## Drinking in Middle Age May Accelerate Cognitive Decline

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January 15, 2014

Middle-aged men who drink 36 grams or more of alcohol a day, or a little more than 2 and a half standard drinks, are more likely to experience faster decline in all cognitive areas — but especially memory — during a period of 10 years, translating into 5.7 years of extra cognitive aging, a new study suggests.

The association for women in the study is less clear, although women who drink 19 or more grams per day of alcohol may experience faster decline in executive function. Interestingly, women who abstain from drinking also have faster declines in certain cognitive domains.

"Excessive alcohol consumption is known to have detrimental short- and long-term effects on the brain, but the effect of consumption of around 3 to 4 drinks per day is less clear," said lead author Séverine Sabia, PhD, Department of Epidemiology and Public Health, University College London, United Kingdom.

Unlike much of the previous research on the impact of alcohol consumption on cognition, the current study included middle-aged persons. "The elderly may have reduced their alcohol consumption due to health concerns," said Dr. Sabia. "In many of the previous studies, the effect of heavy drinking was difficult to assess due to the small number of heavy drinkers."

The study was published online January 15 in Neurology.

## Whitehall II Study

Researchers looked at a sample of 7153 participants in the Whitehall II Study who had the requisite data on alcohol consumption and other covariates. The ongoing study, which includes British civil servants, was started in 1985-1988, with a cohort that was 67% male.

Researchers categorized amounts of reported daily alcohol consumption. The reference category for men in the main analysis was 0.1 to 19.9 grams per day. In women, the reference consumption was between 0.1 and 9.9 grams per day. In the United States, a standard drink is 0.6 fluid ounces — or 14 grams — of alcohol.

The cognitive battery of 4 tests (a short-term verbal memory test and 3 tests of executive function) was carried out starting in 1997-1999 when the participants ranged in age from 44 to 69 years, and then repeated twice during the next 10 years.

The study showed that men who consumed 36 or more grams of alcohol a day showed faster declines on all cognitive measures compared with those consuming 0.1 to 19.9 grams a day.

The difference in 10-year decline in the global cognitive score was -0.10 (95% confidence interval [CI], -0.16 to -0.04; P < .005). The difference in executive function was -0.06 (95% CI, -0.12 to 0.12; P < .05); the difference in memory was -0.16 (95% CI, -0.26 to -0.05; P < .005).

The effect sizes are comparable to 2.4 extra years of cognitive decline in the global cognitive score, 1.5 extra years for executive function, and 5.7 extra years for memory.

"We found that the decline in memory was accelerated by almost 6 years in heavy male drinkers," commented Dr. Sabia. "This means, for example, that a man aged 55 years drinking more than 36 grams of alcohol per day would have a decline in memory comparable to a man aged 61 years."

There was no clear association in relation to beer or wine, which suggests that the effect of the overall alcohol consumption was not driven by a specific beverage, said Dr. Sabia

## Evidence in Women

Because the study did not include enough women who were heavy drinkers, it was impossible to test the effect of the same amount of alcohol as in men. There was only weak evidence in women (P = .09) that drinking more than 19 grams of alcohol per day was associated with a faster decline in executive function, corresponding to 2.4 extra years of decline.

Although abstention did not seem to have an effect on cognitive decline in men, it did have an effect in women. Compared with women consuming 0.1 to 9.9 grams per day, the 10-year abstainers experienced faster decline in the global cognitive score (difference: -0.21; P < .05) and executive functions (-0.17; P < .05) corresponding to about 5 extra years of cognitive decline.

However, said Dr. Sabia, because the number of abstainers was small and their characteristics likely differed from other participants, "this result has to be replicated in other studies, including a higher number of abstainers, before drawing conclusions."

The study did not examine the effect on cognition of binge drinking, but Dr. Sabia pointed to the "large literature on the detrimental effect of binge drinking, particularly in young adults."

The ways in which excessive alcohol consumption might speed cognitive decline are complex, although the main hypothesis focuses on cerebrovascular and cardiovascular pathways, and involves effects that play out over time, said Dr. Sabia.

"Light to moderate alcohol consumption is associated with better vascular outcomes, while both abstinence and heavy alcohol consumption are associated with higher risk of vascular disease, which, in turn, may increase the risk of cognitive impairment," she said. "Furthermore, heavy alcohol consumption has detrimental short- and long-term effects on the brain, including direct neurotoxic effect, proinflammatory effects, and indirect impact via cerebrovascular disease and vitamin deficiency."

The study findings are in line with previous research and with accepted guidelines. According to Dr. Sabia, drinking fewer than 2-3 drinks a day for men and 1-2 drinks for women is "probably not deleterious" for cognitive outcomes.

But these "safe limits" may be too high for older people because of the physiologic and metabolic changes related to aging, said Dr. Sabia. She pointed to recent evidence from a UK Royal College of Psychiatrists report (page 8) that suggests that the upper limit for those older than 65 years is 1.5 units per day or 11 units per week (1 unit = 8 grams).

Some countries have specific consumption guidelines for the elderly. For example, said Dr. Sabia, the US National Institutes of Health (NIH) recommends that people older than 65 years not consume more than 7 drinks a week, and that they have no more than 3 drinks on any given day.

## Statistical Sophistication

Asked to comment on these findings, Iain Lang, PhD, senior lecturer, Public Health, University of Exeter, United Kingdom, who has done research on the impact of alcohol on cognition, noted the study's "aggressive degree of statistical sophistication."

For example, said Dr. Lang, unlike other studies, the researchers used more than a single baseline measure of alcohol consumption.

Another novel aspect to this study, he added, was that it included middle-aged participants. Most previous work was carried out in adults aged 65 years and older.

Nevertheless, the study findings were not unexpected, said Dr. Lang. "I didn't think it was entirely surprising in terms of the results in that they're broadly pretty similar to what we've seen in older adults."

The study may not have included sufficient numbers of women to get a good estimate of the effects of heavy drinking, commented Dr. Lang. However, he added, "it would be rather surprising if this is problematic in men but *not* in women."

The alcohol consumption cut-offs used in the study should be approached with caution, stressed Dr. Lang. In women, for example, there is no way to verify that they are drinking 9.9 grams (the limit for the reference group in women) vs 10 grams a day.

"The general message that drinking a lot is potentially risky is fine, but I think it's problematic to say that if you drink up to 9.9 grams you're good, and if you drink 10 grams or over you're in trouble," said Dr. Lang.

He added, however, that he thought the 9.9 gram a day limit would be "in the ballpark at which you'd expect harm to occur."

As for being unable to point to a particular type of alcohol as the culprit in cognitive deterioration, Dr. Lang said that this is a recurrent challenge. "Unfortunately, for analytical purposes, very few people drink only 1 type of alcohol."

The study was supported by the British Medical Research Council, the British Heart Foundation, the US National Heart, Lung, and Blood Institute, and the US National Institute on Aging. Both Dr. Sabia and Dr. Lang report no relevant financial relationships.

Neurology. Published online January 15, 2014. Abstract

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Cite this article: Drinking in Middle Age May Accelerate Cognitive Decline. *Medscape*. Jan 15, 2014.