Chronic alcohol intake can damage white matter pathways across the entire brain

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Chronic misuse of alcohol results in measurable damage to the brain. Chronic drinking may be particularly damaging to the integrity of frontal white matter tracts, which can interfere with cognitive and inhibitory control that, in turn, is important to achieve and maintain abstinence. A new study has used high-resolution structural magnetic resonance (MR) scans to determine the brain's regional vulnerability to chronic alcohol abuse, finding that abstinent alcoholics have reductions in white matter pathways across the entire brain.

Results will be published in the December 2014 online-only issue of *Alcoholism: Clinical & Experimental Research* and are currently available at Early View.

"The idea that alcohol affects the brain has been established for decades," said Catherine Brawn Fortier, a neuropsychologist and researcher at the VA Boston Healthcare System, assistant professor at Harvard Medical School, as well as corresponding author for the study. "Before advances in neuroimaging technology, the degree to which alcohol affects the brain across different levels of alcohol use, and how it may interact with other health factors, could only be inferred from behavior and through post-mortem studies. We now can use neuroimaging techniques to see, in vivo, that alcohol has wide ranging effects across the entire brain that contribute to a wide range of changes in psychological abilities and intellectual functions."

"Alcohol use among active military and veterans is a major issue in our

care for them at VA Boston Healthcare System and nationwide," said Terence M. Keane, a professor of psychiatry and psychology, as well as assistant dean for research at Boston University School of Medicine. "Many returning veterans use alcohol to cope with PTSD and other wounds of war. Dr. Fortier's study helps us understand how chronic, heavy alcohol misuse affects brain function, which informs our treatment of this group."

"The brain is usually divided into two broad kinds of tissues: gray matter or cortex consisting of neurons, the critical cells that support brain function; and white matter, the connections among large groups of those cells," explained Fortier. "We now know that alcohol impacts both gray and white matter, with the greatest impact affecting parts of the brain called the frontal lobes. These brain areas are critical to learning new information and, even more importantly, in self-regulation, impulse control, and the modification of all complicated human behaviors. In other words, the very parts of the brain that may be most important for controlling problem drinking are damaged by alcohol, and the more alcohol consumed, the greater the damage."

Frontal white matter tracts are the pathways that connect the frontal lobes to the rest of the brain, added Fortier. "The frontal cortex is the integration center for all other parts of the brain that are important to behavior and cognitive function," she said. "These pathways support self-monitoring, planning, judgment, and reasoning. Frontal pathways also allow flexibility in learning and memory, and allow us to change and learn new patterns of behavior. Most importantly, frontal pathways underlie impulse control, which is essential to achieve and maintain abstinence."

Fortier and her colleagues assessed global and regional white matter (WM) microstructure in two groups (n=51) using diffusion MR measures of fractional anisotropy (FA) to create a three-dimensional

measurement of white matter tissue: 31 abstinent alcoholics (20 men, 11 women) with an average of 25 years of abuse and approximately five years of sobriety, and 20 nonalcoholic control participants (13 men, 7 women). Study participants were recruited by way of flyers and newspaper advertisements; the mean age of the alcoholic group was 51, and the control group was matched to the alcoholic group with regard to gender, age, education, and estimated intelligence.

"There were two key findings to our study," said Fortier. "First, recovered alcoholics showed reductions in white matter pathways across the entire brain as compared to healthy light drinkers. This means that the pathways that allow the different parts of their brains to communicate efficiently and effectively are disrupted by alcoholism. Second, the effect of alcohol on the brain appears to be dose specific. Pathology is often thought of as occurring as an all-or-none phenomenon—you either have brain damage or you don't, similar to a stroke. Alcohol, however, is more like sunburn. Our study shows that the damage occurs as a function of quantity and exposure; the more you drink, the greater the damage to key structures of the brain, such as the inferior frontal gyrus, in particular. This part of the brain mediates inhibitory control and decision-making, so tragically, it appears that some of the areas of the brain that are most effected by alcohol are important for self-control and judgment, the very things needed to recover from misuse of alcohol."

"These results further indicate that individuals at high risk for alcoholism may have differences in their brain structure that mediate this risk," added Keane. "These differences could represent an important biomarker for neurobiological vulnerability to alcoholism that could be used to stop alcoholism earlier in the disease process."

"It may be that differences in the inferior frontal gyrus are genetically or congenitally determined - rather than a neurotoxic consequence of

drinking itself," explained Fortier. "Data from other scientists have supported this idea that individuals at high risk for alcoholism may have a neurobiological vulnerability."

"The day-to-day implications of this study are clear: abstinence and light drinking lead to better health and better brain function than heavy drinking," said Keane. "Alcoholism leads to many brain-related changes and dysfunction that decreases one's ability to function and to heal. The brain structures that are the most impacted by alcoholism are the ones that you need to control impulsive behavior and stop drinking. The longer you misuse alcohol the greater your chances are of permanent damage. So if you or someone you know needs help to reduce drinking, do it now."

Fortier agreed. "However, our data demonstrated possible recovery of tissue of the left inferior frontal gyrus with maintained abstinence in those alcoholics who successfully stopped drinking prior to their fifth decade," she said. "This finding is important because it demonstrates a possible critical threshold; excessive heavy drinking after a certain age - our data indicated age 50 - may lead to permanent brain changes, whereas earlier in life there may be more chance for brain recovery with sobriety."

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