: to determine how the brain develops from childhood into adolescence and on into early adulthood.

It is the project of Dr. Jay Giedd (pronounced Geed), chief of brain imaging in the child psychiatry branch at the National Institute of Mental Health. Giedd, 43, has devoted the past 13 years to peering inside the heads of 1,800 kids and teenagers using high-powered magnetic resonance imaging (MRI). For each volunteer, he creates a unique photo album, taking MRI snapshots every two years and building a record as the brain morphs and grows. Giedd started out investigating the developmental origins of attention-deficit/hyperactivity disorder (ADHD) and autism ("I was going alphabetically," he jokes) but soon discovered that so little was known about how the brain is supposed to develop that it was impossible to figure out where things might be going wrong. In a way, the vast project that has become his life's work is nothing more than an attempt to establish a gigantic control group. "It turned out that normal brains were so interesting in themselves," he marvels. "And the adolescent studies have been the most surprising of all."

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Before the imaging studies by Giedd and his collaborators at UCLA, Harvard, the Montreal Neurological Institute and a dozen other institutions, most scientists believed the brain was largely a finished product by the time a child reached the age of 12. Not only is it full-grown in size, Giedd explains, but "in a lot of psychological literature, traced back to [Swiss psychologist Jean] Piaget, the highest rung in the ladder of cognitive development was

about age 12--formal operations." In the past, children entered initiation rites and started learning trades at about the onset of puberty. Some theorists concluded from this that the idea of adolescence was an artificial construct, a phenomenon invented in the post--Industrial Revolution years. Giedd's scanning studies proved what every parent of a teenager knows: not only is the brain of the adolescent far from mature, but both gray and white matter undergo extensive structural changes well past puberty. "When we started," says Giedd, "we thought we'd follow kids until about 18 or 20. If we had to pick a number now, we'd probably go to age 25."

Now that MRI studies have cracked open a window on the developing brain, researchers are looking at how the newly detected physiological changes might account for the adolescent behaviors so familiar to parents: emotional outbursts, reckless risk taking and rule breaking, and the impassioned pursuit of sex, drugs and rock 'n' roll. Some experts believe the structural changes seen at adolescence may explain the timing of such major mental illnesses as schizophrenia and bipolar disorder. These diseases typically begin in adolescence and contribute to the high rate of teen suicide. Increasingly, the wild conduct once blamed on "raging hormones" is being seen as the by-product of two factors: a surfeit of hormones, yes, but also a paucity of the cognitive controls needed for mature behavior.

In recent years, Giedd has shifted his focus to twins, which is why the Manns are such exciting recruits. Although most brain development seems to follow a set plan, with changes following cues that are preprogrammed into genes, other, subtler changes in gray matter reflect experience and environment. By following twins, who start out with identical--or, in fraternal twins, similar--programming but then diverge as life takes them on different paths, he hopes to tease apart the influences of nature and nurture. Ultimately, he hopes to find, for instance, that Anthony Mann's plan to become a pilot and Brandon's to study law will lead to brain differences that are detectable on future MRIs. The brain, more than any other organ, is where experience becomes flesh.

Throughout the afternoon, the Mann brothers take turns completing tests of intelligence and cognitive function. Between sessions they occasionally needle one another in the waiting room. "If the other person is in a bad mood, you've got to provoke it," Anthony asserts slyly. Their mother Nancy

Mann, a sunny paragon of patience who has three daughters in addition to the five boys, smiles and rolls her eyes.

Shortly before 5 p.m., the Manns head downstairs to the imaging floor to meet the magnet. Giedd, a trim, energetic man with a reddish beard, twinkly blue eyes and an impish sense of humor, greets Anthony and tells him what to expect. He asks Anthony to remove his watch, his necklace and a high school ring, labeled KEEPER. Does Anthony have any metal in his body? Any piercings? Not this clean-cut, soccer-playing Mormon. Giedd tapes a vitamin E capsule onto Anthony's left cheek and one in each ear. He explains that the oil-filled capsules are opaque to the scanner and will define a plane on the images, as well as help researchers tell left from right. The scanning will take about 15 minutes, during which Anthony must lie completely still. Dressed in a red sweat shirt, jeans and white K-Swiss sneakers, he stretches out on the examining table and slides his head into the machine's giant magnetic ring.

MRI, Giedd points out, "made studying healthy kids possible" because there's no radiation involved. (Before MRI, brain development was studied mostly by using cadavers.) Each of the Mann boys will be scanned three times. The first scan is a quick survey that lasts one minute. The second lasts two minutes and looks for any damage or abnormality. The third is 10 minutes long and taken at maximum resolution. It's the money shot. Giedd watches as Anthony's brain appears in cross section on a computer screen. The machine scans 124 slices, each as thin as a dime. It will take 20 hours of computer time to process the images, but the analysis is done by humans, says Giedd. "The human brain is still the best at pattern recognition," he marvels.

Some people get nervous as the MRI machine clangs noisily. Claustrophobes panic. Anthony, lying still in the soul of the machine, simply falls asleep.

## CONSTRUCTION AHEAD

One reason scientists have been surprised by the ferment in the teenage brain is that the brain grows very little over the course of childhood. By the time a child is 6, it is 90% to 95% of its adult size. As a matter of fact, we are born equipped with most of the neurons our brain will ever have--and that's fewer than we have in utero. Humans achieve their maximum brain-cell density between the third and sixth month of gestation--the culmination of an explosive period of prenatal neural growth. During the final months before birth, our brains undergo a dramatic pruning in which unnecessary

brain cells are eliminated. Many neuroscientists now believe that autism is the result of insufficient or abnormal prenatal pruning.

What Giedd's long-term studies have documented is that there is a second wave of proliferation and pruning that occurs later in childhood and that the final, critical part of this second wave, affecting some of our highest mental functions, occurs in the late teens. Unlike the prenatal changes, this neural waxing and waning alters not the number of nerve cells but the number of connections, or synapses, between them. When a child is between the ages of 6 and 12, the neurons grow bushier, each making dozens of connections to other neurons and creating new pathways for nerve signals. The thickening of all this gray matter--the neurons and their branchlike dendrites--peaks when girls are about 11 and boys 12 1/2, at which point a serious round of pruning is under way. Gray matter is thinned out at a rate of about 0.7% a year, tapering off in the early 20s. At the same time, the brain's white matter thickens. The white matter is composed of fatty myelin sheaths that encase axons and, like insulation on a wire, make nerve-signal transmissions faster and more efficient. With each passing year (maybe even up to age 40) myelin sheaths thicken, much like tree rings. During adolescence, says Giedd, summing up the process, "you get fewer but faster connections in the brain. The brain becomes a more efficient machine, but there is a trade-off: it is probably losing some of its raw potential for learning and its ability to recover from trauma.

Most scientists believe that the pruning is guided both by genetics and by a use-it-or-lose-it principle. Nobel prizewinning neuroscientist Gerald Edelman has described that process as "neural Darwinism"--survival of the fittest (or most used) synapses. How you spend your time may be critical. Research shows, for instance, that practicing piano quickly thickens neurons in the brain regions that control the fingers. Studies of London cab drivers, who must memorize all the city's streets, show that they have an unusually large hippocampus, a structure involved in memory. Giedd's research suggests that the cerebellum, an area that coordinates both physical and mental activities, is particularly responsive to experience, but he warns that it's too soon to know just what drives the buildup and pruning phases. He's hoping his studies of twins will help answer such questions: "We're looking at what they eat, how they spend their time--is it video games or sports? Now the fun begins," he says.

No matter how a particular brain turns out, its development proceeds in stages, generally from back to front. Some of the brain regions that reach maturity earliest--through proliferation and pruning--are those in the back of the brain that mediate direct contact with the environment by controlling such sensory functions as vision, hearing, touch and spatial processing. Next are areas that

coordinate those functions: the part of the brain that helps you know where the light switch is in your bathroom even if you can't see it in the middle of the night. The very last part of the brain to be pruned and shaped to its adult dimensions is the prefrontal cortex, home of the so-called executive functions--planning, setting priorities, organizing thoughts, suppressing impulses, weighing the consequences of one's actions. In other words, the final part of the brain to grow up is the part capable of deciding, I'll finish my homework and take out the garbage, and then I'll IM my friends about seeing a movie.

"Scientists and the general public had attributed the bad decisions teens make to hormonal changes, says Elizabeth Sowell, a UCLA neuroscientist who has done seminal MRI work on the developing brain. "But once we started mapping where and when the brain changes were happening, we could say, Aha, the part of the brain that makes teenagers more responsible is not finished maturing yet."

## RAGING HORMONES

Hormones, however, remain an important part of the teen-brain story. Right about the time the brain switches from proliferating to pruning, the body comes under the hormonal assault of puberty. (Research suggests that the two events are not closely linked because brain development proceeds on its own schedule even when a child experiences early or late puberty.) For years, psychologists attributed the intense, combustible emotions and unpredictable behavior of teens to this biochemical onslaught. And new research adds fresh support. At puberty, the ovaries and testes begin to pour estrogen and testosterone into the bloodstream, spurring the development of the reproductive system, causing hair to sprout in the armpits and groin, wreaking havoc with the skin, and shaping the body to its adult contours. At the same time, testosterone-like hormones released by the adrenal glands, located near the kidneys, begin to circulate. Recent discoveries show that these adrenal sex hormones are extremely active in the brain, attaching to receptors everywhere and exerting a direct influence on serotonin and other neurochemicals that regulate mood and excitability.

The sex hormones are especially active in the brain's emotional center--the limbic system. This creates a "tinderbox of emotions," says Dr. Ronald Dahl, a psychiatrist at the University of Pittsburgh. Not only do feelings reach a flash point more easily, but adolescents tend to seek out situations where they can allow their emotions and passions to run wild. "Adolescents are actively looking for experiences to create intense feelings," says Dahl. "It's a very important hint that there is some particular hormone-brain relationship contributing to the appetite for thrills, strong sensations and excitement." This thrill seeking may have evolved to promote exploration, an eagerness to leave the



nest and seek one's own path and partner. But in a world where fast cars, illicit drugs, gangs and dangerous liaisons beckon, it also puts the teenager at risk.

That is especially so because the brain regions that put the brakes on risky, impulsive behavior are still under construction. "The parts of the brain responsible for things like sensation seeking are getting turned on in big ways around the time of puberty," says Temple University psychologist Laurence Steinberg. "But the parts for exercising judgment are still maturing throughout the course of adolescence. So you've got this time gap between when things impel kids toward taking risks early in adolescence, and when things that allow people to think before they act come online. It's like turning on the engine of a car without a skilled driver at the wheel."

## DUMB DECISIONS

Increasingly, psychologists like Steinberg are trying to connect the familiar patterns of adolescents' wacky behavior to the new findings about their evolving brain structure. It's not always easy to do. "In all likelihood, the behavior is changing because the brain is changing," he says. "But that is still a bit of a leap." A critical tool in making that leap is functional magnetic resonance imaging (fMRI). While ordinary MRI reveals brain structure, fMRI actually shows brain activity while subjects are doing assigned tasks.

At McLean Hospital in Belmont, Mass., Harvard neuropsychologist Deborah Yurgelun-Todd did an elegant series of FMRI experiments in which both kids and adults were asked to identify the emotions displayed in photographs of faces. "In doing these tasks," she says, "kids and young adolescents rely heavily on the amygdala, a structure in the temporal lobes associated with emotional and gut reactions. Adults rely less on the amygdala and more on the frontal lobe, a region associated with planning and judgment." While adults make few errors in assessing the photos, kids under 14 tend to make mistakes. In particular, they identify fearful expressions as angry, confused or sad. By following the same kids year after year, Yurgelun-Todd has been able to watch their brain-activity pattern--and their judgment--mature. Fledgling physiology, she believes, may explain why adolescents so frequently misread emotional signals, seeing anger and hostility where none exists. Teenage ranting ("That teacher hates me!") can be better understood in this light.

At Temple University, Steinberg has been studying another kind of judgment: risk assessment. In an experiment using a driving-simulation game, he studies teens and adults as they decide whether to

run a yellow light. Both sets of subjects, he found, make safe choices when playing alone. But in group play, teenagers start to take more risks in the presence of their friends, while those over age 20 don't show much change in their behavior. "With this manipulation," says Steinberg, "we've shown that age differences in decision making and judgment may appear under conditions that are emotionally arousing or have high social impact." Most teen crimes, he says, are committed by kids in packs.

Other researchers are exploring how the adolescent propensity for uninhibited risk taking propels teens to experiment with drugs and alcohol. Traditionally, psychologists have attributed this experimentation to peer pressure, teenagers' attraction to novelty and their roaring interest in loosening sexual inhibitions. But researchers have raised the possibility that rapid changes in dopamine-rich areas of the brain may be an additional factor in making teens vulnerable to the stimulating and addictive effects of drugs and alcohol. Dopamine, the brain chemical involved in motivation and in reinforcing behavior, is particularly abundant and active in the teen years.

Why is it so hard to get a teenager off the couch and working on that all important college essay? You might blame it on their immature nucleus accumbens, a region in the frontal cortex that directs motivation to seek rewards. James Bjork at the National Institute on Alcohol Abuse and Alcoholism has been using fMRI to study motivation in a challenging gambling game. He found that teenagers have less activity in this region than adults do. "If adolescents have a motivational deficit, it may mean that they are prone to engaging in behaviors that have either a really high excitement factor or a really low effort factor, or a combination of both." Sound familiar? Bjork believes his work may hold valuable lessons for parents and society. "When presenting suggestions, anything parents can do to emphasize more immediate payoffs will be more effective," he says. To persuade a teen to quit drinking, for example, he suggests stressing something immediate and tangible--the danger of getting kicked off the football team, say--rather than a future on skid row.

Persuading a teenager to go to bed and get up on a reasonable schedule is another matter entirely. This kind of decision making has less to do with the frontal lobe than with the pineal gland at the base of the brain. As nighttime approaches and daylight recedes, the pineal gland produces melatonin, a chemical that signals the body to begin shutting down for sleep. Studies by Mary Carskadon at Brown University have shown that it takes longer for melatonin levels to rise in teenagers than in younger kids or in adults, regardless of exposure to light or stimulating activities. "The brain's program for starting nighttime is later," she explains.

## PRUNING PROBLEMS

The new discoveries about teenage brain development have prompted all sorts of questions and theories about the timing of childhood mental illness and cognitive disorders. Some scientists now believe that ADHD and Tourette's syndrome, which typically appear by the time a child reaches age 7, may be related to the brain proliferation period. Though both disorders have genetic roots, the rapid growth of brain tissue in early childhood, especially in regions rich in dopamine, "may set the stage for the increase in motor activities and tics," says Dr. Martin Teicher, director of developmental biopsychiatry research at McLean Hospital. "When it starts to prune in adolescence, you often see symptoms recede."

Schizophrenia, on the other hand, makes its appearance at about the time the prefrontal cortex is getting pruned. "Many people have speculated that schizophrenia may be due to an abnormality in the pruning process," says Teicher. "Another hypothesis is that schizophrenia has a much earlier, prenatal origin, but as the brain prunes, it gets unmasked." MRI studies have shown that while the average teenager loses about 15% of his cortical gray matter, those who develop schizophrenia lose as much as 25%.

## WHAT'S A PARENT TO DO?

Brain scientists tend to be reluctant to make the leap from the laboratory to real-life, hard-core teenagers. Some feel a little burned by the way earlier neurological discoveries resulted in Baby Einstein tapes and other marketing schemes that misapplied their science. It is clear, however, that there are implications in the new research for parents, educators and lawmakers.

In light of what has been learned, it seems almost arbitrary that our society has decided that a young American is ready to drive a car at 16, to vote and serve in the Army at 18 and to drink alcohol at 21. Giedd says the best estimate for when the brain is truly mature is 25, the age at which you can rent a car. "Avis must have some pretty sophisticated neuroscientists," he jokes. Now that we have scientific evidence that the adolescent brain is not quite up to scratch, some legal scholars and child advocates argue that minors should never be tried as adults and should be spared the death penalty. Last year, in an official statement that summarized current research on the adolescent brain, the American Bar Association urged all state legislatures to ban the death penalty for juveniles. "For social and biological reasons," it read, "teens have increased difficulty making mature decisions and understanding the consequences of their actions."



Most parents, of course, know this instinctively. Still, it's useful to learn that teenage behavior is not just a matter of willful pigheadedness or determination to drive you crazy--though these, too, can be factors. "There's a debate over how much conscious control kids have," says Giedd, who has four "teenagers in training" of his own. "You can tell them to shape up or ship out, but making mistakes is part of how the brain optimally grows." It might be more useful to help them make up for what their brain still lacks by providing structure, organizing their time, guiding them through tough decisions (even when they resist) and applying those time-tested parental virtues: patience and love.

--With reporting by Alice Park/New York

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