Smoking, drinking, and other life style factors and cognitive function in men in the Caerphilly cohort

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Abstract

Study objectives—To examine the cognitive function in a large, ongoing cohort study of older men, and to identify associations with social and lifestyle factors.

Design—A cross sectional study of cognitive function was conducted within the Caerphilly Prospective Study of Heart Disease and stroke.

Setting—The Caerphilly Study was originally set up in 1979–83 when the men were 45–59 years of age. Extensive data are available on a wide range of lifestyle and other factors of possible relevance to cognitive decline. Associations between some of these and cognitive function are reported.

Participants—A representative sample of 1870 men aged 55–69 years.

Main results—Age, social class, medication, and mood were found to be powerful determinants of performance. Self report data on the involvement of the men in leisure pursuits were examined by factor analysis. This indicated that the more intellectual leisure pursuits are the most strongly linked with performance. A measure of social contact showed a weak positive association with the test scores. Current cigarette smokers gave lower test cognitive function scores than either men who had never smoked, or ex-smokers. There was however no evidence of any gradient in cognitive function with the total lifetime consumption of tobacco. The disparity between these two data sets suggests that there had been prior selection of men who had originally started to smoke, but more particularly selection of those who later quit smoking. There was no significant association between alcohol consumption and cognitive function, though ex-drinkers had markedly lower test scores than either current drinkers or men who had never drunk alcohol. This seemed probably to be a consequence of an high prevalence of illness among the ex-drinkers.

Conclusions—Age and social class show strong associations with cognitive function. Leisure pursuits and social contact are also both positively associated. Neither tobacco smoking nor the drinking of alcohol seem to be associated with cognitive function, though there is evidence suggestive of self selection of both men who had never smoked and ex-smokers.

The rising numbers of older people in the community has led to an increasing concern with cognitive decline and dementia, and this has stimulated an increasing interest in aetiological factors other than age.1 2 Holland and Rabbitt1 2 have pointed out that cognitive decline has three components: involutionary decline, which might be accepted as “natural” aging, secondly pathology, and thirdly, socioeconomic factors. None of these has yet been adequately characterised or measured, though Holland and Rabbitt judge the effect of socioeconomic factors to be powerful, and likely to play a major part in the determination of life’s opportunities and histories. Jones et al support this view and claim that the direct effect of age on cognition is “substantially” reduced when social, lifestyle, and physiological variables are taken into account.

In the investigation of how lifestyle factors affect the maintenance of cognitive function an obvious starting point is to evaluate the associations with cognitive function and common everyday factors, such as leisure time activities, physical exercise, and contact from family and friends, in a representative population sample of “younger” elderly subjects. Because of marked disagreement in previous findings, the effects of smoking and drinking are of particular interest.

In this paper we investigate the association of cognitive performance with a variety of lifestyle factors, in particular, smoking, and drinking, within the Caerphilly Cohort, a large representative sample of older men.

Methods

The Caerphilly Study was set up in 1979–83, the aims being the study of lifestyle, dietary, biochemical, and haemostatic factors predictive of ischaemic heart disease. More recently, stroke has been added as an outcome. The study is described more fully elsewhere.5 6 7

Every man included gave signed, informed consent at every phase of the work.

The men in the cohort have been re-examined at four to five year intervals, and in the second re-examinations, the men being 55–69 years, cognitive function was added to the investigations. Full details of the testing of each man are given elsewhere.8 9 10

Men were asked about a wide range of aspects of lifestyle and medical history, and current occupation, or most recent job was used as a basis for social class classification. Cigarette consumption was recorded, both in terms of each man’s current habit, and in terms of an estimated lifetime consumption of
tobacco. The usual alcohol intake was recorded, and a daily consumption over an average week estimated.

Medication, both prescribed and “over the counter” were recorded. Preliminary analyses showed that many drugs have an association with cognitive performance. Therefore one of us (AB), together with a pharmacologist, grouped the drugs that the men in the cohort were taking, into: (1) those unlikely to have any effect on cognitive function; (2) those that may have some effect (such as, antimuscarinics, corticosteroids, digoxin), and (3) those likely to have an appreciable effect (such as antipsychotics, tricyclic antidepressants, phenytoin). This grouping was used as a basis for a process of statistical adjustment to allow for possible confounding effects by medication on other relations.

Using a questionnaire that listed 18 items, subjects were asked to indicate on a five point scale the frequency with which each engaged in a range of leisure pursuits. These were examined first by factor analysis in an attempt to reduce the activities and interests into a small number of separate, uncorrelated items. Relations between these factors and cognitive performance were then examined.

An estimate of the social contact received by each man was obtained from a questionnaire, which asked the average number of persons, family and friends, with whom there was meaningful daily contact.

THE TESTS OF COGNITIVE FUNCTION

Shortly after the clinic attendance, each man was seen at home by one of us (CH). Cognitive function tests were completed by the men, alone, in a quiet room, and they were asked not to smoke during testing. The order of the tests, and the method of application was rigidly standardised. A laptop computer was used for some of the tests. This had a very simple keyboard in place of the usual alpha-numeric keys, and a gas-plasma screen to ensure that each signal disappeared as soon as it had been answered.

Cognitive function was measured with several instruments and these were always applied in precisely the same way and in the same order.

The AH412 comprises a series of 65 items of increasing difficulty alternating between verbal and mathematical reasoning items. These items were presented using a laptop computer and the score used is the total number of correct answers made within a standard limit of 10 minutes.

The Cambridge Cognitive Examination (CAMCOG)13–15 and Mini-Mental State Examination (MMSE)15 were included as tests of cognitive loss. Both are widely used in clinical practice, the CAMCOG being the more precise. They assess a range of functions and skills including language, praxis, perception, memory, attention, and orientation.

In the Choice Reaction Time (CRT) the subject is presented with a stimulus in one of four boxes on the computer screen and is instructed to press the appropriate button on a special four button keyboard. A total of 160 stimuli, balanced for position and latency are presented. Responses under 100 ms were omitted as these indicate anticipation, rather than response. Responses over 30 s were also omitted as was the longest response if it was more than twice the duration of the next longest response as these were considered to have been influenced by distractions. In this report mean response time is derived from all acceptable responses, regardless of whether or not the response was correct.

In addition, a 30 question form of the General Health Questionnaire (GHQ)16 was administered to give an indication of the mood of each man at the time of testing. In the regression analyses that follow, the original score, with some grouping to allow for skew and unevenness in the distribution, is added to the models to allow for any confounding of the cognitive tests by mood. The GHQ is however of some interest as a determinant of performance itself.

STATISTICAL METHODS

The number of possible indices that could be derived from the tests of cognitive function is legion. We made a prior decision to use the following:

AH4: the total number of questions answered correctly within 10 minutes.

CAMCOG: the total score, with a maximum of 104.

MMSE: the total score, with a maximum of 30.

CRT: the mean response time of all the responses.

The associations between these scores and a variety of lifestyle factors of possible relevance is examined and differences in scores between subgroups are adjusted as appropriate for the effects of differences in confounding factors, namely, social class, drug taking, and depression (GHQ score). Adjustment for confounding by age has been done throughout by individual year.

Results

The sample comprised 2154 men aged 55–69 years who were seen in the second re-examination in the Caerphilly cohort study. Of these, 1870 (87%) agreed to cognitive testing. Results from men who had suffered a stroke, or had problems with the testing procedure were omitted, together with those where there had been an equipment failure during testing. Cognitive testing was successful and performance data are therefore available for 1685 men with the AH4, 1781 with the CAMCOG and MMSE, and 1649 with the CRT.

Table 1 displays the mean scores for each test within three age groups. As expected, there are very clear declining trends with increasing age. The data displayed in this table, as in all that follow, have been adjusted for the effects of other factors likely to confound the relations of interest: in this case, the possible confounding effects of social class, medication, and mood at the time of testing have been controlled for.
Table 1  Cognitive function and age

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Men (n)</th>
<th>AH4</th>
<th>CAMCOG</th>
<th>MMSE</th>
<th>CRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>55–59</td>
<td>591</td>
<td>27.5 (10.8)</td>
<td>91.5 (5.8)</td>
<td>27.0 (2.1)</td>
<td>874 (224)</td>
</tr>
<tr>
<td>60–64</td>
<td>536</td>
<td>25.4 (10.1)</td>
<td>89.7 (6.7)</td>
<td>26.5 (2.4)</td>
<td>912 (228)</td>
</tr>
<tr>
<td>65–69</td>
<td>501</td>
<td>23.5 (9.9)</td>
<td>88.0 (7.3)</td>
<td>25.9 (2.5)</td>
<td>988 (279)</td>
</tr>
</tbody>
</table>

Age effect* -0.465 -0.348 -0.105 +11.7
Probability of trend <0.0005 <0.0005 <0.0005 <0.0005

Cases who had a stroke have been excluded in this, and in all subsequent tables.

*The "age effect" shown is the unstandardised regression coefficient of each test on age in years.
The mean scores (SD) for the various tests are shown after adjustment for the effects of social class, drugs, and GHQ score at the time of testing.

Table 2 displays the relations between the tests and a number of possible confounding factors. Clearly social class has very strong relations with each test. After adjustment for the effects of age, medication, and mood at the time of testing (GHQ), the differences across the grouped classes (I+II and IV+V) is equivalent to just over one standard deviation for the AH4 (11.3) and the CAMCOG (6.0), over half a standard deviation for the MMSE (1.5), and just under half a standard deviation for the CRT (100 ms).

Associations of the various tests with mood at the time of testing are strong, even allowing for the effects of the confounding factors, age, social class, and medication (table 2) being just under half of one SD for the AH4, rather less for the CAMCOG and MMSE, and about one quarter of a SD for the CRT. Mood at the time of testing is clearly a most important factor.

There are a few important associations with medication after the effects of confounding factors have been allowed for (table 2). The score in men who were taking drugs that had been judged by the geriatrician and the pharmacologist likely to have definite effects on performance have a mean score for the AH4 (24.4), which is much lower than that of men receiving either no medication, or receiving drugs judged unlikely to affect cognition (26.3 and 27.0). These differences are equivalent to around 20% of the standard deviation for the test. The performance of men taking drugs that had been judged only to have "possible" effects on cognition is intermediate for the AH4 and the CRT. Despite the fact that only a few of the relations with medication are significant, the regression models that follow later have all included medication at four levels, as defined earlier.

The factor analysis of the 18 leisure time pursuits by each man led to the identification of four factors that were judged to be useful in that they each had eigen values greater than one (2.8, 1.9, 1.3, and 1.1 respectively in what follows). These were interpreted as "social" (this included attendance at dances and other social events, being a spectator at sports, visiting a public house or club, playing darts, snooker etc), "cultural" (participation in music or drama, visiting concerts, theatre, cinema or church, doing community or voluntary work, etc), "intellectual" (attending lectures, classes, libraries, museums, playing desk games of skill, involvement in creative arts, etc), and "physical" (garding, walking,jogging, participation in ball games, doing household jobs, etc). Varimax rotation with Kaiser normalisation was used to maximise the variance of the factor loading, but this had no impact on the explanatory power of the factors.

The associations of these leisure "factors" with the cognitive function test results were then examined. Table 3 displays regression coefficients that have been standardised to represent change in cognitive performance in terms of SDs of the cognitive tests, so that direct comparisons can be made between the tests, so they can all be compared. Clearly the strongest relations are those between the cognitive tests and the more "intellectual" activities, and the single most marked association is between these activities and the AH4, the test that is most closely related to reasoning ability. Perhaps surprisingly, the more physical leisure pursuits show the next strongest relations, while the factor for social pursuits shows no association with cognitive performance.

From another questionnaire applied to each man we have an estimate of the social contact each man claimed to receive, in terms of the average number of persons with whom he had meaningful contact in an average week. Associations with cognitive function are weak (table 3), and are best shown by the CAMCOG and the MMSE, the questionnaires that best detect dementia.

Table 4 summarises the effects of smoking on cognitive function. Men who were current smokers at the time of testing gave mean scores on the AH4 (23.9) and the CAMCOG (88.6), which were lower than in men who had never

Key Points
- Leisure time activities show a positive association with cognitive function, especially the more intellectual pursuits.
- Cigarette smoking shows no association, but there is evidence that the more able smokers quit and became ex-smokers.
- Light and moderate drinking shows no association.
The table 3 shows a list of cognitive function, leisure pursuits, and social contacts.

Table 3 Cognitive function, leisure pursuits, and social contacts

<table>
<thead>
<tr>
<th>Leisure pursuit/brain function</th>
<th>Men (n)</th>
<th>AH4</th>
<th>CAMCOG</th>
<th>MMSE</th>
<th>CRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Leisure pursuits&quot; factors (see text)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intellectual</td>
<td>1232</td>
<td>0.198</td>
<td>0.164</td>
<td>0.082</td>
<td>-0.117</td>
</tr>
<tr>
<td>Cultural</td>
<td>1232</td>
<td>0.043</td>
<td>0.056</td>
<td>0.055</td>
<td>-0.003</td>
</tr>
<tr>
<td>Probability</td>
<td></td>
<td>&lt;0.0005</td>
<td>&lt;0.005</td>
<td>&lt;0.005</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Social</td>
<td></td>
<td>NS</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>Probability</td>
<td>1232</td>
<td>0.005</td>
<td>0.031</td>
<td>0.022</td>
<td>-0.064</td>
</tr>
<tr>
<td>Physical</td>
<td>1232</td>
<td>0.069</td>
<td>0.100</td>
<td>0.116</td>
<td>-0.011</td>
</tr>
<tr>
<td>Probability</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.0005</td>
<td>&lt;0.0005</td>
<td>NS</td>
</tr>
</tbody>
</table>

For "leisure pursuits" the figures shown are standardised regression coefficients for the factors identified in the factor analysis described in the text. The coefficients have been adjusted for the effects of age, social class, and GHQ and medication. For social contacts, mean scores (SD) have been adjusted for the effects of age, social class, and GHQ and medication.

Table 4 Cognitive function and smoking

<table>
<thead>
<tr>
<th>Smoking</th>
<th>Men (n)</th>
<th>AH4</th>
<th>CAMCOG</th>
<th>MMSE</th>
<th>CRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>never smoked</td>
<td>290</td>
<td>26.0 (11.0)</td>
<td>90.2 (6.2)</td>
<td>26.5 (2.3)</td>
<td>929 (224)</td>
</tr>
<tr>
<td>ex-smokers</td>
<td>785</td>
<td>26.3 (10.2)</td>
<td>91.0 (6.6)</td>
<td>26.6 (2.4)</td>
<td>906 (244)</td>
</tr>
<tr>
<td>current cigarette</td>
<td>410</td>
<td>23.9* (10.1)</td>
<td>88.6† (7.0)</td>
<td>26.2 (2.4)</td>
<td>939 (270)</td>
</tr>
<tr>
<td>pipe/cigar</td>
<td>110</td>
<td>25.9 (10.0)</td>
<td>91.0 (6.3)</td>
<td>26.7 (2.2)</td>
<td>941 (216)</td>
</tr>
<tr>
<td>Life time cigarette consumption under 183K</td>
<td>548</td>
<td>25.6 (10.1)</td>
<td>89.9 (6.5)</td>
<td>26.5 (2.2)</td>
<td>915 (249)</td>
</tr>
<tr>
<td>17+</td>
<td>467</td>
<td>25.6 (10.4)</td>
<td>90.4 (6.7)</td>
<td>26.7 (2.3)</td>
<td>904 (248)</td>
</tr>
<tr>
<td>Probability of trend</td>
<td></td>
<td>NS</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>NS</td>
</tr>
</tbody>
</table>

Significance levels are for differences from the base groups: men who never smoked. *p<0.005 †p<0.0005.

Mean scores have been adjusted for the effects of age, social class, and drugs.

The test scores in these men are of interest as they are representative of a population of free living older men. Some selection was inevitable, in that 13% of the original cohort refused to be tested, and the data from a further 9% were excluded for technical reasons. In common with other studies, the results for all the tests show a negative skew indicating that there is a small excess proportion of men with scores likely to indicate dementia. Applying criteria commonly used in clinical practice for significant deficit, 179 men (8%) scored below 80 on the CAMCOG and 128 (6%) below 22 on the MMSE. All the tests seem to be sensitive to mood at the time of examination, as judged by the GHQ. The effect is not trivial, the difference between the mean scores in the men likely to be depressed (GHQ scores of 8 or greater) and those with no evidence of depression (GHQ scores of 1 or less) being about 40% of a SD for both the AH4 and the CAMCOG, and about 26% of a SD for the CRT. The state of causality of course arises and cannot be settled by cross sectional data. There is a further complication however in our data in that the results of the CAMCOG indicate a more marked decline in cognitive function with age in the men who seem to be depressed, than in men not depressed. The tests other than the CAMCOG showed no such interaction with mood. Rabb
Smoking, drinking, and other lifestyle factors and cognitive function

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et al\textsuperscript{20} examined this same issue in a much larger sample of volunteers and concluded that age, of itself, is unlikely to increase vulnerability to the effects of depression on cognitive performance. Apart from the CAMCOG results, our data concur with this conclusion.

The effect of social class is very marked (table 2) and the trend across the full range of social classes I to V is consistent and even more marked. The size of this for the MMSE (1.5 in table 2) is very closely similar to that attributed to education (namely 1.7) in the Rotterdam study.\textsuperscript{7} Huppert et al\textsuperscript{6} found that in a population sample in Cambridge, education and social class exerted a significant and independent effect upon performance. Our population sample was however drawn from a former coal mining area where there had been relatively little opportunity for higher education in the 1920–30s and so social class and education are likely to be highly confounded. Elsewhere, however, we present results for both social class and level of educational achievement.\textsuperscript{11}

The evidence on medication and cognitive function that we present in table 2, is confounded with the effects of the diseases for which the drugs were prescribed. This is unavoidable in an observational population study. However, the only use we make of medication in this report is to allow for the confounding effects of drugs on other relations. In a later publication we will examine the relations more closely.

The significant relations we describe with leisure pursuits are to be expected (table 3). The men in our cohort were comparatively young when tested, and so it is not surprising that the clearest relations are shown with the more intellectual component of leisure activities. On the other hand, it is difficult to explain the discrepancy between the absence of any significant relations with the social factor derived from the leisure pursuits, and the significant associations with the independent measure of social contact. These two indices seem however to be measuring rather different things as the correlation between them is low ($r = 0.38; \ p<0.001$).

There are two possible effects of cigarette smoking on performance: acute and chronic. We examined only the second, and have found little evidence of any important effect. Although the men who admitted to cigarette smoking at the time of testing had scores that were lower than those in the men who did not smoke cigarettes, there is no evidence of a gradient with the estimated lifetime consumption of cigarettes (table 4).

The literature seems to give no consistent evidence of smoking on function. Berkman et al\textsuperscript{21} found that 1192 “high functioning” subjects smoked less cigarettes than 162 medium and low functioning subjects. Launer et al\textsuperscript{12} reported that, compared with subjects who had never smoked, current smokers made 20% more errors on the MMSE, and Ferrucci et al\textsuperscript{22} also report a significant effect of smoking. In other studies, however, there is said to have been no association with smoking,\textsuperscript{23} or no modification of the associations with cognitive function when smoking was added to the model.\textsuperscript{24} On the other hand, Dobbs et al\textsuperscript{25} found cigarette smoking to be associated with increased efficiency in a reaction time test, both in 103 subjects with Parkinsonism and in 144 without. Evidence from the Rotterdam cohort study\textsuperscript{7} is consistent with this last in that smoking was found to be less common in subjects with dementia (relative risk, compared with subjects without dementia: 0.35), thus raising the possibility that smoking may protect against cognitive decline. The effects of smoking on cognitive performance may however be complex. While nicotine has both acute and chronic beneficial effects on performance,\textsuperscript{26, 27} other effects of smoking, and in particular on the vascular and haemostatic systems are certainly deleterious.

On the other hand, our data would support the hypothesis that some of the differences in performance between groups of men defined by their smoking habit may be a consequence of self selection out of the smoking groups. In particular, smokers with higher cognitive function scores seem to be more likely to quit and transfer into the ex-smoking group.

Relations between drinking and cognition are of particular interest, and a number of hypotheses have been defined.\textsuperscript{28} There are undoubted harmful effects in chronic alcoholics, but the proportion of these in a community based study such as ours is too small to merit separate consideration. Our data relate more to the effects of “social” drinking. Two hypotheses have been proposed: firstly, that there is a continuum of permanent effects positively related to the usual alcohol intake and, secondly, that there is a “hang over” effect after each drink, with an eventual return to baseline function. Studies of cerebral blood flow would seem to support the former of these hypotheses, as a significant inverse relation has been reported between grey matter blood flow and the usual amount drunk.\textsuperscript{29} Other hypotheses arise from the assumption that personality and cognitive function determine the pattern of drinking and the amount drunk, and in one study such a relation was shown clearly in young adults who had intermittent episodes of immoderate drinking.\textsuperscript{30}

The literature is confused on all these aspects, but this is probably a consequence of the small size of many of the previous studies and the selective nature of the subjects chosen for study. Although we have made every reasonable attempt to ensure that our sample of men is representative of the general population of older men, yet the heaviest drinkers are still likely to be under-represented as they are likely to be less cooperative in any community based study. It would however seem to be reasonable to conclude from our data that social drinking, which describes most of the drinking in our population sample, has little or no chronic affect on cognitive function. There is certainly no evidence in our data to support the conclusion drawn from the smaller Zutphen cohort that alcohol intake is protective against cognitive decline.\textsuperscript{6}
The finding of a marked deficit in performance in the ex-drinkers in our sample is almost certainly a consequence of morbidity that had led to the cessation of drinking. Thus we find that a high proportion of these men were taking medication, and almost half had definite evidence of ischaemic heart disease. A similar result was reported in women by Ensrud et al who found that “former alcohol use” was a significant predictor of impaired function, while current alcohol use was not.

Another approach to the evaluation of smoking and drinking on cognitive function is to examine cerebral blood flow. Thus Rogers et al found a negative and continuous relation between blood flow, and both smoking and drinking habit. While it could be that grey matter that has been impaired by smoking and/or drinking, will require less blood, further results by Rogers et al showed that the quitting of smoking was followed by an improvement in blood flow, suggesting a direct effect. Yet other work by this group showed a decreased vasodilator and vasoconstriction response in cerebral vessels in chronic cigarette smokers.

Clearly, as this cohort ages, the changes in the pattern of associations between the different tests of cognitive function and their likely determinants will be of increasing interest.

We are grateful to Dr Michael Bialus who assisted in the coding of medications.

Funding: the field work described was entirely funded by MRC. The statistical work was done by Janet Pickering, funded by Mental Health Foundation.

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*J Epidemiol Community Health* 1999 53: 9-14
doi: 10.1136/jech.53.1.9

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