ADOLESCENT BRAIN DEVELOPMENT AND ALCOHOL

During adolescence, brain organization and function enter a unique period of flux (Giedd, 2004). As an individual makes the transition from childhood to adulthood, from dependence to independence, changes in behavior are tumultuous (Dahl, 2004). Not surprisingly, so are the changes in brain function that give rise to these behaviors. Circuits that coordinate our behaviors, help us make good decisions and control our impulses, behave appropriately, govern our eating and sleeping habits, etc., are all being remodeled during the teen years. It is thought that much of this remodeling is influenced by an individual's interactions with the outside world, a fact that makes perfect sense given the nature of adolescence as a stage of intense personal evolution that prepares one to survive on their own outside of the nuclear family.

In recent years, it has become clear that, during adolescence, as in childhood, the brain is highly plastic and shaped by experience. A substantial number of synapses are eliminated, or pruned, in the cortex during adolescence, and this process is presumably influenced, at least in part, by interactions with the outside world (Spear, 2004).

It is tempting to conclude that adolescent brain development must simply be an extension of childhood brain development; that it represents a transition stage between childhood and adulthood in a manner similar to how adolescence itself has long been viewed. In actuality, it appears that many of the changes that take place during the second decade of life are novel and do not simply represent the trailing remnants of childhood plasticity.

Studies with both rats and humans suggest that the changes taking place in the brain during adolescence lead them to respond to alcohol differently, in some way, than adults. Below are a few examples with the species on which the work was based listed in parentheses:

- Brain circuitry involved in memory more vulnerable to alcohol in adolescence (rats)
- More brain damage following a four-day drinking binge in adolescents than adults (rats)
- Alcohol prevents cell birth in the brain more potently in adolescents than adults (rats)
- Alcohol impairs memory more in adolescents and young adults relative to adults (rats and humans)
- Alcohol produces less sedation in adolescents and young adults relative to adults (rats and personal experience!)
- Alcohol impairs balance less in adolescents and young adults relative to adults (rats and some human work)
- Repeated alcohol exposure during adolescence alters the way that people respond to alcohol later in life (rats and humans)

In addition to reacting differently to the acute, or initial, effects of alcohol, it appears that adolescents are also affected differently than adults by repeated, heavy drinking.

Many adolescents engage in a pattern of chronic intermittent exposure (CIE) sometimes referred to as binge drinking. Chronic intermittent exposure is a special case of chronic alcohol administration that involves discrete, repeated withdrawals.

There is compelling evidence, from rats, that it is the repeated withdrawals from alcohol that are responsible for many of the CNS effects of chronic alcohol exposure. For example, in laboratory animals, repeated withdrawals from alcohol result in a higher rate of seizures during withdrawal than are observed after *continuous* exposure of the same duration (Becker and Hale, 1993).

The association of repeated withdrawals with withdrawal seizure susceptibility is also indicated in humans. In studies of alcohol detoxification, patients with a history of previous detoxifications were more likely to exhibit seizures during withdrawal (Brown et al, 1988). Although these data from human studies are correlational, the convergence of these findings with those from animal models strongly suggests that discrete, repeated withdrawals from alcohol exposure presents a unique risk for subsequent neurobehavioral impairments.

The available evidence suggests that repeated exposure to alcohol during adolescence could lead to long-lasting deficits in cognitive abilities, including learning and memory, in humans. Much of this work has been pioneered by Drs. Susan Tapert and Sandra Brown, alcohol researchers at the University of California , San Diego (UCSD). Drs. Tapert and Brown have conducted a series of studies examining the impact of alcohol abuse on neuropsychological functioning in adolescents and young adults.

In one such study (Brown et al., 2000), adolescents in an in-patient substance abuse treatment program, at least three weeks sober, were compared to controls from the community on a battery of neuropsychological tests. Ages ranged from 15-16. Frequent drinkers (100 or more total drinking sessions), particularly those that had experienced alcohol withdrawal, performed more poorly than controls on several tests, including tests of learning, memory, and visuospatial functioning.

In a longitudinal study of subjects recruited from treatment programs (ages 13-19), Dr. Tapert and her colleagues observed that a return to drinking after the program led to further decline in cognitive abilities, particularly in tests of attention, over the next four years (Tapert et al., 1999). Once again, withdrawal from alcohol was a

(*cont'd from Page 5*) powerful predictor of such impairments. Similarly, Tapert and colleagues (2002) assessed neuropsychological functioning and substance use involvement at seven time points during an eight year period in subjects beginning, on average, at the age of 16 and ending at 24. Many of the subjects were initially assessed while in treatment and then tracked after their stay in the facility ended. Others were recruited from the community and then followed during the eight year period.

Cumulative levels of substance use, including alcohol use, were correlated with impairments in verbal learning and memory during the final assessment. That is, the heavier one was involved in substance use during adolescence, the lower their scores on tests of learning and memory at year eight, when subjects were in their early twenties. Heavier drinking alone was associated with lower scores on tests of attention, and experiencing withdrawal symptoms from alcohol predicted additional deficits in visuospatial abilities. These studies suggest that heavy use of alcohol and other drugs during the teenage years predicts lower scores on test of memory and attention when one is in their early-mid twenties.

Research by Dr. Tapert and her colleagues clearly suggests that alcohol use during the teen years, particularly when such use is heavy enough to result in withdrawal symptoms upon cessation of drinking, negatively impacts memory and attention, abilities necessary for negotiating the tasks of adolescence and successfully making the transition into adulthood.

These impairments presumably stem from changes in brain function, and that is exactly what additional projects by Tapert and Brown suggest. The authors have conducted several studies employing fMRI to investigate changes in brain activity following alcohol abuse during the teen years. While MRI is used to create images of the anatomy of the brain, fMRI is used to measure changes in oxygen levels in the brain over time, like while subjects perform different tasks. The changes in oxygen levels are used to measure, indirectly, changes in brain activity. In one study on this topic (Tapert et al., 2001), alcohol-dependent young women and healthy controls between the ages of 18-25 performed tests of working memory and vigilance (attention) while brain oxygen levels were measured using fMRI. The sample sizes were not quite big enough to detect significant impairments in working memory, though a clear trend toward such impairments was observed. However, alcohol-dependent subjects exhibited significantly less brain activity while performing the working memory task. Weaker activity was observed in several parts of the frontal lobes and in the parietal lobes. Alcohol-dependent subjects performed just fine during the vigilance task, and their brain activation during the task appeared normal. Such data suggest that the trend toward impaired working memory and the week brain activity that went with it can not simply be explained by lack of interest or motivation on the part of the subject.

A subsequent study with alcohol-dependent young women showed that alcohol-related cues (e.g., words associated with drinking) elicited craving and led to greater increases in brain activity in a variety of regions relative to controls (Tapert et al., 2004), thus establishing a link between craving for alcohol and brain function in key areas and indicating that the brains of alcohol-dependent young women function differently than their peers.

In summary, research with human adolescents clearly suggests that alcohol abuse during the teen years can have lasting deleterious effects beyond the scars of sexual assaults, injuries, violence, etc.

HOW RELEVANT IS THE RAT RESEARCH?

Much of the available data on the potential brain damage caused by exposure to alcohol during adolescence comes from studies done with rats. I am frequently asked how relevant such data could possibly be to the human condition. After all, rats and humans are not exactly the same.

The truth is that, most of what we know about how all drugs—prescription and illicit— affect the brain has been gleaned from research with rats.

Research on Fetal Alcohol Syndrome serves as a prime example of the sometimes beneficial interplay between human and rat research. We know that women who drink during pregnancy can give birth to children with physical and/or cognitive abnormalities. Yet, there is no *proof* from the human work that alcohol *causes* the symptoms seen in Fetal Alcohol Syndrome. However, rat research, in which pregnant rats are given alcohol and their offspring are studied, provides support for the teratogenic effects of alcohol.

It is true that rats are not humans, but our brains are similar enough that insights gleaned from rat research can be used to guide hypothesis-driven research with humans. As time goes by and technology advances, the stack of specifically human research will continue to grow.

Read — Spear LP (2004) Adolescent brain development and animal models. Annof NY Acad Sci 1021: 23-26 — for an excellent overview of issues.

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More material on these topics can be found online at:

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Acknowledgements

Current funding through NIAAA. This document summarizes work done dozens of researchers . Full references are not provided for every statement but are available on my website (see link at left) or by doing scholarly Google searches. If you discover an error in the text, please e-mail me so that I can correct it. Here is a partial list of researchers about whose work I really enjoy reading.

Jay Giedd, NIMH
Ron Dahl, University of Pittsburgh
Linda Spear, SUNY Binghamton
Susan Tapert, UCSD
Sandra Brown, UCSD
Fulton Crews, UNC-CH
Scott Swartzwelder, Duke University
Cheryl Kirstein, University of South Florida
Marisa Silveri, Harvard
Craig Slawecki, Scripps

…and many others

"No animal ever invented anything so bad as drunkenness – or so good as drink."

— G.K. Chesterton