

Evaluating the association of alcohol intake with cognitive functioning

March 22 2012

Many observational cohort studies have shown that moderate alcohol use is associated with better cognitive function. However, since such studies are vulnerable to residual confounding by other lifestyle and physiologic factors, the authors conducted a Mendelian randomization study, using aldehyde dehydrogenase 2 (ALDH2) genotype (AA, GA, or GG) as an instrumental variable in 2-stage least squares analysis. Cognitive function was assessed from delayed 10-word recall score (n = 4,707) and Mini-Mental State Examination (MMSE) score (n = 2,284) among men from the Guangzhou Biobank Cohort Study (2003-2008). The authors had previously reported an association between reported alcohol intake and cognitive function from a larger group of subjects from the same study finding that women reporting occasional alcohol intake and men reporting occasional or moderate intake had better scores related to cognitive function than did abstainers.

In the present Mendelian study, the authors found no significant association between groups defined by the ALDH2 genotype (as an "unbiased" estimate of [alcohol consumption](#)) and the two measures of [cognitive functioning](#). A problem with the present analysis is that ALDH2 genotypes explained only 3% of the variance in reported [alcohol intake](#), which weakens the conclusions of the authors. Further, differences in the predominant type of beverage consumed (rice wine), and probably marked differences in drinking patterns between these subjects and Europeans and Americans, make it difficult to know what the implications of this study are for western industrialized societies.

We agree with the authors that "Causality should be thoroughly verified in a variety of settings using different kinds of evidence, including experimental or [genetic studies](#), rather than relying on simple observations in a particular setting." We strongly support future attempts at using Mendelian randomization studies, hopefully using better instruments for estimating alcohol intake. On the other hand, as stated by recent evaluations of various study designs for determining causality, we appreciate that Mendelian randomization sounds good, but it is not the "Holy Grail."

More information: Au Yeung SL, Jiang CQ, Cheng KK, Liu B, Zhang WS, Lam TH, Leung GM, Schooling CM. Evaluation of moderate alcohol use and cognitive function among men using a Mendelian randomization design in the Guangzhou Biobank Cohort Study. *Am J Epidemiol* 2012; pre-publication release. [DOI: 10.1093/aje/kwr462](https://doi.org/10.1093/aje/kwr462)

Provided by Boston University Medical Center

Citation: Evaluating the association of alcohol intake with cognitive functioning (2012, March 22) retrieved 3 May 2024 from <https://medicalxpress.com/news/2012-03-association-alcohol-intake-cognitive-functioning.html>

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