

Do Brain Abnormalities Predate Marijuana Use?

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MONTREAL — Teens who report heavy alcohol use have reduced hippocampal volume, compared with their nondrinking peers, but those who combine marijuana with heavy drinking do not show these abnormalities, Susan Tapert, Ph.D., reported at the annual conference of the EEG and Clinical Neuroscience Society.

"It's possible there could be some neu-

roprotective effect of marijuana against the effects of alcohol," said Dr. Tapert of the University of California, San Diego, noting that simultaneous marijuana and alcohol use has been shown to reduce blood alcohol levels.

However, another potential explanation is that "there may be competing pathologies that cancel each other out," she said in an interview. "Microstructural hippocampal changes related to marijuana use may include increased glial prolifera-

tion and white matter density, as well as reduced gray matter density," which might result in "relatively normal hippocampal volumes ... despite functional pathology," she wrote in a recent study (*Neurotoxicol. Teratol.* 2007;29:141-52). "This is speculative, and spectroscopic, diffusion, and segmentation studies will be needed to verify these impressions," she stressed.

In the study, which she presented at the meeting, her group used magnetic resonance imaging to compare hippocampal

volumes in 16 adolescent alcohol users, 26 marijuana and alcohol users, and 21 abstainers. The subjects were aged 15-18 years, and MRI was performed after at least 2 days of abstinence from all substances.

The smaller hippocampal volume seen in the alcohol users resulted in an abnormal pattern of right-to-left hippocampal asymmetry, compared with both controls and users of marijuana plus alcohol—and this abnormal asymmetry was related to memory function.

"In the nonusing control group, right-to-left hippocampal ratios were linearly related to best performance on verbal learning tasks, with right greater than left ratios linked to the best performances," Dr. Tapert said. "In contrast, adolescent drinkers

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and adolescent users of marijuana plus alcohol did not show any relationship between hippocampal asymmetry and learning performance. This could indicate underlying pathology in the substance-using teens, in

which hippocampal ratios no longer index encoding ability."

She went on to speculate that the pathological lack of correspondence between performance and volumes might be attributable to a combination of simultaneous microstructural factors, such as edema, atrophy, altered myelination, and altered synaptic pruning.

Brain volume studies may show little effect of marijuana use, but brain function tests tell another story, Dr. Tapert said. In another recent study by her group, although marijuana-using adolescents who had abstained for 28 days performed similarly to nonusers on an inhibition task, functional MRI showed evidence of more brain processing effort to achieve adequate performance levels in the users (*Psychopharmacology [Berl]* 2007;194:173-83).

And in another study by her group, 31 marijuana-using adolescents were compared with 34 controls on neuropsychological functioning. Users had slower psychomotor speed and poorer complex attention, verbal learning and memory, and planning and sequencing ability, even after more than 23 days of abstinence (*J. Int. Neuropsychol. Soc.* 2007;13:807-20).

Dr. Tapert suggested that some brain function abnormalities noted in adolescent marijuana users may not be caused by substance use but could possibly predate it.

"For performance on inhibition tasks, there is not much evidence to suggest that marijuana is accounting for the abnormalities, and there is a suggestion of premorbid differences," she said. "In contrast, abnormalities in verbal learning and memory do not appear linked to premorbid functioning and may possibly relate specifically to heavy marijuana use during adolescence." ■

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