The Cognitive Consequences Of Alcohol Use

By Ronald Devere, MD FAAN

In my experience as director of an Alzheimer’s disease (AD) and memory disorders center, it appears that an increasing number of my cognitively impaired patients are drinking alcohol more regularly. As clinical neurologists, our training in the neurological complications of alcohol use/abuse mainly focus on Wernicke’s encephalopathy, Korsakoff’s Syndrome, peripheral neuropathy, and cerebellar ataxia. Nonetheless, one of the most intriguing aspects of this topic from a neurological perspective is the cognitive impact of chronic mild to moderate continuous alcohol use and binge drinking. This topic has become more important because a significant number of patients over 65 are developing cognitive decline and experts in addiction medicine are beginning to realize that cognitive function is important in management of these individuals. According to various studies, 50 to 80 percent of these individuals present with impaired cognitive function.

The role of alcohol in cognitive decline, especially in the presence of multiple small strokes, Parkinson’s disease, Alzheimer’s disease, and frontal dementia, is difficult to decipher because little information is available on the effect of drinking in these disorders. On the contrary, a good deal of information exists regarding cognitive function and alcohol use by itself. In an article published in Neurology last year, authors concluded that regular and episodic drinking were not consistently associated with cognitive function.1 Worse cognition in participants who stopped drinking during follow-up suggested that inclusion of less healthy ex-drinkers may partly explain poor cognition in non-drinkers. This certainly challenges the notion that mild to moderate drinking is healthy for your heart and brain.

Ahead is a brief survey of literature on the topic.

ALCOHOL AND COGNITION

One of the most comprehensive studies on alcohol is a meta-analysis of 143 papers from 250 countries covering 1997-2011. It describes the relationship between moderate drinking of alcohol and aspects of cognition.2 The authors divided the papers into two distinct categories: those that provided ratios of risk between drinkers and non-drinkers (74 papers), and those that did not provide ratios but allowed cognition in drinkers to be rated as “better,” “no difference,” or “worse” than in non-drinkers. They also determined that cognitive testing varied between two different eras: 1977 to 1997, during which neuropsychological testing was used in mostly young to middle-aged adults, and 1998-2011, during which most used the mini mental status exam (MMSE) evaluating mostly older individuals. In studies in which no ratios and standard neuropsychological testing was used in 111,709 subjects younger than 55 years old, heavy drinking of four to six drinks per day was associated with cognitive impairment and higher risk for dementia. Notably, no significant difference in cognition was observed between light to moderate drinkers and non-drinkers.

In studies with ratios of risk in patients older than 55 years of age, 87 percent used MMSE. Eighty percent of these studies took place since 1998 in multiple countries. These studies showed a decreased risk of dementia and cognitive impairment in light to moderate drinkers in older adults by...
20 percent, but no significant benefit against rate of cognitive decline.

It is worth noting that this analysis was subject to criticism because some of the studies it used included previous drinkers that quit, which can bias the results. Nineteen of the ratio studies excluded these former drinkers. The meta-analysis showed that most studies did not distinguish the type of alcohol used. Some studies said wine was better, whereas others found no difference between beer or spirits. Of course, another inherent criticism is that male and female drinkers were combined for analysis and it is known the two sexes have different drinking patterns, which may mask a genuine difference among types of alcohol. In this meta-analysis, 23 ratios in the worse cognitively impaired group were carefully reviewed to see why mild to moderate drinking was associated with worse cognitive impairment. After accounting for +APOE4 allele and heavy drinking noted in these cases, the worse group represented only 2.2 percent of the total study. Unfortunately, few studies have looked at +APOE4, drinking, and cognitive decline, therefore more are needed to answer this question.

Another notable aspect about the meta-analysis is that accounting for age, education, sex, and smoking produced no change in the alcohol effects. There was also no difference in outcome between longitudinal or cross-sectional studies. Mental status exams were more often associated with finding better cognition in drinkers while neuropsychological tests were more often associated with no difference in cognition between drinkers and non-drinkers. Importantly, the findings suggested that moderate drinking had no impact on dementia in general, AD, or vascular dementia. Other meta-analyses have failed to find a significant benefit of alcohol use against cognitive decline, as well.3

In general, the association of moderate drinking and cognitive risk was found in a majority of the countries studied, however, the authors noted the absence of studies from Eastern Europe and Russia. As for why the MMSE test results were positive in reducing cognitive risk of decline compared to neuropsychological testing group in light to moderate drinkers, the authors pointed out that because many studies used MMSE to increase the validity of the results, while 60 percent of the studies used additional measures of cognition, the judgement of dementia and cognitive impairment were more reliable. The authors also stated that heavy drinking (i.e., greater than three to four drinks a day) is associated with an increased risk of cognitive impairment and dementia in addition to the usual social and society issues in general. Light to moderate drinking of two drinks per day or less in adult men and one drink or less in adult women, does not increase risk of cognitive decline, cognitive impairment, or dementia.

Defining Cognitive Impairment in Heavy Drinkers

There are four profiles of cognitive impairment in heavy drinkers:

1. No cognitive impairment
2. Isolated executive deficits with normal memory and global cognitive efficiency
3. Mild executive dysfunction with memory impairment and preserved global cognitive efficiency
4. Global impairment (executive function, memory and impaired cognitive efficiency)

These impairments can generally affect working memory, mental flexibility, attention, decision making, problem solving, processing speed, and planning. Encoding and retrieval tend to be affected most, while memory storage was normal.23 Executive impairment includes disorders of inhibition, flexibility, multitasking, and episodic memory. Visual spatial impairment is also predominantly affected, as studies have shown impaired visual spatial processing, visual learning, and visual spatial construction tasks.45

— Ronald Devere, MD

1. Ihara H et al, Group and case study of the dysexecutive syndrome in alcoholism without amnesia. JNAP 2000 68: 731-2
2. Pitel A et al, Genuine Episodic memory deficits and executive dysfunction in alcohol subjects early in abstinence. Alcohol Clinical Experimental Research. 2007 31; 1169-78

These results were echoed by findings from another comprehensive review evaluating the same factors.4

More recently, a study evaluated the relationship of alcohol consumption and cognitive decline in early old age.5 The cohort was the Whitehall II, a British study of civil servants which started in 1985 to 1988 composed of 10,308 participants, 67 percent of which were men men, with an age range of 35 to 55. Participants completed a self-administered questionnaire followed by clinical exams over future years from 1991 to 2009 (four assessments). Mean alcohol consumption was calculated for each participant via questions on frequency and amount of alcohol use and which source of alcohol consumed. Alcoholic drinks were converted to grams and divided by seven to obtain daily consumption in
grams/day. Those consuming alcohol but not in the third assessment were classified under “alcohol cessation” in the last 10 years. Those that drank but not in the last few weeks in all assessments were classified as “occasional” drinkers. Investigators used cognitive testing in the middle of the study (ages 44-69) and repeated in 2002-04, and 2007-09 (age range 55-80). Short-term memory and executive function (fluency and inductive reasoning, Math, etc.) were used. At inception, roughly 7,500 out of 10,000 participants participated at least one of three cognitive assessments and constituted the analytic sample. Thirteen percent partici-

Dosage Moderate Drinking Have Indirect Benefits?

While heavy drinking has been associated with cognitive impairments in addition to other detriments to health, there is some evidence to suggest that moderate alcohol consumption may have a positive impact. For example, one study found that low to moderate drinking reduced the risk of Myocardial Infarction (0.38) in male patients, even in non-smokers, those with a BMI of under 25 BMI, and who exercised 30 minutes per day. Another study found that low alcohol consumption of moderate drinking was found among those in poor health behavior (no exercise, poor diet and smoking).

The mechanism involved between alcohol consumption and cognition is complex. The main theory focuses on cerebral and cardio-pathways that play out over extended period of time. Light to moderate alcohol consumption leads to better vascular outcome. Both abstinence and heavy consumption is assisted with higher risk of vascular disease, which leads to increased cognitive impairment. Heavy alcohol use has neurotoxic effects on the brain, pro-inflammatory effects, cerebral vascular disease, and vitamin deficiency.

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Assessing Cognitive Impairment in Patients Who Have Stopped Drinking

For patients on a return visit who have abstained from alcohol since the previous visit, it may be appropriate to order an MRI of the brain and basic labwork, including TSH, B12, folate, vitamin D and homocysteine, metabolic profile, and CBC to see if there are any abnormalities to treat. A thiamine replacement might be necessary, as well. The MRI or CT scan may unveil chronic subdural, multiple strokes, etc., which may or may not change your evaluation before the patient returns after withdrawal from alcohol. Neuropsychological testing is not indicated until the patient has been off of alcohol for two to three months or longer, re-evaluated, and determined to have cognitive impairment. The neurologist should insist that the patient’s medications and vitamins be given by the caregiver. My mantra in cognitively impaired individuals is, “If the medication has not been seen swallowed it has not been taken.”

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554 Finnish Twins who provided data on alcohol consumption in questionnaires in 1975 and 1981 and were followed for 25 years. Participants were 65 years or older at the time of dementia assessment in 1999-2001. The assessments were done by telephone interviews, which have shown a strong correlation with mental assessment face to face. By the end of the follow-up, 103 participants developed dementia, however, the cause of dementia could not be determined from the telephone interview. The study considered binge drinking as five bottles of beer or one bottle of wine on one occasion at least monthly. This was associated with a relative risk of 3.2 (95% confidence interval = 1.2-8.6) for dementia. Also, blacking out during the heavy drinking periods at least twice during the previous year as reported in 1981 was associated with a higher risk for dementia in drinkers. The study found that binge drinking and passing out were risk factors even after controlling for alcohol consumption or after excluding from the analysis that were heavy drinkers. Of note, the follow-up period of 25 years was considered longer than most other studies. Participants in studies such as this frequently misreport their drinking habits for 25 years due to perhaps memory problems. Of note, a large proportion of the study population was composed of abstainers (24 percent). It did not appear that abstainers were less healthy than the other study members.

Interestingly, another study found that light to moderate drinkers with occasional binge drinking had a higher mortality than those light to moderate drinkers with such occasions. Additionally, a Russian study in 2001 showed that the risk of death from cardiovascular disease was increased in binge drinkers. We also know that recurrent head injuries are not uncommon in heavy and binge drinkers and may well be missed in questionnaires and history taking in any study. These data suggest that binge drinking in midlife is associated with increased risk of dementia.

THE EFFECT OF ALCOHOL OVERUSE AND ABSTINENCE ON THE BRAIN

When it comes to the exactly how alcohol use affects the brain, the severity of brain lesions depends on various factors including the extent of alcohol consumption, age, gender, and neuropsychological comorbidities. The most susceptible brain structures are the neocortex in the frontal lobes, the limbic system and the cerebellum. Gray matter reduction involves the frontal parietal regions while white matter reduction is diffuse. This latter study showed a 20 percent reduction of the gray matter of the dorsolateral prefrontal cortex and that the aging brain is more sensitive to the deleterious effects of excessive alcohol consumption. While this is not terribly surprising, the key word here is “age.” Regardless of the amount of heavy drinking, greater age leads to greater frontal lobe damage. The limbic system, especially the hippocampus, which is involved in episodic memory, is also impaired. The hypothalamus and mammillary bodies are very susceptible to chronic excessive alcohol use and when accompanied by thiamine deficiency leads to well-known Wernicke’s encephalopathy and Korsakoff’s syndrome we all know about. The cerebellum shows reduction of white matter volume in the vermis and cerebellar hemisphere, and connections between cerebellum and frontal lobe viapons and thalami are impaired.

On the other hand, abstaining from alcohol can have very positive effects. Studies have shown that in the first month of abstinence, brain volume begins to increase, sulci and ventricles start to decline, and evidence of improved executive function and verbal episodic memory begins. In another study, investigators 54 alcoholics and 54 matched controls matched for age (48 years) and education (very few women) and performed baseline neuropsychological tests assessing episodic memory and executive function and then again after six months of alcohol abstinence. The results over the six-month interval showed that episodic memory and executive function moderately improved and some returned to normal, whereas relapers performed lower in executive function. There was no significant differ-
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due to its reduced cardiovascular morbidity (see sidebar on page 59).

It is very clear that heavy drinking beyond three or more drinks per day increases cognitive decline, cognitive impairment and risk of dementia, but when it begins that rate of decline does not correlate with this or other level of drinking. Increased cardiovascular morbidity plays a big role in its negative affect. Binge drinking has been studied less but drinking greater than five beers or one bottle of wine at one time, a minimum of one time a month, has been shown to increase cognitive decline and dementia.

The good news is that abstinence from heavy drinking can lead to improvement in cognitive impairment and in many cases return the patient to normal in three months to one year, depending on length of alcohol abuse and the age of the individual. This is very important to neurologists who see numerous individuals with cognitive impairment on a daily basis. If a detailed alcohol history is taken from the patient—or, perhaps more importantly, the caregiver—and it appears the patient has been drinking heavy or binge drinking, it would make sense to try to encourage the patient to stop drinking and return to the clinic in two to three months sober, if possible. While other neurodegenerative and vascular causes of cognitive impairment do not improve, curbing the overuse of alcohol can in fact result in improvement.

TAKEAWAY POINTS ABOUT ALCOHOL USE AND COGNITIVE FUNCTION

Regardless of the limitations of many studies, it is quite clear that heavy drinking is detrimental to brain function, with effects ranging from impairment of memory (encoding and retrieval), executive function, and global cognition, to an increased risk of dementia. The data suggest that mild to moderate drinking (equal to or less than two drinks/day in men, or equal to or greater than one drink/day in women) does not increase risk for cognitive decline or dementia, but actually appears to reduce future cognitive impairment, likely


19. Chournaud S et al, Rewiring the brain to compensate for impairment in recovering alcoholics. Cerebral Cortex 2013, 23: 97-104