ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #404

Title: Correlation of Amount add Type of Alcohol Intake on MRI Changes in the Brain

Abbreviated Title: Alcohol and Brain MRI

Writing Group: Eigenbrodt M, Mosely T, Hutchinson R, Folsom A
Correspondence: Preventive Cardiology/ARIC, UMC, 2500 N. State St., Jackson, MS 39216 Phone: (601} 984-5644, Fax (601) 984-5693, E-mail: aric@fiona.umsmed,edu

Rationale:
It has long been recognized that alcoholism may result in a number of syndromes or injuries such as Wernicke's and Korsakoff's encephalopathies, central pontine myelinolysis, Marchiafava-Bignami syndrome, hepatocerebral degeneration, and head trauma (Charnes 1993). Some damage may result from direct neurotoxicity, from nutritionaI deficiencies (predomirsantly thiate) or a combination (Charness 1993) Many of the syndromes have been associated with gross anatomic changes within the brain. With the advent of magnetic resonance imaging (MRI) there have been multiple clinical studies in chronic alcoholics which have found one or more of the following changes: ventricular enlargement, loss of white matter, increased T2 signal around the aqueduct and third ventricle and atrophy of the mammillary bodies, atrophy of the cerebellar and cortical gray matter (seen as enlarged sulci) and reduction in subcortical gray matter structures, increased T2 signal or cystic areas of decreased Tl signal within the corpus callosum, increased T1 signal or increased T2 signal within the basis pontis, and an increase in cerebral spinal fluid (Charness l993, Pfefferbaum 1992 and 1995, Kroft 1991, Zipursky 1989, Agartz 1991 and Chick 1989). It has been suggested that alcoholics lose a disproportionate amount of subcortial white matter as compared with cortical gray matter. However, there has not been uniform agreement. While the majority of alcoholics will have enlargement of the cerebral ventricles and sulci on MRI, the findings do not correlate consistently with either the duration of drinking or the severity of cognitive impairment (Charness 1993). A number of studies also investigated the change in ventricular and sulcal size and change in gray matter in abstinent alcoholics (Pfefferbaum l995, Mann 1995, Shear l994, Kroft l991, Zipursly 1989) with most studies indicating at least some shrinkage of the ventricles toward normal. Kroft, 1991, however, found no significant change in ventricular size in ten alcohol dependent women before or after abstinence, and suggested that women may not respond identically to men to the intake of alcohol. The variation in significant findings among studies may be due to the small number of patients found in most studies, variation in type of alcohol dependent persons studied, or lack of control for other factors that may contribute to brain changes. The studies rarely controlled for other possible diseases or factors which can contribute to brain lesions such as atherosclerosis, hypertension, and diabetes. The MRI findings are reported in patients almost exclusively with severe long standing alcoholism. While several population based studies have evaluated cerebral lesions on B1, They have not included the effect of alcohol in those seldies (Liigren lO94, Breteler t994, Manolio 1994). The ARIC data presents the chance to evaluate the effect that intake of different levels and types of alcohol has on MRI changes while controlling for numerous other factors.

Main Study Questions: The following MRI changes are available for evaluation: ventricular size grade, sulcal size grade, white matter disease grade, bifrontal horn/inner table grade/ central sulcus width, brain steln disease measurement. white matter disease distribution, perivascular space assessment, anterior vs posterior circulation, and infarct size and distribution.

We plan to evaluate the correlation of brain MRI changes with lifetime alcohol intake, current level of

alcohol intake, as well as changes in alcohol intake.

1. Compared to never drinkers, are different levels of current alcohol intake associated significantly with MRI changes? Do
these associations remain significant after controlling for age, gender, race, history of prior stroke, TIA, history of MI,
hypertension, diabetes, and medications.

2. Compared to never drinkers, are different levels of lifetime alcohol consumption correlated with MRI changes? Do these
associations remain significant after controlling for age, gender, race, history of prior stroke, TIA, history of MI,
hypertension, diabetes, and medications.

3. Among drinkers with similar lifetime alcohol consumption, does the status of current versus former correlate with MRI
changes? Do these associations remain significant after controlling for age, gender, race, history of prior stroke, TLA,
history of MI, hypertension, diabetes, and medications.

4. In patients with equivalent levels of alcohol intake do the findings on MRI vary
with type beer, wine, or hard liquor) of alcohol intake? Do these associations remain significant after controlling for prior
stoke, TIA, history of MI, hypertension, diabetes, race, age, gender, and medications.

5. Do the MRI findings in participants with similar levels of alcohol intake vary in those with vs without cognitive function
changes? Dc these associations remain significant after controlling for prior stroke, TIA, history of MI, hypertension,
diabetes, race, age, gender, and medications

6. In patients with significantly different alcohol intake from visit 1 to visit 3, is there a
correlation with change in cognitive function?

7. Do the above questions vary with the % kca1 that alcohol intake represents or the level of thiamine intake?

Data (Variables, source):

Exclude patients with Parkinson's disease, epilepsy, and cancer.
Visit 1: level of alcohol intake (gms/week), cognitive function
Visit 3: ever vs never consumption of alcohol, current vs former alcohol intake, level of current alcohol intake (gms/weeks), type of alcohol intake, %kcal alcohol represents, lifetime alcohol intake in grams, cognitive function, age, gender, race, history of prior stroke. TIA, history of MI, hypertension, diabetes, medications, and MRI findings.

References:

Agartz I, Saaf J, Wahlund LO, Wettterberg L. Tl and T2 relaxation time estimates and brain measures during withdrawal in alcoholic men. Drug and Alc Dependence 1991;29:157-

Breteler MMB, Van Amerongen NM, Swieten JC, et.al. Cognitive correlates of ventricular

enlargement and cerebral white matter lesions on magnetic resonance imaging: the Rotterdarnstudy. Strokeli94;25:1I09-1115.

Breteler MMB, Van Swieten JC, BDtS ML, et.al. Cerebral white matter lesions vascular risk factors, and cognitive function in a population-based study: the Rotterdam study Neurology 1994;44:I246-1252.

Charness ME. Brain lesions in alcoholics. Alc Clin Exp Res 1993;17:2-11.

Chick JD, Smith MA, Engleman, et.al. Magnetic resonance imaging of the brain in alcoholics: cerebral atrophy, lifetime alcohol consumption, and cognitive deficits. Arc Clin Exp Res 1989;13:512-518

Kroft CL, Gescuk B, Woods BT; et.al. Brain ventricular size in female alcoholics: an MRI study. Alcohol 1991;8:31-34.

Lindgren A, Roijel A, Rudling A, et.al. Cerebral lesions on magnetic resonance imaging, heart disease, and vascular risk factors in subjects without stroke: a population-based study. Stroke 1994;25:929 934.

Mann K, Mundle G, SkayIe MX Wakat p. Neuroimaging in alcoholism: CT and MRI results and clinical correlates. J Neuro transmission 1995;99: l 45-155.

Manolio TA, Krormal RA, Burke GL, Poirier V, et al. Magnetic resonance abnormalities; and cardiovascular disease in older adults: ie cardiovascular health study. Stroke 1994;25:31 8-397.

Piederbaum A, Lim KO, Zipursky RBX, et.al. Brain gray and white matter volume loss accelerates with aging in chronic alcoholics: a quantitative MRI study. Alc Clin Exp Res 1992; 1078--1089.

Piederbaum A, Sullivan ER, Mathalon DH, et. al. Longitudinal changes in magnetic resonance imaging brain volumes in abstinent and relapsed alcoholics. Alc Clin Exp Res 1995;19:1177-1191.

Shear PK, Jernigan TL, Butlers N. Volumetric magnetic resonance imaging quantification of Longitudinal brain changes in abstinent alcoholics. Alc Clin Exp Ru 1994;18:172-176,

Smith MA, Chick JD, Engleman HM, et al. Brain hydration during alcohol withdrawal in alcoholics measured by magnetic resonance imaging. Drug Alcohol Depend; 1988;21:2S-28.

Storaeter AJ, Nilsen G, Smevik O, Rinck P. Minor structural brain changes in young drug abusers: a magnetic resonance study. Acta Neurol Scand 1993; 87:210-214.

Zipursky RB, Lim KO, Pfefferbaum A. MRI study of brain changes with short-term abstinence from alcohol. Alc Clin Exp Res 1989;13:664-666.