

New research indicates that teenagers who drink too much may lose as much as 10 percent of their brainpower—the difference between passing and failing in school . . . and in life

# getting S u i d

By Bernice Wuethrich Photographs by Danielle Levitt

*Sarah, a high school senior, drinks in moderation, but many of her friends do not. At one party, a classmate passed out after downing more than 20 shots of hard liquor and had to be rushed to a local emergency room. At another party a friend got sick, so Sarah made her drink water, dressed her in a sweatshirt to keep her warm, and lay her in bed, with a bucket on the floor. Then she brushed the girl's long hair away from her face so that it wouldn't get coated with vomit. "Every weekend, drinking is the only thing people do. Every single party has alcohol," says Sarah. (The names of the teenagers in these stories have been changed to protect their privacy.)*

THE MOST RECENT STATISTICS FROM THE U.S. Substance Abuse and Mental Health Services Administration's National Household Survey on Drug Abuse indicate that nearly 7 million youths between the ages of 12 and 20 binge-drink at least once a month. And despite the fact that many colleges have cracked down on drinking, Henry Wechsler of the Harvard School of Public Health says that two of every five college students still binge-drink regularly. For a male that means downing five or more drinks

in a row; for a female it means consuming four drinks in one session at least once in a two-week period.

Few teens seem to worry much about what such drinking does to their bodies. Cirrhosis of the liver is unlikely to catch up with them for decades, and heart disease must seem as remote as retirement. But new research suggests that young drinkers are courting danger. Because their brains are still developing well into their twenties, teens who drink excessively may be destroying significant amounts of mental capacity in ways that are more dramatic than in older drinkers.

Scientists have long known that excessive alcohol consumption among adults over long periods of time can create brain damage, ranging from a mild loss of motor skills to psychosis and even the inability to form memories. But less has been known about the impact alcohol has on younger brains. Until recently, scientists assumed that a youthful brain is more resilient than an adult brain and could escape many of

the brain that is similar in rats and humans. Six years ago, when Swartzwelder published his first paper suggesting that alcohol disrupts the hippocampus more severely in adolescent rats than in adult rats, "people didn't believe it," he says. Since then, his research has shown that the adolescent brain is more easily damaged in the structures that regulate the acquisition and storage of memories.

Learning depends on communication between nerve cells, or neurons, within the hippocampus. To communicate, a neuron fires an electrical signal down its axon, a single fiber extending away from the cell's center. In response, the axon releases chemical messengers, called neurotransmitters, which bind to receptors on the receiving branches of neighboring cells. Depending on the types of neurotransmitters released, the receiving cell may be jolted into action or settle more deeply into rest.

But the formation of memories requires more than the simple firing or inhibition of nerve cells. There must be

lescent brain tissue much more than in adult tissue. Next, Swartzwelder identified a likely explanation. Long-term potentiation—and thus memory formation—relies in large part on the action of a neurotransmitter known as glutamate, the brain's chemical kingpin of neural excitation. Glutamate strengthens a cell's electrical stimulation when it binds to a docking port called the NMDA receptor. If the receptor is blocked, so is long-term potentiation, and thus memory formation. Swartzwelder found that exposure to the equivalent of just two beers inhibits the NMDA receptors in the hippocampal cells of adolescent rats, while more than twice as much is required to produce the same effect in adult rats. These findings led him to suspect that alcohol consumption might have a dramatic impact on the ability of adolescents to learn. So he set up a series of behavioral tests.

First, Swartzwelder's team dosed adolescent and adult rats with alcohol and ran them through maze-learning tests.

## The younger the brain, the more it may be at risk

the worst ills of alcohol. But some researchers are now beginning to question this assumption. Preliminary results from several studies indicate that the younger the brain is, the more it may be at risk. "The adolescent brain is a developing nervous system, and the things you do to it can change it," says Scott Swartzwelder, a neuropsychologist at Duke University and the U.S. Department of Veterans Affairs.

Teen drinkers appear to be most susceptible to damage in the hippocampus, a structure buried deep in the brain that is responsible for many types of learning and memory, and the prefrontal cortex, located behind the forehead, which is the brain's chief decision maker and voice of reason. Both areas, especially the prefrontal cortex, undergo dramatic change in the second decade of life.

Swartzwelder and his team have been studying how alcohol affects the hippocampus, an evolutionarily old part of

some physical change in the hippocampal neurons that represents the encoding of new information. Scientists believe that this change occurs in the synapses, the tiny gaps between neurons that neurotransmitters traverse. Repeated use of synapses seems to increase their ability to fire up connecting cells. Laboratory experiments on brain tissue can induce this process, called long-term potentiation. Researchers assume that something similar takes place in the intact living brain, although it is impossible to observe directly. Essentially, if the repetitive neural reverberations are strong enough, they burn in new patterns of synaptic circuitry to encode memory, just as the more often a child recites his ABCs, the better he knows them.

Swartzwelder's first clue that alcohol powerfully disrupts memory in the adolescent brain came from studying rat hippocampi. He found that alcohol blocks long-term potentiation in ado-

Compared with the adult rats, the adolescents failed miserably. To see whether similar results held true for humans, Swartzwelder recruited a group of volunteers aged 21 to 29 years old. He couldn't use younger subjects because of laws that forbid drinking before age 21. He chose to split the volunteers into two groups: 21 to 24 years old and 25 to 29 years old. "While I wouldn't argue that these younger folks are adolescents, even in their early twenties their brains are still developing," Swartzwelder says. After three drinks, with a blood-alcohol level slightly below the National Highway Traffic Safety Administration's recommended limit—.08 percent—the younger group's learning was impaired 25 percent more than the older group's.

Intrigued by these results, Swartzwelder's colleague Aaron White, a biological psychologist at Duke, set out to discover how vulnerable the adolescent brain is to long-term damage. He gave

a young person had been drinking, the smaller his hippocampus. The average size difference between healthy teens and alcohol abusers was roughly 10 percent. That is a lot of brain cells.

De Bellis speculates that the shrinkage may be due to cell damage and death that occurs during withdrawal from alcohol. Withdrawal is the brain's way of trying to get back to normal after prolonged or heavy drinking. It can leave the hands jittery, set off the classic headache, generate intense anxiety, and even provoke seizures, as neurons that had adjusted to the presence of alcohol try to adjust to its absence. Because alcohol slows down the transmission of nerve signals—in part by stopping glutamate from activating its NMDA receptors—nerve cells under the influence react by increasing the number and sensitivity of these receptors. When drinking stops, the brain is suddenly stuck with too many hyperactive receptors.

Mark Prendergast, a neuroscientist at the University of Kentucky, recently revealed one way these hyperactive receptors kill brain cells. First, he exposed rat hippocampal slices to alcohol for 10

that if overexcitability during alcohol withdrawal was causing cell death, blocking the receptors should minimize the carnage. It did, by about 75 percent.

Now Prendergast is examining what makes the receptors so lethal. By tracking radioactive calcium, he found that the overexcited receptors open floodgates that allow calcium to swamp the cell. Too much calcium can turn on suicide genes that cause the neuron to break down its own membrane. Indeed, that is exactly what Prendergast observed during alcohol withdrawal: Overactive receptors opened wide, and the influx of calcium became a raging flood.

Prendergast says that four or five drinks may cause a mild withdrawal. And, according to Harvard's Wechsler, 44 percent of college students binge in this manner. More alarming, 23 percent of them consume 72 percent of all the alcohol that college students drink.

*Chuck was 15 the first time he binged—on warm beers chugged with friends late at night in a vacant house. Six years later, celebrating his 21st birthday, he rapidly downed four shots of vodka in his dorm*

Brown, Susan Tapert, and Gregory Brown have been following alcohol-dependent adolescents for eight years. Repeated testing shows that problem drinkers perform more poorly on tests of cognition and learning than do nondrinkers. Furthermore, "the single best predictor of neuropsychological deficits for adolescents is withdrawal symptoms," says principal investigator Sandra Brown.

The psychologists recruited a group of 33 teenagers aged 15 and 16, all heavy drinkers. On average, each teen had used alcohol more than 750 times—the equivalent of drinking every day for two and a half years. Bingeing was common: The teens downed an average of eight drinks at each sitting. The researchers matched drinkers with nondrinkers of the same gender and similar age, IQ, socioeconomic background, and family history of alcohol use. Then, three weeks after the drinkers had their last drink, all the teens took a two-hour battery of tests.

The teens with alcohol problems had a harder time recalling information, both verbal and nonverbal, that they had learned 20 minutes earlier. Words such as *apple* and *football* escaped them. The

## Hyperactive receptors can cause cell death

days, then removed the alcohol. Following withdrawal, he stained the tissue with a fluorescent dye that lit up dead and dying cells. When exposed to an alcohol concentration of about .08 percent, cell death increased some 25 percent above the baseline. When concentrations were two or three times higher, he wrote in a recent issue of *Alcoholism: Clinical and Experimental Research*, the number of dead cells shot up to 100 percent above the baseline.

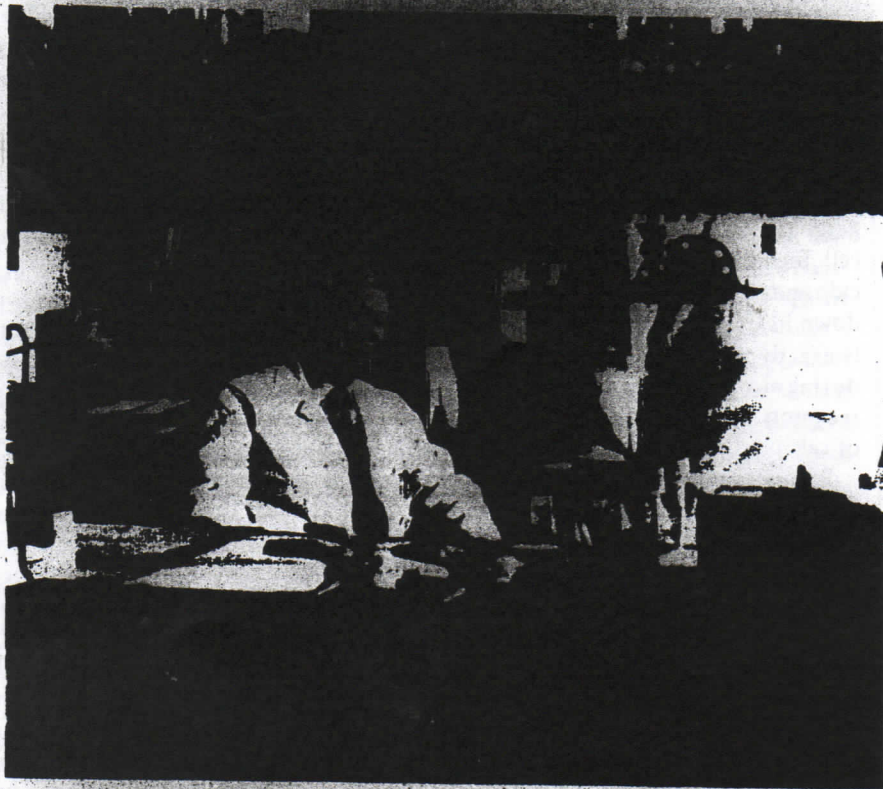
Prendergast says that the younger brain tissue was far more sensitive. Preadolescent tissue suffered four to five times more cell death than did adult tissue. In all cases, most of the death occurred in hippocampal cells that were packed with NMDA receptors. To home in on the cause, he treated another batch of brain slices with the drug MK-801, which blocks NMDA receptors. He reasoned

*room. Then he and his friends drove through the snowy night to a sorority party at a bar, where he consumed another 16 drinks. Chuck's friends later told him how the rest of the night unfolded. He danced in a cage. He spun on the floor. He careened around the parking lot with a friend on his back. Halfway home, he stumbled out of the car and threw up. A friend half carried him home down frozen roads at 2 a.m. "I don't remember any of this," Chuck says. But he does remember the hangover he lived with for two days, as his brain and body withdrew from the booze.*

RECENT HUMAN STUDIES SUPPORT a conclusion Prendergast drew from his molecular experiments: The greatest brain damage from alcohol occurs during withdrawal. At the University of California at San Diego and the VA San Diego Health Care System, Sandra

performance difference was about 10 percent. "It's not serious brain damage, but it's the difference of a grade, a pass or a fail," Tapert says. Other tests evaluated skills needed for map learning, geometry, or science. Again, there was a 10 percent difference in performance.

"The study shows that just several years of heavy alcohol use by youth can adversely affect their brain functions in ways that are critical to learning," Sandra Brown says. She is following the group of teenagers until they reach age 30, and some have already passed 21. "Those who continue to use alcohol heavily are developing attentional deficits in addition to the memory and problem-solving deficits that showed up early on," Brown says. "In the past we thought of alcohol as a more benign drug. It's not included in the war on drugs. This study clearly demonstrates



Alcohol triggers "a lower sedative response" in the brains of adolescents than in adults, says Fulton Crews, director of the Center for Alcohol Studies at the University of North Carolina at Chapel Hill. As a result, teenagers "can drink more and damage their brains more."



"We think that a blackout is alcohol shutting down the hippocampus. During that time, the hippocampus can no longer form new memories," says biological psychologist Aaron White (right), with neuropsychologist Scott Swartzwelder in their Duke University lab.

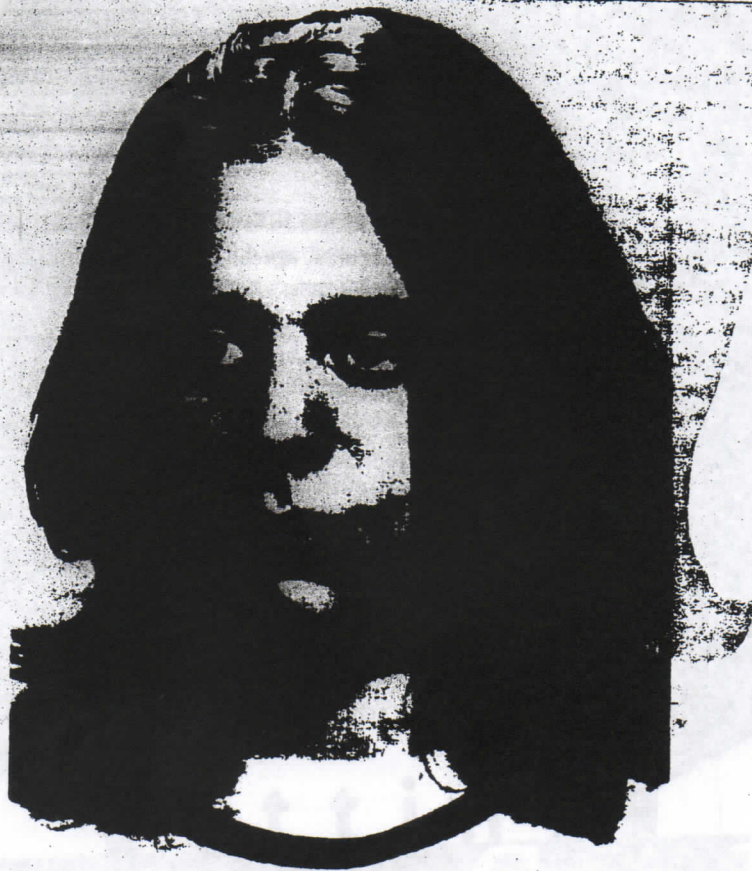
adolescent and adult rats large doses of alcohol every other day for 20 days—the equivalent of a 150-pound human chugging 24 drinks in a row. Twenty days after the last binge, when the adolescent rats had reached adulthood, White trained them in a maze-memory task roughly akin to that performed by a human when remembering the location of his car in a parking garage.

Both the younger and older rats performed equally well when sober. But when intoxicated, those who had binged as adolescents performed much worse. "Binge alcohol exposure in adolescence appears to produce long-lasting changes in brain function," White says. He suspects that early damage caused by alcohol could surface whenever the brain is taxed. He also suspects that the NMDA receptor is involved, because just as alcohol in the system inhibits the receptor, the drug's withdrawal overstimulates it—which can kill the cell outright.

*During the fall semester last year, at least 11 college students died from alcohol-related causes—at California State University at Chico, Colgate University in New York, Old Dominion University in Virginia, the University of Michigan,*

*Vincennes University in Kentucky, Washington and Lee University in Virginia, and Washington State University. No one knows how many other students were rushed to emergency rooms for alcohol poisoning, but at Duke, 11 students had visited local ERs in just the first three weeks of school, and in only one night of partying, three students from the University of Tennessee were hospitalized.*

STUDENTS WHO DRINK HEAVILY sometimes joke that they are killing a few brain cells. New research suggests that this is not funny. Some of the evidence is anatomical: Michael De Bellis at the University of Pittsburgh Medical Center used magnetic resonance imaging to compare the hippocampi of subjects 14 to 21 years old who abused alcohol to the hippocampi of those who did not. He found that the longer and the more



Cindy, 18

**DRINKING HISTORY:** First drink: age 14, at a party. "In high school I drank every weekend."

**MOST ALCOHOL EVER**

**CONSUMED:** three shots vodka, four shots rum, two screwdrivers, one strawberry daiquiri, and one beer.

**AFTEREFFECTS:** "In high school I had all B+'s and A-'s. I don't drink that much in college, and I have a B/B- average. Go figure. I put more effort into my college work though because I'm not rushing out at 6 o'clock to get a good six hours in of drinking."

that the most popular drug is also an incredibly dangerous drug."

Brown's research team is also using functional magnetic resonance imaging to compare the brain function of alcohol abusers and nondrinkers. Initial results show that brains of young adults with a history of alcohol dependence are less active than the brains of nondrinkers during tasks that require spatial working memory (comparable to the maze task that White conducted on rats). In addition, the adolescent drinkers seem to exhibit greater levels of brain activity when they are exposed to alcohol-related stimuli. For instance, when the drinkers read words such as *wasted* or *tequila* on a screen, the nucleus accumbens—a small section of the brain associated with craving—lights up.

The nucleus accumbens is integral to the brain's so-called pleasure circuit, which scientists now believe undergoes major remodeling during adolescence. Underlying the pleasure circuit is the neurotransmitter dopamine. Sex, food, and many drugs, including alcohol, can all induce the release of dopamine, which

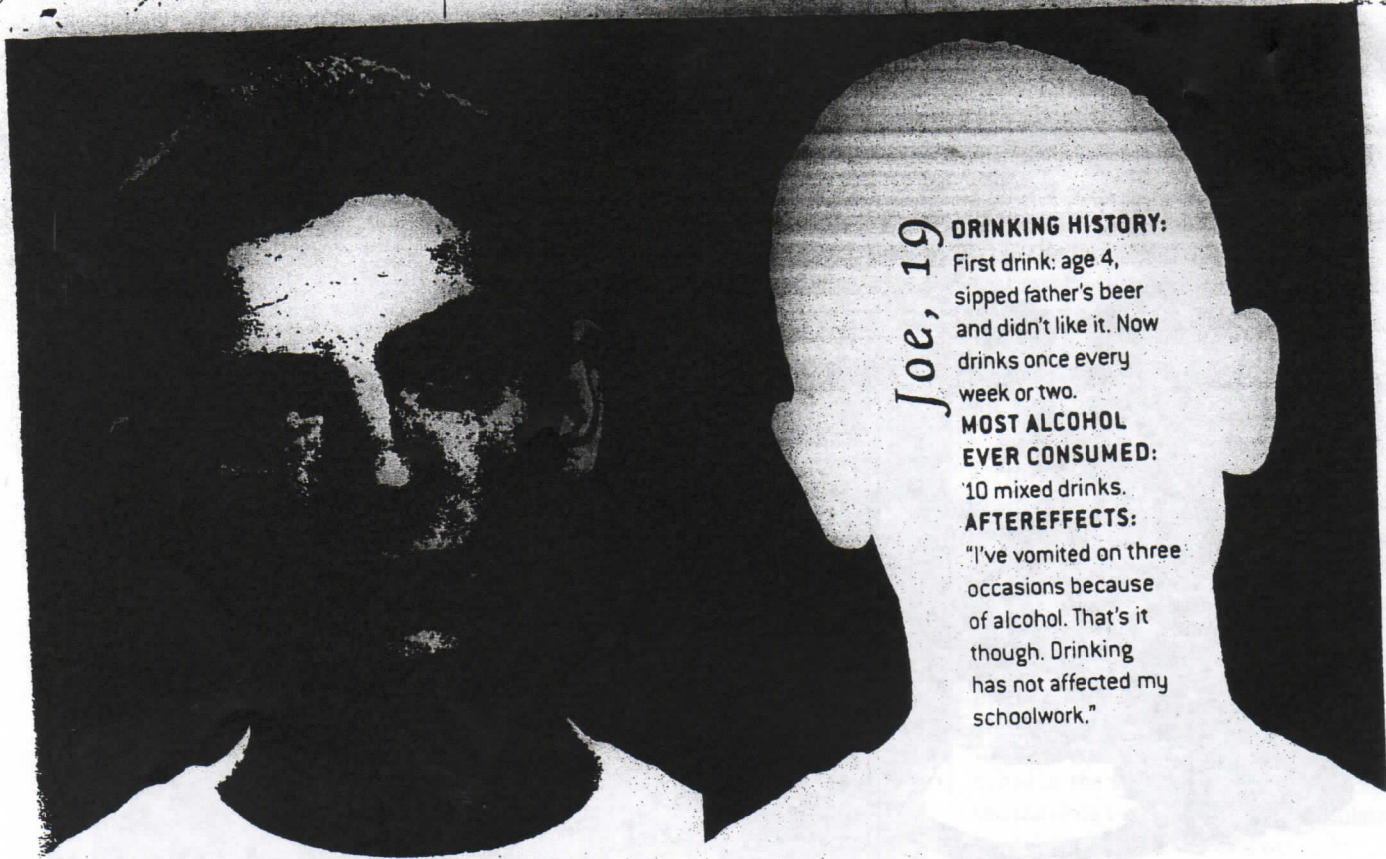
creates feelings of pleasure and in turn encourages repetition of the original behavior. During adolescence, the balance of dopamine activity temporarily shifts away from the nucleus accumbens, the brain's key pleasure and reward center, to the prefrontal cortex. Linda Spear, a developmental psychobiologist at Binghamton University in New York, speculates that as a result of this shift in balance, teenagers may find drugs less rewarding than earlier or later in life. And if the drugs produce less of a kick, more will be needed for the same effect. "In the case of alcohol, this may lead to binge drinking," she says.

*When Lynn was a freshman in high school, she liked to hang out at her friend John's apartment. More often than not, his father would be drinking beer. "He was like, 'Help yourself,'" Lynn says. Friends would come over and play drinking games until four or five in the morning. The longer the games continued, the tougher the rules became, doubling and tripling the number of drinks consumed. One night, Lynn came home drunk. Her*

*mother talked her through her options, sharing stories of relatives who had ruined their lives drinking. Lynn struggled with her choices. A year later she still drinks, but she's kept a pact with her girlfriends to stop bingeing.*

DURING ADOLESCENCE, THE PREFRONTAL cortex changes more than any other part of the brain. At around age 11 or 12, its neurons branch out like crazy, only to be seriously pruned back in the years that follow. All this tumult is to good purpose. In the adult brain, the prefrontal cortex executes the thought processes adolescents struggle to master: the ability to plan ahead, think abstractly, and integrate information to make sound decisions.

Now there is evidence that the prefrontal cortex and associated areas are among those most damaged in the brains of bingeing adolescents. Fulton Crews, director of the Center for Alcohol Studies at the University of North Carolina at Chapel Hill, has studied the patterns of cell death in the brains of adolescent and adult rats after four-day drinking



Joe, 19

**DRINKING HISTORY:**

First drink: age 4, sipped father's beer and didn't like it. Now drinks once every week or two.

**MOST ALCOHOL EVER CONSUMED:**

10 mixed drinks.

**AFTEREFFECTS:**

"I've vomited on three occasions because of alcohol. That's it though. Drinking has not affected my schoolwork."

bouts. While both groups showed damage in the back areas of the brain and in the frontally located olfactory bulb, used for smell, only the adolescents suffered brain damage in other frontal areas.

That youthful damage was severe. It extended from the rat's olfactory bulb to the interconnected parts of the brain that process sensory information and memories to make associations, such as "This smell and the sight of that wall tell me I'm in a place where I previously faced down an enemy." The regions of cell death in the rat experiment corresponded to the human prefrontal cortex and to parts of the limbic system.

The limbic system, which includes the hippocampus, changes throughout adolescence, according to recent work by Jay Giedd at the National Institute of Mental Health in Bethesda, Maryland. The limbic system not only encodes memory but is also mobilized when a person is hungry or frightened or angry; it helps the brain process survival impulses. The limbic system and the prefrontal cortex must work in concert for a person to make sound decisions.

Damage to the prefrontal cortex and the limbic system is especially worrisome because they play an important role in the formation of an adult personality. "Binge drinking could be making permanent long-term changes in the final neural physiology, which is expressed as personality and behavior in the individual," Crews says. But he readily acknowledges that such conclusions are hypothetical. "It's very hard to prove this stuff. You can't do an experiment in which you change people's brains."

Nonetheless, evidence of the vulnerability of young people to alcohol is mounting. A study by Bridget Grant of the National Institute on Alcohol Abuse and Alcoholism shows that the younger someone is when he begins to regularly drink alcohol, the more likely that individual will eventually become an alcoholic. Grant found that 40 percent of the drinkers who got started before age 15 were classified later in life as alcohol dependent, compared with only 10 percent of those who began drinking at age 21 or 22. Overall, beginning at age 15, the risk of future alcohol de-

pendence decreased by 14 percent with each passing year of abstinence.

The study leaves unanswered whether early regular drinking is merely a marker of later abuse or whether it results in long-term changes in the brain that increase the later propensity for abuse. "It's got to be both," Crews says. For one thing, he points out that studies of rats and people have shown that repeated alcohol use makes it harder for a person—or a rat—to learn new ways of doing things, rather than repeating the same actions over and over again. In short, the way alcohol changes the brain makes it increasingly difficult over time to stop reaching for beer after beer after beer.

Ultimately, the collateral damage caused by having so many American adolescents reach for one drink after another may be incalculable. "People in their late teens have been drinking heavily for generations. We're not a society of idiots, but we're not a society of Einsteins either," says Swartzwelder. "What if you've compromised your function by 7 percent or 10 percent and never known the difference?" ☒

"Getting Stupid" Discover March 2001

1. Binge drinking consists of \_\_\_\_\_ drinks in a row for males, and \_\_\_\_\_ for females.
2. What effect does excessive alcohol consumption over long periods of time have on adults?
3. Teen drinkers are more susceptible than adults to damage to what 2 parts of the brain? What functions does each part have?
4. Scientists believe that the change in neurons that allows you to learn new information occurs in the \_\_\_\_\_.
5. Swartzwelder discovered that alcohol blocks \_\_\_\_\_ in \_\_\_\_\_ brain tissue much more than in adult tissue.
6. The equivalent of just \_\_\_\_\_ beers inhibits (blocks) memory formation in adolescent rats while more than \_\_\_\_\_ as much beer is required to have the same effect on adult rats.
7. When adult and adolescent rats were both given equivalent amounts of alcohol and tried to learn to run a maze, which rats did better?
8. What effect does withdrawal have on NMDA cells?
9. What did Michael De Bellis find when he compared the hippocampi of those who abused alcohol and those who did not?
10. What is withdrawal?
11. What are the physical symptoms of withdrawal?
12. What does Prendergast mean when he says that young brain tissue is "far more sensitive?"
13. Where did most of the cell death occur?
14. Recent Human studies support Prendergast's conclusion that:
15. How did the psychologists at the University of California set up their experiment? Summarize the results of the experiment.
16. What happens when teen drinkers read words such as *wasted* or *tequila*?
17. Where is dopamine activity mainly located in adolescence?
18. What effect does that have on the "kick" drugs give adolescents?
19. What is the possible effect of that?
20. During adolescence, the \_\_\_\_\_ changes more than any other part of the brain.
21. What does the prefrontal cortex do in adults?
22. The study at UNC suggests that \_\_\_\_\_ are the areas most damaged in the brains of bingeing adolescents.
23. Damage to the prefrontal cortex and the limbic system is especially worrisome because it could cause permanent changes in an adolescent's \_\_\_\_\_.
24. What relationship is there between your age at first drink and alcoholism?
25. The way alcohol changes the brain makes it increasingly difficult over time to \_\_\_\_\_.
26. List two facts in this article about the effects of alcohol that you think most adolescents don't know.