Alcohol Intake, Carotid Plaque, and Cognition
The Northern Manhattan Study

Clinton B. Wright, MD, MS; Mitchell S.V. Elkind, MD, MS; Tatjana Rundek, MD, PhD; Bernadette Boden-Albala, DrPh; Myunghee C. Paik, PhD; Ralph L. Sacco, MD, MS

Background and Purpose—Moderate alcohol intake has been associated with better cognitive performance, implicating vascular and neurodegenerative processes. Few studies to clarify the importance of vascular disease have included direct measures of atherosclerosis or minority populations at higher risk of vascular disease and dementia.

Methods—The Northern Manhattan Study includes stroke-free community based Hispanic (54%), black (25%), and white (22%) participants. We performed a cross-sectional study of alcohol intake and performance on the Mini-Mental State Examination (MMSE) in subjects with sonographic measurement of maximal carotid plaque thickness and adjusted for sociodemographic and vascular risk factors.

Results—The median MMSE score was 27 (interquartile range 24 to 29; n=2215). Reported alcohol intake was divided into 5 groups: never (n=509), <1 drink/week (n=300), 1/week to ≤2 drinks/day (n=796), and >2 drinks/day (n=116). Drinking 1 drink weekly up to 2 daily was associated with better performance on the MMSE (odds ratio = 1.19; 95% CI, 1.10 to 1.26) compared with nondrinkers in women (P≤0.0001) but not in men, adjusting for sociodemographic and vascular risk factors. Maximal carotid plaque thickness (mean 1.1 mm; SD 1.2 mm) was not associated with alcohol intake and did not mediate the relationship between alcohol and cognition.

Conclusions—Moderate alcohol consumption was independently associated with better cognitive performance in women from this multiethnic sample. Carotid plaque was not a mediator of this association suggesting alcohol may impact cognition through a separate vascular or degenerative pathway. (Stroke. 2006;37:1160-1164.)

Key Words: alcohol drinking ● carotid artery diseases ● cognition

Moderate alcohol consumption may lower the risk of cognitive decline and dementia.1–7 The benefit may be mediated by a protective effect against vascular disease, as moderate alcohol consumption lowers the risk of stroke as well as subclinical infarcts and white matter disease on brain imaging.8,9 Moderate alcohol intake may also lower the risk of Alzheimer disease (AD).10 However, most studies have been limited to white subjects, and only a few studies have included blacks or Hispanics.7,11–13 Blacks and Hispanics have higher rates of cerebrovascular disease, dementia, and AD.14,15 Thus, additional data are needed to clarify the mechanism, especially in minority populations.

Carotid plaque has been associated with poor cognitive function independent of other vascular risk factors.16 The relationship between alcohol and carotid plaque is unclear, with some studies reporting moderate alcohol consumption was associated with less carotid atherosclerosis and others none.17,18 We hypothesized that moderate alcohol intake would be associated with better cognitive performance and examined carotid plaque and vascular risk factors as potential mediators of this relationship in a multiethnic cohort.

Methods
The Northern Manhattan Study (NOMAS) includes a stroke-free sample identified through random digit dialing as described previously.19 Community participants were eligible if they had never been diagnosed with a stroke, were ≥40 years of age, and had been residents of Northern Manhattan for at least 3 months in a household with a telephone. Subjects were recruited from the telephone sample for an in-person assessment with an overall response rate of 68%.

The ethics committee of Columbia University approved the study. Data were collected through interviews by trained bilingual research assistants using standardized data collection instruments, review of medical records, physical and neurological examinations by study physicians, and fasting blood samples. Standardized questions about vascular risk factors were adapted from the Centers for Disease Control and Prevention Behavioral Risk Factor Surveillance System as defined previously.20 Hypertension, diabetes, heart disease, and physical inactivity were defined as described previously.19 Race-ethnicity was based on self-identification and the distribution at enrollment was ~63% Hispanic, 20% black, and 15% white. Depression was defined as a Hamilton Depression Rating Scale score >10 or a history of antidepressant use.

Cognitive Assessment
Cognitive status was assessed at baseline by bilingual trained research assistants using the 30-point Mini-Mental State Examina-
tion (MMSE) in English or Spanish depending on the language spoken by the subject at home.\textsuperscript{21,22}

**Alcohol Consumption Assessments**

Alcohol use was assessed using structured interviews adapted from food frequency questionnaires as previously described.\textsuperscript{8} We asked about the average amount consumed in the past year, and on average during the participant’s drinking lifetime. There were 9 possible responses from none to 7 or more drinks per day of wine (120 mL or 11 g), beer (360 mL or 12.8 g), and liquor (45 mL or 14 g). Responses for each beverage type were summed for an overall quantity.

**Assessment of Carotid Plaque**

Carotid artery plaque was assessed by high-resolution B-mode ultrasound on a GE LOGIQ 700 system with a multifrequency 9 to 13 MHz linear-array transducer with the subject in a supine position according to a standard scanning and reading protocol.\textsuperscript{23,24} We imaged the extracranial carotid arteries in transverse (short axis) and longitudinal planes (anterior, lateral and posterior views). Internal and common carotid arteries as well as the bifurcations were examined for atherosclerotic plaque, defined as an area of focal entire arterial wall thickening or protrusion into the lumen at least 50% greater than the surrounding wall thickness. Maximum carotid plaque thickness (MCPT) in millimeters was measured at the peak plaque prominence from any of the 3 artery segments using the semiautomatic IMAGE-Pro V.5.2 software (Microsoft). If no plaque was identified, MCPT was recorded as 0. Within and between reader variability for repeated plaque measurements were carried out as follows: the intraclass correlation coefficient type 3 (ICC3,1) represented by the algorithm: (ICC3,1) = (BMS − EMS)/(BMS + (k−1)×EMS) was used. Each subject was assessed by the same k raters (k=2 readers). BMS was the between-targets (readers) mean square and EMS was the within-targets (reader) mean square. In a sample of 88 stroke-free subjects, the correlation coefficients for within and between reader variability for repeated plaque measurements ranged from 0.87 to 0.94.

**Laboratory Assessments**

Baseline fasting blood samples were drawn into serum tubes and spun within 1 hour at 3000\textsuperscript{g} and 4°C for 20 minutes and immediately frozen at −70°C. High-density lipoprotein cholesterol (HDL-C) levels were measured using an automated spectrometer (Hitachi 705; Boehringer).

**Statistical Analyses**

Statistical analyses were carried out using SAS software (version 8.02; SAS Institute). We created 5 alcohol intake categories: (1) never (reference), (2) past, (3) \textless 1 drink/week, (3) 1 drink/week–\textless 2/day, and (4) \textless 2 drinks/day (Table 1). We excluded participants with a prior alcohol-related hospitalization (n=58).

We fit generalized linear models with a binomial distribution assuming the MMSE score is a random variable that is the sum of products of the number of questions correctly answered times the corresponding scores (20 questions: 16 of 1 point, 3 of 3 points, and 1 of 5 points). This random variable is distributed as a convolution of a product of 3 independent binomials and the corresponding likelihood function is proportional to a binomial distribution with 30 independent trials (maximum score (n) of 30). Odds ratios (OR)

### TABLE 1. Characteristics of Study Sample by Reported Alcohol Intake

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall %</th>
<th>Never</th>
<th>Past</th>
<th>&lt;1 Drink Weekly</th>
<th>1 Drink Weekly to 2 Daily</th>
<th>&gt;2 Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age mean (SD)</td>
<td>67.9 (9.7)</td>
<td>69.1 (9.7)</td>
<td>68.8 (9.0)</td>
<td>68.5 (10.1)</td>
<td>66.8 (9.8)*</td>
<td>64.8 (8.6)*</td>
</tr>
<tr>
<td>Women, %</td>
<td>59</td>
<td>84†</td>
<td>54</td>
<td>67</td>
<td>50</td>
<td>22</td>
</tr>
<tr>
<td>\textless 8 years education, %</td>
<td>38</td>
<td>47†</td>
<td>46</td>
<td>34</td>
<td>29</td>
<td>25</td>
</tr>
<tr>
<td>Medicaid or no insurance, %</td>
<td>41</td>
<td>51†</td>
<td>48</td>
<td>37</td>
<td>34</td>
<td>33</td>
</tr>
<tr>
<td>Race-ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic, %</td>
<td>54</td>
<td>61†</td>
<td>58</td>
<td>53</td>
<td>48</td>
<td>42</td>
</tr>
<tr>
<td>Black, %</td>
<td>25</td>
<td>21</td>
<td>28</td>
<td>26</td>
<td>24</td>
<td>36</td>
</tr>
<tr>
<td>White, %</td>
<td>21</td>
<td>18</td>
<td>15</td>
<td>21</td>
<td>28</td>
<td>22</td>
</tr>
<tr>
<td>Married</td>
<td>34</td>
<td>29†</td>
<td>33</td>
<td>28</td>
<td>40</td>
<td>37</td>
</tr>
<tr>
<td>\textless 3 friends, %</td>
<td>13</td>
<td>16†</td>
<td>17</td>
<td>11</td>
<td>9</td>
<td>17</td>
</tr>
<tr>
<td>Physical inactivity, %</td>
<td>38</td>
<td>37†</td>
<td>45</td>
<td>44</td>
<td>33</td>
<td>35</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>73</td>
<td>77†</td>
<td>78</td>
<td>70</td>
<td>67</td>
<td>72</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>21</td>
<td>24†</td>
<td>26</td>
<td>21</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Cardiac disease, %</td>
<td>21</td>
<td>23†</td>
<td>25</td>
<td>24</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;30, %</td>
<td>29</td>
<td>27†</td>
<td>30</td>
<td>24</td>
<td>32</td>
<td>29</td>
</tr>
<tr>
<td>25 to 30, %</td>
<td>43</td>
<td>40</td>
<td>42</td>
<td>42</td>
<td>45</td>
<td>52</td>
</tr>
<tr>
<td>\textless 25, %</td>
<td>28</td>
<td>33</td>
<td>28</td>
<td>33</td>
<td>23</td>
<td>20</td>
</tr>
<tr>
<td>Depression, %</td>
<td>12</td>
<td>16†</td>
<td>14</td>
<td>14</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>HDL-C mean (SD)</td>
<td>46 (15)</td>
<td>47 (14)</td>
<td>44 (14)*</td>
<td>46 (15)</td>
<td>47 (15)</td>
<td>46 (15)</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>17</td>
<td>9</td>
<td>15</td>
<td>16</td>
<td>21</td>
<td>43</td>
</tr>
<tr>
<td>MMSE median (SD)</td>
<td>27 (3.4)</td>
<td>27 (3.6)</td>
<td>27 (3.7)</td>
<td>27 (3.4)</td>
<td>28 (3.0)*</td>
<td>28 (2.9)*</td>
</tr>
</tbody>
</table>

*Significant difference compared to nondrinkers (unadjusted; P<0.05); †P<0.05 for trend (unadjusted).
TABLE 2. MCPT by Race-Ethnic Group

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Hispanic</th>
<th>Black</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>2215</td>
<td>1163</td>
<td>539</td>
<td>471</td>
</tr>
<tr>
<td>MCPT, mean (SD)</td>
<td>1.1 (1.2)</td>
<td>0.9 (1.1)†</td>
<td>1.4 (1.3)</td>
<td>1.4 (1.2)</td>
</tr>
<tr>
<td>Plaque, %</td>
<td>58</td>
<td>49</td>
<td>65</td>
<td>71</td>
</tr>
</tbody>
</table>

There were 47 participants of “other” race-ethnicity not included in this table. †Odds Ratio comparing different levels of alcohol intake to abstainers.

Results

There were 2215 participants with cognitive assessments, reported alcohol intake, and carotid plaque measurements. Compared with those with missing cognitive and alcohol data (n = 1083), participants in the study sample were more likely to be younger (<70 years, 42% versus 60%; P < 0.0001), more likely to be male (41% versus 30%; P < 0.0001), and to have Medicaid (70% versus 58%; P < 0.0001). Regarding vascular risk factors, this group was less likely to have a BMI > 30 (30% versus 34%; P for trend < 0.08), hypertension (73% versus 76%; P = 0.03), cardiac disease (21% versus 29%; P < 0.0001), or to be depressed (12% versus 18%; P < 0.0001).

Participants had a mean age of 69 (interquartile range 62 to 76; 54% Hispanics, 24% blacks, and 21% whites). Reported drinking is presented in Table 1. Performance on the MMSE (mean score 26; interquartile range 24 to 29) differed by drinking category; current drinkers had higher MMSE scores than never or past drinkers (Table 1). In univariate analyses, mean MMSE scores were lower for those who were older (P < 0.0001), female (P < 0.0001), less educated (P < 0.0001), black (P < 0.0001) or Hispanic (P < 0.0001) compared with white, had Medicaid or no insurance (P < 0.0001), were unmarried (P = 0.0002), or had < 3 friends (P = 0.0001). MMSE scores were also lower for those with hypertension (P = 0.03), diabetes (P = 0.0005), cardiac disease (P = 0.003), physical inactivity (P ≤ 0.0001), and depression (P < 0.0001).

Carotid plaque was present in 58% (mean 1.1 mm; Table 2) and was more prevalent in the following groups in univariate analysis: black (OR = 1.4; 95% CI 1.0, 1.8) and white (OR = 2.6; 95% CI 2.1, 3.3) participants versus Hispanics, those > 70 years (OR = 3.2; 95% CI 2.6, 3.8), those with > 8 years education (1.5; 95% CI 1.3, 1.8), having Medicare or private insurance (OR = 1.6; 95% CI 1.3, 1.8), and having > 3 friends (OR = 1.5; 95% CI 1.1, 1.9). Hypertension (OR = 1.6; 95% CI 1.3, 2.0), diabetes (OR = 1.5; 95% CI 1.2, 1.8), cardiac disease (OR = 1.7; 95% CI 1.4, 2.2), and current smoking (OR = 1.6; 95% CI 1.3, 2.1) were associated with carotid plaque. There was no association between MCPT and reported alcohol intake or with performance on the MMSE.

Moderate drinking (1 drink/week–2 drinks/day) was associated with better performance on the MMSE than never drinking, adjusting for age and education, but not past, lighter, or heavier drinking (Table 3, model 1). Adjusting for other social factors, only moderate drinking was associated with better cognitive performance (Table 3, model 2). Adjusting for vascular risk factors did not attenuate this effect (Table 3, model 3) and adding MCPT to the model did not diminish the strength of the association (Table 3, model 4). There was an interaction by gender such that the association

TABLE 3. Relation Between Reported Alcohol Intake and Performance on the MMSE

<table>
<thead>
<tr>
<th>Reported Alcohol Intake</th>
<th>Never</th>
<th>Past</th>
<th>&lt;1 Drink Weekly</th>
<th>≥1 Drink Weekly to 2 Daily</th>
<th>&gt;2 Drinks Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>OR (95% CI)</td>
<td>P</td>
<td>OR (95% CI)</td>
<td>P</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>1. Adjusted for age and education</td>
<td>Ref</td>
<td>1.01 (0.94, 1.09)</td>
<td>0.69</td>
<td>1.10 (1.01, 1.20)</td>
<td>0.03</td>
</tr>
<tr>
<td>2. Model 1 + gender, race-ethnicity, Medicaid, marriage, and friendships</td>
<td>Ref</td>
<td>1.02 (0.95, 1.10)</td>
<td>0.59</td>
<td>1.07 (0.98, 1.18)</td>
<td>0.12</td>
</tr>
<tr>
<td>3. Model 2 + hypertension, diabetes, cardiac disease, body mass index, HDL-C, current smoking, physical inactivity, and depression</td>
<td>Ref</td>
<td>1.03 (0.95, 1.11)</td>
<td>0.47</td>
<td>1.09 (0.99, 1.20)</td>
<td>0.08</td>
</tr>
<tr>
<td>4. Model 3 + MCPT</td>
<td>Ref</td>
<td>1.03 (0.96, 1.12)</td>
<td>0.42</td>
<td>1.09 (0.99, 1.20)</td>
<td>0.08</td>
</tr>
<tr>
<td>5. Model 4 in Women</td>
<td>Ref</td>
<td>0.98 (0.90, 1.08)</td>
<td>0.74</td>
<td>1.09 (0.97, 1.21)</td>
<td>0.15</td>
</tr>
<tr>
<td>6. Model 4 in Men</td>
<td>Ref</td>
<td>1.01 (0.84, 1.22)</td>
<td>0.92</td>
<td>1.01 (0.81, 1.25)</td>
<td>0.95</td>
</tr>
</tbody>
</table>

†Odds Ratio comparing different levels of alcohol intake to abstainers.
between moderate alcohol intake and better cognitive performance was limited to women ($P = 0.04$). Stratification showed a significant positive effect of moderate alcohol intake on cognition for women (OR 1.26, 95% CI, 1.14 to 1.38) but not men.

**Discussion**

In this stroke-free multiethnic sample we found an independent association for women between moderate drinking and better cognitive performance compared with abstainers. This is in agreement with some other studies, but few studies have included black and Hispanic subjects living in the same community. We found that carotid plaque was not a mediator of the association between alcohol and cognitive performance.

Moderate alcohol intake may be protective against subclinical cerebrovascular disease, which perhaps is on the pathway between moderate alcohol consumption and cognitive impairment. In this study, moderate alcohol consumers had better cognition independent of vascular risk factors, and current drinkers did not have higher HDL-C levels, another potential mediator. Because moderate alcohol intake is protective against stroke in both our case-control and prospective studies, these findings could suggest alcohol acts through a separate vascular mechanism. The lack of a mediating effect of MCPT suggests that large vessel atherosclerosis is not a key pathway and small vessel damage may be one. However, alcohol has inhibitory effects on platelets and could lead to fewer ischemic lesions. Indeed, the effect of alcohol on platelets and interactions with plaque characteristics may be more relevant than the mere presence of plaque.

The independent relationship between moderate alcohol intake and better cognitive performance may implicate AD. Moderate intake of wine has been shown to be associated with a lower risk of dementia and AD. The mechanism is not clear, but animal data suggest alcohol may increase brain acetylcholine levels which could result in improved cognitive function. Separately, ethanol may decrease systemic inflammation that could interact with vascular and neurodegenerative processes.

The chronic dose effect of alcohol on cognition is unclear with some studies showing a graded association, or 1 that is J-shaped, or 1 that is U-shaped. In this study, past drinking was associated with better cognition only in univariate analysis but was no longer adjusting for age and education. However, past drinkers are heterogeneous, including those that had not taken alcohol in years with those that had stopped recently. A trend for light drinkers to perform better on the MMSE than abstainers suggests a possible dose effect with moderate drinkers showing an even larger association. Heavier drinkers did not differ by MMSE from abstainers but the sample was small.

Several cross-sectional studies have found a benefit of moderate alcohol intake in relation to cognitive function in women but not in men. Another study found a trend toward less cognitive decline in women but not men moderate drinkers. Data from Framingham suggested women had better cognition than men at light and moderate levels of alcohol intake but that men had better performance when they took >4 drinks a day. The British 1946 birth cohort study found the opposite; alcohol intake prevented memory decline in men only. Here, women were older and more socially disadvantaged than men and few men abstained. Thus, we may have been unable to detect effects in men.

This study has several limitations. Being cross-sectional we cannot make causal inferences. Current drinkers may be healthier than nondrinkers if the latter have stopped drinking because of health problems. Although this is a potential problem, we separated never from past drinkers to help limit this. Another potential source of bias is that those who reported moderate alcohol intake may have had better cognition than never drinkers, but we adjusted for relevant sociodemographic confounders. We did not use an MMSE cutoff for cognitive impairment because no established cutoffs are well validated in populations with Caribbean Hispanics. Despite this, it remains an appropriate global measure of cognition because it has been translated and validated in many cultures. Finally, this sample with MCPT measurements was healthier than the overall cohort and our results may not be generalizable. However, the prevalence of vascular risk factors in the sample is similar to many urban multiethnic populations in the United States.

This cross-sectional study of reported alcohol intake and cognitive performance suggests moderate drinking may be protective in women in a multiethnic community. The lack of a mediating effect of large vessel atherosclerosis provides evidence that other mechanisms may be involved and future studies that clarify the importance of small vessel damage, platelet function, and inflammation are needed.

**Acknowledgments**

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**References**


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