Cognitive Function after 11.5 Years of Alcohol Use: Relation to Alcohol Use

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The authors investigated the relation between alcohol use and cognitive decline after 11.5 years in a community sample. Findings were based on a study of 1,488 participants in the Baltimore arm of the Epidemiologic Catchment Area study, who completed the Mini-Mental State Examination (MMSE) at three time points in 1981, 1982, and 1993–1996. The participants were divided into five groups based on the amount and frequency of alcohol intake and the Diagnostic and Statistical Manual of Mental Disorders: DSM IIIR diagnosis of alcohol use disorders. The relation between level of alcohol use and MMSE score change between waves 2 and 3 of the study was examined using analysis of variance, which was then adjusted for the effects of age, race, and education. Alcohol use was associated with significantly less cognitive decline in alcohol drinkers when compared with nondrinkers for both sexes. When adjusted, a trend toward significantly less cognitive decline was seen in women drinkers, but not in men. Among female users, there was a trend toward less cognitive decline in women who used alcohol habitually as compared with those who were nonusers or heavy users. The authors conclude that, over long time periods, alcohol use is not associated with cognitive decline and, in women, may be associated with less decline.

alcohol drinking; cognition; dementia; women

Abbreviations: DSM-IIIR, Diagnostic and Statistical Manual of Mental Disorders: DSM IIIR; MMSE, Mini-Mental State Examination.

The relation of alcohol consumption to the risk of cognitive impairment or dementia has been studied extensively over the past two decades. However, results have been conflicting. This is, in part, due to the lack of longitudinal follow-up studies of the cognitive functioning of people who consume different amounts of alcohol over a long period of time, that is, years. Another area of interest is the differential effect of alcohol use by gender. Although the effect of alcohol on women’s health is increasingly becoming a focus of attention (1), little attention has been paid to the effect of alcohol consumption on cognition in women.

Several studies have examined, cross-sectionally, the relation between alcohol intake and cognitive impairment, in the absence of intoxication. Some found an increased risk of visuospatial and executive dysfunction (2, 3) and decreased psychomotor speed and recent memory (4) in chronic alcoholism. In contrast, others reported no association between chronic alcohol consumption and cognitive impairment, unless a more defined brain syndrome, such as Korsakoff’s, is present (5).

It has been argued that the studies finding no association between alcohol use and cognitive impairment did not administer neuropsychologic tests with “ecologic validity,” that is, relevance to every day cognitive tasks (6). In studies using neuropsychologic tests with such ecologic validity, chronic alcoholics, who do not meet criteria for a particular brain syndrome, appear to exhibit significant cognitive deficits, severe enough to interfere with the demands of daily life (6). Nonetheless, cross-sectional studies are still limited in determining the long-term effects of alcohol consumption on cognition, in part because of differential survival rates between alcohol users and nonusers. In addition, cross-sectional studies are often hampered by the acute effects of alcohol use. Hence, they may have little bearing on understanding the long-term effects of alcohol use on cognition.

Of the few prospective studies examining the long-term association of alcohol consumption and cognitive impair-
ment, results have been inconsistent. Two studies (7, 8) had only a 3-year follow-up. One reported that men who had low to moderate alcohol intake were protected from cognitive impairment (7). The other, however, found no consistent relation between either alcohol use or smoking and cognitive decline (8). In contrast to these shorter studies, Edelstein et al. (9) followed a cohort (n = 521) of older men and women aged 55 or more years prospectively over 13–18 years. No global effect on cognition, as assessed by the Mini-Mental State Examination (MMSE) scores, was seen. In addition, alcohol consumption over time did not affect cognition in men, whereas moderate drinking in women may have been associated with impaired long-term recall.

We recently reported findings from a 13-year follow-up of 1,488 persons of all ages who had participated in the Baltimore, Maryland, portion of the Epidemiologic Catchment Area study (10). The MMSE (11), a widely used quantitative measure of cognition, was administered to participants during wave 1 in 1981 and during two follow-up waves in 1982 and 1993–1996. The design of the study allowed us to examine cognitive decline between waves 2 and 3 in a large epidemiologic sample. We found that cognitive decline occurred in all age groups. Age, education, and minority status were all significantly associated with greater cognitive decline. In a later study, we found no association between cannabis use and cognitive decline as assessed by the MMSE (12).

In this paper, we focus our investigation on the same population. We had two goals: 1) to investigate any long-term association between alcohol use and cognitive decline and 2) to further delineate the association between alcohol consumption and cognitive decline in men and women separately. We used a study design proposed by Pope et al. (13) and previously used by Lyketsos et al. (12) in examining the relation between cognitive decline and cannabis use.

MATERIALS AND METHODS

The Baltimore Epidemiologic Catchment Area follow-up

The Epidemiologic Catchment Area program has been described in detail elsewhere (14, 15). Briefly, the National Institute of Mental Health Epidemiologic Catchment Area program is a national study with the aim of assessing the incidence and prevalence of mental disorders in the general population. Over 20,000 participants 18 or more years of age were interviewed at five study sites between 1980 and 1983. The Epidemiologic Catchment Area study estimated the lifetime prevalence of specific mental disorders in the population using the Diagnostic Interview Schedule that was designed for large-scale epidemiologic studies.

The Baltimore arm of this five-site study first entered the field in 1981, when the first wave of in-person assessments was completed. A second wave of assessment (including wave 2 administration of the MMSE) was conducted 1 year later, in 1982. The Baltimore Epidemiologic Catchment Area target population consisted of the adult household residents of eastern Baltimore City, an area with 175,211 inhabitants. During wave 1, a total of 4,238 individuals were designated for interview by probability sampling methods, and 3,481 (82 percent) completed interviews. Of these persons, 2,695 completed interviews during wave 2.

Wave 3 was conducted in 1993, approximately 11.5 years after wave 2. In wave 3, all 3,481 initial participants were targeted for tracing and interviewing. A total of 848 participants were found to have died; the remaining 2,633 were presumed to be alive, but 415 of them could not be successfully traced. Of the 2,218 persons located, 288 refused to participate, and 1,920 completed interviews. Of these 1,920 persons, 1,488 were found to have completed the MMSE during all three waves and were included in the present analysis. Diagnoses according to the Diagnostic and Statistical Manual of Mental Disorders: DSM III-R (DSM-III-R) were made using the Diagnostic Interview Schedule. All study participants signed informed consent statements approved by the Institutional Review Board of the Johns Hopkins University School of Hygiene and Public Health.

Participants

In these analyses, we included only those Epidemiologic Catchment Area study participants who completed the MMSE during all three study waves (n = 1,488), as we did in previous studies (10, 12).

Classification of participants according to use of alcohol. Participants were separated into five groups based on their self-reported alcohol use during all three waves of the study. The highest rated alcohol intake reported for the past month during any of the three study waves was used for each participant. The decision to assign the highest rated alcohol intake during any of the three waves was made after a separate analysis of the data using only information collected at the first two waves showed highly comparable findings to using data obtained from all three waves. Group 1 (nonusers) comprised those who reported in all three waves that they had never used alcohol (n = 319; 21.4 percent) and had never met criteria for alcohol abuse and dependence. This group reported that they had never used alcohol at any point in their lives. Group 2 (mild-moderate, infrequent, or “social” drinkers) comprised participants who had four drinks or less of alcohol per day, had never used it daily, and drank fewer than 20 days per month (n = 778; 52.3 percent). Group 3 (mild-moderate, frequent, or “habitual” drinkers) comprised participants who had four drinks or less of alcohol per day but drank on 20 or more days per month (n = 194; 13 percent). Group 4 (heavy, infrequent users) comprised those who had used more than four drinks per day on fewer than 20 days per month, that is, not daily use (n = 139; 9.3 percent). Finally, group 5 (heavy, frequent, or “heavy” drinkers) comprised those who reported more than four drinks per day on 20 or more days per month or “daily” (n = 58; 3.9 percent). In the Epidemiologic Catchment Area study, we define a drink as equal to one beer (16 ounces), one glass of wine, or 2 ounces of spirits (1 ounce = 29.57 ml). There was no overlap between the groups.

In a secondary analysis, the groups were also divided and analyzed on the basis of two additional classifications. First, participants were divided into those who were alcohol “users,” that is, having used alcohol on at least one of the three waves, versus alcohol “nonusers,” that is, never having
used alcohol at all three waves. Second, participants were divided into those with a DSM-III R diagnosis of alcohol abuse or dependence at one or more waves versus those with no diagnosis of alcohol abuse or dependence at any study wave. After complete description of the study to the subjects, written informed consent was obtained.

**Measurement of cognitive decline.** For each participant, an MMSE score difference was calculated by subtracting the wave 3 (1993–1996) MMSE score from the wave 2 (1982) MMSE score. The mean time interval between the points at which these MMSEs were administered was 11.6 years (standard error, 0.01 years). The median interval was 11.5 years, the 25th percentile was 11.3 years, and the 75th percentile was 11.9 years. The change in MMSE score (reported as a minus value) between waves 2 and 3 was the primary dependent variable in the analyses reported here.

**Other variables associated with cognitive decline used as covariates.** Information on other variables associated with cognitive decline was recorded at wave 1. Gender was indicated as male or female. Age was grouped as follows: 18–30, 31–40, 41–50, 51–60, 61–70, and more than 70 years. Minority status was indicated as African American or Hispanic versus other ethnicity (non-Hispanic White). Five educational subgroups were developed: 0–8 years, 9–11 years, 12 years, 13–15 years, and 16 or more years, in conformity with common educational landmarks. It is possible that some study participants, especially those in younger age groups at wave 1, completed their education after wave 1 and were thus misclassified.

**RESULTS**

Mean MMSE change scores in this cohort between waves 2 and 3 (with 95 percent confidence intervals) have been reported elsewhere (10). The mean change in MMSE score (with its 95 percent confidence interval) by level of alcohol use was estimated for the total group and for men and women separately. The relation between level of alcohol use and MMSE score change between waves 2 and 3 was examined using analysis of variance. Analysis of covariance models were then estimated with age, race, and education as covariates to adjust for the effect of other variables associated with cognitive decline. In the analysis of covariance, we also estimated adjusted mean declines (and 95 percent confidence intervals) in MMSE scores for the different alcohol use groups. Drug use was not included in the analysis as long-term cannabis use was found not to have a significant effect on cognitive decline (12).

**TABLE 1. Sociodemographic characteristics of the Baltimore Epidemiologic Catchment Area study cohort at wave 1 (n = 1,488) in 1981 and mean Mini-Mental State Examination score at waves 1–3 in 1981–1994**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–30</td>
<td>545</td>
<td>37</td>
</tr>
<tr>
<td>31–40</td>
<td>319</td>
<td>21</td>
</tr>
<tr>
<td>41–50</td>
<td>179</td>
<td>12</td>
</tr>
<tr>
<td>51–60</td>
<td>185</td>
<td>12</td>
</tr>
<tr>
<td>61–70</td>
<td>207</td>
<td>14</td>
</tr>
<tr>
<td>&gt;70</td>
<td>53</td>
<td>4</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>546</td>
<td>37</td>
</tr>
<tr>
<td>Female</td>
<td>942</td>
<td>63</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minority (African American or Hispanic)</td>
<td>516</td>
<td>35</td>
</tr>
<tr>
<td>Nonminority others</td>
<td>972</td>
<td>65</td>
</tr>
<tr>
<td>Education (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–8</td>
<td>245</td>
<td>16</td>
</tr>
<tr>
<td>9–11</td>
<td>318</td>
<td>21</td>
</tr>
<tr>
<td>12/GED*</td>
<td>576</td>
<td>39</td>
</tr>
<tr>
<td>13–15</td>
<td>222</td>
<td>15</td>
</tr>
<tr>
<td>≥16</td>
<td>127</td>
<td>9</td>
</tr>
<tr>
<td>MMSE* score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wave 1 (1981)</td>
<td>28.7</td>
<td>1.90</td>
</tr>
<tr>
<td>Wave 2 (1982)</td>
<td>28.5</td>
<td>1.87</td>
</tr>
<tr>
<td>Wave 3 (1993–1994)</td>
<td>27.1</td>
<td>2.59</td>
</tr>
</tbody>
</table>

* GED, General Equivalency Diploma; MMSE, Mini-Mental State Examination; SD, standard deviation.

**Association between alcohol use and MMSE score decline**

Table 2 displays the mean change in MMSE score by the level of alcohol use for the entire cohort and for men and women separately. The table displays the mean MMSE decline between wave 2 and wave 3 for each level of alcohol use or the estimated decline after adjustment for age, race, and education from the analysis of covariance. The 95 percent confidence intervals of this decline (negative numbers indicate a decline, positive numbers indicate an increase) are also reported after adjustment for age, race, and education. For each comparison across alcohol use levels, table 2 also shows the value of the F statistic from the analysis of variance or covariance, along with the relevant p value.

As can be seen in table 2, and as we have reported before (10), participants, on average, exhibited a mean decline of more than one MMSE point after 11.5 years. Declines were significantly greater for nonusers of alcohol, especially among women. After adjustment for age, race, and education, declines were comparable across levels of alcohol use in men but...
different for women. Women nondrinkers exhibited almost one point greater MMSE decline than did heavy, frequent drinkers and about two thirds of a point greater decline than did habitual users. Overall, however, even among women, differences in cognitive decline by level of alcohol use were small and only at the “trend” level of statistical significance.

Similar analyses of variance were then undertaken to compare the change in mean MMSE score between men and women for those with a DSM-IIIR diagnosis of alcohol use and/or dependence as compared with those who did not have this diagnosis. No statistically significant difference was found between the groups at the conventional level of $p < 0.05$. After adjustment for other variables such as age, education, and minority status, using an analysis of covariance, we found no association between the diagnosis of alcohol abuse and/or dependence and cognitive decline.

As seen in table 3, when comparing overall (men and women) alcohol “users” (i.e., used any amount of alcohol with any frequency during at least one wave) with “nonusers” (i.e., never used alcohol in all three waves), there was significantly less cognitive decline in the “users.” When examining results from men and women separately, we

<table>
<thead>
<tr>
<th>Level of alcohol use</th>
<th>Mean change* in MMSE† for total group</th>
<th>Mean change in MMSE for men</th>
<th>Mean change in MMSE for women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted‡</td>
<td>Adjusted§,¶</td>
<td>Unadjusted#</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>95% CI†</td>
<td>Mean</td>
</tr>
<tr>
<td>Nonusers (n = 319)</td>
<td>–1.99</td>
<td>–2.3, –1.69</td>
<td>–1.60</td>
</tr>
<tr>
<td>Social users (n = 778)</td>
<td>–1.29</td>
<td>–1.16, –1.40</td>
<td>–1.41</td>
</tr>
<tr>
<td>Habitual users (n = 194)</td>
<td>–1.02</td>
<td>–0.76, –1.29</td>
<td>–1.25</td>
</tr>
<tr>
<td>Binge users (n = 139)</td>
<td>–1.31</td>
<td>–0.93, –1.68</td>
<td>–1.30</td>
</tr>
<tr>
<td>Heavy, frequent users (n = 58)</td>
<td>–1.26</td>
<td>–0.37, –2.14</td>
<td>–1.37</td>
</tr>
</tbody>
</table>

* Change scores reported with minus signs.
† MMSE, Mini-Mental State Examination; CI, confidence interval.
‡ $F_{4,1483} = 7.37; p < 0.0001$.
§ Adjusted estimates account for the effects of age, education, and race.
¶ $F_{4,1480} = 0.97; p = 0.42$.
# $F_{4,158} = 1.12; p = 0.35$.
** $F_{4,158} = 0.216; p = 0.93$.
†† $F_{4,937} = 6.41; p < 0.0001$.
‡‡ $F_{4,934} = 1.70; p = 0.148$.
§§ Nonusers: total group (n = 319), men (n = 72), and women (n = 247).
¶¶ Alcohol users: total group (n = 1,169), men (n = 474), and women (n = 695).

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found that both groups had significantly less cognitive decline in the “user” group. When adjusted for age, education, and race, we found that no significant differences were seen in a comparison of “users” with “nonusers.” However, in women, a trend toward significantly less cognitive decline in “users” was seen. Hence, it appears that long-term alcohol use does not have an adverse effect on global cognitive decline in either men or women and may even be protective against decline in women. Finally, when stratifying the analysis by each of the six age groups, we found that no interaction with age and cognitive change and “use” or “nonuse” status was seen.

DISCUSSION

Few long-term, large, prospective population studies have investigated the relation between alcohol use and cognitive decline. In this study, among women, a trend toward less cognitive decline was seen for women with higher levels of alcohol use as well as when comparing alcohol “users” with “nonusers.” Among men, no such difference was evident. This lack of association between alcohol use and cognitive decline was confirmed in the secondary analysis that compared cognitive decline in those with or without a diagnosis of an alcohol use disorder. These results reflect data collected after an 11.5-year period following baseline examination, making this one of the two longest prospective, follow-up studies to examine the long-term effect of alcohol use on cognition.

These results are consistent with those from several other smaller or cross-sectional studies. For example, a meta-analysis of the risk of alcohol and tobacco consumption for the development of Alzheimer’s disease revealed no association between Alzheimer’s disease and increasing alcohol use (16). Likewise, according to a recent study from the Netherlands (5), which examined the neuropsychologic profiles and magnetic resonance imaging brain structure volumes of 14 patients with Korsakoff’s syndrome, compared with 15 patients with chronic alcoholism and 16 healthy controls, no cognitive and brain structure abnormalities were found in the non-Korsakoff’s, chronic alcoholism group. The authors of this study concluded that, if severe cognitive impairment is present in chronic alcoholic patients, it is more likely to be due to an underlying specific brain syndrome, such as Korsakoff’s, rather than due to the alcohol consumption per se. This notion is supported by studies that have found no evidence for the existence of “alcoholic dementia” or a dementia syndrome due to alcohol consumption alone (17, 18). Finally, the Bordeaux study (19), which was a cross-sectional, community-based study, showed no association between the level of wine consumption and the risk of low MMSE scores, that is, an MMSE score of less than 24.

Other studies have shown the opposite association between alcohol use and cognitive decline in women but not in men. That is, greater cognitive decline has been associated with alcohol use in women. For example, Edelstein et al. (9), in one of the few prospective studies, examined the association of cigarette smoking and alcohol consumption with the risk of cognitive impairment over a 13- to 18-year period. At final follow-up, their sample consisted of 521 surviving, noninstitutionalized men and women aged 55 or more years. A battery of cognitive tests, including the MMSE, were administered. The mean weekly level of alcohol consumption was divided into quartiles to reflect increasing amounts of use. With increasing levels of use, a decline in some cognitive scores, that is, the long-term recall portion of the Visual Reproduction Test, was seen in both sexes. However, statistical significance was reached only in women. In addition, women had more impaired savings scores with increasing levels of alcohol use. Finally, in women, moderate baseline and recent consumption of alcohol (about two drinks per day) was associated with worse performance on the Buschke long-term recall test. No such association was seen in men. The authors do concede that, because of the large number of comparisons and overall inconsistency of their results, the positive findings may simply be spurious. In fact, our data tend to support the latter conclusion.

In spite of our negative findings, it is possible to explain the trend seen in our study by survival bias. That is, in any prospective study, there is a risk that exposure to a particular factor of interest may result in death or dropout prior to the outcome of interest’s having been determined. This might explain the less impaired cognitive scores seen in the “heavy” and “binge” groups. However, the conclusions drawn from these groups are somewhat limited because of the smaller sample size in the latter subgroups. Many epidemiologic studies of the effects of alcohol use in women have found that the percentage of women who have two or more alcoholic drinks per day is relatively small (1), suggesting that few women would have dropped out of the higher intake groups. In addition, this study was designed to address the effect of alcohol use on cognition, not mortality, and therefore we cannot rule out that there may be a subgroup of patients who developed severe cognitive impairment and subsequently died. Finally, a point of concern is that, because the amount of alcohol intake was based on each individual’s recall, there is the potential of poor recall reliability among participants. Unfortunately, their information could not be verified by proxy.

Other study limitations include the MMSE’s being too insensitive to pick up specific cognitive changes or more subtle global cognitive decline. However, as we have proposed before, the MMSE is sensitive enough to detect “clinically significant” decline (10, 12). Hence, the absence of change is notable and clinically relevant. In addition, the MMSE is not designed to detect improvement in cognition, and there may be a ceiling effect for those who are functioning in the higher ranges of the MMSE. An improvement in cognition in male alcoholic individuals over a 13-month period of abstinence has been reported (20). Such a change would be difficult to pick up in this study, because of the “ceiling effect” of the MMSE. A more detailed cognitive battery might have detected important differences. However, the database did not provide any more detailed measures.

It could be argued that small differences in such a large sample (n = 1,488) might be due to a possible Meehl effect (statistically significant but unimportant and often nonreproducible differences found often in very large samples). However, most of our findings were not statistically signifi-

Am J Epidemiol 2002;156:747–752
cant, even though the point estimates were generally consistent in their direction for women.

As is consistent with the findings in our study, the negative effects of “social drinking” have not yet been fully determined. Problems arise in that different definitions of “social drinking” have been used across studies. Parsons (21), in a thorough review of the question, proposed a series of hypotheses to explain the presumed relation between alcohol consumption and cognitive-perceptual performance in sober social drinkers. In spite of this, it was determined that considerable research on the cognitive effects of social drinking is still necessary. One study (22), comparing nondrinkers, social drinkers, and long-term and short-term sober alcoholics, revealed no difference in performance on perceptual and memory tests between social drinkers and long-term abstinent alcoholics. Both groups performed worse than did the nondrinkers. The overall conclusion was that a simple dose-response relation between alcohol consumption and performance on cognitive testing most likely does not exist.

In summary, findings from this prospective epidemiologic study suggest that long-term social and habitual consumption of alcohol is not associated with an increased risk of cognitive decline in men and may even protect against cognitive decline in women.

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