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Brain CT Changes in Alcoholics: Effects of Age and Alcohol Consumption

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A computerized tomographic (CT) brain scan and assessments of lifetime alcohol consumption, body size, and cognitive performance were performed in 37 male alcoholics, aged 26–62 years. Hematocrit and mean corpuscular volume (MCV) were also measured. CT data were analyzed using a semiautomated scoring system yielding measures of percentage of fluid at the ventricles and cortical sulci. Normative brain CT data from 57 community controls spanning the adult age range allowed Z-score assessment of deviation from age norms for each alcoholic. Across the entire group, alcoholics had significantly enlarged ventricles and sulci for their age. Enlargement at both sites correlated significantly with lifetime alcohol consumption. Sulcal enlargement in alcoholics was found across all ages. In contrast, ventricular enlargement was apparent only in older alcoholics and became increasingly exaggerated with age. Measures of body size, hematocrit, and MCV correlated with ventricular but not sulcal enlargement, suggesting that nutritional factors play a role in ventricular enlargement. Associations between neuropsychological performance and CT changes or alcohol consumption were less pronounced and at times counterintuitive. The findings support a modest dose-effect relationship between ethanol exposure and changes in brain morphology, and suggest that ventricles and sulci show a different time course of response. The role of nutritional status needs to be more closely investigated.

THERE HAVE BEEN several reports of "brain damage" in chronic alcoholics based on analysis of computerized tomographic (CT) images of the brain. The data suggest an association between chronic alcohol use and loss of brain tissue and are consistent with long-standing observations of deficits in performance of certain cognitive tasks among alcoholics. However, despite the plausibility of a causal model, there is a surprising lack of evidence demonstrating a clear association between actual alcohol consumption and CT assessment of brain atrophy on the one hand or neuropsychological impairment on the other.[1,2]

One reason for this situation is the complex and multifactorial nature of the relationship between chronic alcohol consumption and observed changes in brain structure or function.[3] The extent to which subject characteristics such as age, premorbid intelligence, and health status either exacerbate and/or mitigate the effects of alcohol consumption is unknown. In addition, head trauma, malnutrition and hepatic disease, commonly found in association with chronic alcohol use, have been associated with either brain atrophy or with neuropsychological impairment, independently of any association with alcoholism.[4–6]

CT studies of the alcoholic brain have been quite consistent in reporting cerebral atrophy. See Wilkinson[7] and Ron[1] for excellent reviews and critiques of the field. While early applications of CT to study the alcoholic brain were retrospective, and used "normal" CT scans drawn from hospital files as controls,[8] more recently there have been several prospective studies in which alcoholics have been compared with community controls.[1,9–11] While some studies may report higher incidences of atrophy than others, or note greater change at sulci than ventricles,[10,11] the general direction of the data is quite consistent and corroborates autopsy data on reduced brain weight[12,13] and increased pericerebral space[14] in alcoholics.

Much work has also been done to evaluate cognitive changes in alcoholics, and the existence of cognitive deficits in people who have been chronic excessive drinkers is well documented.[15–18] General intelligence, as measured by tests such as the Wechsler Adult Intelligence Scale (WAIS) and the Bender-Gestalt, often is not significantly impaired in alcoholics, but a closer examination of performance on specific subtests of the WAIS reveals a discrepancy between summarized scores on verbal (VIQ) and performance (PIQ) subtests.[1] Verbal skills in general are retained and provide a measure of premorbid abilities. Performance skills, on the other hand, decline. Thus the difference between VIQ and PIQ (VIQ − PIQ) has been interpreted as a measure of cognitive loss. It would be plausible to expect an association between this measure and a measure of brain structural change.

In spite of the considerable amount of work which has been done in this field, there are still significant gaps in our knowledge. For example, it is not known whether there is an age-related increase in vulnerability of brain structure or function to alcohol, how much accumulated alcohol consumption is likely to produce a measurable morphological or neuropsychological effect, and whether

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concurrent change in a patient's nutritional status contributes to observed changes in brain structure and function.

One factor impairing the detection of relationships between alcohol consumption and brain structure has been the limited ability to measure small changes in brain structure, inherent in many popular techniques for CT scan assessment. Another factor has been failure to appropriately account for the influence of age, which exerts strong effects on measures of both brain structure and function. Studies of CT variables in alcoholics have generally adopted the approach of age-matching alcoholic and control populations. However, this avoids rather than investigates the influence of age. Another approach is to use age as a covariate in the analysis. Unfortunately, this technique can partial out the influence of variables, such as amount of alcohol use, which tend to be closely associated with age. Yet another approach is to test healthy community members spanning the adult age range and use regression analysis to derive the predicted (mean) value for each age, as well as quantify variability (standard deviations) for each age. In our normative work[19] we have demonstrated an increase with age of both the mean and the variance of CT measures of atrophy. Therefore, we use Z-score computations to assess deviations from age norms. This score is derived by subtracting the predicted value (from the regression curve for subject's age) from the observed value and dividing by the predicted standard deviation for that age. The mean of such Z-scores from the control population will be zero. Individual patient Z-scores will provide an estimate of deviation from control age norms, and the mean of Z-scores from patient groups will reflect the extent to which those patients, as a group, demonstrate pathology independent of their individual ages.

The following paper reports on an exploratory study which provides data relevant to the following questions: (*a*) Do alcoholics as a group have enlarged ventricles for their age? (*b*) Do alcoholics as a group have enlarged sulci for their age? (*c*) Are either the ventricles or the sulci more vulnerable to the effects of alcohol? (*d*) Are ventricular or sulcal changes seen in young alcoholics, or do they only become apparent in older alcoholics? (*e*) Does the amount of alcohol consumed over a lifetime contribute to the extent to which CT measures deviate from age norms? (*f*) Do any physiological indices of nutritional status contribute to the extent to which CT measures deviate from age norms? (*g*) Are there any associations between CT change and neuropsychological deficits?

SUBJECTS AND METHODS

Alcoholic Subjects

Alcoholic subjects were recruited from the Palo Alto Veterans Administration Medical Center's 30-day alcohol rehabilitation ward. Criteria for admission to this program include meeting DSM-III (Diagnostic and Statistical Manual of Mental Disorders, Ed. 3) criteria for alcohol dependency, willingness to participate in a voluntary, cognitively oriented program, and absence of acute medical or psychiatric condition. During a 5-month period, the charts of all admissions to the ward were carefully reviewed. Subjects were not considered for the study if they had a definite history of schizophrenia or major affective psychosis, seizures unrelated to alcohol abuse, head injury, or trauma involving documented significant loss of consciousness, stroke, migraine, or other neurological disorders unrelated to alcohol use, or if their admission workup [which included serum glutamic oxaloacetic transminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) liver enzyme tests] indicated seriously compromised liver function. Eight of the subjects in this study had one or both liver enzymes elevated on admission. In all but one subject, these values had returned toward normal by the time of discharge. Subjects who appeared to meet criteria were further screened by interview and their informed consent obtained. Postanalysis file review revealed a discharge diagnosis of "possible paranoid schizophrenia" for one alcoholic subject.

The complete protocol included electrophysiological[20] and neuropsychological testing as well as CT scanning. Of the 42 subjects who originally agreed to participate in the study, three withdrew before their CT scan was obtained and two declined the CT scan. Neuropsychological testing and CT scanning occurred some time during the second to fourth week on the ward. For 80% of the subjects, this was within 14–28 days of their last drink (as reported on intake interview). Actual test times ranged from 11 to 63 days from last drink.

Alcoholism Descriptors

All alcoholics completed an alcohol dependence scale (ADS)[21] to assess alcoholic dependence. This self-administered questionnaire consists of 29 items taken from an alcohol use inventory[22] designed to assess withdrawal symptoms, obsessive-compulsive drinking style, and loss of behavioral control. Skinner and Allen[21] report that the total score has good test-retest reliability and correlates well with physical symptoms, social problems from drinking, and quantity of alcohol used.

Patients were also questioned, using a structured interview, regarding their total lifetime alcohol consumption. This interview follows the general format described by Skinner,[23] but does not differentiate between types of drink or probe for information related to style of drinking. In this format, subjects are asked to recall when they first started drinking and then to conceptualize their life into a series of drinking stages. Subjects are asked to link these stages to specific milestones or events in their lives. Subjects are then asked how many drinks *on average*, and how much was the *maximum* they would drink at each stage. Drinks were standardized so that 12 oz beer = 5 oz wine = 1.5 oz spirits = 13.5 g ethanol. The number of 'average' and 'maximum' drinking days a month are estimated, and the total number of drinks a month calculated. Lifetime totals of ethanol consumed can then be obtained by summing monthly totals within and across each drinking stage. Subjects are also asked to estimate their weight during each stage to allow correction of alcohol consumed for weight. From this interview, the following measures were derived to characterize the alcohol consumption of each subject: total lifetime ethanol in kg (corrected for mean lifetime kg weight), number of years of "alcoholic drinking" (exceeding 80 g/day), and amount of ethanol consumed in 6 months prior to current admission.

Demographic, Physiological, and Other Variables

Several additional variables were recorded from the patient's medical record including admission laboratory values for SGOT, SGPT, alkaline phosphatase, total and direct bilirubin, albumin, hematocrit, hemaglobin, mean corpuscular volume, blood urea nitrogen (BUN), creatinine, and electrolytes. Admission height and weight were used to compute a body mass index (wt/ht^2). In addition, admission weight was subtracted from average lifetime weight to yield an estimate of possible recent weight loss. Age, years of education, whether or not either parent "had problems with alcohol," number of cigarettes smoked, and current and previous use of medications and recreational drugs were also noted.

Control Subjects

Healthy community members were recruited by word of mouth and newspaper advertisement. They were initially screened by phone interview, and then by questionnaires, to exclude those with a history of significant psychiatric or neurological disease, recent use of psychoactive drugs, or alcohol consumption exceeding 50 g/day. Previously reported CT data from 57 control subjects, ranging in age from 22 to 84 years were used to determine age norms for CT variables.[19] 51 of these subjects also completed the neuropsychological test battery. The age, education and alcohol consumption (data available for only 29) of these subjects are listed in Table 1. (Note that older controls may have total lifetime alcohol consumption exceeding that of young alcoholics.)

Test Procedures

CT scans were obtained on an EMI 1010 scanner. Ten to 14, 8-mm thick, contiguous sections were collected beginning at +15° to the canthomeatal and proceeding rostrally. Scans were filmed for routine clinical evaluation, and were also recorded on magnetic tape as a 160 × 160 pixel image with a CT number resolution of one count per Hounsfield unit (HU). These data were transferred to our laboratory VAX 11/730 computer for quantitative analysis using a technique recently developed in this laboratory.[19] Briefly, this semiautomated scoring technique first applies a two-dimensional filter to minimize spectral shift (beam hardening) artifact, and then employs a movable one-bit display to identify the CT number which visually differentiates cerebrospinal fluid (CSF) from tissue on each section. These data are then used to define the percentage of fluid in the ventricles [medial segments of five sections beginning from an index section (selected to include some anterior horn of the lateral ventricle, the third ventricle and the quadrigeminal cistern) and proceeding superiorly through the ventricles] and sulci [peripheral segment of the next (sixth) section]. The data were initially expressed as percentage of fluid (fluid area/total intracranial area) and then arcsin transformed (arcsin of the square root of the proportion).

Table 1. Demographic, Alcohol Consumption, and Physiological Data for Alcoholic Subjects with Demographic and Alcohol Consumption Data for Control Subjects

	Min	Max	Mean	SD	Kurtosis
Alcoholic patients (N = 37)					
Age	26	62	45.6	10.54	−1.05
Education (yrs)	5	19	12.96	2.6	1.73
VIQ	77	143	112.08	14.42	−0.27
PIQ	79	139	108.89	11.78	0.91
MQ	89	143	119.00	17.88	−1.19
Alcohol dependency scale	3	41	24.54	10.57	−1.15
Lifetime alcohol (kg ethanol)	135	3088	1001.32	730.47	1.58
Lifetime alcohol/weight	1.3	47.5	14.2	11.2	1.33
Yrs drinking >80 g/day	0	36	13.35	10.11	0.49
Alcohol use last 6 months (kg)	4	106	36.5	24.45	0.97
Cigarettes/day	0	60	24.42	14.29	−0.15
Body mass index (ht/wt^2)	16.2	31.2	23.47	3.34	−0.15
Admission weight (kg)	50	104	75	13.44	−0.40
Alkaline phosphatase U/liter (N = 35)	37	166	94.14	32.64	−0.05
Bilirubin direct mg/dl (N = 35)	0	3	1.0	0.57	3.87
Albumin g/dl (N = 35)	3.7	5	4.2	0.27	0.55
Hematocrit % (N = 35)	30.9	53.1	44.41	4.59	1.93
Mean corp. vol. μm^3 (N = 35)	82	112	97.03	5.73	0.98
SGOT U/liter (N = 35)	13	202	38.89	37.59	8.47
SGPT U/liter (N = 35)	2	227	51.57	56.39	2.88
BUN mg/dl (N = 34)	5	22	11.71	3.61	0.63
Creatinine mg/dl (N = 34)	0.8	1.6	1.09	0.19	0.01
Control subjects					
Age (N = 57)	20	82	54.32	18.5	−1.09
Education (N = 56)	9	20	15.18	2.7	−0.62
VIQ (N = 51)	83	146	123.04	12.86	0.91
PIQ (N = 51)	101	144	119.26	10.28	−0.54
Lifetime alcohol (kg ethanol) (N = 29)	0	544	110.86	131.1	2.6
Lifetime alcohol use/weight (N = 29)	0	7.9	1.59	1.9	2.77

The cognitive battery included the following tests, administered in a standardized manner by psychology technicians trained and supervised by an experienced psychometrician. The full Wechsler Adult Intelligence Scale,[24] the Wechsler Memory Scale (WMS),[25] Trailmaking Test from the Halstead-Reitan battery,[26] a Mini Mental Status (MMS) exam,[27] and a Verbal Paired Associates Learning test.[28]

DATA ANALYSIS

The control population in this study was used principally to provide age norms for CT variables. The control group differed from the patient group on education status and thus assessments of neuropsychological impairment in the alcoholic group relative to these controls will not be made. However, associations between neuropsychological performance, alcohol consumption, and CT variables within the alcoholic group were examined.

Two types of analysis were performed. The first was designed to test if alcoholics were deviant for their age on CT measures. This was accomplished by comparing the CT variable Z-scores of alcoholics (relative to age-regression values in the control group) to those of controls. We made the following *a priori* predictions which were tested at the 0.05 α level: (*a*) Alcoholics will have enlarged ventricles for their age; (*b*) alcoholics will have increased sulcal area for their age.

The second analysis was designed to identify associations, within the alcoholic population, between CT measures of ventricular and sulcal enlargement for their age and measures of alcohol exposure, as well as selected physiological and neuropsychological variables. This was done by entering variables which prior reports in the literature suggested could contribute to, or be a comanifestation of, ventricular and/or sulcal change, into a large exploratory correlational matrix. The variables selected can be broadly grouped into the following categories: age itself, alcohol use, body size, nutritional status, liver function, and cognitive performance. Additionally, an attempt was made to reduce the effect of underlying differences in premorbid intelligence, as evidenced by VIQ differences, by using the standardized residuals (derived from regression of cognitive scores against VIQ) as well as the actual cognitive scores in the correlation matrix.

RESULTS

Table 1 presents data describing the alcoholic population, which ranged in age from 26 to 62 years. As a group, these alcoholics were well educated [mean, 12.96-year education, with the mode (38%) having had some college], of higher than average intelligence (mean VIQ = 112, mean PIQ = 109), and memory ability [mean memory quotient (MQ) = 119 on the WMS]. While all patients met DSM-III criteria for alcohol dependence, necessary for admission to the treatment program, they exhibited quite a range both in scores on the Alcohol Dependence Scale (3–41; mean, 24.5), and in years of alcoholic (>80

g/day) drinking (0–36; mean, 13.6 years) and lifetime consumption of ethanol (135–3088; mean, 1001 kg).

Figure 1 plots percentage of fluid at ventricles and sulci for the alcoholic subjects by age, with control mean and standard error of the regression lines superimposed. The difference between alcoholics and controls for these values was evaluated by t test comparison of Z-scores (t = mean Z/standard error of mean Z). As a group, the alcoholics had more cerebrospinal fluid and less brain tissue than controls for both ventricular (mean Z = +0.56, t = 2.34, $p < .005$) and sulcal (mean Z = +1.53, t = 4.91, $p <$ 0.001) CT measures. However, visual inspection of data in Fig. 1 suggests that ventricular enlargement beyond age norms is not seen in younger alcoholics, but becomes increasingly exaggerated in older alcoholics. Sulcal enlargement, in contrast, is present across the entire age range. This relationship is confirmed by a significant correlation between age and Z-score for the ventricular but not the sulcal measure (see Fig. 2 and Table 2).

Correlations between CT Z-scores and selected variables for the alcoholics are listed in Table 2. These statistics represent associations between various subject characteristics and deviation from age norms, not the absolute size, of the CT regions measured.

The amount of ventricular enlargement beyond age norms was strongly associated with the patient's age, but sulcal enlargement was not. Both ventricular and sulcal enlargement were associated with the total amount of alcohol consumed over a lifetime. Adjusting the lifetime alcohol consumption for the subject's estimated weight strengthened the association with CT measures. A chronological measure of alcohol exposure, the number of years of alcoholic drinking, was also associated with these CT measures, but not as well as the quantity measure. In contrast with these simple measures of alcohol exposure, the ADS, a multivariable measure of alcohol dependence, showed no association with any CT measure. The number of days since last drink did not correlate with any CT measure.

While exposure to alcohol was associated with CT measures of both central and cortical atrophy, measures of body weight and the body mass index were associated only with the central, ventricular measure. The association implies that greater ventricular enlargement is seen in lower weight, lower body mass patients. Furthermore, there was an association between a crude estimate of apparent weight loss and ventricular enlargement. The assumption that these associations are mediated by nutritional status factors is supported by strong associations with measures of hematocrit and mean corpuscular volume (MCV). The alcoholics with larger ventricles tended to have a hemogram consistent with macrocytic anemia, increased MCV and decreased hematocrit (see Fig. 3). Hematocrit was significantly negatively correlated with ventricular size ($r = -0.59$, $p < 0.001$), but not sulcal size ($r = -0.19$, NS). Similarly, MCV was significantly positively correlated with ventricular size ($r = +0.54$, $p < 0.01$) but not sulcal size ($r = +0.24$, NS). Age normative MCV data provided by Robert Marcus, MD, allowed us to age correct the alcoholic's data. After age correction, the relationship between MCV and ventricular size was still significant ($r = +0.51$, $p < 0.01$) and the relationship between MCV and sulcal size was not ($r = +0.25$, NS). Self reported current smoking behavior (in cigarettes/day) was available on 29 of the 37 alcoholics. Smoking was not significantly correlated with hematocrit ($r = +0.15$, NS) or MCV ($r = +0.03$, NS), nor was it correlated with the CT measures. None of the correlations of liver enzymes (SGOT, SGPT) with CT measures showed a significant association (see Table 2). Most other measures from the blood sample were also unrelated to CT measures.

Associations between cognitive and CT measures were primarily seen for ventricular rather than sulcal measures. The association between VIQ and ventricular enlargement was positive, indicating that in this sample, alcoholics with higher VIQ scores also had greater ventricular enlargement for their age. This causally implausible association accounts for the predicted association, VIQ − PIQ (a hypothetical measure of cognitive deterioration) and ventricular enlargement. MQ, which correlated highly ($r = 0.82$)

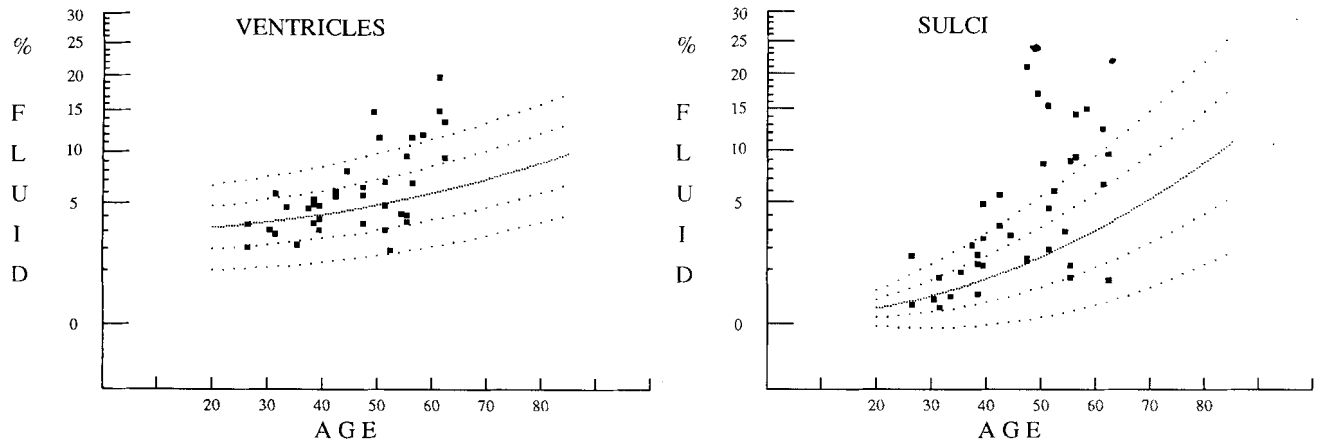

Fig. 1. Percentage of fluid (arcsin transformed) at ventricles and sulci for alcoholics, plotted against control norms. Dark line, age-predicted value; light lines, 1 and 2 standard deviations from the regression.

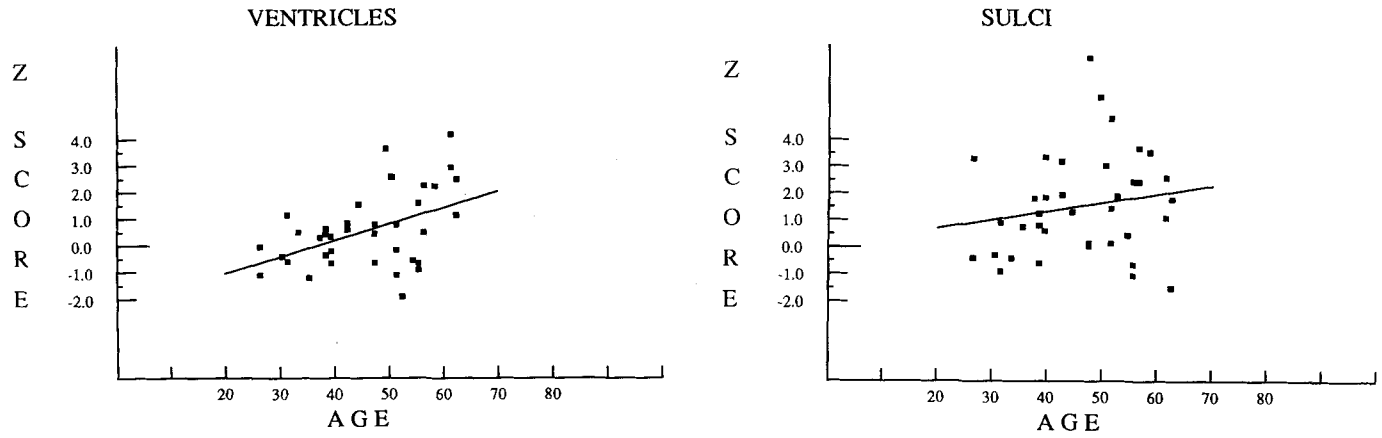

Fig. 2. Z-scores (deviations from age norms) for ventricles and sulci from alcoholic subjects plotted as a function of their age. The increase with age in these age-corrected values is significant for the ventricles but not the sulci.

Table 2. Pearson Product Moment Correlations between CT Variables and Alcohol Use, Body Size, Nutrition, and Liver Enzyme Variables for Alcoholic Subjects

	Ventricles	Sulci
Age ($N = 37$)	0.46*	0.18
Alcohol use ($N = 37$)		
Lifetime alcohol	0.40†	0.39†
Lifetime alcohol/wt	0.44*	0.43†
Years drinking >80 g/day	0.42†	0.31‡
Alcohol Dependence Scale	0.10	0.27
Days since last drink	0.06	−0.15
Body size ($N = 37$)		
Admit weight	−0.44*	−0.15
Percentage of weight change	0.37†	0.20
Body mass index	−0.32‡	−0.19
Nutrition ($N = 35$)		
Albumin	−0.29‡	0.24
MCV	0.54*	0.24
Hematocrit	−0.60§	−0.19
Liver enzymes ($N = 35$)		
SGOT	−0.15	0.22
SGPT	0.06	0.04

† $p < 0.05$ (two-tail).
‡ $p < 0.05$ (one-tail).
* $p < 0.01$ (two-tail).
§ $p < 0.001$ (two-tail).

with VIQ, showed a similar pattern. Correlations between cognitive variables, controlled for VIQ, and ventricular and sulcal enlargement illustrate that controlling for VIQ uncovers the underlying relationship between digit symbol substitution, block design and ventricular enlargement (Table 3). Block design was also associated with sulcal enlargement, a relationship which was weakened slightly by correcting for VIQ. After correcting for VIQ, all these associations were in the expected direction, i.e., poorer performance being associated with more CSF and less brain tissue.

Only one neuropsychological score, block design from the WAIS, was associated with lifetime alcohol consumption. The composite scores (VIQ, PIQ, and MQ) were not related at all. Controlling for VIQ enhanced relationships with lifetime alcohol consumption slightly. Associations between neuropsychological performance and amount of alcohol consumed in the last 6 months were generally lower than with total lifetime consumption. The one exception, digit symbol substitution, showed a positive association suggesting higher scores with greater alcohol consumption, a causally implausible result.

DISCUSSION

This study, using continuous measures of dependent and independent variables was able to demonstrate a modest "dose effect" relationship between ethanol exposure and changes in brain morphology. It also suggests that while the neurotoxic effects of ethanol are marked at both sulcal and ventricular locations, these broadly defined anatomical regions may respond differently to ethanol exposure. The enlarged sulci in young alcoholics may imply that the cortex is less resilient to the neurotoxic effect and gives way first, or that some sulcal enlargement may even precede excessive alcohol consumption. Ventricular enlargement, by contrast appears to be the outcome of a number of different things. Nutritional status is suggested by our data, but a more detailed account of this variable is needed. As the years pass, the ventricles appear to become increasingly vulnerable, and enlargement accelerates.

The paucity of associations between neuropsychological, CT, and alcohol consumption data was disappointing. The global nature of the CT measures used minimized the probability of detecting associations which may exist between specific neuroanatomical regions and cognitive abilities. Greater differentiation of our measure of atrophy into more regionally specific assessment of the frontal and temporal lobes, perisylvian fissure, and third ventricle may improve our ability to detect relationships between neuroanatomy and performance. Furthermore, premorbid dif-

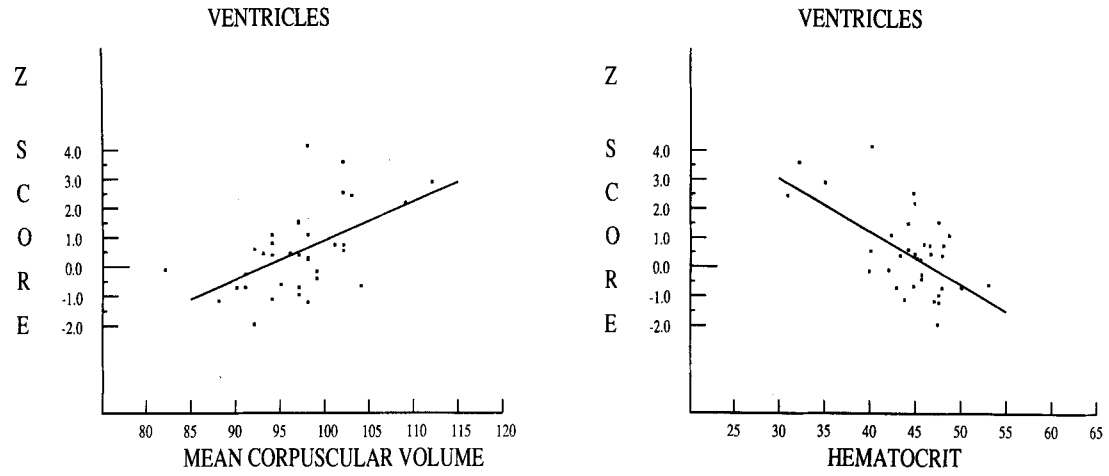

Fig. 3. Z-scores (deviations from age norms) for ventricles from alcoholic subjects plotted as a function of mean corpuscular volume and hematocrit.

Table 3. Pearson Product Moment Correlations Between Cognitive Variables, CT and Alcohol Consumption Variables: Correlations with Actual Cognitive Score and VIQ-adjusted Scores are Presented

	Ventricle		Sulci		Lifetime Alc use		Last 6-M Alc Use	
	Actual score	VIQ-adjusted	Actual score	VIQ-adjusted	Actual score	VIQ-adjusted	Actual score	VIQ-adjusted
VIQ	0.35†		−0.14		0.17		0.04	
VIQ-PIQ	0.34†	0.16	−0.02	0.09	0.17	0.08	−0.02	−0.06
PIQ	0.06	−0.16	−0.15	−0.09	0.02	−0.08	0.07	0.06
Digit symbol substitute	−0.21	−0.34†	−0.21	−0.18	−0.05	−0.11	0.33†	0.34†
Block design	−0.23	−0.34†	−0.35†	−0.32‡	−0.35†	−0.41†	−0.12	−0.14
MQ	0.47*	0.32‡	−0.10	0.03	0.21	0.13	0.16	0.22
Assoc. learning	0.23	0.06	−0.25	−0.21	−0.15	−0.28	0.15	0.14

† $p < 0.05$ (two-tail).
‡ $p < 0.05$ (one-tail).
* $p < 0.01$ (two-tail).

ferences in cognitive ability probably suppress superimposed changes associated with alcohol consumption.

Sampling bias probably accounts for the improbable association between large ventricles and high VIQ and MQ. Such bias can both obscure genuine relationships as well as highlight spurious ones.[29] Strategies to overcome this are hard to establish, given the fact that participation in research protocols is voluntary, and we are drawing subjects from a limited segment of the population of alcoholics (e.g., veterans living in a geographic catchment area characterized primarily by high-technology and service-oriented industry, voluntarily entering an educationally oriented treatment program). Perhaps only patients who start at extremely high premorbid levels survive the rigors of alcoholism, seek treatment at our medical center, and are willing to participate in research protocols. Significantly enough, one of the patients, a 61-year-old retired teacher, had both the highest ventricular Z-score and the highest VIQ score. The enlarged ventricles on his CT scan raised the question of occult hydrocephalus. However, further neurodiagnostic and cognitive testing indicated he was well within normal limits for his age. Two years later he is still alive and well.

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