

# Adolescent Addiction Centers Light Up on Cue

BY DEBRA L. BECK

FROM THE ANNUAL MEETING OF THE SOCIETY FOR ADOLESCENT HEALTH AND MEDICINE

TORONTO — Functional magnetic resonance imaging has shown that even very low levels of nicotine exposure can cause detectable changes in the adolescent brain's addiction centers, some of which differ from nicotine-related changes seen in adult brains, a study showed.

Previous research has also revealed differences in the effects of smoking on adolescents, compared with adults, Dr. Mark L. Rubinstein of the University of California, San Francisco, said at the meeting.

"We know that people who start smoking as teenagers are more likely to become lifelong smokers than those who start smoking as adults. In addition, teens seem to be more susceptible to nicotine addiction, reporting addiction with much lower levels of smoking—sometimes even without smoking daily."

Pharmacotherapy for smoking cessation is also less effective in teens than in adults. The current research aimed to discover underlying brain effects that might account for these differences.

In adult smokers, functional MRI has shown that both nicotine and smoking cues produce activity in the mesolimbic addiction system, specifically in the amygdala, the orbital frontal complex, the hippocampus, and the prefrontal

cortex. Previous studies of heavy smokers in their teens found similar results. However, because the majority of adolescents smoke only two to five cigarettes per day, Dr. Rubinstein's research used 12 light smokers (one to five cigarettes per day [mean 3.6] for at least 6 months) aged 13-17, along with 12 smoking-naïve adolescents of the same age as controls.

"We wondered if this might give us a better indication of the way adolescent brains work, and also a better idea of how early addiction processes work in the brain," he said.

Because cue exposure has the same effects on brain activity as actual nicotine, participants passively viewed a set of smoking-related images, then a set of neutral images, with process repeated eight times.

Functional analysis of their brains during this process found that nonsmokers showed no brain activation in any area.

In smokers, however, smoking cues were significantly associated with activity in the anterior cingulate (in the frontal cortex), the middle occipital gyrus, and the hippocampus—all of which lie within the brain's addiction centers.

"The hippocampus is involved with memory, specifically drug reward memories and conditioned responses," Dr. Rubinstein said. "The cingulate gyrus, which is in the frontal lobe, is involved in inhibitory control, and importantly, the frontal cortex, specifically the pre-

frontal cortex, is the last part of the teenage brain to develop.

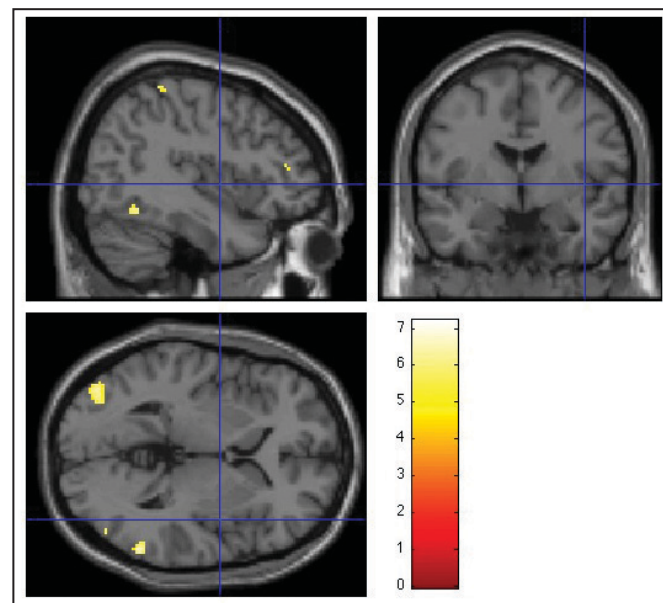
The medial occipital lobes are involved in visuospatial processing; this is subtracting the activation that occurs when smokers stare at neutral images, so they're paying more attention to the smoking images, which is no surprise but has been associated with addiction in adults."

Although these results were similar to those seen

in adult smokers, a significant difference was found: In adults, the lateral orbital frontal complex is usually activated, but in these teenaged light smokers, the medial orbital frontal complex was affected.

"The orbital frontal complex is involved in reward-related learning and impulse control, and a lot of people think that the medial orbital frontal complex might be the most important in impulse control," said Dr. Rubinstein.

"One of our theories is that the medial orbital frontal complex may be



IMAGES COURTESY DR. MARK L. RUBINSTEIN

**In teen smokers, smoking cues were significantly associated with activity in the brain's addiction centers.**

important in the development of addiction rather than the maintenance of addiction."

This is supported by the observation that these teen smokers scored only 2.8 on the modified Fagerström Tolerance Questionnaire, indicating no or very light addiction.

"Clinically, this says to us that even at very light/low levels of nicotine exposure, you may already be causing changes in the brain," he concluded.

Dr. Rubenstein reported no relevant financial relationships. ■

## Preteen Marijuana Use Boosts Risk for Depression, PTSD

VITALS

**Major Finding:** Starting marijuana use in the preteen years instead of the teen years was associated with a significantly greater likelihood of current posttraumatic stress disorder (16% vs. 6%) and a history of suicide attempts (32% vs. 19%).

**Data Source:** Retrospective study of 139 teenagers in residential treatment for substance dependence disorder.

**Disclosures:** Dr. Mahfoud said the investigators have no pertinent conflicts of interest. The study was funded by the National Institute on Alcohol Abuse and Alcoholism and the John Templeton Foundation.

BY SHERRY BOSCHERT

FROM THE ANNUAL CONFERENCE OF THE AMERICAN SOCIETY OF ADDICTION MEDICINE

SAN FRANCISCO — Substance-dependent young people who started smoking marijuana in their preteen years entered treatment with greater impairments than did those who started using marijuana as teenagers in a study of 136 patients in residential treatment.

Among the cohort of 14- to 18-year-olds, 57 (42%) began smoking marijuana before age 13 and 79 (58%) started marijuana use during their teenage years. Those whose marijuana use started before age 13 were more likely to have comorbid posttraumatic stress disorder (PTSD)—9 patients (16%) vs. 5 patients (6%)—and to have a history of suicide attempts—18 patients (32%) vs. 15 patients (19%)—at the time they entered treatment for substance dependence.

Preteen initiation of marijuana use also was associated with a history of past traffic violations, in four pa-

tients (7%) compared with one patient (1%), Dr. Youssef Mahfoud and his associates reported at the annual conference of the American Society of Addiction Medicine.

Marijuana dependence was significantly more likely in preteen users than in later users—54 patients (95%) vs. 61 (77%). Hallucinogen dependence also was more common in those who started marijuana as preteens: 25 patients (44%) vs. 21 patients (27%), said Dr. Mahfoud, a fellow in



**Marijuana might pose special risks for preteen users, whose adolescent brain growth peaks around age 12.**

DR. MAHFOUD

the psychiatry department of Case Western Reserve University, Cleveland.

In general, those young people who began using marijuana as preteens were more likely to be dependent on more than one substance.

The preteen marijuana users smoked more cigarettes per day (11 per patient) compared with the teen marijuana group (8 per patient) and were younger when they entered treatment (15.9 years vs. 16.5 years).

The associations between preteen marijuana use and more problems at the time youths enter treatment are not necessarily causal, Dr. Mahfoud noted. Preteens with PTSD, for example, might be using marijuana to self-medicate.

The increased rate of suicide attempts in preteen marijuana users might be attributable to a potentially increased rate of comorbid depression, but the study did not assess depression rates, he added.

"Marijuana, the most commonly used illicit substance in the United States, is perceived by many youths to be harmless," but it might pose special risks for preteen users, whose adolescent brain growth peaks around age 12, he said.

Previous studies have shown that marijuana use commonly is associated with increased rates of anxiety, legal problems, dropping out of school, and cognitive impairment with long-term use, he noted.

Dr. Mahfoud and his associates retrospectively studied data from semistructured interviews of patients, medical charts, and reports by the youths, parents, and clinicians. Because these were treatment-seeking patients, the findings might not be representative of other populations.

The cohort was 66% white. Preteen marijuana use was more common among Hispanics (8 patients, or 14%) than among non-Hispanics (2 patients, or 3%) and among patients with less-educated parents.

Overall, 57% of patients had a parent with a substance dependence disorder, and 57% came from single-parent households.

The study is the largest of substance-dependent young people that contained a generally gender-balanced cohort—47% male, 53% female, Dr. Mahfoud said.

Future research should investigate the way in which preteen marijuana might interfere with the brain's major growth spurt at age 12, Dr. Mahfoud suggested. ■