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Effects of Diet and Alcohol Use on Neuropsychological
Functioning, Neuroanatomical Structure and Serum Biochemistry

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Dissertation in partial fulfillment of
requirements for
Doctorate of Philosophy
Department of Psychology
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September, 1983

CARLETON UNIVERSITY

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Abstract

One hundred and ten outpatient neuroradiological referrals were administered psychological tests of abstract reasoning, visual-spatial skills, verbal abilities, conceptualization, verbal and non-verbal fluency and mood disturbances. In addition to their CAT-scans, routine biochemical measures were available. The Parker Alcohol Use Inventory and a three-day diet diary also were completed. The sample was predominantly caucasian and upper middle-class, reporting generally high dietary quality. While drinking ranged from abstinence to heavy reported drinking, most subjects were light social drinkers. Multivariate analysis of variance revealed that general neuropsychological performance was associated with general dietary quality, serum potassium and sodium levels, and density of the white matter of the ascending corona radiata, but not to alcohol use. Mood disturbance was strongly related to alcohol use, serum calcium level, and density of gray and white matter of the frontal lobes. Implications for the neuro-anatomical and biochemical mechanisms of the neuropsychological effects of diet and alcohol use are discussed.

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INTRODUCTION

Research in the clinical neurosciences has outlined strong relations of neuropsychological performance with alcohol consumption and with diet. The present study will examine the association of both diet and alcohol use and their interaction with neuropsychological performance.

The finding that neuropsychological performance is adversely affected by alcoholism has been well documented (Eckhardt & Ryback, 1981; Parsons & Farr, 1982). Specifically, alcoholics tend to have deficits in concept formation and shifting, and in visual spatial tasks. Such conceptual abilities are known to involve the frontal lobes (Milner, 1964), while visual-spatial tasks tend to be mediated by the right hemisphere (Jones & Parsons, 1971). Thus it has been postulated that excessive alcohol use specifically impairs the frontal lobes and right-hemisphere of the brain (Parsons & Leber, 1981). Neuroanatomical studies of alcoholics have confirmed that alcohol-related abnormalities are seen primarily in the cortex of the frontal lobes (Cala & Mastaglia, 1980; Ron, 1980), and in the anterior regions of the lateral ventricles (Cala & Mastaglia, 1980; Lee, Hardt, Moller, Haubek & Jenson, 1979).

It also has been found that alcohol-related neuropsychological decrements in conceptualization and visual-spatial tasks are apparent in social drinkers. Parker and Noble (1977; 1980) and Parker, Birnbaum, Boyd and Noble (1980)

found that mean amount of alcohol consumed per occasion in social drinkers was predictive of neuropsychological decrements in abstraction abilities. This finding has been essentially confirmed by MacVane, Butters, Montgomery and Farber (1982). In addition, neuroanatomical (CAT-scan) research on social drinkers suggests that the anterior region of the lateral ventricles and cortical sulci are larger in heavy social drinkers than in light-drinking controls (Bergman, Borg & Hindmarsh, 1980). One of the major problems with alcohol research in humans, however, is the fact that alcohol use may be confounded with dietary restriction, as the number of calories consumed per day may be somewhat limited. The nutritional quality may be expected to decline as alcohol use increases.

The research on diet and behaviour generally supports the finding that malnutrition results in impaired cognitive development in children (Pollitt & Thomson, 1977). Similarly, in adults, anorexia nervosa or self-starvation, has been found to be related to severe depression and cognitive rigidity (Ben-Tovim, Marilov & Crisp, 1979). More subtle forms of undernutrition have also been found to predict cognitive performance. For example, attentional impairment has been associated with diets adequate in protein and calories, but deficient in iron (Brown, Lubin, Smith & Oski, 1972; Pollitt, Greenfield & Liebel, 1978; Sulzer, 1973; Webb & Oski, 1973). Neuroanatomical studies have revealed that general dietary inadequacy impairs the myelinization process

(Shoemaker & Bloom, 1977) and number of **synapses** (Bedi, Thomas, Doares & Dobbing, 1980) in rats. Anorexia nervosa has been associated with cortical shrinkage (Cala et al., 1980), which is apparently reversible with the reinstatement of adequate nutritional status (Enzmann & Lane, 1977; Heinz, Martinez & Haenggeli, 1977). Tucker and Sandstead (1981) found that iron deficiency was related to EEG indices of arousal or attention.

These and other studies in the field of the neuropsychology of alcohol use and diet have raised a number of intriguing questions for further research. This thesis will address the major question of whether alcohol use is associated with cognitive decrements when dietary quality is controlled. Related to this central thesis are the following issues:

- (1) What degree of alcohol use and dietary insufficiency is necessary before neuropsychological sequelae become apparent? That is, are deficits associated with diet, and alcohol use apparent in well-nourished social drinkers, or only in alcoholics and clinically malnourished patients?
- (2) What are the specific alcohol-use measures and dietary nutrients which relate to neuropsychological impairment? Relevant to this issue is the neuropsychological specificity of dietary and alcohol use effects. For example, is mean amount of alcohol consumed per occasion the most critical variable in predicting

neuropsychological decrements, or does it merely predict a different type of impairment than does frequency of consumption? Do specific vitamin and mineral deficiencies selectively affect different neuropsychological systems? (e.g., does iron deficiency affect performance measures other than attention, and is attention affected by other nutrient levels?).

(3) What are the biochemical and or neuroanatomical mechanisms which mediate the relationships of neuropsychological performance with diet and alcohol consumption? Are there distinct neurological systems related to diet and alcohol use? For example; the neuropsychological literature suggests that alcohol-related impairment may be primarily frontal, while diet-related impairment is more subcortical. A related issue in this case is the extent to which neuropsychological performance is related to specific patterns of neuroanatomical and biochemical status.

Obviously no single study can provide definitive answers to these questions. However it is the purpose of this research to examine the validity of alcohol-related impairments when dietary quality is controlled, and to address each of the related issues as they have been outlined.

There are three major problems with previous research in these areas:

(1) The validity of diet and alcohol use studies is often questioned. Diet and alcohol use are generally

confounded not only with each other, but also with socioeconomic status (SES), unrelated diseases or trauma, and acute symptoms of withdrawal, intoxication, or hunger.

(2) The issue of causality is generally not addressed.

Thus it remains unclear as to whether diet or alcohol use problems resulted in neuropsychological impairment, or, perhaps, vice versa.

(3) The reliability and validity of self-report measures of diet, and especially of alcohol use, has been questioned.

Further reference to these caveats will be made in reviewing the literature on the neuropsychology of alcohol use and diet. The manner in which these issues are addressed in the present study will be described following the literature review.

II

NEUROPSYCHOLOGY OF ALCOHOL USEImpairments of Sober Alcoholics

Alcoholics have been reported to show definite cognitive and neuropsychological deficits, which vary in type and degree depending on the age of the alcoholic, duration of alcohol abuse, amount of alcohol consumed per occasion, and period of abstinence from alcohol. Excellent reviews of the neuropsychological and cognitive research on alcohol-related deficits have been written by Kleinknecht and Goldstein (1972), Ron (1977), and Parsons and Farr (1982). A specific pattern of neuropsychological dysfunction is apparent in recently detoxified (i.e., approximately 2 weeks abstinence) alcoholic patients on batteries such as the Wechsler Adult Intelligence Scale (WAIS), Halstead Reitan Battery (HRB), Luria Nebraska Battery (LNB), Shipley Institute of Living Scale (SILS), and other neuropsychological tests. In addition, cognitive tests of memory and learning reveal a fairly consistent type of alcohol-related dysfunction. With only two weeks of abstinence, however, acute effects of intoxication and detoxification may still be prevalent, thus confounding the effects of chronic alcohol abuse.

* Wechsler Adult Intelligence Scale (WAIS) Performance

In a recent review, Parsons and Farr (1981) considered 14 well-controlled studies in which the WAIS had been administered to chronic alcoholics who were generally well-nourished and without clinical signs of neurological and

hepatic impairment, who had been detoxified for approximately two weeks, and who were inpatients in alcoholic treatment programs. The mean Verbal IQ (VIQ) of the alcoholics in these 14 studies was 108.7; the mean Performance IQ (PIQ) was 104.7. Clearly these subjects did not suffer from any global intellectual deterioration. Eight of the studies reviewed had compared alcoholics to matched controls. Only three of these found the alcoholics' VIQ to be significantly lower than that of controls, while 6 found significantly lower PIQ's among the alcoholics than among controls. All 8 studies reported that alcoholics had significantly lower scores on Block Design; 7 found significantly lower scores on Object Assembly; 6 revealed alcoholics had significantly lower Digit Symbol scores than controls. Tarter (1976) reviewed three studies which consistently found significantly lower Block Design performance in alcoholics than in controls. Thus, alcoholics seem to suffer from a specific pattern of deficits in visual-spatial construction and perceptual-motor speed.

This pattern of deficits clearly indicates that some of the performance subtests are more sensitive to alcohol-related dysfunction than are the verbal subtests. Jones and Parsons (1971) have suggested that right-hemisphere functions may be more vulnerable to the effects of alcohol than are left-hemisphere functions. Jones and Parsons (1971) maintain that the type of brain dysfunction associated with alcoholism is mild and diffuse rather than focal. This type of impairment disrupts the right-hemisphere functions which are thought to be

more diffusely represented than left-hemisphere functions, which are presumably more focally and specifically localized. However, it is not clear why specific left-hemisphere tasks would not be mildly disrupted as well, if this were the case.

Parsons and Leber (1981) have demonstrated that aged subjects, who are believed to have mild diffuse cortical atrophy, are impaired on a variety of neuropsychological tests including both verbal and visual-spatial paired-associate learning tasks. However, alcoholic subjects are impaired on visual-spatial paired-associate learning and perform normally on the verbal paired-associates. Parsons and Leber (1981) argue that these results reflect a qualitative difference in patterns of neuropsychological performance between alcoholics and aged subjects. They suggest that while the brain dysfunction associated with aging is mild and diffuse, alcoholic brain dysfunction may be more specifically localized.

Alternatively, it is possible that the distinction between alcoholics and aged subjects is one of degree, rather than type of impairment. That is, the right-hemisphere performance tasks may be more difficult, or the right hemisphere may be less apt to recover than the left hemisphere, as it is less frequently activated in normal daily functioning. Thus, if alcoholics are less severely impaired than aged subjects, deficits may be apparent only on "right-hemisphere" tasks.

Kleinknecht and Goldstein (1972) have suggested that lower WAIS-Performance scores than verbal scores in alcoholics may reflect the prevalence of peripheral neuropathy in alcoholics

without involving CNS damage. Motor impairments associated with the acute effects of detoxification may disrupt performance on these tasks with only 2 weeks of abstinence.

Halstead-Reitan Battery Performance

Parsons and Farr (1981) reviewed 15 studies which investigated the performance of alcoholics on the Halstead-Reitan Battery (HRB). Again, the average period of detoxification was two to three weeks. In 13 of these studies, the alcoholics' Impairment Index indicated a significantly greater incidence of brain damage when compared to controls. However, the mean Impairment Index score of the alcoholics in these studies was .49, which is within ~~the~~ borderline range of impairment. Those studies finding alcoholics with Impairment Indices in the impaired range were based on older subjects who were less well-educated. The Impairment Index Score is a measure of general brain damage (Reitan & Davison, 1977); it is known to decline with aging in normal subjects over age 45, and is sensitive to other physiological parameters such as differences in serum-cholesterol levels (Reitan, 1967). Blucewicz, Dustman, Schenkenberg and Beck (1977) found that young alcoholics tended to have higher (mean score of .50) Impairment Indices than subjects with histories of less severe drinking problems. Age-matched controls had an Impairment Index of .16. However, the alcoholics were not as impaired as an aged control group, who had a mean Impairment Index of .68.

The HRB subtest on which alcoholics are most consistently impaired is the Category test. Parsons and Farr (1981) report

that 13 of the 15 studies reviewed found alcoholics to be significantly impaired on this test. Similar results have been reported by Tarter (1976), and Blucewicz et al. (1977). Parsons and Farr report that alcoholics were found to be impaired on the Tactual Performance Test (TPT)-time in 12 of the 15 studies reviewed, on TPT-location on 10 of these studies, and on the Trails-B test in 11 studies. Eight of these studies found alcoholics to be impaired on speech-sounds perception, and only 4 studies found them to be impaired on tests of rhythm, finger tapping, and TPT-memory. However, Tarter (1975) reported that finger tapping performance is one of only 4 HRB subtests which successfully discriminated alcoholics from controls. Blucewicz et al. (1977) found that alcoholics performed as poorly as aged subjects on only two HRB subtests: Category, and TPT-memory. These conflicting results reveal the importance of controlling for the factors of age, duration of excessive alcohol use, and presence of peripheral neuropathy. Eckhardt, Parker, Noble, Feldman and Gottschalk (1978) found deficits in TPT-memory only in alcoholics with prolonged histories of alcohol abuse, and not in those with shorter histories, regardless of age. Thus, while complex abstracting abilities (Category test), spatial problem-solving (TPT-time), spatial orientation (TPT-location), and spatial-motor abilities are impaired in alcoholics, others such as spatial memory (TPT-memory) and motor speed (finger-tapping) appear to be impaired only in aged subjects and those with longer histories of alcohol abuse.

Grant, Adams and Reed (1979) found no significant differences in HRB performance among alcoholics detoxified for 3 weeks, alcoholics detoxified for 18 months, and light drinking controls. However, age was negatively related to neuropsychological performance. Grant attributes the lack of neuropsychological impairment in this sample of alcoholics to the fact that they were younger (late thirties) than the alcoholics traditionally studied. They were also of relatively high IQ and educational status. The authors conclude with "...cautious optimism that even very heavy alcohol use (80 g/day or more) is not related to neuropsychological impairment in the alcoholic who is in his or her late thirties." In contrast, Eckhardt, Parker, Pautler, Noble and Gottschalk (1980) tested 59 alcoholics within 7 days of their last drink, and 20 within 14-31 days of their last drink. Both groups were in their mid-thirties, and more than 50% had college educations. Both groups were equally impaired on approximately half of the 24 neuropsychological tests administered. On the HRB, both groups were impaired on TPT-time, TPT-location, finger tapping, Trails, and Category. Multivariate analyses revealed that these impairments were unrelated to medical or neurological ailments, other drug use, or mean days of abstinence. However, degree of neuropsychological impairment was related to recent and chronic alcohol consumption, to age, and to education. The authors conclude that the lesser impairment on Grant et al. (1979) subjects is due to their reduced intensity and chronicity of excessive alcohol use compared to typical

alcoholic samples. That is, with more typical amounts (e.g., 2.4 g/kg per occasion) and duration (e.g., 12 years) of abuse, clinically detectable cognitive impairment is commonly observed, even with 3 weeks of abstinence.

Reitan (1967) has developed the Brain-Age-Quotient (BAQ) as a sensitive indicator of brain damage which is known to increase with age. The BAQ is comprised of the HRB tests TPT^u time, TPT-location, Trails, Category, and the WAIS subtests Block Design, and Digit Symbol. These are the tests which most specifically and consistently distinguish alcoholics from controls. Thus, it appears that alcoholics suffer from a relatively complex and subtle, but general form of brain damage typical of aging. Similarly, Blucewicz et al. (1977) found that alcoholics' neuropsychological deficits were the same as those of normal aged subjects, and suggestive of the global cortical damage of premature aging, rather than of focal cortical, or peripheral damage.

Luria Nebraska Battery (LNB)

Studies employing the LNB have resulted in similar conclusions regarding alcohol-related brain damage as have those using the WAIS and HRB. Chmielski and Golden (1980) found that alcoholics of mean age of 50, who had been detoxified for 15-20 days were significantly more impaired than age- and education-matched controls on 6 of the 14 LNB subscales. The results indicated that more complex functions subserved by the broad cortical association areas of the brain, rather than by focal or subcortical areas, were most impaired in the alcoholics.

While basic visual, spatial, and mnemonic skills were intact, tasks which required the abstract cortical integration of these skills were performed significantly more poorly by alcoholics than by controls. This deficit was most apparent in tasks involving spatial, as opposed to verbal, components. The authors suggest that it may be the more diffuse organization of the right hemisphere and association areas which make the functions subserved by these regions more susceptible to the broadly damaging effects of alcoholism.

Parsons and Farr (1982) report that an unpublished paper by de O'Baldia compared 30 middle-aged alcoholics to 15 healthy age-matched controls. The alcoholics performed significantly worse on every subscale of the LNB except reading. Again, it was concluded that the brain damage associated with chronic alcoholism is a mild but diffuse form.

Other Neuropsychological Tests

Ornstein (1977) found that alcoholics who had been abstinent for 3 months were significantly impaired, compared to controls, on the Shipley-Hartford Conceptual Quotient (SHCQ) and on the Hooper visual organization tests, while performance of the alcoholics was normal on the Shipley-Hartford Vocabularly test and Wechsler-Bellvue IQ scale. Again, it appears that alcoholics retain normal levels of intellectual and verbal abilities, but show deficits in abstract reasoning and spatial organization. Tarter (1976) reports that alcoholics were found to be unimpaired on the Shipley-Hartford and Wechsler scales of intellectual competence, but were significantly more impaired

than controls on the Stroop test (a measure of perceptual shifting capacity), and the Purdue Pegboard (a test of perceptual-motor abilities). In addition, Tarter (1976) found that alcoholics show consistent deficits in maintaining set persistence on the Wisconsin Card Sort Test (WCST), a test of conceptual reasoning and shifting. Long-term alcoholics show perseverative deficits on the WCST in that they are unable to shift from one sorting criterion to another, or to appropriately utilize error information. However, these alcohol-related deficits on the WCST are not found if words are substituted for pictures on the stimulus cards. Thus, alcoholics seem to maintain the capacity for verbal conceptualization.

Alcoholics consistently have been found to be more field-dependent than controls on Witkins' Rod and Frame test, and thus seem to suffer from a deficiency in spatial orientation (Karp, Witkin & Goodenough, 1965; Tarter, 1976). However, this impairment is substantially reduced if alcoholics are first subjected to sensory deprivation (Sugarman & Schneider, 1977), which presumably enables a re-focusing on internal stimuli and the appropriate integration of internal and external information in otherwise externally-bound subjects. The results of these studies lend further support to the notion that alcoholics suffer from a disability in integrating neuropsychological functions, especially on spatial tasks, and performing tasks of abstract conceptualization.

Learning and Memory

The results of research on cognitive deficits in memory :

and learning among alcoholics are inconsistent, due to the lack of standardization of tests used, and differences in age, duration and severity of drinking, and period of abstinence among the alcoholic subjects. In alcoholics who had been abstinent for longer than two weeks, Miglioli (1979) found that initial deficits in long-term and short-term verbal memory had substantially improved. However, there was no improvement in long-term and short-term non-verbal memory performance assessed by the Memory-for Designs Test. Similarly, other studies have shown alcoholics to have verbal and non-verbal memory impairments after only 2 weeks of detoxification (Riege, Miklusak & Buchhalter, 1975), although verbal memory improves with longer periods of abstinence (Page & Linden, 1974; Smith & Rayden, 1972). Parsons and Prigatano (1977) found that after 3 weeks of detoxification, alcoholics in their thirties were unimpaired in verbal memory, while older alcoholics still had verbal memory deficits. Thus, while non-verbal memory impairment is typically seen in chronic alcoholics, deficits in verbal memory appear only with very short periods of detoxification, or in older subjects. Parsons and Leber (1981) found that alcoholics were impaired on a visual-spatial paired-associated learning (PAL) task but showed no deficit on a verbal PAL task. Aged subjects were impaired on both tasks. Again, these results provide support for the hypothesis that functions subserved by the right hemisphere are more vulnerable to disruption in alcoholics than are functions subserved by the left hemisphere.

Reversibility of Neuropsychological Impairment

Certain skills such as verbal, motor, and tactical abilities seem to recover with short (i.e., within a month) periods of abstinence (McLaughlin et al., 1979) and may be attributable to recovery from the effects of acute detoxification and from peripheral neuropathy. Prolonged abstinence (i.e., more than a year) does not appear to influence the limited recovery of visual-spatial skills (Hill & Mikael, 1979) although visual-spatial recovery may occur in younger alcoholics within a month of abstinence (Ayers, Templer, Ruff & Barthlow, 1978). While limited recovery of abstracting abilities may occur with periods of abstinence of more than a year (Long & McLaughlin, 1974) this reversibility appears only among alcoholics with very moderate degrees of initial impairment and again, may be the result of recovery from acute effects of detoxification. Thus, it might be hypothesized that the verbal, motor and sensory abilities which recover with short periods of abstinence are the result of temporary central and/or peripheral nervous system dysfunction related to alcohol abuse. The visual-spatial and abstracting deficits which are more resistant to recovery may be the result of permanent alcohol-induced brain damage as they are apparent in studies which have controlled for the confounding factors of peripheral neuropathy (Long & McLaughlin, 1974), and secondary factors likely to cause brain damage such as head trauma, malnutrition, and liver disease (Eckhardt et al., 1978). Unfortunately, no single study has controlled for all of these factors.

Summary

To what extent may the neuropsychological deficits, observed in alcoholics with at least 2 to 3 weeks of abstinence, be attributed to the direct toxic effects of chronic alcohol ingestion on the brain? Unfortunately, the studies reviewed to this point do not enable a conclusive answer to this question. With only 2 weeks of abstinence, the observed impairment may be influenced by the acute effects of detoxification or to chronic or acute peripheral neuropathy. Alternatively, the role of genetically transmitted and/or early developmental factors is unknown. That is, neuropsychological impairment in the subjects may have existed since childhood and may have operated to predispose the individual to alcoholism. Unfortunately, there are no comprehensive longitudinal neuropsychological studies of pre-alcoholic children or adolescents followed through to alcoholism in adulthood. One major research effort, the Oakland Longitudinal Study (Jones, 1968; Jones, 1971) has revealed that significant personality differences among adult alcoholics, heavy drinkers, moderate drinkers, light drinkers and abstainers are evident in pre-drinking adolescence and may predispose individuals to a particular drinking pattern in adulthood. Furthermore, Blouin, Bornstein and Trites (1978) have demonstrated that, with differences in school difficulty controlled for, adolescent neuropsychological profiles of hyperactivity are associated with patterns of greater alcohol use five years later. Thus, neuropsychological differences may operate to

predispose the alcoholic towards his drinking habits.

Specificity to alcohol. No single study has compared the neuropsychological deficits seen in alcoholics with those seen in subjects with other forms of substance abuse or nutritional deficits. However, the pattern of dysfunction (i.e., mild and general non-verbal and conceptual functional impairment, with relative integrity of verbal functions) may be distinguished from the pattern of specific deficits seen in patients with localized brain damage. The pattern of alcoholic dysfunction is similar to that seen in aged subjects and it has been suggested that alcoholism causes a premature aging of the brain. However, Parsons and Leber (1981) have shown that alcoholics differ from aged subjects in the nature of neuropsychological impairment. That is, although both groups are deficient on visual-spatial learning, aged subjects also perform poorly on verbal learning tasks while alcoholics perform in the normal range.

Localization of alcoholic brain damage. In general, it appears that the WAIS performance subtests such as Block Design and Object Assembly, and other non-verbal tests, such as spatial memory show consistent deficits among alcoholics, while verbal functions are less impaired. These non-verbal tests are believed to assess the integrity of the right-hemisphere. Thus, this pattern of neuropsychological impairment might suggest that the right hemisphere is more damaged by the effect of alcohol than is the left-hemisphere. However a specific vulnerability of the right hemisphere to mild and

diffuse damage has not been demonstrated conclusively.

Alternatively, Kleinecht and Goldstein (1972) have noted that the low performance scores in alcoholics may reflect merely a peripheral neuropathy rather than localized cortical damage.

Another pattern of neuropsychological deficits seen in alcoholics (i.e., perservation, and impaired abstraction ability) led Tarter (1976) to suggest that alcohol impairs the functioning of the frontal lobe and related subcortical structures more than it disrupts the posterior regions of the brain. Alcoholics are typically impaired on such tests as the WCST and Category test, which are particularly sensitive to frontal lobe damage (Milner, 1964; Reitan & Davison, 1977). Thus, Tarter (1976) postulated that alcoholic brain damage is primarily localized in the frontal lobes. However, while alcoholics do perform poorly on classically "frontal lobe" tests such as the WCST and Category test, these tests are also sensitive to more general forms of brain damage such as the global deterioration seen in aging (Reitan, 1967). Furthermore, alcoholics perform well on other tests of verbal perservation such as the verbal form of the WCST (Tarter, 1976), while frontal lobe patients are known to perform poorly on verbal fluency tests due to perseverative errors (Jones-Gotman & Milner, 1976). In addition, alcoholics do poorly on simple non-verbal tasks such as the performance subtests of the WAIS, while frontal lobe patients are typically unimpaired on these tests (Black, 1976). Thus definitive support for the hypothesis of specifically localized brain damage in

alcoholics has yet to be found in the neuropsychological literature.

Social Drinkers

Parker and Noble (1977) examined the relationship between alcohol consumption and cognitive performance in non-alcoholic, social drinkers with high socioeconomic status. Neither total lifetime consumption, nor frequency of drinking was significantly related to cognition. However, the mean amount of alcohol consumed per drinking occasion was inversely related to abstraction (Shipley-Hartford Abstraction score) and concept formation (Halstead Category test, Wisconsin Card Sort test, Shipley-Hartford Conceptual quotient). When the heavy drinkers (more than 5 drinks per occasion and more than 4 occasions per week) were excluded from the sample (36%), only performance on the Halstead Category test was related significantly to amount of alcohol consumed per occasion.

Two other studies by Parker and her associates have found a relation between alcohol use and cognitive decrements. First, a study of male college students found that amount of alcohol consumed per occasion was inversely related to sober performance on the Shipley-Hartford Scale (Parker et al., 1980). Second, an epidemiological study of 1,367 employed men and women in the Detroit area found the same association between amount of alcohol consumed per occasion and cognitive decrements (Parker & Parkér, 1982). Similarly, a study of female social drinkers reported that sober memory performance in moderate drinkers was significantly worse than in light drinkers (Jones & Jones, 1980).

In a recent study by MacVane et al. (1982), male social drinkers were divided into two groups of heavy and light drinkers, according to the criteria of Cahalan, Cisin and Crossley (1969) employed by Parker and Noble (1977). In both groups, mean amount of alcohol consumed per occasion was associated inversely with short-term memory scores. In the heavy drinkers, amount per occasion was positively related to the perseverative error ratio on the Wisconsin Card Sort test, but not to the total error rate, or to mean trials needed to reach criterion (which Parker and Noble (1977) had found to be most sensitive to amount per occasion). In the light and moderate drinkers, amount consumed per occasion was related positively to total errors and mean trials to criterion on the Wisconsin test. It is worth noting that the light and heavy drinking groups did not differ on any measure of memory or Wisconsin Card Sort test performance. In the total sample, amount per occasion was inversely related to memory but not to Wisconsin test performance, or the digit symbol task. MacVane et al. (1982) also caution that some of their heavier drinkers may have been alcoholic and/or intoxicated at the time of testing. In addition, Parsons and Fabian (1982) have raised questions regarding the validity of self-report alcohol use questionnaires. Therefore, given these factors and "the generally low correlations between drinking indices and cognitive scores, ...these findings should be interpreted with caution" (MacVane et al., 1982, p. 93).

Another reason for viewing these results with caution is, as Parker and Noble (1977) point out, the fact that unmeasured

factors such as life stress might be contributing both to increased alcohol consumption and decreased cognitive performance, while the latter two are not directly causally related. As Parsons and Fabian (1982) contend, "the discrepancy between the correlational and the group-differences approaches indicates the presence of other variables which remain to be identified" (p. 182). In summary, there does not appear to be any question that there is an inverse association between amount of alcohol consumed per occasion and psychological functioning. However it has not been demonstrated that this relation is direct, causal, or, indeed, continuous across abstaining, light-drinking, heavy-drinking, and alcoholic groups.

If 'social' drinking has a direct effect on neuropsychological performance which parallels that seen with alcoholism, then it should also be predictive of the same qualitative neuroanatomical and biochemical changes which accompany neuropsychological impairment in alcoholics, albeit to a lesser extent. If, for example, life stress and the accompanying mood disturbance were the cause of both increased social drinking and subtle cognitive decrements, then one would not expect that the increased alcohol consumption would be associated with neuroanatomical and/or biochemical abnormalities. The two chapters which follow the discussion of methodological considerations in alcohol research will review the neuroanatomy and biochemistry of alcoholism. This will provide a framework for investigating these factors among

sub-alcoholic drinkers in the present study.

Methodological Considerations

The obvious problem with neuropsychological research on alcohol use is that human subjects cannot be randomly assigned to alcohol and non-alcohol groups. Without such random assignment, the research design is, at best, quasi-experimental but more often is considered as correlational or survey research, and therefore precludes addressing the issue of causality. One approach to this problem is that of animal research, wherein random assignment to alcoholic and nonalcoholic groups is possible. However, this approach is of limited utility in the neuropsychology of alcohol use as the primary form of impairment most commonly observed in alcoholics is one of conceptualization or abstract reasoning, behavior which is difficult to assess with an animal model. Thus, neuropsychological research on alcohol-use has focused primarily on human subjects and has attempted to eliminate confounding variables through methods of experimental or statistical control. Experimental control has involved matching alcohol users and controls on variables such as age, socioeconomic status, IQ, nutritional status, peripheral neuropathy, or reported incidence of head trauma. Statistical control of these and other confounding variables has been attempted through analysis of covariance and hierarchical regression techniques. However, complete control of the many possible confounds in this area of research has not been achieved in any one study. In addition, the systematic control of variables related to subjects' drinking history such as duration of alcohol use, amount drunk

per occasion relative to body weight, and frequency of drinking occasions per week has not been achieved. These factors are apparently related to neuropsychological performance and may account for inconsistent results in the literature, but the nature of this relationship is unclear. Thus, the two major methodological drawbacks in this research are lack of control of variables confounded with extreme alcohol use (internal validity) and lack of control of alcoholic subject variables (external validity). These various threats to the validity of neuropsychological research in alcoholism will be discussed in turn.

Internal Validity

The following threats to internal validity stem primarily from the traditional focus on alcoholic samples. The investigations of alcohol use in non-alcoholic social drinkers are less vulnerable to these problems of internal validity, with the exception of confounds of mood state and dietary quality.

Dietary insufficiency. Malnutrition is commonly seen in alcoholics of lower socioeconomic status (Freund, 1976); however, less severe manifestations of dietary insufficiency probably accompany more subtle patterns of alcohol use as alcohol may compete with other nutrients as the number of calories one can ingest in a given day may be limited.

Dietary insufficiency is known to result in a variety of symptoms of cognitive dysfunction and attentional deficits, which will be reviewed more thoroughly in Chapter 5.

Mood state. Probably the most overlooked confound in

studies of alcohol's relation to cognition is the mediating factor of mood. Nathan, Titler, Lowenstein, Solomon and Rossi (1970) reported significant elevations of tension, depression and anger, measured by the Profile of Mood States (POMS), in alcoholics during periods of prolonged drinking, compared to non-drinking periods. In addition, scores for vigour on the POMS were significantly lower during drinking periods. While it is unclear whether drinking preceded or resulted from the mood disturbance, it is obvious that cognitive performance may be adversely affected by alcohol use simply as a function of mood disturbance.

Peripheral neuropathy. Alcohol is believed to exert toxic effects on the functioning of the peripheral nervous system, which can be classified into 3 types: sensory, motor, and autonomic (Freund, 1976). Sensory symptoms such as hyperesthesia and numbness generally precede motor involvements such as weakness and muscle atrophy. Position sense and reflexes may become impaired. Autonomic complications range from hypotension to vocal cord palsy. Although the precise etiology of alcoholic polyneuropathy is a subject of much controversy, it is widely believed that alcohol exerts its toxic effect via primary axonal degeneration; however, it is also thought that malnutrition plays an important role in the development of alcoholic peripheral neuropathy (Freund, 1976).

Secondary brain damage. Damage to the central nervous system may occur due to a variety of secondary factors associated with alcoholism, rather than due to the direct toxic effects

of alcohol use. Hepatic encephalopathy is a severe liver disease which may be related to alcoholism and results in impairments in intellectual functions, concentration, memory, abstract thinking, and motor control. Subdural hematoma following head trauma is common in alcoholics and may result in profuse brain damage.

Acute effects of alcohol. One of the most common methodological drawbacks of the neuropsychological research on alcoholism is the failure to control for the acute effects of intoxication. Through their effect on the neuronal membrane, and the activity of the sodium-potassium "pump", ethanol and its metabolite acetaldehyde exert profound acute disruptive effects on the pharmacological activity of the brain. The rate of norepinephrine (NE) turnover (synthesis, metabolism and re-uptake) is decreased (Kissin, 1979; Lahti, 1973; Ryback, 1973) as are the absolute levels of NE, especially in the hypothalamus, hippocampus, and midbrain (Anokhina, 1979). During the post-intoxication period, a rebound phenomenon may occur, resulting in excessively high levels of brain NE (Kissin, 1979). Similarly disruptive effects of acute intoxication occur with regard to dopamine (Anokhina, 1979), serotonin (Ballenger, Goodwin, Major & Brown, 1979; Kissin, 1979), GABA (Rawat, 1973) and acetylcholine (ACH) (Majchrowicz, 1979). In addition, acetaldehyde binds to the biogenic amines to form false neurotransmitters which further disrupt the normal pattern of neuronal activity (Smith, 1973). There is evidence that the acute toxic effects of alcohol on neuro-

transmitter activity may vary as a function of the anatomical site within the brain (Majchrowicz, 1979). This fact may account for the many conflicting reports regarding acute neuropharmacological effects of alcohol. Kissin (1979) notes that the disruptive effects of acute intoxication on neurotransmitter activity may persist for several days, or even weeks, following acute intoxication.

Acute intoxication may impair the functioning of the brain in other ways as well. That is, it may result in dehydration of the neurons which causes the brain to appear shrunken in size; electrolyte imbalances and shifts in the brain's normal osmotic pressure also occur with intoxication. Estimates of the duration of these acute effects range from one week to a month (Wilkinson & Carlen, 1980). Thus, it is crucial that a period of one month of abstinence from alcohol be imposed on alcoholics when testing for the effects of chronic abuse. Otherwise, the results are confounded by the acute effects of intoxication and detoxification.

External Validity

Conflicting results regarding the nature of neuropsychological deficits associated with alcohol use may be attributable to inconsistencies regarding subjects' ages, duration of alcoholism, amount drunk per occasion, frequency of drinking, IQ, education and socioeconomic status.

These variables threaten external validity when their restricted range limits the generalizability of results. They threaten internal validity when confounded with the independent measures.

Age. Certain effects of alcohol use may be found only in aged subjects, but not in younger alcohol users. For example Grant et al. (1979) found no deficits in young alcoholics. Such an interaction was found for social drinking effects by Parker and Noble (1980). This observation implies that either these effects associated with chronic alcohol use are cumulative and appear only after many years of consumption, or that there is some specific form of vulnerability of the aging brain to impairment associated with alcohol use.

Duration of alcohol abuse. ~~It~~ is interesting to note that the severity of some alcohol-related deficits depends on the duration of alcohol-use while others depend on the age of the subject, but not the length of his drinking history (Parsons & Leber, 1980). This factor must be more carefully examined in future research.

Amount drunk per occasion. Parker and Noble (1977) have demonstrated that deficits in cognitive performance of social drinkers are most reliably predicted by the amount of alcohol per kg. of body weight drunk per occasion. This factor is often ignored in alcoholism research or, at least, is not reported. Unfortunately, the same is true of the frequency with which the subject drinks. The role of these drinking variables in neuropsychological functioning generally has not been adequately controlled.

Other subject variables. Many neuropsychological studies compare alcohol users and controls without controlling for differences in education, socioeconomic status, and verbal

abilities between the two groups. These factors are known to influence neuropsychological performance (Hecaen & Albert, 1979); it is unknown whether the effects of alcohol use are seen only in subjects with such specific characteristics or are, indeed, generalizable to well-educated, high socioeconomic status groups with adequate diets.

In summary, a variety of factors must be controlled in neuropsychological research on human alcoholics to avoid substantial threats to external and internal validity. The present research proposes to address these issues of validity.

III

BIOCHEMISTRY OF ALCOHOL USE

Common laboratory blood tests have been used in studies of alcoholism for two major reasons: first, to seek a valid, reliable and inexpensive biochemical method for the early diagnosis of alcoholism and second, to examine the nature and extent of alcohol-induced biochemical disruption. The most recent work in the area of biochemical diagnosis of alcoholism has been done by Ryback and associates. Basically their work demonstrates that 100% of medical ward alcoholics, and 100% of non-alcoholic medical controls can be correctly classified with fairly routine biochemical tests. Similarly, 96% of treatment program alcoholics and 89% of the non-alcoholic medical controls were correctly classified with the same tests (Ryback, Eckhardt, Pautler & Feldman, 1978). The nine tests which most reliably discriminate alcoholics from controls are bilirubin, SGOT, SGPT, CO₂, red blood cell count, hemoglobin, hematocrit, MCV and MCH. These tests reflect on the integrity of vital physiological symptoms and are diagnostic of such diseases as anemia and liver dysfunction. These findings currently are being applied in clinical settings, and enable physicians to diagnose alcoholism without having to rely on patients' self-reports. Thus, if alcohol use has a continuous adverse effect on biochemical parameters, as it has been postulated to have on cognitive functions (Parker & Noble, 1980), then the biochemical profile discussed by Ryback et al. (1978) could provide a useful method of establishing the concurrent

validity of self-report questionnaires of social drinking practices.

Alcoholism has been found to be associated with biochemical indices of specific nutrient deficiencies. One common reason for global nutritional deficiencies in alcoholics is that many do not receive adequate diets. However, more specific nutrient deficiencies have been noted in well-nourished alcoholics due to the adverse effects of ethanol on the metabolism and utilization of ingested nutrients. These have been thoroughly reviewed by Tabakoff, Noble and Warren (1979). Ethanol has been found to reduce serum levels of both calcium and magnesium, although the precise mechanism for this phenomena has not been established (Tabakoff et al., 1979). While the administration of magnesium to hypomagnesic animals rapidly returns serum and CSF magnesium levels to normal, the increase in brain tissue magnesium is relatively slow, and the characteristically hyperexcitable state persists beyond the time that CSF magnesium levels become normal (Tabakoff et al., 1979). Calcium deficiency has been found to cause depletion of brain thiamine in rats, and magnesium deficiency has been shown to cause a refractoriness to thiamine treatment in alcoholics suffering from Wernicke-Korsakoff syndrome (Tabakoff et al., 1979). However, there is no evidence that chronic alcohol ingestion directly produces a thiamine deficiency in rats and baboons (Shaw, Gorkin & Lieber, 1981), or in man (Wood, Goode, Buttigieg & Breen, 1981).

In summary, besides the effects on neurotransmitter systems discussed earlier, prolonged and heavy alcohol use is known to disrupt a variety of biochemical parameters of general bodily functioning and nutritional state. The chronicity of these alcohol-related biochemical alterations is presently unknown. Clinical observations indicate that they are reversible with abstinence (N. Nayer, M.D., personal communication, 1983).

IV

NEUROANATOMY OF ALCOHOL USE

Investigations of the neuroanatomical correlates of chronic heavy alcohol consumption reveal that alcoholics have a significantly higher incidence of brain abnormalities, such as sulcal widening and ventricular enlargement, than do the normal population. Both sulcal widening and ventricular enlargement have been considered indices of brain cell atrophy, as a consequence of the direct neurotoxic effects of ethanol. However, alternative explanations for these results must also be considered. Initial conclusions in this area were based on autopsy data from alcoholics. This method was refined with the later use of air encephalogram (AEG) technology, which permitted the investigation of the brains of live subjects. More recently, computerized axial tomographic scan (CAT-scan) technology has been developed which has enabled live neuro-anatomical examinations which are noninvasive.

Autopsy Research

One of the earliest and most comprehensive neuroanatomical investigations of chronic alcoholics was done by Courville (1955). He examined the brains at autopsy of 124 confirmed alcoholics. The major finding was that of progressive atrophy of the dorsolateral area of the frontal lobes, pre- and post-central gyri, and superior parietal lobes. In more advanced cases of alcoholism, there was evidence of ventricular enlargement, cerebellar degeneration, and spinal chord cellular alterations. Courville attributed this atrophy to cellular

damage occurring during acute intoxication and in delirium tremens. He describes the process as "wet brain" or brain edema caused by excessive amounts of CSF and hemorrhaging. Microscopically, the alcoholics' brains had alterations of the ependyma and choroid plexus, and vascular and perivascular edema. Deterioration and loss of pyramidal cells was seen in the frontal; central and parietal lobes, as well as the neurons of the basal ganglia, mamillary bodies and hypothalamus.

In another autopsy study by Victor and Adams (1953), 11 alcoholics with severe neurological symptoms were examined. In these cases, degeneration of the cerebellar cortex, especially the Purkinje cells, was observed. The major cerebral damage occurred in the dorsomedial nucleus of the thalamus and the mamillary bodies.

Very little can be concluded from these early studies as the brain damage observed may be attributable to such uncontrolled factors as malnutrition (which was apparent in 75% of Victor and Adams (1953) cases), head trauma, or liver damage. Furthermore, the absence of information concerning duration of alcohol use, average daily consumption, and time since last drink limits the interpretation of these data.

AEG Studies

Studies of live patients, using the AEG and more recent CAT-scan techniques have enabled more comprehensive investigations of the neuroanatomical factors related to alcoholism. Lereboullet (1956) compared the results of AEGs in 65 alcoholics and 23 controls matched for age (mean age was 50 years).

Subjects with clinical symptoms of neurological damage were excluded. The alcoholics had been drinking for a mean of 10 years. Unfortunately, the average daily consumption, and duration of abstinence at AEG testing were not stated. There was evidence of a greater degree of malnutrition in the alcoholic group. It was found that the alcoholics had a significantly more enlarged third ventricle than the control group. Since the period of abstinence was not stated, however, this observation may have been the result of brain dehydration, or to abnormalities in the brain's osmotic pressure or electrolyte concentration. These acute physiological effects of alcohol ingestion may lead to the erroneous conclusion of brain cell atrophy in AEG and CAT-scan examinations, and may require at least one week of abstinence from alcohol to subside (Wilkinson & Carlen, 1980). However, despite this drawback, and the obvious nutritional confound, Lereboullet's study was valuable in prompting further research into the relation between alcoholism and structural brain damage.

Brewer and Perret (1971) investigated 33 alcoholics, of mean age 50, using the AEG technique. In addition, two psychometric tests (WAIS and Bender Visual Retention Test) were administered. The subjects had been drinking at least 7 glasses of beer or its equivalent daily for an unspecified number of years, but again, the period of abstinence at time of testing was not stated. In general, the alcoholics appeared to be, and reported being well nourished, and had no evidence of liver disease, or clinical symptoms

of neurological impairment. Although there was no control group, the authors reported that all but two subjects showed evidence of both cortical and ventricular atrophy. On the basis of their experience with the AEG technique, this damage was considered to range from moderate to severe. Two thirds of these patients appeared to have diffuse structural atrophy in the frontal and parietal areas, while another 9 had damage solely in the frontal lobe. There were significant correlations ranging from .3 to .5 between the extent of apparent brain atrophy and impaired performance on the psychometric tests. In addition, similar correlations were found between the indices of brain damage and age of the subjects. Unfortunately, the lack of a defined period of abstinence in these subjects, and failure to include a control group renders these intriguing results difficult to interpret.

Computerized Axial Tomography (CAT-scan) Research

The CAT-scan method is preferred to the use of the AEG as it is noninvasive and carries no risk of discomfort for the patient. Osborne (1979) maintains that the CAT-scan is the most sensitive, reliable and valid noninvasive neuroradiologic procedure ever developed. The validity of the CAT-scan has been demonstrated through its extensive clinical use and documented in clinical research (Huckman, Grainer & Clasen, 1977) and studies employing phantom or simulated brains of known tissue density and volume (Penn, Bellanger & Yasnoff, 1978). Penn et al. (1977) have demonstrated that, while CAT-scan measures based on Polaroid print, or planimetry measures

are of limited reliability and validity, computer-generated volume and density measurements of tissue and ventricles are 84% to 99% accurate, using the EMI scan machine. The validity of localizing specific tissue or ventricular measures depends on maintaining a precisely specified orientation of CAT slices. In addition the possibility of artifacts due to motion of the patient's head, the presence of high density foreign materials in the brain (e.g., plates, clips), or low density air in the ventricles must be considered (Huckman et al., 1977).

Nonetheless, the interpretation of CAT-scan measures may be difficult. For example, Kenneth Till, a former neurosurgeon at the Great Ormon St. Hospital for Sick Children, London, is quoted in Science (Vol. 210, 12, 1980, p. 1232): "Interpreting brain scans can be very tricky. There can be a great deal more brain tissue in the cranium than is immediately apparent".

One reason for this is that acute shifts in osmotic pressure or electrolyte balance (which can occur with malnutrition or dehydration) can alter the fluid retention of the brain.

This might result in the erroneous conclusion of brain atrophy.

Measures of tissue density may also be misleading. Density is measured in Hounsfield units; water or CSF has a value of 0, protein or cellular material has a positive value, while lipids or myelin has a negative value. Thus, an increase in the Hounsfield unit of an area of brain tissue does not necessarily reflect increased cellular density, but may reflect (a) dehydration, (b) demyelination, or (c) vascular edema or hyperemia. Similarly while lower Hounsfield units may

reflect tissue atrophy, they may also represent (a) edema, (b) increased myelination, or (c) vascular constriction. The implications for neurological functioning vary considerably depending on which interpretation is made.

Few studies have addressed the related issue of CAT-scan reliability. However, reliability has been indirectly addressed by those studies which sought to demonstrate reversible "atrophy" in alcoholics following prolonged abstinence. For example, Carlen, Holgate, Wilkinson and Rankin (1978) reported in Science that of 8 cases investigated, 5 of 6 abstinent alcoholics had reduced ventricular and sulcal volume measures from the first scan after approximately 1 month of abstinence to the second scan after approximately a year of abstinence. This change corresponded with clinical improvements in all 6 patients. Ventricular and sulcal measures were the same (i.e., indicative of atrophy) at both first and second scans in 2 of the 8 alcoholics who continued drinking. There was no clinical improvement in these 2 patients. If the scans were unreliable, one would expect that at least 3 of these measures would increase by chance, and that there would be no relation between ventricular and sulcal volume, and clinical improvement. Similarly, Artmann, Von Gall and Hacker (1981) found that, among 11 abstinent alcoholics, 9 showed some improvement in sulcal or ventricular volume on the CT-scan between initial hospital admission and 1 year later. Four patients who were not abstinent maintained the exact same measures of cortical and ventricular volume with the two CT-scans. The authors

report a notable lack of significant increase in "atrophy". However, they caution that "it is still uncertain whether dehydration together with decreasing serum albumin due to malnutrition or to neuronal degenerative processes are responsible" (Artmann et al., 1981, p. 27).

With these issues of validity and reliability in mind, the literature will be reviewed on CAT-scans and alcohol use.

CAT-scans of alcoholics

Fox, Ramsey, Huckman and Proske (1976) compared the CAT results of 7 male and 5 female alcoholics who had been drinking heavily for 5 to 40 years, with the CAT-scans of 60 neurological patient controls. The mean age of the subjects was 46.4 years. Subjects were neurological referrals and thus, were apt to be more impaired than both alcoholics and nonalcoholics in the normal population. The nutritional status of the subjects, and period of abstinence from alcohol was not stated. All of the alcoholics had some form of liver disease. The authors found that the alcoholics had significantly larger ventricles than the control group (2/3 of the alcoholics compared to 1/4 of the controls), despite the fact that the alcoholics tended to be younger than the controls. There was a significant relation between age and ventricular size in both groups. There were no differences between the two groups with respect to the size of cortical sulci. While the enlarged ventricles of the alcoholics may have been caused by brain atrophy, they also may have been caused by dehydration, osmotic pressure abnormalities or electrolyte imbalances

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as a result of acute intoxication since the period of alcohol abstinence was not stated. Furthermore, the effect of alcoholism on the brain may be confounded by possible malnutrition and definite liver problems.

Cala, Jones, Mastaglia and Wiley (1978) gave CAT-scans to 26 alcoholics whose mean duration of alcohol abuse was 14.2 years, and whose mean age was 30.3 years. There was no control group. The CAT-scans were given for experimental purposes, rather than for the investigation of clinical symptoms of neurological impairment. Although 1/2 of the subjects reported their diet to be nutritionally insufficient, thiamine levels were in the normal range and a minority had fairly mild symptoms of liver disease. There was some indication of a higher than normal rate of head injury in these subjects. Seventy-three percent showed evidence of cortical sulcal enlargement, and 50% had enlarged ventricles. In addition, 64% appeared to have cerebellar atrophy. The degree of cerebral structural atrophy was positively related to the subjects' age, to the duration of alcoholism, and to the degree of impairment on the WAIS performance subtests. The apparent cortical atrophy was diffuse and symmetrical, but most pronounced in the area around the cingulate gyrus of the frontal lobe. The absence of a definite period of abstinence, lack of a control group, and nutritional and neurological confounds are an obvious drawback to the interpretability of this study.

Lee et al. (1979) conducted CAT-scans on 37 male

alcoholics who had been drinking an average of 50 g. of alcohol a day for an average of 10 years. The average age of these subjects was 30 (10 to 20 years younger than in previously reported studies); they had no obvious clinical signs of neurological impairment, and their nutritional status was reported as very good. Although it is stated that they were abstinent from alcohol at the time of testing, the actual period of abstinence was not reported. Approximately half had abnormally functioning livers, but the degree of liver damage was unrelated to the results of the CAT-scan; 48% of the subjects showed evidence of sulcal widening on the scan, which was most prominent in the interhemispheric fissure of the frontal lobes. Thirty percent had evidence of cerebellar atrophy¹, while only 13% showed signs of ventricular atrophy. Apparently ventricular enlargement is more linearly related to age than is sulcal widening, and is rarely seen in young alcoholics (Bergman, Borg & Hindmarsh, 1980). Fifty-nine percent of the subjects were impaired on the WAIS and on cognitive tests of memory and learning. However, psychometric performance was unrelated to CAT-scan results. This study suffers mainly from the lack of a control group, and the unreported length of abstinence from drinking.

The first study which did control all of the methodological weaknesses of the CAT-scan research previously reported found no evidence of greater brain atrophy in alcoholics than

¹This 30% rate of cerebellar damage was also found by Haubeck and Lee (1979), in younger (i.e., mid-thirties) alcoholics.

in controls. Hill and Mikhael (1979) performed CAT-scans on 15 alcoholics, 15 heroin abusers and 15 controls, matched for age, education, and socio-economic status. The alcoholics, whose mean age was 34, had been drinking an average of a 1/5 of liquor a day for 14.3 years. Their nutritional status was good, and they showed no clinical signs of neurological impairment. The heroin abusers had not abused any other drugs to a significant extent, nor had the controls used alcohol, heroin, amphetamines or other drugs to a substantial degree. The subjects had been abstinent for at least one month, some for six months. Ventricular enlargement on the CAT-scan was measured with a hand planimeter from the scanner-computer print-out, and was expressed as the sum of the areas of the ventricles divided by the sum of the areas of the cranium. This provided the ventricle/brain ratio (VBR). Previous studies have employed a cruder method of direct measurement of the sulci and ventricles from the CAT-scan Polaroid print. Hill and Mikhael (1979) measured sulcal width in this conventional manner. The results correspond closely to those of Lee et al. (1979). That is, 45% of the alcoholics were judged as having sulcal widening, but this rate did not differ from the incidence of 25% in the control group. The cerebral sulci of the heroin abusers were smaller than both the controls and the alcoholics. The authors found that 13% of the alcoholics showed evidence of ventricular enlargement but, again, this was not statistically different from that of the controls (8.3%). The heroin abusers tended to have smaller ventricles than the alcoholics

and controls. Thus, there was a nonsignificant trend for alcoholics to have enlarged ventricles and sulci compared to controls. Heroin abusers were found to have smaller ventricles and sulci than alcoholics and controls. In addition to the neurological test, neuropsychological assessments were performed on these subjects using the Halstead-Reitan battery (HRB). The alcoholics were more impaired than both the heroin abusers and controls, especially on the Category test and TPT-time. However, the subjects were all within the normal ranges of intelligence as measured by the Shipley-Hartford and Peabody Picture Vocabulary tests. The absence of evidence of cerebral atrophy among the alcoholics, and comparably low rates among Lee et al.'s (1979) subjects, may reflect the younger ages of these alcoholics. That is, structural brain damage suggested by earlier studies to result from alcoholism may only occur in older subjects either as a function of duration of alcohol abuse, or an interaction with age itself. Alcohol may promote premature aging of the brain which only approaches the brain-damaged range in older alcoholics. The relationship of age with CAT-scan results was not reported by Lee et al. (1979), or by Hill and Mikhael (1979).

Ron (1980) compared the CAT-scans of 100 male alcoholic referrals to those of 41 age-matched controls. The controls tended to have a higher verbal IQ than the alcoholics. The alcoholic group had a mean age of 43.5, and had been drinking an average of 463 grams of alcohol a day for 17.3 years. They had been abstinent for 12 to 120 days (mean of 34 days). The

ventricle-to-brain ratio (VBR) measure was 9.5 in the alcoholics, compared to 6.1 in the controls, a difference significant at the .001 level. The VBR measure was not related to performance on either the WAIS or the Wisconsin Card Sort test. However, in older subjects it was inversely related to the length of abstinence from alcohol.

Two recent studies by Carlen et al. (1978), and Carlen and Wilkinson (1980), have shed further light on the issue of alcohol-related brain atrophy. In the later study (Carlen & Wilkinson, 1980), 96 alcoholics were compared with 146 controls on CAT-scan measures. It was found that the alcoholics had a significantly higher than normal incidence of sulcal widening and ventricular enlargement (77% and 60%, respectively). These subjects appeared not to suffer from any symptoms of malnutrition or liver disease and reported no history of head trauma. However, there was evidence of a greater degree of brain atrophy in both groups than in the subjects of Hill et al.' study. In the first study, 8 alcoholics of mean age 48.7, with a drinking history of 18.5 years, were given CAT-scans after an average of one month abstinence from drinking, and again one year later. Carlen et al. (1978) found that after an average of one year of further abstinence from alcohol, clinical improvement was observed in 6 of the 8 patients. In 4 of these 6, the extent of ventricular and sulcal enlargement was substantially reduced. The authors maintain that, because initial scans were performed between 2.5 and 11 weeks of abstinence, these reversible atrophy effects cannot be attributed

to re-hydration, or to normalizing shifts in osmotic pressure and electrolyte balance following acute intoxication. The authors suggest that re-growth of damaged neurons and/or supporting glial and vascular tissues may have occurred after prolonged abstinence, perhaps due to increased levels of protein synthesis. This reversibility suggests that the structural brain damage associated with chronic and prolonged (i.e., more than 18 years) alcohol abuse in older subjects (i.e., more than 45) may be an effect of ethanol toxicity, which improves with the removal of the toxic agent. Previous studies were not designed to test the direction of a possible causal relationship between alcoholism and brain damage. However, the small Ns in this study did not permit the statistical analyses necessary to validate the conclusion of reversibility. In addition, it might be argued that some acute affects of alcohol require more than 4 weeks of abstinence in order for detoxification to occur. Thus, the initial conclusion of alcohol-induced structural brain damage in the 4 subjects who improved may be questioned.

Hill and Mikhael (1979) have argued that Carlen et al.'s (1978) conclusion of reversible atrophy in alcoholics is not valid. First, statistical analysis does not support a difference in ventricle size from scan 1 to scan 2. Second there was no control group so that initial abnormality on scan 1 was not demonstrated. Third, the standard error in the linear measurement method employed by Carlen et al. (1978) is at least as large as the average sulcus measured. In a rebuttal

of these criticisms, Carlen, Wilkinson and Wortzman (1979) maintain that in later comparisons with age-matched controls, the conclusion of initial abnormality was supported. In addition, they maintain that their method of measurement is highly reliable ($r = .83$ to $.93$) and that concurrent validity has been established between their method of measuring ventricular volume and an interactive computer system of measurement developed by Penn (1978).

Bergman et al. (1980) compared the CAT-scans of 130 alcoholics; with mean age of 44.2 and a drinking history of more than 11 years to 195 age-matched controls. In addition, 18 heavy social drinkers were examined. Careful medical examinations were given to exclude other disorders and typical confounds of previous research in this area. These alcoholics were thus less impaired than those of Carlen et al. (1978, 1980). Evidence of sulcal widening was evident in 62% of the alcoholics and 40% of the heavy drinkers, which was significantly greater than the incidence of 15% among the controls. Thirty-six percent of both alcoholics and heavy drinkers showed evidence of ventricular enlargement, compared to 11% of the controls. Finally, 35% of the alcoholics had cerebellar atrophy, compared to 5% of the controls.

CAT-scans of social drinkers

Two recent studies have suggested that CAT-scan abnormalities are associated with social drinking practices. Cala and Mastaglia (1980) examined 59 heavy drinkers, who had not suffered from delirium tremens, withdrawal seizures or liver disease,

and "who would regard themselves as no more" than heavy social drinkers" (p. 38). However, the authors do not report the frequency or average amount of alcohol consumption in these subjects. Control subjects included 19 abstinent church members and 43 light drinkers, who were at least 10 years younger on average, than the heavy drinkers. A significant correlation was found between length of drinking history and cerebral (especially frontal and temporal) and cerebellar atrophy. Greater atrophy was related to cognitive impairment on the WAIS, especially on the performance subtests. Unfortunately, the confound of the age with drinking history in this population limits the validity of the alcohol-use variable.

Sarabia and Bowden (1980) examined the CAT-scans of 50 psychiatric referrals, of mean age 44.1, who were classified as heavy drinkers. They had consumed an average of 8 oz. of liquor or 36 ounces of beer a day for 10 or more years, and had been abstinent less than one week. Controls were 50 psychiatric referrals with mean age 38. The authors found that 56% of the drinkers had atrophy of the ventricles or sulci or both, compared to only 6% of controls. This study is limited by the confounds of age, and fairly short period of abstinence in these subjects.

Bergman et al. (1980) examined a random selection of 200 male subjects, of whom 18 were designated as heavy drinkers (consuming 40 g. of alcohol a day for more than 10 years). The remainder consumed a mean of 16 g. per day. Unfortunately,

the authors do not report the mean ages of the two groups. The heavy drinkers were found to have a significantly higher frequency of cortical and ventricular abnormalities on the CAT-scan, and neuropsychological deficits than did the light drinkers. However, neuropsychological performance and CAT-scan measures were unrelated when the effects of age were partialled out.

These studies with social drinkers suggest that morphological changes in the brain may be associated with even sub-alcoholismic levels of drinking. However, further research which controls for the effects of age and investigates relevant drinking variables such as frequency and amount of alcohol consumed is needed to confirm these preliminary findings.

Summary

There is only limited evidence that cortical atrophy and ventricular enlargement are the direct result of the neurotoxic effects of chronic alcoholism. First, the atrophy has been found to be related to the duration of alcohol use. However, duration of drinking is generally confounded with aging, which is known to be related to cerebral atrophy in nonalcoholic populations. Second, the removal of alcohol for up to a year may lead to the reversal of neuroanatomical damage (Carlen and Wilkenson, 1980). However, this study must be replicated with a larger number of subjects so that valid conclusions can be drawn regarding reversibility of neuroanatomical damage with abstinence from alcohol.

Specificity of alcoholic brain damage. The pattern of sulcal widening and ventricular enlargement does not occur exclusively in patients with alcoholism. Cases of nonalcoholic liver disease (Victor et al., 1965), malnutrition (Strom, 1978), and simple aging (Osborn, 1979) have been documented with similar evidence of brain atrophy, or shrinkage. However, this pattern can be distinguished from that of heroin abusers, who tend to have smaller ventricles and sulci than normal subjects and alcoholics (Hill & Mikhael, 1979).

Localization of brain damage. Severe neuroanatomical studies based on the AEG (Brewer & Perrett, 1971), and CAT-scan (Cala et al., 1978; Lee et al., 1979), techniques have found that, while brain atrophy associated with alcoholism occurs symmetrically over broad areas of the brain, damage is especially prominent in the frontal lobes. Cala et al. (1978) found that the cingulate gyrus in the frontal area was most substantially atrophied, while Lee et al. (1979) found damage to be most prominent in the area of the interhemispheric fissure of the frontal lobe. It is unclear as to why the frontal lobes might be more vulnerable to alcohol-related damage than other areas of the brain. It is worth noting, however, that in the three studies which found the frontal cortex to be most prominently affected, the period of subjects' abstinence from alcohol at the time of testing was not stated. Thus, the apparently enhanced atrophy of the frontal area may have been an artifact of neuronal dehydration, electrolyte imbalance, or abnormalities of osmotic pressure.

It is possible that in the frontal cortex, which is less well-supported by subcortical structures than is the rest of the cortex, the temporary shrinkage phenomenon associated with acute intoxication is more visually apparent on CAT-scans and AEG prints. Conversely, the neuronal structure of the frontal cortex may render it more vulnerable to damage with chronic alcoholism. That is, the frontal cortex is predominantly agranular (i.e., there is a higher ratio of stellate cells to pyramidal cells), while the more posterior portions of the cortex are granular in nature. In addition, myelinization of the frontal lobes occurs much later in life (i.e., around puberty) than it does in more posterior regions. These differences could be the basis for the greater vulnerability of the frontal lobes. Von Gall (1979) has suggested that the phylogenetic recency of the development of the frontal area renders it more vulnerable to the disruptive effects of alcohol and a variety of other psychiatric and neurological degenerative processes. Additionally, it is possible that the frontal lobes may degenerate in alcoholics as a result of primary damage to the dorsomedial thalamus which has direct connections with the prefrontal cortex. Early autopsy studies (Victor, 1953) have found the dorsomedial thalami and mammillary bodies, which lie adjacent to the third ventricle, to be the most damaged areas of the brain in alcoholic subjects. The question of greater frontal lobe impairment with alcohol, and its cause, awaits confirmation through further neuro-anatomical research. However, it should be noted that

electrophysiological studies, using ERP and CBF measures also suggest greater impairment of the frontal lobes in alcoholics.

Relation between neuroanatomical and neuropsychological indices of impairment. Because several of the neuroanatomical investigations of alcohol-related brain damage included the administration of neuropsychological tests, it was possible to examine the relation between indices of brain atrophy and impaired cognitive functioning. Brewer and Perret (1971) found a significant correlation between AEG indices of atrophy and overall performance on the WAIS and Benton Visual Retention test. Correlations also were found between the degree of brain atrophy and age. Similarly, Cala et al. (1978) found significant correlations between global estimates of cerebral atrophy on the CAT-scan, and the WAIS performance subtests. In addition, degree of apparent brain atrophy was significantly related to the subjects' age and duration of alcohol abuse. Carlsson et al. (1979) found that psychometric performance was related to ventricular size, but not to sulcal width, in a sample of 34 neurologically impaired alcoholics. Size of the third ventricle was related inversely to performance on Block Design ($r = .46$), configural organization ($r = .45$), the Gottschaldt test ($r = .44$) and tests of perseveration ($r = .37$) and inversion capacity ($r = .40$).

Bergman et al. (1980) found Evan's ratio (width of the anterior horns divided by inner skull width) was significantly and inversely related to performance on the Block Design subtest of the WAIS, and on several Halstead-Reitan subtests.

When age was partialled out, Evan's ratio remained significantly related only to Block Design ($r = -.15$) and the Tactual Performance test ($r = -.16$), and these correlations accounted for less than 3% of the variance. In a second study, reported in the same article, Bergman et al. (1980) report that ventricular and central CAT-scan changes are related to learning and memory performance, while sulcal changes relate to other tests of neuropsychological performance, not learning and memory. However, no statistics are reported to support this contention.

While these studies found a consistent relation between neuroanatomical and neuropsychological indices of alcoholic brain damage, three other studies failed to find such a relationship. Fox et al. (1976) found their alcoholics to be unimpaired on a series of cognitive tests measuring learning and memory despite the fact that there was CAT-scan evidence of significantly more ventricular enlargement in the alcoholics than control subjects. In addition, Hill et al. (1979) found no evidence of greater brain atrophy in their alcoholic sample, despite the fact that these subjects were significantly more impaired than controls on several subtests of the HRB, such as the Category test and TPT. Performance on these tests were minimally related to the degree of cortical atrophy. Lee et al. (1970) also found limited evidence of cortical atrophy (48%) and ventricular atrophy (16%) in their alcoholic sample. Although 59% were impaired on the WAIS and cognitive tests of learning and memory, the psychometric indices were

unrelated to the extent of atrophy. In the latter two studies, finding no relationship between neuropsychological performance and brain atrophy, the subjects were relatively young, with shorter drinking histories. Carlen and Wilkinson (1980) found significant correlations between CAT-scan measures and 76 of 102 neuropsychological tests, including the WAIS, Wechsler Memory Scale and HRB in their alcoholic sample. When age was partialled out of this relationship, only 2 of the neuropsychological tests were related to degree of brain atrophy, which is even fewer than might be expected by chance alone. The authors concluded that age has an accelerating effect on both functional and neuroanatomical impairment due to alcoholism. In summary, there is some indication of a relationship between neuroanatomical and neuropsychological impairment as a function of chronic heavy alcohol abuse. However, this relationship may depend on the accelerating effects of age, and perhaps of duration of alcohol abuse.

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V

NEUROPSYCHOLOGY OF DIET AND NUTRITION

Both dietary and nutritional status have been found to affect neuropsychological performance, although the two do not parallel each other as closely as one might expect. Diet refers to nutrients which the individual ingests, typically assessed by self-report dietary recall or diet dietary methods. Nutrition refers to the biochemical balance of nutrients within the body, usually measured by blood, urine, or other biochemical assay methods. There is generally a weak but positive relation between chronic dietary ingestion and serum levels of nutrients such as some minerals (e.g., iron) and fat-soluble vitamins (e.g., vitamin D). In contrast levels of other nutrients such as glucose, and water soluble vitamins fluctuate acutely throughout the day with each meal. Serum levels of other minerals, such as calcium and phosphorous are closely controlled by hormones (e.g., parathormone in the case of calcium and phosphorous); thus dietary effects within a near-normal range are very subtle.

Knowledge about the neuropsychological sequelae of specific dietary and nutritional deficiencies is relatively scant. There is a fair amount known of the neurochemical effects of specific vitamin deficiencies in experimental animals. In humans, there has been a growing body of research on the association of vitamin and mineral deficiencies (specifically iron-deficiency anemia) and protein-calorie malnutrition, with behavioural and learning disorders in

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children. With adults there has been some research on psychiatric correlates of nutritional deficiencies and anorexia nervosa. In addition, there is a growing interest in the acute behavioural effects of ingestion of glucose and of dietary precursors of neurotransmitter synthesis (Lieberman & Wurtman, 1982). This review will confine itself to the chronic psychological effects of general calorie-protein intake, and more specific essential vitamin and mineral ingestion.

Calorie-Protein Undernutrition

According to recent estimates, approximately one-fourth of the world population is suffering from varying forms of undernutrition (Dreyfus & Geel, 1981). Particular attention has been directed to the large proportion of this population represented by children, as the brain is known to be the most susceptible to environmental insult during the period of 30 weeks gestation to 2 years of age. This is the critical period during which growth of neuronal processes and myelogenesis is most rapid, although such development is known to continue in the frontal lobes until the teen years. In the rat, protein-calorie undernutrition has been found to result in impaired cellular proliferation and myelin development, immature myelin concentration and composition, and altered levels of brain amino acids and neurotransmitters. The nature and extent of these abnormalities depends on the timing and duration of the period of undernutrition (Dreyfus & Geel, 1981).

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An important question is the reversibility of these neurological abnormalities. Most research favours the view that while alterations occurring during a critical phase of brain development are irreversible, those occurring during a later phase may be reversed with the reinstatement of adequate nutrition (Dreyfus & Geel, 1981).

It has been difficult to address properly the issue of whether behaviour and learning capacity are altered by dietary inadequacy. Generally, studies of undernourished children are confounded by nonnutritional variables such as disease, socioeconomic and cultural differences, and psychological factors. However, there have been several field studies which have controlled experimentally for these factors. Studies of undernourished children vs. well-nourished controls in India (Singh, Anand, Gupta & Dhingra, 1976), Nepal (Graves, 1978), Cali, Columbia (McKay, Sinisterra, McKay, Gomex & Lforeda, 1978), Nigeria (Ashem & Janes, 1978), Korea (Winick, 1979), Jamaica (Richardson, 1980), Mexico (Brozek, 1979), and Chile (Monckeberg, 1979) tend to concur: poor nutrition and impaired cognitive performance are associated in children. More specifically, the undernourished children are less active and exploratory and thus interact less with their environment than well-nourished controls. However, a consistent confound in these studies, even when socioeconomic status is controlled, is that children from the undernourished groups tend to receive a lower level of home stimulation (Brozek, 1981).

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In an excellent review of the literature on protein-calorie malnutrition and behaviour, Pollitt and Thomson (1977) reach the following conclusion:

Despite a lack of specific information on the nature of the nutrition-intelligence relationship, available evidence indicates that protein-calorie malnutrition has an adverse effect on the ontogenetic process, retarding the rate of developmental change. However, except for those cases of severe and chronic under-nutrition with an onset during the prenatal period or early postnatal life, protein-calorie deficiency does not arrest development (p. 300).

Several studies support the conclusion that nutritional supplementation increased the IQs of malnourished children, compared to non-supplemented controls (e.g., Chavez, Martinez & Yaschine, 1974). McKay et al. (1978) have demonstrated that low IQ and poor psychological performance in moderately malnourished children are amenable to improvement in an enriched environment which includes nutritional supplementation. However, short-term memory did not improve. Persisting short-term memory deficits are the most commonly reported impairment in undernourished children, a finding generally attributed to an attentional deficit (Pollitt & Thomson, 1977). Nonetheless, Levitsky (1971) has noted that performance of such tests of intellectual performance may be compounded by emotional and maturational deficits and other variables arising from non-nutritional causes. Thus, Dreyfus and Geel (1981) conclude that coexisting variables of disease, cultural differences, and psychological factors interacting with malnutrition render the interpretation of results difficult. Furthermore, interpretation is clouded by the fact that data are usually obtained

from a clinical sample of unknown medical history and compared to an inadequate control group. Nonetheless, there is ample evidence suggestive of diet-related intellectual decline to warrant further investigation in a relatively healthy, upper-class, well-educated sample.

In North America, clinical malnutrition is far less prevalent than in developing and Third World nations. Thus, further understanding of the consequences of malnutrition here has been achieved through the study of groups such as anorexia nervosa patients, suffering from the effects of self-inflicted starvation.

Anorectics have not been found to have lower IQs than well-nourished controls, but have been found to be significantly more depressed and obsessive than controls (Ben-Tovim et al., 1979; Solyom, Freeman & Miles, 1982). It is not entirely clear whether depression and obsessiveness precede or result from impaired nutritional status. Nevertheless, Ben-Tovim et al. (1979) have concluded that "...the early morning waking that characterises the anorectic population and which weights them for depression...is a feature of impaired nutritional status and is unrelated to affective state" (p. 324).

There have been a number of studies investigating the effects of "orchonutritional dietary treatment programs (Gowans, 1980) and other diet, exercise and education regimens (Merzbacher, 1979) on various measures of psychological functioning. In such studies the independent variable, diet,

is generally either poorly and vaguely defined (e.g., the "orthonutritional approach") or else confounded with a variety of other lifestyle-change factors (e.g., Merzbacher, 1979). Thus, interpretation of a dietary effect in these studies is not really possible.

Specific Vitamin and Mineral Deficiencies

There is ample evidence that specific vitamin and mineral deficiencies affect psychological functioning in humans. Again, the majority of this work has focused on children as dietary deficiencies are believed to have their most debilitating effects on the developing brain.

Vitamin Deficiencies

Vitamins are organic compounds, necessary in small quantities to sustain basic metabolic processes (Herbert, 1977). Vitamins combine with enzyme proteins to form holoenzymes which are necessary for specific metabolic reactions. Once the enzyme protein is saturated with its respective vitamin, the vitamin serves no useful function and must be excreted. The water-soluble vitamins (B-complex and C) are generally quickly excreted, but the acute effect of large doses of niacin, for example, may cause hot flushes, circulatory disturbances, cardiac arrhythmias, liver damage, hyperglycemia, hypernutrition, and lower cholesterol and blood lipids (American Academy of Pediatrics, 1976; Golden, 1980; Lipton & Wheless, 1980). The fat-soluble vitamins (A, D, E, and K) are even more toxic if taken in excess, as they are stored

most clearly regulate man's affective and emotional state, as well as the neuropsychological abilities described above.

Unfortunately, previous research in this area has failed to control adequately for affective state. Thus, the neuropsychological deficits commonly seen in alcoholics and heavy social drinkers may be secondary to disturbed affect rather than simply a direct effect of frontal lobe dysfunction associated with alcohol use.

Previous research in this area also has failed to control adequately for dietary inadequacy commonly found in alcoholics (Tabakoff et al., 1979). In addition, it is not known to what extent the relation between alcohol use and neuropsychological dysfunction may be secondary to alcohol's adverse effect on the metabolism of nutrients such as calcium and magnesium.

Alcohol has been associated definitively with neuro-anatomical changes measured by instruments such as the CAT-scan. At the present time, the interpretation of these findings is quite controversial. It is not known whether the shrinkage, seen most notably in the frontal cortex but also in tissue surrounding the lateral ventricles, represents actual neuronal atrophy, electrolyte imbalances and/or shifts in osmotic pressure, or some other factors. Recent advances in CAT-scan interpretation based on tissue density measures (Bruce, Alavi, Bilaniuk, Dolinska, Obrist & Uzzel, 1981) may allow more precise determination of the etiology of such shrinkage and its relation to neuropsychological performance.

Because less research has been done on the neuropsychological

on a variety of symptom checklists.

Two studies aimed at studying the effects of pyridoxine (B6) treatment, however, found positive results. Rimland, Calaway and Dreyfus (1978) performed a double-blind crossover study, administering either pyridoxine or placebo to 16 autistic children. The children were reported on home and school ratings and symptom checklists as being significantly improved while on pyridoxine. However, it is not clear that, in fact, performance did not deteriorate during the placebo phase due to withdrawal from pyridoxine dependence. Coleman, Steinberg, Tippet, Bhagavan, Coursin, Gross, Lewis and Deveau (1979) selected hyperactive children who responded to methylphenidate, and had serotonin levels lower than 50% of the normal range, for a double-blind crossover study. The children were administered high and low doses of methylphenidate, pyridoxine, and placebo. At each stage, Conners Parent and Teacher Rating Scales were completed. The children had significantly better behavioural patterns while on pyridoxine, as well as significantly higher serotonin levels, than while on methylphenidate or placebo. It was concluded that the subset of hyperactive children with abnormally low serotonin levels respond positively to pyridoxine treatment. However, this study has not been replicated. While other researchers have failed to find serotonin deficiencies in hyperactive children (Ferguson, Pappas, Trites, Peters & Taub, 1981), such a subgroup may, indeed, exist. It should be noted that the diagnostic specificity of pyridoxine treatment has not

been established, since Rimland et al. (1978) found it to be effective in treating autism, in which a serotonin deficiency has not been found.

Deficiencies of other B-complex vitamins are known, clinically, to have specific neuropsychiatric sequelae (Schuster, 1980). For example, thiamine deficiency produces Wernicke's encephalopathy, manifested by memory deficit, confabulation, apathy, ataxis and progressive dementia. Lesser degrees of thiamine deficiency produce depressive symptoms, fatigue, irritability, and lack of drive. Niacin deficiency is known to be associated with deficiencies in the amino acid, tryptophan. This may result in symptoms of hyperkinesia, irritability, apathy, anxiety, and memory defect which are responsive to niacin therapy. Psychotic behaviour may occur in more advanced stages of niacin or tryptophan deficiency (Schuster, 1980), and may be irreversible. Serum B12 deficiency has been found to be associated with intellectual impairment on psychological tests (Roca & Willanger, 1977) and disturbances of memory and affect (Sullivan, 1970).

Mineral Deficiencies

There is growing evidence that specific mineral deficiencies are associated with decrements in psychological functioning. In contrast to vitamins, minerals are inorganic compounds, also necessary in small amounts to sustain the normal metabolic life processes. While excessive amounts of minerals may be as detrimental as deficiencies, this review will focus on deficiency states as they are most commonly

caused by factors such as alcohol ingestion and dietary insufficiency.

Calcium is the most prevalent cation in the body and is maintained in plasma under strict control of homeostatic mechanisms, such as parathormone, vitamin D, circulating levels of inorganic phosphorous, and, possibly, calcitonin. Thus, in the normal dietary range, calcium ingestion is only slightly correlated with serum calcium levels. The strong effect of parathormone is such that serum levels of calcium and phosphorous are inversely related, although a 1:1 ratio is most desirable. Calcium is directly involved in the stabilization of cell membranes and the regulation of membrane permeability and thus has an important effect of impulse initiation and propagation (Winokur & Beckman, 1977). Calcium is also known to have an important role in the release of neurotransmitters such as norepinephrine and acetylcholine. Lowering calcium levels increases the excitability of neural tissue, clinically manifested by reflex hyperactivity, nervousness and irritability (Webb & Gehl, 1980). The multitude of mental symptoms associated with hypocalcemia range from anxiety and emotional lability to catatonic states (Webb & Gehl, 1980). Pitts and McClure (1967) proposed that in certain predisposed individuals, stress produced a buildup of lactate (a calcium metabolite) which subsequently reduced calcium levels and precipitated anxiety attacks.

Phosphorous, the major intracellular anion has received less attention than calcium, despite its many biological

functions. Phosphorous is vital to all synthetic and catabolic processes and proper central nervous system function (Webb & Gehl, 1980). Experimentally induced phosphorous deficiency was found to result in weakness, tremulousness and irritability (Lotz, Zismann & Bartter, 1968). Clinical deficiency is also associated with apprehension and confusion (Webb & Gehl, 1980). The mechanisms by which phosphorous deficiency affects central nervous system function is through the impairment glucose metabolism and anoxia (Webb & Gehl, 1980) associated with red cell abnormalities.

Sodium deficiency, or hyponatremia, often results from dietary restriction and a variety of systemic diseases. McCance (1936) experimentally lowered sodium levels in healthy volunteers and found that the result was impaired taste, anorexia, clouded sensorium, and general exhaustion. Weiner and Epstein (1972) found that acute symptoms of hyponatremia include headache, impaired orientation and concentration and decreased attention span.

Potassium is the major cation of intracellular fluid, and plays a central role in maintaining the membrane potential. Total body potassium is maintained by dietary intake of other nutrients (Webb & Gehl, 1980), the acid base balance and losses from various tissues. Depletion (hypokalemia) is common in patients with anorexia nervosa, vomiting and diarrhea and various renal disorders. Psychological symptoms of hypokalemia include nervousness, irritability, headaches and depression (Webb & Gehl, 1980). Cognitively, symptoms

include diminished concentration, attention span, memory and abstracting abilities. Shaw and Coppen (1966) found that intracellular potassium levels were low in depressed patients compared to normal controls. Similarly, Shaw, Frizel, Camps and White (1969) found potassium concentrations in the brains of suicide victims were below normal when compared to a control group.

Magnesium is essential for the activity of many enzymatic systems, and is thought to be the main electrolyte required for uptake of catecholamines into neural vesicles (Euler & Lishajko, 1963). Magnesium and calcium act as co-regulating factors; for example, the central nervous system depression produced by hypercalcemia can be overcome by intravenous injections of magnesium (Webb & Gehl, 1980). While calcium deficiency results in profound anxiety, depression is the more common psychiatric symptom of hypomagnesemia (Hall & Joffe, 1973).

By far the most compelling work concerning the neurotoxic effects of trace mineral deficiencies has focused on neuropsychological performance in relation to iron deficiency, but this work has been done almost exclusively with children. Sulzer, Hausche and Koenig (1973) found that 'iron-poor' children had lower IQs and vocabulary test scores, and were unable to effectively integrate previously learned associations, compared to controls with adequate iron levels. There were, however, no differences in attention span between the two groups. Webb and Oski (1973) examined attention, perception and

scholastic achievement in 12- to 14-year olds, and found that anemic children's scores were lower than those of nonanemic controls. The authors concluded that scholastic achievement of the anemics was a result of attentional and perceptual deficits typical of conduct disorder. 7

Pollitt and Liebel (1976) maintain that it is unclear, in these ex post facto studies, whether the cognitive deficits reported were consequences of iron deficiency alone, or of general nutritional inadequacy. In addition, when appropriate controls for environmental differences between iron-deficient and control groups are introduced, results are less conclusive (Deinard, 1981). However, a longitudinal study by Cantwell (1974) supports the conclusion that anemia in children with adequate protein-calorie nutrition is one cause of possibly permanent MBD. At 6 to 18 months of age, 32 of 61 children were identified as being anemic, but not malnourished. Unfortunately, levels of other dietary minerals were not reported. At 6 to 7 years of age, blind ratings revealed that the previously anemic children had a higher incidence of "soft" neurological signs, inattentiveness and hyperactivity than controls of comparable socioeconomic status. A major weakness of this study is that it is correlational in nature, and the possibility that other factors were confounded with anemia remains strong.

The most compelling argument that cognitive deficits result from iron deficiency would involve the reversibility of such deficits with iron supplementation. This has been

conclusively demonstrated with animals (Massaro & Widmayer, 1981). Oski and Honig (1978) found improved scores on the Bayley Infant Development scale after iron-deficient infants were treated with intramuscular iron. Placebo treatment yielded no improvement. Lieber et al. (1981) compared cognitive performance of 15 iron-deficient but non-anemic children to 15 IQ-matched controls, after several months of iron therapy. The iron-deficient children showed significantly more improvement in attentiveness and learning tasks than the iron-replete controls. However, as Connors (1982) points out, since the experimental group had significantly lower pre-treatment cognitive test scores than controls, regression to the mean for cognitive performance may well account for the results. Ideally, such groups should be matched in baseline attentiveness and learning ability.

Clinically, depression has been associated with iron-deficiency, but not with hemoglobin concentration. Thus, specific iron-related biochemical and enzymatic changes are the more likely cause of the depression than is hemoglobin concentration. For example Mackler, Person, Miller and Finch (1979) have shown significant alterations in pathways of serotonin degradation in adult iron-deficient rats.

Summary

Dietary and nutritional deficiencies have been demonstrated both clinically and experimentally to affect cognitive performance and psychiatric mood state. General dietary restriction of protein-calorie intake appears to affect inversely general

cognitive development in children, and especially attentional mechanisms. These deficits may be reversible with the reinstatement of adequate diet.

Severe clinical deficiencies in B-complex vitamins (thiamine, niacin, B12) are associated with impairments of memory, affect, and with general apathy and depression. Treatment with B-complex supplements substantially alleviates these symptoms. More subtle degrees of deficiency of vitamin B6 have been associated with hyperactive and autistic behavioural disorders in children which the initial data suggest are at least partially amenable to B6 supplementation.

Mineral deficiencies also have been conclusively associated with psychiatric and cognitive disturbances in both clinical and experimental research. Sodium, magnesium, iron, and potassium deficiencies are known to result in depression, while hypocalcaemia more typically causes anxiety. While deficiencies of these minerals and phosphorous are known to result in general cognitive decline, there have been no well-controlled studies aimed at investigating effects on specific cognitive processes. However, iron-deficiency has been found to be associated with retarded cognitive development and impaired attention in children, while iron supplements reduced these deficits.

Several biochemical mechanisms for the psychological effects of diet and nutrition have been proposed throughout this section. The next chapter will explore these mechanisms in greater depth.

VI

BIOCHEMISTRY OF DIET AND NUTRITION

Dietary ingestion of the nutrients reviewed in the preceding chapter does not directly affect blood concentrations in all cases. Serum levels of calcium, phosphorous and magnesium are controlled more by hormonal regulation than by diet. Nevertheless, serum calcium and phosphorous have been found to be reduced significantly by chronic alcohol use (Tabakoff et al., 1976), which suggests that alcohol may disrupt hormonal mechanisms such as parathormone. Serum sodium and potassium, on the other hand, do vary directly with general dietary intake (Webb & Gehi, 1980), and serum iron levels are known to increase with elevated dietary ingestion of iron. With these associations between diet and nutrition in mind, the research on biochemical effects of nutrition will be reviewed briefly.

Dietary restriction and the resulting protein-calorie undernutrition have a multitude of biochemical effects, as essentially every nutrient required by the body to sustain its metabolic processes is deficient. For example, both undernutrition and anorexia nervosa result in disturbances of hypothalamic function, with increased production and decreased metabolism of cortisol (Walsh, 1982). In anorexia nervosa there is a further disturbance in thyroid functioning resulting in a decrease of thyroid hormones and in noradrenaline receptor sensitivity. This reduced noradrenaline receptor sensitivity may be a central factor in the increased risk of depression in anorectics (Walsh, 1982).

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In undernourished rats at weaning, several studies have found that absolute levels of noradrenaline and dopamine are reduced; however, if these levels are expressed as concentration per gram of brain, the noradrenaline and dopamine values of the undernourished animals would be slightly, but not significantly higher than that of controls (Shoemaker & Bloom, 1977).

Regarding more specific nutrients, there has been limited research on biochemical and neurotransmitter abnormalities associated with specific nutritional deficiencies. Pyridoxine (vitamin B6) deficiencies have been associated with diminished serotonin levels. In fact Coleman et al. (1976) reported that the improved behaviour of hyperactive children while receiving pyridoxine supplements was paralleled by increased levels of serotonin in plasma. Niacin deficiency has been associated with deficiencies in the amino acid tryptophan, a dietary precursor of serotonin. Niacin and accompanying tryptophan deficiencies have been found to be associated with hyperkinesis, anxiety, and memory impairments (Schuster, 1980).

In the case of dietary minerals, more is known of the biochemical actions of calcium than of the other minerals. Calcium plays an important role in regulating neurotransmitter release. Baksi and Hughes (1982) have demonstrated that dietary manipulation resulting in reduced serum calcium in rats produces significant increases in the dopamine and noradrenaline content of the cortex and hypothalamus. This result may be the basis for the clinically observed anxiety (Pitts &

McClure, 1967), irritability and reflex hyperactivity in hypocalcemic patients (Webb & Gehl, 1980).

▲ The effects of phosphorous deficiency on neurotransmitter activity have not been examined. However, it is thought that the CNS mechanism of phosphorous deficiency is the impairment of glucose metabolism and red cell anoxia (Webb & Gehl, 1980). Finally, iron deficiency has been found to disrupt serotonin degradation in adult rats (Mackler, Person, Miller, Inamdar & Finch, 1978).

◆ In summary, severe caloric restriction impairs the functioning of practically every bodily system. Effects on hormonal systems (e.g., hypothalamic and thyroid) have been most well documented. Pyridoxine, niacin and iron deficiencies have been found to disrupt serotonin synthesis and degradation. Calcium deficiency, on the other hand, produces abnormally elevated concentrations of dopamine and norepinephrine in the cortex and hypothalamus. Phosphorous deficiency results in red cell anoxia and impaired glucose metabolism in the brain.

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VII

NEUROANATOMY OF DIET AND NUTRITION

As is the case with neuropsychological and biochemical studies of diet and nutrition, there has been little research on the neuroanatomy of dietary and nutritional status. In the work that has been done, there has been an almost exclusive focus on the prenatal and developing brain as it is believed to be most vulnerable to the neuroanatomical effects of nutritional insult. Thus knowledge of the effects of undernutrition on adults, and the effects of specific nutrients on the brain remains unknown.

In prenatal and infant brains, undernutrition appears to result in reduced number and size of both neurons and myelin cells, which is irreversible with subsequent nutritional rehabilitation (Shoemaker & Bloom, 1977; Johnston, 1977). From 2-3 weeks of life, onset of nutritional deficiency results mainly in the reduction of the number of myelin cells which subsequently develop (Shoemaker & Bloom, 1977). From two years onward, however, the effect of undernutrition is not to reduce the number of myelin cells, but to reduce the size of the cell due to decreased lipid content (Johnston, 1977). Indeed, in clinical reports of adult humans, the central feature of undernutrition has been found to be myelinolysis (Lopez & Collins, 1968). Thus the cells were unable to adequately perform the natural functions of myelination.

It is thought that myelinated axons reduce their conductance speed when myelination is deficient (Shoemaker & Bloom, 1977).

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A second possible role of myelin involves brain nutrition. It is believed that myelin cells store carbohydrates and release them to neuronal cells during periods of food restriction (Shoemaker & Bloom, 1977). These functions could certainly account for a diet-related functional deficit.

In rats, the effect on myelin development has been found to be reversible, in that nutritional rehabilitation results in lipid content being raised from 70% to 87% of that of well-nourished controls (Fishman, Madhyastha & Prensky, 1971). Johnston (1977) notes that protein deprivation has been found to curtail myelination more seriously than does general under-nutrition. Others have reported that the central dietary feature affecting retarded myelination is a fat deficiency, and especially an essential fatty acid deficiency (Johnston, 1977). Unfortunately, as mentioned earlier, most of this research has focused on immature or developing brains so that the questions of (1) effects of undernutrition on the adult brain, and (2) specific nutrients involved in this effect in adults remain unanswered.

Four studies of neuroanatomical changes seen in anorectics do shed light on the issue of the effects of adult undernutrition on the brain. In CAT-scans of adolescent girls with anorexia nervosa, generalized diffuse and uniform cerebral atrophy has been found (Enzmann & Lane, 1977; Cala & Mastaglia, 1980; Heinz et al., 1977; Sein, Searson, Nicol & Hall, 1981). In all three of these studies (Enzmann & Lane, 1977; Heinz et al., 1977; Sein et al., 1981), the previously observed atrophy

disappeared as dietary intake improved and weight approached normal.

Only one study could be found which was relevant to the issue of specific nutrients involved in the neuroanatomical effects of undernutrition in adults. Tucker and Sandstead (1981) examined the spectral EEG correlates of serum iron status in adult men. Measures of resting delta frequency were significantly related to iron status in two groups of men, and were interpreted as indicating alertness or arousal level.

In summary, it is apparent that undernutrition may produce substantial neuroanatomical effects. In adults, these are related, perhaps exclusively to a general process of reduction in myelin size and function. On the CAT-scan this process would manifest itself as apparent shrinkage of the brain but, more specifically, as increased brain density (lipids, i.e., myelin, has a negative density value, while protein, i.e., neurons, have a positive value). It remains unknown however, at what point in the continuum of well nourished to undernourished status these effects would be seen, which specific nutrients are most responsible for these effects, and finally, what might be the functional significance of the neuroanatomical alterations of undernutrition.

VIII

RATIONALE FOR PRESENT STUDY

The review of the literature provides considerable evidence for neuropsychological, biochemical and neuroanatomical effects of alcohol use and diet. However, it also raises many questions and issues for further research.

It is clear that alcohol use in 'alcoholics' and in 'social drinkers' is associated with decrements in neuropsychological performance. The tests which most consistently demonstrate alcohol-related decrements are tests specifically sensitive to frontal lobe functioning, such as the Wisconsin Card Sort Test, and "right-hemisphere tests" such as Block Design and Digit Symbol. In addition, tests of general conceptual and abstraction abilities, such as the Shipley Institute of Living Scale, are sensitive to alcohol use. Performance on tests of verbal abilities and vocabulary, on the other hand, appears not to be adversely affected by alcohol use. Because of the emphasis on frontal- and right-hemisphere-related dysfunction in alcohol research, one also would expect that heavy drinkers and alcoholics would be most impaired on tests sensitive to right frontal lobe lesions, such as the Design Fluency test (Jones-Gotman & Milner, 1972), and only moderately impaired on tests sensitive to left frontal lobe lesions, such as a Verbal Fluency test. On the basis of these neuropsychological patterns, Tarter (1976) has proposed the very popular theory that excessive alcohol use results in a specifically frontal-limbic dysfunction. The frontal-limbic system is known to

most clearly regulate man's affective and emotional state, as well as the neuropsychological abilities described above.

Unfortunately, previous research in this area has failed to control adequately for affective state. Thus, the neuropsychological deficits commonly seen in alcoholics and heavy social drinkers may be secondary to disturbed affect rather than simply a direct effect of frontal lobe dysfunction associated with alcohol use.

Previous research in this area also has failed to control adequately for dietary inadequacy commonly found in alcoholics (Tabakoff et al., 1979). In addition, it is not known to what extent the relation between alcohol use and neuropsychological dysfunction may be secondary to alcohol's adverse effect on the metabolism of nutrients such as calcium and magnesium.

Alcohol has been associated definitively with neuro-anatomical changes measured by instruments such as the CAT-scan. At the present time, the interpretation of these findings is quite controversial. It is not known whether the shrinkage, seen most notably in the frontal cortex but also in tissue surrounding the lateral ventricles, represents actual neuronal atrophy, electrolyte imbalances and/or shifts in osmotic pressure, or some other factors. Recent advances in CAT-scan interpretation based on tissue density measures (Bruce, Alavi, Bilaniuk, Dolinskas, Obrist & Uzzel, 1981) may allow more precise determination of the etiology of such shrinkage and its relation to neuropsychological performance.

Because less research has been done on the neuropsychological

biochemical and neuroanatomical effects of diet and nutrition, there remain even more unanswered questions than is the case with the effects of alcohol use. It has been established that children from underdeveloped nations have deficits in cognitive development and myelin formation, associated with dietary and nutritional deficiencies. Similar results have been found with iron-deficient children in North America. In addition, anorectic adults from upper socioeconomic status environments have a higher incidence of affective disturbances, diffuse CAT-scan abnormalities and biochemical deficiencies compared to controls. However, it is not known to what extent dietary and nutritional inadequacy are directly responsible for these abnormalities as they are generally confounded either with environmental factors or with other disease states, or both. In addition, neuropsychological deficits associated with diet and nutrition have not been demonstrated in adults, nor have the specific nutrients involved in this relationship been identified. Each of these issues will be investigated in this study.

This research will examine the relationship of alcohol use with neuropsychological performance and neuroanatomical measures while controlling for dietary quality in middle- and upper-class adults. The questions related to this major issue, outlined in the introduction, may be stated as:

- 1) What degree of alcohol use and dietary insufficiency is necessary before neuropsychological sequelae become apparent?

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- a) While neuropsychological, neuroanatomical and biochemical impairment are the well-documented sequelae of alcoholism and childhood malnourishment, do subtle degrees of these deficits related to diet and alcohol use occur in social drinking adults with adequate protein-calorie intake?
 - b) Are the alcohol-related deficits independent of dietary status, and of affect or are they secondary to the effect of these factors on neuropsychological performance?
 - c) Are diet-related deficits independent of socio-economic status and age or do they occur only in very young and economically deprived groups?
- 2) What are the specific patterns in the association of diet and alcohol use with neuropsychological performance?
- a) Is the effect of alcohol use "frontal" as previous literature suggests, affecting mainly performance on tests specifically sensitive to frontal lobe functioning, and the integrity of particular frontal lobe neuroanatomical measures?
 - b) What are the alcohol-use parameters (e.g., amount or frequency of consumption) which appear most critical in influencing neuropsychological and neuroanatomical factors?
 - c) Is the effect of diet more subcortical, primarily affecting myelination and general attentional mechanisms as the literature indicates?

- d) What are the specific dietary nutrients (e.g., vitamins, minerals, protein) which are responsible for these effects?
- 3) What are the roles of biochemical and neuroanatomical mechanisms in mediating the relationships of diet and alcohol use with neuropsychological performance?
- a) Based on the analysis of CAT-scan tissue-density measures and biochemical indices, is it possible to determine whether the commonly observed cerebral shrinkage of undernourished and heavy-drinking groups is primarily the result of neuronal atrophy, myelin impairment, fluid/electrolyte-imbances, or some other process?
- b) To what extent is neuropsychological impairment related to neuroanatomical (linear and tissue density) measures and to biochemical factors?

One common criticism of previous research on the effects of alcohol use and diet is the question of the validity and reliability of the measurement of these two factors. It is believed by many for example, that alcoholics are notorious for under-reporting their alcohol use (Summers, 1970). Thus the issues of reliability and validity of self-report measures of diet and alcohol use, such as those used in the present study, will be reviewed.

Validity of Self-Reported Alcohol use

There have been several investigations of the validity and reliability of self-report questionnaires concerning alcohol

use. Generally it has been found that the self-report method can indeed provide quite valid and reliable alcohol-use information, especially in a largely non-alcoholic population.

The judgement that alcoholics' self-reports are unreliable derives from studies such as that conducted by Summers (1970). Low inter-interviewer reliability was found for a pretreatment drinking history with alcoholics. It is noteworthy that in this study, one-third of the subjects were intoxicated when interviewed, and at least half of the questions were of an attitudinal nature rather than factual. In contrast, Sobell and Sobell (1975) interviewed 39 alcoholics twice regarding social and drinking history. Validity of self-reports concerning alcohol and non-alcohol related questions was assessed through official records and documents. Of all interview answers, 92% were found to be reliable, while 86% were found to be valid. Surprisingly, where there were discrepancies in actual and reported incarcerations, the alcoholics tended more to over-report than under-report. The authors conclude that "...accepting self-reports at face value does not lead to erroneous assumptions about drinking history severity..." (p. 41).

In a later study, Sobell and Sobell (1978) found that alcoholics gave equally valid answers to alcohol-related and non-alcohol related questions (validity was assessed using official documents and records) regardless of whether they were voluntary outpatient alcoholics (88% valid), court-referred (i.e., coerced) outpatient alcoholics (83.6% valid), or voluntary

inpatient alcoholics (80% valid). The discrepancies which did exist were generally in the direction of over-reporting than under-reporting such things as arrests for being publicly drunk, drunk in an automobile, drinking while driving, and drunken driving.

Kirsch et al. (1965) conducted 81 interviews (under house-to-house "public opinion survey" conditions) with persons who were listed on the rolls of an alcoholic clinic as having sought help. Parallel interviews with 81 persons of same age, sex, race and socioeconomic status were also done. The authors found that questions of frequency and amount of past and present drinking sharply distinguished between the two groups. These questions were therefore judged as being sufficiently accurate to be used as the basis for a subsequent nationwide survey of drinking practices (Cahalan, Cisin & Crossley, 1970). It is this set of questions on which the questionnaire used in the present study is based.

Polich et al. (1978) conducted a comparison of the validity of the two most often used survey techniques for assessing alcohol use in normal populations: the N.I.A.A.A. Typical Consumption Measure (Armor, Polich & Stambul, 1978), and the Cahalan National survey questionnaire (Cahalan & Room, 1974). Data on beverage sales at 13 Air Force Bases was compared with these two self-report measures. The beverage sales estimates imply an average consumption of 1.14 ounces/day per capita for this 90% male population. This compares favourably with national estimates based on nationwide beverage sales

which are 1.25 ounces/day for males and .63 ounces/day for females. Polich et al. (1978) found that both the N.I.A.A.A. and Cahalan survey methods resulted in estimates of approximately 50% of the beverage sales estimates. However, when reported amount and frequency of atypical periods of drinking were taken into account, the mean consumption for the Cahalan method rose to 1.01 ounces/day, or 88.6% of the beverage sales estimate. A second reason for the relatively low rate of reporting is probably not due to subject distortions, but to the fact that the Cahalan method does not account for occasions of drinking more than 12 drinks. Thus, binge drinkers who may consume up to 20 drinks per occasion are not represented adequately (Polich et al., 1978). As a result of these findings, the Cahalan interview schedule served as the basis for the Parker Alcohol Inventory used in the present study. However, it differs from the Cahalan interview in that atypical drinking behaviour is calculated into the estimate of amount of alcohol consumed per occasion, and the questions allow for reporting of up to more than 20 drinks per occasion, rather than 12. The Parker Alcohol Inventory is included as Appendix I.

Validity of Self-Reported Dietary Intake

There are several methods of assessing dietary intake available, and these have been reviewed carefully by Young (1981). For individuals, the most commonly used methods include the 24-hour recall, the diet diary kept from 1 to 7 days, diet histories based on interviews with a nutritionist,

food frequency checklists, and weighed intake where all food is measured and weighed prior to each meal and at the end of the meal by a nutritionist or trained investigator. By far the most valid method is the weighted intake, which requires an institutional setting whereby the investigator is sure that the subject did not ingest any foods other than those offered to him, weighed and measured by the staff. The other methods, based on self-report, have been compared to the weighted intake method to ascertain their validity and reliability.

The 24-hour recall method has been used most often (Young, 1981) because of its ease of administration and relatively high response rate. Madden, Goodman and Guthrie (1976), using subjects aged 60 years and older, compared weighted intake with 24-hour recall. No significant differences were found between the two methods for any of eight nutrients except calories. Large caloric intakes tended to be under-reported while small intakes were over-reported (the flat slope syndrome). Similarly, Samuelson (1970) found acceptable comparisons between weighted intake and 24-hour recall. Gersovitz, Madden and Wright (1978) compared both 24-hour recall and 7-day diet diary methods to that of weighted intake. Both the 24-hour recall and 7-day diet diary methods were found to be valid. Again, however, the 24-hour recall method was more prone to under-reporting high intakes and over-reporting low intakes. Another drawback of the 24-hour recall method is that intake cannot be considered to be representative of typical diet as only one day is sampled. For this reason, longer periods

(i.e., 3 to 7 days) are preferred.

More researchers are turning to the diet diary method as there is a smaller tendency for the "flat-slope" syndrome to occur (Gersovitz et al., 1978), and the representativeness of reported intake is likely to be higher (Young, 1981). For example, Cellier and Hankin (1963) have found that weekend days give different results than week days; thus the days sampled should approximate the typical 2:5 ratio of weekend to week days. Response rate has been found to decline in studies where the subject was asked to keep a diet diary for 7 days or longer, while 3 day diaries have been found to give reliable estimates of average dietary intake in sufficiently large groups (Young, 1981).

The validity of other methods is more problematic. Diet history interviews have been found to be quite valid, but only if done by highly-skilled interviewers with sufficient available time (at least one hour per day being sampled) (Bruke, 1947). The food frequency checklist method has not been found to be valid when compared to Burke's (1947) diet history method (Epstein, Reshef & Abramson, 1970), but was found to provide an adequate estimate of sugar intake when compared to the 7-day diary method (Yudkin, 1966). In summary, it appears that the most consistently valid and representative means of obtaining self-report data on dietary intake is the 3-day diet diary method. For this reason, a 3-day diet diary which had been used previously with obvious success (Barrows, 1969) was employed in the present study. A copy of this diary appears as Appendix II.

Rationale and Validity of the Psychological Test Battery

Because alcohol use has been found to be associated more with performance decrements related to the anterior (frontal) and central (parietal) lobes, rather than temporal or occipital lobes, the neuropsychological battery was designed to focus on tests sensitive to the functions of these areas. In addition, the battery was designed to include separate tests of right and left hemisphere functioning, in order to investigate the hypothesis, based on previous research, that alcohol-related deficits may be lateralized more to the right hemisphere. Such anatomical specificity of the effects of dietary deficiencies could not be proposed due to the limited nature of previous research in that area. Furthermore, a test of attention was included generally as attentional impairments have been reported as a primary result of dietary inadequacy.

In addition to the neuropsychological tests, a mood scale was administered in order to assess the possibly confounding association of alcohol use with mood (Profile of Mood States, McNair, 1971). As discussed earlier, this relation may be a strong mediator of the well-documented association between social drinking and cognitive performance, as it has not been controlled in previous studies.

Tests of psychiatric and alcoholic status chosen for use at the National Institute of Mental Health (Research Diagnostic Criteria, 3rd Edition, 1977) and finger tapping speed and grip strength (Trites, 1977) were given so that alcoholic and/or psychotic subjects, and those with peripheral motor symptoms

could be excluded from the study.

The following neuropsychological tests were used: (1) tests of left frontal functions (Wisconsin Card Sort test, Milner, 1963; Thurstone Verbal Fluency test, Milner, 1964); (2) test of right frontal functions (Design Fluency test, Jones-Gotman & Milner, 1977); (3) tests of anterior-central right-hemisphere functions (Block Design and Digit Symbol performance subtests of the Wechsler Adult Intelligence Scale (WAIS), Wechsler, 1955); (4) tests of anterior-central left hemisphere functions (Shipley Institute of Living Scale Abstraction test, Paulson & Lin, 1970); (5) a test of verbal (usually left temporal) abilities (Shipley Institute of Living Scale Vocabulary test, Paulson & Lin, 1970).

Performance on the Wisconsin Card Sort test has been found by Milner (1963) to be a reliable and valid discriminator of patients with prefrontal lesions compared to control patients with comparable lesions in other areas of the brain. Prefrontal patients have trouble in switching their response set to a new sorting rule and perseverate on earlier solutions. Milner (1963) has found this impairment to be greater in left-hemisphere dorsolateral-frontal patients than in right-hemisphere dorsolateral patients. In addition, Milner (1964) found that the left-prefrontal patients were significantly more impaired than control patients on a test of verbal fluency, although verbal recall memory abilities were normal. Right prefrontal and left temporal patients were moderately impaired on this task while right temporal and parietal

patients showed no verbal fluency deficits.

Jones-Gotman and Milner (1977) found that in a non-verbal test of design fluency, right prefrontal patients were maximally impaired. These patients produced fewer designs but, more strikingly, they perseverated in re-producing the same basic design. Left frontal and right temporal patients were moderately impaired on design fluency; the latter group produced the smallest quantity of designs.

The sensitivity of the WAIS Block Design and Digit Symbol subtests to right hemisphere lesions has been well documented (Hecaen & Albert, 1978; Lezak, 1983). However, Lezak (1983) notes that performance decrements in both tests occur with lesions of any size or location in the brain. For most adults, Digit Symbol is a test of psychomotor performance, and is relatively unaffected by memory, learning or general intelligence -- however, performance appears to be strongly mediated by a variety of factors such as attention, response speed, and visuomotor coordination. As such it is not surprising that it is sensitive to a diffuse array of types and locations of lesions. It is generally considered to be more sensitive to brain damage than any other WAIS subtest (Lezak, 1983).

Block Design is generally recognized as the best measure of visuospatial abilities in the WAIS battery (Lezak, 1983) and is relatively unaffected by the patient's academic and cultural background. Block design scores are generally depressed

For this reason, some have preferred the term "shrinkage" to describe alcohol-related CAT-scan changes. Nonetheless, linear CAT-scan measures are clearly not amenable to the precise understanding of the CAT-scan abnormalities resulting from alcohol use and dietary insufficiency.

Measures of tissue density may be able to provide more information regarding CAT-scan changes related to diet and alcohol use. Tissue density is measured on the CAT-scan in Hounsfield units. For every pixel (the smallest square unit measured by the CAT-scan) a density value ranging from -100 to 100 is given. Water has a value of 0, proteins (e.g., vascular and neuronal tissue) have a positive value, while lipids (e.g., myelin cells) have a negative Hounsfield value. Thus, with tissue shrinkage, one may have an increase in the density of the remaining tissue which may reflect either vascular dilation, dehydration or loss of lipid material. Alternatively there may be a decrease in tissue density, reflecting neuronal atrophy, vascular constriction, or edema. Thus, knowledge of tissue density changes provides an increased understanding of the most probable etiology of alcohol- and diet-induced CAT-scan abnormalities. For this reason, density readings in both the grey and white matter of the frontal lobes (most vulnerable to alcohol-related abnormalities), and in the thalamus, and corona radiata were done in the present study. As with the linear measures, these were done on both the right and left sides, in order to enable the investigation of lateralized effects.

with any type of brain injury but especially lesions on the right side, parietal lobe, and prefrontal cortex (Lezak, 1983).

The Shipley Institute of Living Scale (SILS) contains both a Verbal and Abstraction test. It was originally designed as a test of organicity, to be used with psychiatric patients. Shipley (1940) and Shipley and Burlingame (1944) found that the derived Conceptual Quotient (a ratio of the abstraction and verbal scores) was a reliable discriminator of organic psychotics, functional psychotics, and non-psychotic patients. Since then, the scale has been used more widely with non-psychotic groups. Paulson and Lin (1970) have reviewed the studies concerning the reliability and validity of the SILS, and report reliability coefficients ranging from .87 to .92. Regarding validity, the SILS Conceptual Quotient has been found to be strongly related to WAIS-Full Scale IQ ($r = .78$ to $r = .90$) (Paulson & Lin, 1970). Parker and Noble (1980) report that the SILS Abstraction test is very sensitive to the well-documented cognitive decline associated with aging.

The Profile of Mood States (POMS) has been thoroughly examined for its reliability and validity (McNair, 1971). Reliability has been difficult to measure in psychiatric groups due to their typical emotional lability. However, in such groups, reliability estimates taken first at admission and then just prior to treatment onset, range from .65 to .74. In validity studies, the POMS has been found to be sensitive to changes associated with psychotherapy (Lorr, McNair, Weinstein & Michaux, 1961; Pugatch, Haskell & McNair, 1969), tranquilizers

with psychotherapy (Lorr, McNair & Weinstein, 1964), psychoactive medication alone (McNair, Fisher, Sussman, Droppleman & Kahn, 1970), and emotion-arousing conditions (e.g., viewing an anxiety-inducing film) (Pillard & Fisher, 1967).

Attention was assessed by means of the Continuous Performance Test. This assessment of attention has very high concurrent validity when compared to other tests of attention, and is also highly reliable (Rosvold, Mirsky, Sarason, Bransome & Beck, 1956).

In summary, each test of the psychological test battery was chosen on the basis of several factors. First, sensitivity to alcohol use and/or dietary deficiency; second, evidence regarding neuroanatomical specificity or localization; finally, established reliability and validity. It is generally apparent that the tests meet these criteria very well.

Reliability and Validity of Computerized Axial Tomography (CAT-scan) Measures

The general reliability and validity of computer-generated volume and density measures of brain tissue and ventricles has been found to be 84% to 99% accurate, based on studies employing phantom or simulated brains of known density and volume (Penn et al., 1978). Nevertheless, the correct interpretation of these measures in the human brain requires very careful consideration.

Previous studies of CAT-scan measures associated with alcohol use have relied almost exclusively on linear measures of sulci and ventricles, made by non-radiologists, or on global assessments of "atrophy" on scales of 0-3. Of these measures,

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the following have been found to be related to the presence or absence of alcoholism: (1) Evan's ratio (the maximum width of the anterior horns of the lateral ventricle divided by the maximum inner skull width; Bergman et al., 1980); (2) Hucksman's measure (the sum of the widths of the lateral ventricles at the level of the anterior horns plus the width at the level of the caudate; Fox et al., 1976; Wilkinson & Carlen, 1980); (3) the ventricle-to-brain ratio (VBR) (the area of the lateral ventricle, measured by planimeter, divided by the area of the whole brain; Ron et al., 1980); (4) global ratings of ventricular enlargement on a scale of 0 to 4 (Cala & Mastaglia, 1978; 1980) and on a scale of 1 to 3 (Von Gall et al., 1978; Artmann et al., 1980); (5) the sum of the widths of the 4 largest sulci (including the Interhemispheric and Sylvian fissures) (Fox et al., 1976; Carlen et al., 1978; Wilkinson & Carlen, 1980); (6) global ratings of sulcal size (Artmann et al., 1980; Bergman et al., 1980; Cala et al., 1980; Ron et al., 1980); (7) and various cerebellar measures (Bergman et al., 1980; Cala et al., 1980).

Based on the review of their reliability and validity, several linear CAT-scan measures and the VBR measure were chosen for use in the present study. However, for many of these measures, values for the right and left hemispheres were calculated separately in order to enable the investigation of lateralized effects. Thus the measures used (made by Dr. C. Bickham, chief of neuroradiology, Suburban Hospital, Bethesda, Md.) included (1) global assessments of the size of both

sulci and ventricles; (2) the sum of the widths of 4 largest sulci; (3) the width of the interhemispheric fissure; (4) the widths of both the left and right frontal lobes at the medial-frontal gyrus' widest point, (5) the width of the space between the frontal cortex and skull at the same point, on both the right and left sides; (6) the width of the third ventricle at the level of the thalamus; (7) the width of the lateral ventricles at the frontal horns plus the width at the caudate nucleus - this is Huckman's measure; (8) the ventricle-to-brain ratio (VBR).

For several reasons, the present study did not rely solely on the use of linear and volumetric measures of cortical and ventricular size, but also employed indices of tissue density. First, although there are several studies which have found these measures to be related to alcohol use, very few have been able to demonstrate a relation between linear CAT-scan measures and neuropsychological performance. For example, both Lee et al., (1979) and Cala and Mastaglia (1980) found that Evan's ratio (width of anterior horns divided by inner skull width) was not related to performance on any of the WAIS subtests or on tests of memory and learning, although Bergman et al. (1980) found very low but significant correlations between Evan's ratio and Block Design ($r = -.15$) and the Tactual Performance Test ($r = -.16$). Wilkinson and Carlen (1980) found no association between Huckman's ratio and the Halstead-Reitan Impairment Index. The VBR measure was found to be unrelated to performance on the WAIS, or the Wisconsin Card Sort

Test (Ron et al., 1980), the Shipley Institute of Living Scale (SILS) or Halstead Reitan Battery (Hill et al., 1980) with the exception of the Category test (Hill et al., 1980). Conflicting results with sulcal enlargement have been found by Wilkinson and Carlen in that the sum of widths of eight sulci was found not to be related to performance on the Halstead Reitan Battery (Wilkinson & Carlen, 1980), but in a larger group of alcoholics this sulcal size measure was reportedly related to performance on the HRB sub-tests of Aphasia, Trails (B), Tactual Performance Memory, Category Test and Impairment Index. Thus the association of these linear measures with neuropsychological performance is, at best, equivocal.

The second major problem with linear CAT-scan measures is the question of their interpretation. That is, the validity of linear measures of sulcal and ventricular size as indices of tissue atrophy has not been demonstrated, although this interpretation is almost always made. Carlen and Wilkinson (1978) found that, with 8 to 28 months of abstinence, 4 out of 8 alcoholics' atrophy on the CAT-scan, based on Huckman's measure, had virtually disappeared. This was referred to as reversible atrophy, and attributed to re-growth of damaged neurons or glia with increased protein synthesis. Similar recovery has been found with the ventricular enlargement of previous anorectics (Enzmann & Lane, 1977). Based on these findings, the use of the term atrophy seems particularly problematic as neuronal tissue is known not to "regrow".

For this reason, some have preferred the term "shrinkage" to describe alcohol-related CAT-scan changes. Nonetheless, linear CAT-scan measures are clearly not amenable to the precise understanding of the CAT-scan abnormalities resulting from alcohol use and dietary insufficiency.

Measures of tissue density may be able to provide more information regarding CAT-scan changes related to diet and alcohol use. Tissue density is measured on the CAT-scan in Hounsfield units. For every pixel (the smallest square unit measured by the CAT-scan) a density value ranging from -100 to 100 is given. Water has a value of 0, proteins (e.g., vascular and neuronal tissue) have a positive value, while lipids (e.g., myelin cells) have a negative Hounsfield value. Thus, with tissue shrinkage, one may have an increase in the density of the remaining tissue which may reflect either vascular dilation, dehydration or loss of lipid material. Alternatively there may be a decrease in tissue density, reflecting neuronal atrophy, vascular constriction, or edema. Thus, knowledge of tissue density changes provides an increased understanding of the most probable etiology of alcohol- and diet-induced CAT-scan abnormalities. For this reason, density readings in both the grey and white matter of the frontal lobes (most vulnerable to alcohol-related abnormalities), and in the thalamus, and corona radiata were done in the present study. As with the linear measures, these were done on both the right and left sides, in order to enable the investigation of lateralized effects.

Reliability and Validity of Biochemical Measures

A major direct mechanism by which diet and alcohol are thought to affect psychological functioning is through their effects on central nervous system (CNS) levels of essential nutrients and electrolytes. Normally serum measures are taken for reasons of ease and practicality of performing routine blood tests. However, this raises the issue of the extent to which the easily measured serum levels of these nutrients reflect the levels which would be found in the central nervous system. The relationship between serum and CNS levels appears to vary with the specific properties of the various nutrients - most specifically, with the relative ease with which they cross the blood-brain barrier.

Calcium

There is evidence that significant elevations and depressions of serum calcium may be accompanied by normal and constant concentrations of CSF calcium (Webb & Gehi, 1980). However, the prominence and character of mental symptoms produced by hypercalcemia are related to its serum levels (Webb & Gehi, 1980), which suggests that CNS manifestations may be related to a breakdown of the blood-brain barrier (Cramer, 1977).

Phosphorous

Although mental symptoms are known to be related directly to hypophosphatemia (Webb & Gehi, 1980), the precise relationship of serum levels to CNS levels of phosphorous has not been

established. It is known that the mechanisms by which phosphorous affects CNS function include impairment of glucose metabolism and anoxia due to diminution of 2, 3 DPG in the red cell.

Potassium

Serum potassium concentration should not be equated with total body stores since 98% of the latter is located intracellularly. Nevertheless, Lindeman (1976) maintains that the serum concentration is the only practical way to measure potassium stores. Differences between CNS and serum levels of potassium have not been found.

Sodium

In contrast to potassium, sodium is the major extracellular cation. The nervous system is particularly sensitive to changes in sodium and potassium concentrations (Webb & Gehi, 1980). Depressed patients have been found to have equivalent decreases in serum sodium (Gibbons, 1960) and CSF sodium levels (Ueno, Aoki, Yabuki & Kuraishi, 1961). Similarly, Shaw et al. (1969) found that the brains of depressed patients who committed suicide had decreased concentrations of sodium and potassium and increased water content compared to the brains of controls. No differences in these patients were found between CSF and serum levels of sodium.

In summary, the present study utilized serum measures of the nutrients calcium phosphorous, sodium, potassium as it was the most practical and expeditious method available for determining their concentrations in the body. In addition, hemoglobin

and hematocrit measures were taken to assess iron-related anemia (Edwards, 1980). Blood glucose was also measured as it is known to be directly related to CNS glucose levels (Popkin & MacKenzie, 1980). Both iron levels (Edwards, 1980) and serum glucose (Popkin & MacKenzie, 1980) have been reported to be directly related to cognitive and psychiatric functions. The foregoing discussion illustrates that serum levels of these nutrients are, at the very least, highly correlated with the levels normally found in the brain. Thus the assumption that the serum levels may also reflect brain nutrient concentrations appears valid.

Summary

This review of the literature regarding the neuropsychology of alcohol use and nutrition indicates that there are several theoretical and methodological issues which must be addressed by further research. First, while neuropsychological, neuro-anatomical and biochemical impairment are well-documented correlates of alcoholism and social drinking, it is unclear to what extent such deficits may be secondary to dietary inadequacy. Furthermore, it is not clear whether or not these effects are secondary to frequently confounding variables such as disturbed affect (especially in social drinkers), socio-economic status, age, sex, education, incidence of trauma or other diseases, acute effects of intoxication, withdrawal or hunger, and peripheral neuropathy.

A related issue to be addressed by this research is that of specificity of the relationships of diet and alcohol use with

neuropsychological performance. As yet, the exact dietary nutrients and alcohol consumption indices have not been definitely identified in relation to localized patterns of neuropsychological performance. However previous research does suggest that amount of alcohol consumed per occasion may be specifically associated with neuropsychological² and neuroanatomical indices to frontal lobe impairment. In addition general dietary inadequacy and particularly iron deficiencies have been found to be related to subcortical impairment, in the form of disturbed myelin structure and attentional deficits.) The replicability of these findings in a non-alcoholic non-malnourished group, in which the potential confounds listed above are controlled, remains to be established.

Another issue to be investigated in this study is that of the mediating role of biochemical and neuroanatomical factors in the associations of alcohol use and diet with neuropsychological performance. It is clear that alcohol use is associated with fairly specific biochemical disruptions, and with neuroanatomical abnormalities in the frontal cortex and lateral ventricles. Similarly, malnutrition has been associated with disturbances of the myelination process. However, studies of alcoholics and social drinkers which have examined both neuroanatomical and neuropsychological indices have failed to find a correspondence between the two methods regarding the localization of dysfunction. Similarly equivocal results have been found in studies of diet and nutrition. One possible

explanation for this is the insensitivity of the linear and volumetric measurements from CAT-scans typically used.

Measures of tissue-density may yield clearer results.

Specific Aims

The primary aim of this research was to examine the influence of specific parameters of alcohol use (i.e., amount and frequency of consumption) on mood state and neuropsychological performance while controlling for dietary quality, in a group of adequately nourished, non-alcoholic drinkers. The potentially confounding variables such as peripheral and central neurological impairment, psychiatric impairment, acute intoxication, hunger and alcohol withdrawal were controlled experimentally in this study by excluding subjects with these symptoms. Statistical control of age, sex, and education will be achieved through partialling out these effects from the analyses. A second aim of this study is to examine the extent to which associations are mediated by the effects of biochemical and neuroanatomical indices. This was achieved through the method of path analysis which enables the decomposition of the neuropsychological effects of diet and alcohol use into those that are direct, and those which are indirect or primarily the result of the mediating effects of biochemical and neuroanatomical factors. A third aim of this study is the examination of the association of localized linear and tissue-density indices of neuroanatomical status with corresponding measures of neuropsychological performance.

This investigation will examine these questions using the

previously described self-report measures of diet and alcohol use, psychological tests, neuroanatomical measures and biochemical indices. The following chapter will describe more precisely the methods employed in conducting this study.

IX
METHODS

Subjects

One hundred and ten neuroradiological referrals for CAT-scan testing to Suburban Hospital, Bethesda, Md., served as subjects in this study. Every patient receiving a CAT-scan between January 1981 and July 1982 was screened for eligibility for inclusion in the study. This was done by distributing to each patient a form briefly describing the study, inviting their participation, and asking about the incidence of the following factors which would exclude them from the study. Patients were excluded for the following reasons: incidence of recent head trauma (N = 97); did not complete exclusion criteria form (N = 83); history of seizures (N = 44); history of stroke accompanied by unconsciousness (N = 35); history of cancer possibly invading the CNS (N = 16); had had brain surgery (N = 10); were on strong psychoactive medication (N = 8); were apparently demented (N = 6). When a patient was selected, on the basis of the exclusion criteria form, as being suitable for the study, their referring physician was then contacted to ensure that there was no medical or personal reason for not inviting the patient to participate in the study. At this point, 14 patients were excluded at the request of the referring physician. Next, the subject was contacted and invited to participate in the study. Only 13 subjects could not be reached. The nature of the study was fully explained to the subjects and they were offered \$36.00 for participating.

At this point, 41 subjects refused to participate. If they agreed, they were asked to come in to the National Institute of Health for blood tests, 2 1/2 hours of psychological test administration, and the completion of self-report inventories on diet and alcohol use.

Of the patients included in the study, 36 had been referred for the CAT-scan because of headaches, 17 for fainting or dizzy spells, 7 for transient problems with vision, 8 for minor head injuries, 8 for suspected minor strokes not involving loss of consciousness, 2 for cancer not invading the nervous system, 1 for suspected seizure, 1 for memory problems and 20 for "other" reasons such as tics, circulatory problems, or peripheral nervous system symptoms; 10 subjects neglected to specify the reason for their referral.

Thus the sample was comprised of 58 males and 52 females who ranged in age from 18 to 79 years with a mean age of 45.7 years. Their mean educational level was 14.9 years and the mean family income was approximately \$31,000.00. Ninety-six percent were Caucasian. Thus the sample was predominately a very well-educated, white, upper-middle class group. Such a population is typical of the Bethesda area in which Suburban Hospital is located.

As might be expected of a sample of this nature, the subjects generally had qualitatively superior diets and drank slightly less alcohol than does the normal population. Their mean diet was low in carbohydrate (59.3% Recommended Dietary

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Allowance or R.D.A.¹), high in protein (141.9% R.D.A.) and moderate in fat (95.3% R.D.A.). They tended to eat a lot of expensive meats, dairy products, fruits and vegetables, but little bread and sweets. The mean R.D.A. for all essential vitamins was well over 100% (e.g., 211.5% for vitamin A to 351.6% for vitamin C). Fifteen of the subjects took vitamin supplements. The mean R.D.A. for minerals was lower: 82% for calcium and magnesium, 110% for iron, 133.8% for phosphorous. The mean frequency of drinking was approximately 3 times per week, while the mean amount drunk per occasion was 1 to 2 drinks.

Only 33 of these subjects were not on medication, while 77 were. By far the most common form of medication was pain killer or aspirin for headaches, although some subjects were taking medications for blood pressure, or anxiety states.

Subjects were asked to abstain from alcohol for at least 12 hours prior to the testing session. Nevertheless, 4 subjects tested reported having had a drink within the last 6 hours, and another 5 subjects reported having had a drink within the last 12 hours. Every subject in the study was given a breathalyser test for acute intoxication and not a single subject showed evidence of even mild intoxication.

It is clear that these subjects were not representative of the population at large, but are a sub-group of neurological referrals, many of whom were on medication. They were well-

¹This was determined by the Nutriquest program, to be discussed later.

educated, and this is reflected in their very high Verbal Abilities score on the Shipley test (mean = 32.3/40). Their mean Abstraction Abilities score was somewhat lower, 25.8/40, giving them a normal range Conceptual Quotient (C.Q.) of 90. A fair amount of intellectual impairment is not unexpected in a neurological sample; however it is evident that the strict exclusion criteria in this study were fairly successful in eliminating the more impaired patients: the CQ of 90 is at the 62nd percentile (that is 62% receive CQ's lower than 90) in a standardization group of 1,046 normal subjects (Shipley, 1940). Similarly, the mean Block Design score, adjusted for sex and age was 12.16 (10 is the norm) and the adjusted Digit Symbol score was 12.53. Clearly, despite the fact that this is a neurological sample, their mean cognitive performance is generally above normal, and as such is consistent with their high socioeconomic and educational status.

Procedure

The subjects came to the National Institute of Health (NIH) for testing, usually in the morning at about 8:30 am. They had abstained from eating breakfast as a requirement of the blood tests. Once admitted as outpatients at NIH, they were taken to the phlebotomy lab, where 5 evacuated test tubes (Terumo Medical Corp., Elkton, Maryland) of blood were routinely drawn. Blood chemistry samples were collected in 15 cc red top Vacutainer tubes and hematology samples were collected in 7 cc lavender top Vacutainer tubes, kept at room temperature until processing. Blood chemistry analyses were performed by

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technicians using an SMA-C-2 automated analyzer (Technicon Instruments, Tarrytown, New York). Hematology samples were analyzed by a Coulter S-SR automated counter (Coulter Corp., Hialeah, Florida). The following tests were thus obtained: total protein, albumin, calcium, alkaline phosphatase, cholesterol, uric acid, creatine, total bilirubin, inorganic phosphorous, SGOT, SGPT, chloride, carbon dioxide, sodium, potassium, urea nitrogen, glucose, white blood cell, red blood cell, hemoglobin and hematocrit. The mean values for each of these tests was within the normal range (Clinical Chemistry Laboratory, Normal Range Values, National Institute of Health).

Following the blood tests, subjects were given the breakfast of their choice (most chose bacon, eggs, toast, juice and coffee or tea, although some chose only bran muffin, juice and coffee). At this time, subjects were free to ask the investigator any and all questions he/she had about the study.

On completion of breakfast, the psychological test battery was administered to the subject in the following order:

<u>Test</u>	<u>Approximate Time</u>
1. Test of mood state Profile of Mood States (POMS)	10 mins.
2. Alcohol use questionnaire Parker Alcohol Inventory	25 mins.
3. Research Diagnostic Criteria (RDC) Interview Schedules for Psychiatric State and Alcoholism	20 mins.
4. Test of Attention Continuous Performance Test (CPT)	20 mins.
5. Test of verbal and abstraction abilities Shipley Institute of Living Scale (SILS)	15 mins.

6. Motor tests	
a) Grip Strength Parts 1 and 2	5 mins.
b) Finger Tapping Parts 1 and 2	5 mins.
7. Blood Alcohol Concentration Breathalyzer test	5 mins.
8. Thurstone Verbal Fluency test	5 mins.
9. Jones-Gotman Design Fluency test	5 mins.
10. Wisconsin Card Sorting Test	20 mins.
11. WAIS Block Design	5 mins.
12. WAIS Digit Symbol	5 mins.
	<hr/>
Total	2 hrs., 25 mins.

On completion of the testing, subjects were given the following materials to complete at home: (1) a personal and family medical history questionnaire; (2) a three-day diet diary; (3) a second but shorter version of the Parker Alcohol Inventory.

The rationale, validity and reliability for each of these tests has already been discussed. The instructions, scoring forms and actual questionnaires used are included as Appendix III. The POMS, Parker Alcohol Inventory and 3-day diet diary were administered by questionnaire rather than interview as this method has been used successfully and most often in previous studies. However, each subject was given very careful instructions in completing the Parker Alcohol Inventory and the Diet Diary to ensure that they understood what constituted a single drink in terms of amount and alcoholic content, and the method to be used when reporting amounts of foods eaten at each meal. Subjects were encouraged to call the investigator should questions arise in completing the

diary at home (several did call) and to draw on a piece of paper the portion size of what they drank or ate if unsure of its volume or weight (many did this, as well). The information from the diet diary was analysed by the Nutriquest software package, a commercially available program which can be run on an APPLE II micro-computer. This program provides the total amounts, and percentages of the Recommended Dietary Allowance of the following nutrients: calories, protein, carbohydrates, fats, vitamins A, B6, B12, C, thiamine, niacine, riboflavin, calcium, phosphorous, magnesium and iron. The Research Diagnostic Criteria schedules for psychiatric symptoms and alcoholism were done by means of interview. The present investigator was trained to conduct these interviews by the Principal Investigator and psychiatrist on the overall project at N.I.H., Dr. T.P. Bridge.

The Continuous Performance Test was performed using a CPT machine made by Sunrise Systems Ltd., Baltimore, Md. For this task, the X-Fixed Pace, AX-Fixed Pace, and X-Dynamic Pace phases were used. In the X-Fixed Pace task, letters appeared one at a time, at a fixed pace, and in random order on the screen and the subject was asked to press a button in his hand every time he saw an X. The machine recorded the number of hits, misses, false-positives, correct-rejections, and mean time to response. In the AX-Fixed Pace task, the subject was asked to push the button when he saw an X, but only if it came after an A. In the X-Dynamic Pace, the subject was asked to press the button every time he saw an X, but the pace of letter-

presentation sped up gradually as the test continued and the period of time for which each letter could be seen on the screen decreased. Each task continued for 5 minutes.

Grip strength was measured using a hand dynamometer, and finger tapping speed was assessed with a standard finger-tapping board. Both of these tests were performed in two phases as recommended by Trites (1977), once before and again after the breathalyzer tests. The Wisconsin Card Sort test was conducted in the standard manner described by Grant and Berg (1966). However, due to time limitations, subjects were stopped after 4 categories rather than 6. The remainder of the tests, the Shipley Institute of Living Scale, Verbal and Design Fluency, and the WAIS Block Design and Digit Symbol were performed in the standard manner. Complete instructions and scoring forms for all psychological tests used appear in Appendix III.

The Design Fluency test requires a certain amount of subjective interpretation in scoring. The scoring instructions of Jones-Gotman and Milner (1977) were carefully followed. To ensure comparability of our scoring, the first 20 Design Fluency sheets were sent to Jones-Gotman who was kind enough to score them for us. Initial calculations indicated a low ($r = .64$) reliability coefficient. This was attributable to the present investigator being overly lenient in scoring drawings as perseverative. Once this source of discrepancy became clear, the sheets were shuffled and re-scored. Subsequently a reliability of $r = .89$ and $r = .87$ was reached in

scoring the number and perseverative rate of the drawings, respectively. Means and standard deviations for reported diet and alcohol use, and psychological test performance appear as Appendix VII.

The psychological testing was conducted within 0 to 3 weeks of CAT-scan testing. The mean period of time was 8 days. The scans were conducted using the GE8800 scanner, regarded by clinicians as one of the most technologically sophisticated scanners with the highest resolution status of its kind in use today. The CT-scan was obtained at the standard 25° to the base line (the orbitomeatal line), with 8 mm collimation. Normally 10 slices, from the most rostral to most dorsal, were taken. The scans were available for scoring on 66 of the 110 patients. Fifty-two of the 66 scans were done without the use of contrast material, while 14 subjects only had scans for which contrast material (iodine substance) had been injected into the patient just prior to the scan. This has the effect of systematically increasing the density values of brain tissue on the scan, and is often done to enhance the resolution of the scan. It has no effect on the volume of the tissue or ventricle. In the present study differences in density values attributable to the use of contrast material was statistically partialled out and the density values used in all analyses reported here are the residual values subsequent to partialling out the effect of contrast material. The 14 subjects who had had contrast-enhanced scans did not differ significantly from the non-contrast group in terms of age, sex, education or reason of referral. A typical example of the scans appears on the next page, with an enlargement of slice 6 on the following page.

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The reliability and validity of various CAT-scan measures has already been discussed. In the present study, all CAT-scan measures, with the exception of the ventricle-brain ratio (VBR), were taken by Dr. C. Bickham, Chief of Radiology, Suburban Hospital, Bethesda, Md., who was blind as to the identity of the subjects on each scan. The scoring form used is included in Appendix IV. Global ratings of sulci and ventricles were obtained on a 1 to 5 scale, using standards of sulcal and ventricular atrophy used by Zatz et al. (1977). The cortical and ventricular linear measurements, including Huckman's measure were made in the following manner: for each subject, the CAT-scan tape was mounted on the computer and the visual display of each slice of the scan was then available for viewing and scoring on the cathode ray tube (CRT). A cursor attached to the CRT was then used to trace the widths of (a) the 4 largest sulci, (b) the interhemispheric fissure, (c) the subdural space between the inner table of the skull to the frontal lobe on both right and left sides, at the point where the medial gyrus appears largest, (d) the frontal lobe at the same point, (e) the third ventricle at the thalamic level, (f) the lateral ventricles at the frontal horns, and (g) the lateral ventricles at the level of the caudate. (The sum of the latter two measures provides Huckman's measure.).

The density measures in the various regions of interest also were performed with the aid of the cursor. For each density measure, a reading was taken from a 5x5 pixel area. This was done for both the left and right sides of the brain

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in (a) the grey matter of the frontal cortex (Brodman areas 9 and 10), (b) the frontal white matter (just anterior to the frontal horns of the lateral ventricles), (c) the thalamus, (d) the ascending white matter of the corona radiata, and (e) the brain stem.

The decision regarding the CAT-scan slice, or anatomical level at which these various measures should be taken was based on the classical work of Gado (1979). Thus, the clinical or global ratings were generally done at level 6, the level at which the lateral ventricles appear largest. The widths of the lateral ventricles both at the frontal horns and the caudate-level also were measured at level 6. The width of the third ventricle was measured at level 5. The sum of the widths of the 4 largest sulci was performed on one of the highest cuts, level 9, as sulci are most clearly visible on higher cortical slices, and because previous studies also had used the highest two slices for this measure (Lee et al., 1979; Fox, 1976). The widths of the interhemispheric fissure, the frontal subdural area and the frontal lobe were measured at levels 4 and 5 which traverse the dorsolateral area of the frontal lobes (the area most commonly involved in performance on tasks such as the Wisconsin Card Sort Test (Milner, 1964) which is sensitive to alcohol-related impairment. The density ratings of the frontal lobes were also done at levels 4 and 5. In addition, the thalamic and corona radiata measures were done at level 4 or 5, depending on which slice provided the largest view of these structures.

The volume of the lateral ventricles and of the inner skull, to obtain the ventricle-to-brain ratio (VBR) were taken by the author, blind regarding subjects' identity. This was done with the aid of a planimeter, using the procedure described by Weinberger et al. (1982).

The reliability of the CAT-scan measures was generally quite high. The mean intra-rater reliability for the linear measures on the CRT, and for the average of four 5x5-pixel readings per subject for each of the density measures was $r = .89$. The intra-rater reliability for the VBR was $r = .92$, while the inter-rater reliability was $r = .87$. Reliability measures were obtained by blindly re-scoring all CAT-scan measures twice, on a subsample of 20 subjects. The mean pearson correlation between the 2 scores for all measures was then calculated.

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X

ANALYSES

Description of Analyses

Statistical analysis was conducted in the following stages:

1) Validity of self-reported alcohol use. The two measures of alcohol use which Parker and Noble (1980) and others (e.g., McVane et al., 1982) have found to be most sensitive to alcohol-related dysfunction are (1) the calculated mean amount of alcohol reportedly consumed per occasion and (2) reported frequency of alcohol consumption. These two measures were correlated with 7 of the biochemical indices which Ryback et al. (1978) have found to reliably discriminate alcoholics from controls.

2) Reliability of alcohol use. The Parker Alcohol Inventory was completed twice by the subjects: once during the testing session and a shorter version again at their homes. The two alcohol measures, amount and frequency of consumption, derived from the at-home questionnaire, were correlated with the corresponding measure from the test-session questionnaire, to provide reliability estimates.

3) Relationship of biochemical indices with reported dietary intake. Multiple regressions of serum calcium, phosphorous, glucose, sodium and potassium were examined with dietary intake of protein, carbohydrates, minerals and vitamins. This was done in order to investigate the relationship of self-reported dietary intake with the obtained biochemical parameters.

4) Validity of neuropsychological measures. A major issue of interest in this study is the anatomical specificity of the

associations among neuroanatomical and neuropsychological measures. That is, does performance on tests presumably sensitive to the integrity of localized areas of the brain (e.g., right vs. left hemisphere; anterior vs. posterior regions) relate to the linear, and density measures of those specific neuroanatomical sites? To address this issue, tests of functions normally subserved by the left hemisphere (verbal and card-sorting tests), right hemisphere (WAIS performance subtests and design fluency), and frontal lobe (design fluency, card-sorting, and abstraction tests) were entered into multiple regression analyses with the corresponding neuroanatomical measures as dependant variables.

5) Data reduction. The primary purpose of this study was to examine the relationships of diet and alcohol use with neuropsychological, neuroanatomical, and biochemical indices of brain dysfunction. However, as the data set consisted of 15 nutritional variables, 19 biochemical measures, approximately 60 psychological indices and 21 CAT-scan measures, data reduction procedures were obviously required. Two alternative methods, canonical correlation and factor analysis were conducted. The canonical correlations were unsatisfactory for the following reasons: only 38 subjects had both biochemical and CAT-scan data. Using canonical correlation with pairwise deletion of missing data resulted in invalid results, (e.g., correlations greater than one). Using listwise deletion, the degrees of freedom were reduced to the point that canonical correlations of .7 to .9 (i.e., eigenvalues explaining 50-80% of the variance) did not reach the .05 level of significance.

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Thus the factor analysis method of data reduction (combined with multiple regression analyses) was found to provide the most valid and meaningful statistical approach to the data.

Separate factor analyses were performed on (a) nutritional data, (b) psychological measures, (c) CAT-scan indices, and (d) biochemical data. In each case, 2-5 orthogonal factors were obtained. In most cases (i.e., unless otherwise stated), these were added to the existing data set by calculating the factor score for each case, using factor score coefficients.

6) Multiple Regressions. Multiple regression of the nutritional, biochemical and CAT-scan factor scores, and the two alcohol variables were performed on each of the orthogonal psychological factors. In order to make maximal use of the available data, the first set of multiple regressions examined only the influence of nutrition and alcohol use on the psychological factors (N = 110). The second set repeated this, but entered the biochemical factors into the equation before the nutrition and alcohol factors (N = 52); the third entered the CAT-scan factors into the equation before the nutrition and alcohol factors (N = 66). Thus, the second and third multiple regressions essentially performed two functions: (1) the examination of the psychological effects of the biochemical and CAT-scan indices; (2) sub-group "cross-validation" of the initial analysis of the psychological effects of diet and alcohol use was performed with two sub-groups of (a) subjects who had biochemical data (N = 52) and (b) subjects who had CAT-scan data (N = 66). Thirty-five subjects had both biochemical and CAT-

scan data.

7) Path analyses. Based on the results of the multiple regression analyses, three path analysis models were examined. These were designed to examine the nature of effects of general dietary quality and alcohol use (amount and frequency) on psychological measures. More specifically, the path analyses investigated the extent to which the psychological effects of diet and alcohol use were mediated by the biochemical and neuro-anatomical factors. The rationale for the models used will be discussed in greater detail below.

In summary these analyses were conducted with the following objectives in mind: (1) to address the questions of reliability and validity of the alcohol and nutritional consumption inventories; (2) to investigate the neuroanatomical validity of the neuropsychological measures; (3) to reduce the very large amount of data to a meaningful and manageable data set; (4) to examine the specific effects of diet and alcohol consumption, on neuropsychological performance; and (5) to investigate whether biochemical and/or neuroanatomical factors mediate these effects. For ease of reference, tables of the zero-order correlations among the variables and factors used in these analyses are provided in Appendix V.

Concurrent Validity of Self-Reported Alcohol Use

In order to establish the concurrent validity of the Parker Alcohol Inventory, seven biochemical measures known to discriminate alcoholics from controls (Ryback et al., 1978) were correlated with reported amount and frequency of alcohol consumption. As Table 1 indicates, four of the seven measures were found to

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Table 1

Correlations of the Biochemical Predictors of Alcoholism with
Reported Frequency of Alcohol Consumption (N=52)

<u>Biochemical Predictor</u>	<u>Pearson's r</u>	<u>p</u>
SGPT	.306	.015
RBC	-.195	.08
HGB	-.205	.08
HCT	-.23	.05
Bili	N.S.	1
SGOT	N.S.	1
CO ₂	N.S.	1

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be significantly related, in the predicted direction, to frequency of alcohol use in this sample, but were not related to amount consumed per occasion. These included SGPT, RBC, HGB, and HCT. The tests for Bili, SGOT and CO_2 were unrelated to alcohol use in this sample of social drinkers.

Reliability of Self-Reported Alcohol Use

In order to obtain a measure of the reliability of the Parker Alcohol Inventory (PAI), 72 subjects were administered the Inventory a second time; that is, in addition to completing the PAI during the testing session, they were given the PAI to complete at home. The Pearson correlation, or reliability coefficient for calculated mean total amount of alcohol consumed per occasion was $r = .624$ ($p < .000$), while the reliability coefficient for reported frequency of alcohol consumption was $r = .932$ ($p < .000$). As might be expected, there was a slight tendency for some subjects to report greater alcohol consumption while in the privacy of their home, than was the case during the test session when the examiner was in the room. However, the mean amount reported at home ($\bar{x} = 3.48$) did not differ significantly from that reported during testing ($\bar{x} = 3.27$), nor did the means for frequency of consumption differ significantly at home ($\bar{x} = 163.3$) vs. at testing ($\bar{x} = 164.8$).

Relation of Nutritional Status to Dietary Intake

Serum levels of protein, calcium, phosphorous, glucose, potassium and sodium were entered into multiple regressions with the RDA levels of nutrients derived from the 3-day diet diaries. The multiple regressions for serum calcium and phosphorous were

significant ($F = 5.36$; $p < .05$ and $F = 4.89$; $p < .05$ respectively). As seen in Table 2, serum calcium was found to be positively related to protein intake, and inversely related to intake of thiamine, riboflavin, niacin, vitamins B6 and B12. Conversely, serum inorganic phosphorous was positively related to these B-complex vitamins. Serum levels of glucose, sodium and potassium were significantly correlated with reported dietary intake of iron, magnesium, and vitamin A. However, the multiple regression for these latter three serum measures were not significant.

Relation of Neuroanatomical to Neuropsychological Measures

In order to more closely examine the relationships between psychological factors and neuroanatomical (CAT-scan) factors multiple regressions of the 19 CAT-scan measures on 10 of the psychological variables were done. The purpose of these analyses was to determine whether performance on tests which are presumably sensitive to the functioning of particular areas of the brain are, indeed, correlated with the density ratings and linear measures for those areas. More specifically, (1) are verbal abilities related to the CAT-scan ratings of the left vs. right hemisphere? (2) are performance, or non-verbal abilities related to the CAT-scan measures of the right hemisphere? (3) are "frontal" tests exclusively related to the frontal-lobe measures.

Lateral Assymetries.

Three tests which are presumably related predominantly to left-hemisphere functioning were examined. These included the

Table 2

Correlations of Serum Nutrient Levels with Reported Dietary

Intake of Nutrients

Dietary Nutrient	Serum Nutrient				
	Calc.	Phos.	Glucose	Sodium	Potassium
Protein	.255 (p=.05)				
Thiamine	-.366 (p=.008)	.340 (p=.013)			
Riboflavin	-.356 (p=.01)	.346 (p=.011)			
Niacin	-.414 (p=.003)	.370 (p=.007)			-.247 (p=.05)
Vit. B6	-.421 (p=.002)	.365 (p=.008)			
Vit. B12	-.496 (p=.000)	.419 (p=.003)			
Iron				.259 (p=.049)	.236 (p=.06)
Magnes.			.255 (p=.049)	.334 (p=.014)	.285 (p=.03)
Vitamin A		.237 (p=.06)	.247 (p=.05)		

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SILS:Verbal abilities, Verbal fluency (quantity), and Wisconsin Card Sort Test:Trials to Criterion measure (WCST:TTC). Although performance on the two verbal tests were correlated at the .05 level of significance with the CAT-scan measures of tissue density, the multiple regressions for verbal abilities and verbal fluency were not significant. Furthermore, no trend towards neuroanatomical lateralization was apparent in the zero-order correlations. Performance on the WCST:TTC, however, was significantly related to the CAT-scan measures ($F=2.35$, $df = 18,20$; $p < .05$). Specifically, the number of trials required to reach criterion was positively related to the width of the space between the left frontal cortex and skull ($b = .669$; $F = 3.09$; $df = 1,20$; $p < .09$). In addition, the density of the left corona radiata was positively related to trials required to reach criterion on the WCST ($b = .887$; $F = 7.08$; $df = 1,20$; $p < .01$).

Tests presumably sensitive to right-hemisphere functioning were found to be specifically associated with right-hemisphere CAT-scan measures. Design fluency (quantity) performance was related to the CAT-scan measures ($F = 1.45$; $df = 18,19$; $p < .1$).¹ This was due to the significant inverse contribution of the distance between the right frontal cortex and skull ($b = -.512$; $F = 4.28$; $df = 1,38$; $p < .05$). Performance on the SILS: Abstraction index also was related to the CAT-scan measures ($F = 1.73$; $df = 18,20$; $p < .1$) due, in part, to the inverse effect of the density rating of the right thalamus ($b = -.524$;

¹Because of the extremely restrictive degrees of freedom, the $p < .1$ level of significance was adopted for this analysis. (Harris, R. A Primer of Multivariate Statistics, New York: Academic, 1975, p. 12).

$F = 3.55$; $df = 1,39$; $p < .07$).

Anterior-Posterior Assymetries

Four neuropsychological tests, Shipley Abstraction, Design Fluency, Block Design and Wisconsin Card sort, which are apparently particularly sensitive to frontal lobe dysfunction were examined in relation to specifically frontal CAT-scan measures. For all four tests, the multivariate relationship to the CAT-scan measures was significant at the $p < .1$ level of significance. The CAT-scan measure, width of the inter-hemispheric fissure, was significantly and inversely related to performance on the Shipley Abstraction test ($b = -.628$; $F = 8.2$, $df = 1,38$; $p < .01$), Block Design test ($b = -.596$, $F = 7.06$; $df = 1,38$; $p < .02$), and Wisconsin test (Trials to Criterion measure) ($b = -.615$; $F = 8.13$; $df = 1,38$; $p < .01$).

As discussed above, performance on the Design Fluency and Wisconsin Card Sort tests also were inversely related to the width of the space between the right, and left (respectively) frontal cortex and the skull.

The multiple regressions of the CAT-scan measures and verbal fluency (perseverative score) and the Wisconsin Card Sort perseverative to non-perseverative error ratio were not significant. Nevertheless, it is interesting to note that the density of the left frontal cortex was positively related to both of these measures. The partial correlation with verbal perseveration was $b = .789$ ($F = 2.96$; $p < .1$), and with Wisconsin perseveration was $b = .75$ ($F = 2.66$; $p < .1$).

Table 3 illustrates the associations among neuropsychological

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The Relationship Between Neuropsychological and Neuroanatomical Measures

	SILS:VA	SILS:AA	Verbal Fluency Quantity	Design Fluency Novel R's	WCTS:TTC	Design Flu. Persev.	Block Design	Att'n: XDP
Multivariate Significance	N.S.	F=1.73 p < .1	N.S.	F=1.45 p < .1	F=2.35 p < .05	N.S.	F=1.61 p < .1	N.S.
Width of Inter-hemispheric fissure		b=-.628 r=-.455		r=-.276	b=.784 r=.361		b=-.596 r=.248	r=-.352
Width of right frontal skull-to-cortex				b=-.512 r=-.455		r=.259	r=-.229	r=-.293
Width of left frontal skull-to-cortex					b=+.669 r=.453	r=.331	r=-.28	r=-.25
Sum of 4 largest sulci		r=-.214		r=-.223	r=.231			r=-.208
Density of right frontal white matter	r=-.23						r=-.24	
Density of left frontal white matter			r=-.275					
Density of right thalamus	r=-.266	b=-.524 r=-.283		r=-2.95				
Density of left thalamus			r=-.29					
Density of right corona radiata		r=-.254	r=-.226				r=-.293	122
Density of left corona radiata		r=-.205	r=-.213		b=.887 r=.122		r=-.212	

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and neuroanatomical measures.

Factor Analyses

Four separate factor analyses were conducted on the separate groups of data. The first factor analysis included all available psychological data, a second on the dietary intake data, a third on the biochemical (blood work) data, and a fourth on the neuroanatomical CAT-scan measures.

Factor Analysis of Psychological Data

Nine factors with eigenvalues of greater than 1.0 were extracted for varimax-rotation. The following description of these factors is based on variables with factor loadings of greater than .3. Rotation revealed that the first, fourth, sixth and eighth factors represented performance on the Continuous Performance Test. The first factor, labelled general attention, had significant loadings from mean time to respond and number of correct responses from the three CPT phases, but especially the X:dynamic phase. The fourth factor has been labeled attentional impulsivity, as it had highest loadings from incorrect or false-positive responses on all three phases of the CPT. The sixth factor reflected general performance on the X-Fixed Pace Phase, while the eighth factor represented performance on the AX-Fixed Pace Phase.

The second factor reflected mood disturbance. High loadings were obtained on all subscales of the Profile of Mood States (POMS) questionnaire. The highest loading was obtained from the Depression subscale. Because the subscales were so highly correlated with one another, the POMS Total Mood Disturbance

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score was used in subsequent analyses.

The third factor represented general Wisconsin Card Sort Test Performance, with high loadings from mean trials to criterion, perseverative errors and other (non-perseverative) errors. For theoretical reasons, two WCST variables were used. The first was the ratio of perseverative to non-perseverative errors, the measure which Milner (1963) found to be maximally sensitive to frontal-lobe impairment. The second was the mean number of trials to reach criterion score which Parker et al. (1982) found to be most sensitive to impairment associated with alcohol consumption.

The fifth factor reflected motor performance, with loadings exceeding .6 from left- and right-hand grip strength and finger-tapping tests. Block Design, which is known to require manual dexterity, also loaded onto this factor ($r=.4$).

The seventh factor represented general neuropsychological performance. High loadings were obtained from the Shipley Verbal and Abstraction tests, Design Fluency test, Verbal Fluency tests, Block Design, and Digit Symbol WAIS subtests. The ninth factor was labelled the "neuropsychological rigidity" factor. It obtained negative loadings from the Shipley Abstraction and Conceptual Quotient, and positive loadings from the perseverative scores on the verbal and design fluency tests. Table 4 provides the factor loadings for these two factors.

As a result of this factor analysis, six psychological measures were used in the subsequent multiple regression

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Table 4

Factor Loadings for Neuropsychological Factors Used In Sub-
sequent Analyses*

<u>Variable</u>	<u>General Neuropsych. Performance Factor</u>	<u>Rigidity Factor</u>
SIIS:Verbal	.472	
SIIS:Conceptual	.38	-.734
Verbal Fluency	.684	
Design Fluency	.39	
Block Design	.75	-.359
Digit Symbol	.54	-.33
Design Perseveration		.388
Verbal Perseveration		.451

*only loadings exceeding .3 are reported.

ADDITIONAL INFORMATION

analyses. The variable which accounted for the majority of the variance, in the general attention factor, X:Dynamic Pace (correct responses) was employed in the multiple regressions. The Profile of Mood States (POMS) Total Mood Disturbance score, a calculated summary score of the highly correlated POMS subscales also was used. The four neuropsychological variables included were (1) the general neuropsychological performance factor, (2) the rigidity factor, (3) WCST:Trials to criterion, and (4) WCST:ratio of perseverative to non-perseverative errors. The two neuropsychological (i.e., general and rigidity) factors were derived from the actual factor score coefficients. This method of creating factors for subsequent analyses has several advantages over the unit-weight method. The main advantage is that factor score coefficients most accurately define the factors, and thus are more likely to reflect the properties of the hypothetical factors (such as orthogonality, which is essential to the subsequent analyses in this study) (Blouin & Conners, 1983).*

The POMS:Total Mood Disturbance score was employed rather than the actual POMS factor, since the summary score can be easily calculated from the actual data, would facilitate later replication of results based on this measure, and was highly correlated ($r = .90$) with the obtained POMS factor. For the same reason, the X:Dynamic Pace correct responses variable was used as the attentional measure. The two WCST variables were used in place of the single WCST factor as previous research with this test provided a strong rationale for the inclusion

*Blouin, A., and Conners, C.K. The independence of hyperactivity from conduct disorder. Methodological considerations submitted to Journal of Abnormal Child Psychology, Sept. 1983.

of both of these particular measures. Despite using actual test scores for 5 of the 7 measures, rather than the obtained factors when represented, orthogonality of the psychological variables was not substantially affected. Table 5 demonstrates that, with the exception of the two Wisconsin Test scores, the remaining variables share little common variance.

Dietary Factors

The total amounts of all nutrients provided by the Nutriquest program were entered into factor analyses. Two factors were obtained, which reflected (1) general dietary quality (especially calorie-protein, and trace mineral intake), and (2) B-vitamin intake (See Table 6). Again, the nutritional factors were created for subsequent analyses from the factor score coefficients.

Biochemical Data

The serum levels of the minerals sodium, potassium, calcium, inorganic phosphorous, and alkaline phosphate, the blood cell measures red blood cell count, hemoglobin and hematocrit, and total protein and glucose were entered into the factor analysis. Three factors were obtained which are shown in Table 7. The first was labelled the hemoglobin factor, as it received its highest loadings from hemoglobin, red blood cell count, and hemotocrit. The second factor, the potassium factor, reflected primarily potassium, sodium and alkaline phosphatase. Total protein loaded negatively on this factor. The third factor was named the "calcium" factor, as that mineral loaded most highly on it. Inorganic phosphorous loaded

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Table 5
Shared Variance (R^2) Among the Six Psychological Measures

General Neuropsych. Performance	General Neuro-psych. Performance Factor	Rigidity Factor	WCTS:TTC	WCTS: Perseverative Ratio	Attention X:Dynamic Pace Hits
Rigidity	.021				
WCST:TTC	.078	.15			
WCST:Persev. Ratio	.09	.15	.59		
Attention (X:Dynamic Pace Hits)	.073	.00	.00	.00	
POMS:Mood Disturbance	.02	.00	.013	.00	.00

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Table 6

Factor Loadings for Dietary Factors*

<u>Variable</u>	<u>General Dietary Quality Factor</u>	<u>B-Vitamin Factor</u>
Calories	.919	
Carbohydrates	.754	
Protein	.820	
Fats	.850	
Vitamin A		.358
Thiamine		.964
Niacin		.976
Vitamin C		.446
Calcium	.670	
Phosphorous	.920	
Iron	.586	
Magnesium	.748	
Vitamin B6		.590
Vitamin B12		.861

*only factor loadings exceeding .3 are reported.

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Table 7
Factor Loadings for Biochemical Factors*

<u>Variable</u>	<u>Hemoglobin Factor</u>	<u>Potassium Factor</u>	<u>Calcium Factor</u>
Sodium (Na)		.575	
Potassium (k)		.806	
Red Blood Cell	.606		
Hemoglobin	.945		
Hematocrit	.863		
Calcium			.980
Inorg.Phos.			-.565
Alk.Phosph.		.563	
Total Protein		-.503	

*only factor loadings greater than .3 are reported.

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negatively on this factor. Glucose was included in subsequent analyses as a separate "factor" since it did not have a loading of greater than $r = .3$ on any of the three biochemical factors. As with the other factors, factor score coefficients were employed to create these factors for subsequent analyses.

Neuroanatomical Factors

Nineteen measures derived from the CAT-scan were entered into a factor analysis. Five separate factors were obtained (see Table 8). The first factor was labelled the ventricular factor, as highest loadings were from the measures (a) general ventricular size, (b) width of lateral ventricles at level of the caudate, and frontal horns, and (c) width of third ventricle. This factor correlated highly ($r = .694$) with the ventricle/brain ratio (VBR) measure used by others (Weinberg et al., 1980). The second factor was labelled the frontal density factor as it received highest loadings from the region-of-interest measures on the right and left sides of the frontal lobes both in white and grey matter. The third neuroanatomical factor reflected the density of the left and right ascending corona radiata (white matter). The fourth factor was labelled the sulcal size factor as highest loadings were from the (a) general sulcal size measure, (b) width of the spaces between the frontal cortex and the skull, on both sides, and (c) sum of the widths of the four largest sulci. The fifth factor represented the density of the right and left thalamic nuclei. Again, subsequent analyses using CAT-scan data were based on these factors, created using factor score coefficients.

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Table 8

Factor Loading for CAT-Scan Factors*

Variable	Ventricle Factor	Frontal Density	Corona Rad. Density	Sulcal Size Factor	Thalamic Density
Sulcal size	.595			.409	
Ventric. size	.845				
4 largest sulci	.572			.504	
Width I.H. Fissure	.459			.320	
Width skull to F.L. (rt)				.676	
Width skull to F.L. (lt)				.732	
Width Frontal lobes	.488				
Width 3rd V.	.689				
Width lat. V. Fr.	.773				
Width lat. V. Caud.	.879				
Density Frontal Lat. (rt)		.848			.713
Density Frontal Lat. (lt)		.873			.715
Density Frontal Ant. (rt)		.753			
Density Frontal Ant. (lt)		.732			
Density Thalamus (rt)					
Density Thalamus (lt)					
Density Cor. Rad (rt)			.720		
Density Cor. Rad (lt)			.715		
Brain Stem Density			.376		
VBR	.694				

*only loadings of greater than .3 are reported.

ALL INFORMATION CONTAINED

Multiple Regressions on Psychological Factors

Three multiple regressions of the independent variables nutrition, alcohol use, biochemical status, and CAT-scan indices were performed on the psychological factors. In order to present a clear visual representation of the results, bar-graph figures are presented. In all cases, the independent measure (i.e., alcohol use, diet, biochemistry or CAT-scan) was broken down to four groups so that each group contained approximately the same number of subjects. (This was not possible with the alcohol measure as 52% of the subjects reported drinking 1-2 drinks per occasion.) The rationale for choosing four groups was that the small number enabled both ease of visual display of the results and yet provided enough groups to test the significance of a non-linear trend with analysis of variance.

First Multiple Regression: Diet and Alcohol Use

Since approximately half of the subjects did not have biochemical and/or CAT-scan data, the first multiple regression on the psychological factors was performed only on the demographic, diet and alcohol use variables. Pairwise deletion was employed. As only 91 subjects had completed the diet diaries, regressions based on nutritional data were calculated with $N = 91$. For each psychological factor, the demographic variables, age, sex, and education, were entered into the regression equation first, while the dietary factors, general dietary quality and B-vitamins, and alcohol variables, mean amount consumed per occasion (amount) and frequency of consumption (frequency), were entered on the second step.

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General neuropsychological performance. This factor was significantly related to the demographic variables, age, sex, and education ($F = 10.27$; $df = 3,85$; $p < .001$). This was primarily due to the effect of education on neuropsychological performance ($F = 23.03$; $p < .001$). When the dietary and alcohol consumption variables were added to the equation, it remained significant ($F = 6.62$; $df = 7,81$; $p < .001$). The only two independent variables significantly related to general neuropsychological performance then were education ($F = 20.54$, $p < .001$) and general dietary quality ($F = 11.14$, $p < .001$). In summary, when demographic, and alcohol consumption variables are partialled out, the general dietary quality factor is positively related to general neuropsychological performance ($b = .312$), alone accounting for 9.31% of the variance. Figure 1 demonstrates this relationship in bar-graph form. The significance of the analysis of variance of neuropsychological performance with the four nutritional groups is $F = 3.59$ ($df = 4,86$; $p = .0093$). The linear effect ($F = 9.83$; $p = .002$) accounts for the majority of the variance, while the non-linear effect is not significant. Alcohol consumption, on the other hand, was not related to general neuropsychological performance. Figure 2 provides a visual display of this non-significant relationship.

Mood disturbance. The demographic variables, age, sex, and education were not significantly related to mood, although there was a tendency for education to be related inversely to mood disturbance. When the nutritional and alcohol variables

Figure 1

The Relationship between General Dietary Quality and General Neuropsychological Performance*

*The general neuropsychological performance variable is the residual value, after age, sex, and education have been partialled out of the standardized factor score. General Nutrition units are standardized factor scores.

Figure 2

The Relationship between Alcohol Consumption and General
Neuropsychological Performance*

(Not Significant)

*The general neuropsychological performance variable is the residual value, after age, sex, and education are partialled out of the standardized factor score. Amount/occasion represents the average reported number of drinks consumed per occasion.

were entered into the equation there was a significant effect ($F = 4.33$; $df = 7,81$; $p < .001$) due to the fact that both amount ($F = 7.30$, $p < .01$) and frequency ($F = 7.74$, $p < .01$) of alcohol consumption were significantly and positively related to mood disturbance. Figure 3 represents this relationship. The analysis of variance of Mood disturbance with the four alcohol consumption (amount per occasion) groups ($F = 6.97$; $df = 4,97$; $p < .0001$) had both a significant linear trend ($F = 13.04$, $p < .0005$) and non-linear trend ($F = 4.95$, $p < .003$). Thus it appears that light drinkers have the least mood disturbance, followed by abstainers and moderate drinkers, while heavy drinkers have the most mood disturbance. The large amount of variance accounted for (21%) is due to the very small amount of error variance in this association. When the demographic and dietary factors are partialled out, amount and frequency of alcohol consumption together account for 21.15% of the variance in mood disturbance.

Wisconsin Card Sort Test (a) Perseverative error ratio.

Of the demographic variables entered into the equation on the first step ($F = 2.03$; $df = 3,84$; $p < .1$), age was the most influential ($F = 4.04$, $p < .05$). Older subjects made more perseverative errors relative to non-perseverative errors than did younger subjects. Neither diet nor alcohol consumption influenced this variable.

(b) Mean trials to criterion. This variable was not significantly affected by the demographic variables, diet, or alcohol use.

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Figure 3

The Relationship Between Alcohol Consumption and Mood
Disturbance

STATISTICAL SIGNIFICANCE

*The mood disturbance variable is the standardized POMS (Total Mood Disturbance Score) residual value, after age, sex, and education are partialled out. Amount/occasion represents the average reported number of drinks consumed per occasion.

Rigidity. The rigidity factor was very strongly related to the demographic variables ($F = 10.39$; $df = 3,85$; $p < .001$) due to the effect of age ($F = 29.15$; $p < .001$). Although dietary quality tended to be related inversely, and alcohol consumption tended to be positively related to rigidity, the effects were no longer significant when the influence of age was partialled out.

General attention. This CPT measure was significantly affected by the demographic variables ($F = 4.13$; $df = 3,85$, $p < .01$). Older people ($F = 4.25$; $p < .05$) and females ($F = 9.27$; $p < .01$) performed more poorly than younger subjects and males. Neither this factor, nor the attentional impulsivity factor was influenced by the diet factors or by alcohol consumption.

Second Multiple Regressions: Biochemistry

The second set of multiple regressions was similar to the first, with the exception that the biochemical factors, hemoglobin, potassium, calcium and glucose were entered into the equation on the second step, after the demographic variables were partialled out. The dietary and alcohol consumption variables were entered on the third step. Listwise rather than pairwise deletion of missing data was employed as the discrepancies in available data for the biochemical factors ($N = 52$) compared to the dietary and alcohol use variables ($N = 92$) would have yielded inaccurate and unreliable results; thus these analyses were based on a sample size of 52. The major purpose of this analysis was to examine the effects of the biochemical

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factors on the psychological measures. In addition, this analysis enabled a sub-sample validation of the dietary and alcohol use results.

General neuropsychological performance. As with the larger sample, the demographic variables ($F = 7.76$; $df = 3,38$; $p < .001$), and especially education ($F = 16.59$; $p < .001$) were related significantly to general neuropsychological performance. When the demographic variables were partialled out, biochemical factors accounted for an additional 16.5% of the neuropsychological variance ($F = 4.22$; $df = 7,34$; $p < .01$). This was due primarily to the positive influence of the potassium factor ($b = .231$; $F = 3.24$; $p < .05$). Figure 4 demonstrates this relationship. The analysis of variance of neuropsychological performance did not reveal a significant effect of the four potassium groups, although the linear effect approached significance ($F = 2.06$; $df = 1,45$; $p = .15$). The demographic-partialled correlation of general dietary quality with neuropsychological performance remained significant in this sub-sample both before inclusion of the biochemical factors ($b = .363$; $F = 5.61$; $p < .05$) and after their inclusion ($b = .339$; $F = 4.29$; $p < .05$). Thus, it appears that the effect of nutrition on performance is at least partially mediated by the effect of potassium, and is as strong in the subgroup of subjects having biochemical data as in the larger sample of all subjects.

Mood disturbance. When the demographic variables were in the equation, there was a tendency for the biochemical factors

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related. Indeed, this is the case in the present sample ($r = -.541$; $p < .001$). However, there are some dietary factors which are known to affect calcium absorption, and thus influence serum calcium levels. For example, diets rich in protein tend to facilitate calcium retention. In the present sample, the percentage of Recommended Dietary Allowance (RDA) for protein was positively related to serum calcium levels ($r = .255$; $p < .05$). Conversely, ingestion of foods such as cereal seeds which contain phytic acid and, incidentally, abundant supplies of the B-complex vitamins have been found to be related inversely to serum calcium levels. In the present study, calcium levels were found to be inversely related to the percentage RDA of thiamine ($r = -.36$; $p < .01$), riboflavin ($r = -.36$; $p < .01$), niacin ($r = -.41$; $p < .003$), vitamin B6 ($r = -.42$, $p < .002$) and vitamin B12 ($r = -.49$; $p < .001$). Conversely, ingestion of these B vitamins was related positively to serum inorganic phosphorous. Beyond these relatively subtle effects, however, the associations between dietary intake of the essential vitamins and minerals and serum levels of calcium, phosphorous, glucose, sodium, potassium and hemoglobin are not strong.

Relationship of Neuroanatomical and Neuropsychological Measures

Only one neuropsychological measure, Wisconsin Card Sort Test performance, was related significantly ($p < .05$) to the multiple regression of the neuroanatomical indices. This was primarily the result of its strong association with the following linear measures of frontal lobe status: Wisconsin performance

to influence mood ($F = 1.64$; $df = 7,34$; $p < .1$). This was due primarily to the inverse effect of the calcium factor on mood disturbance ($F = 4.45$; $p < .05$). Figure 5 represents this effect. The analysis of variance revealed that only the linear effect of the four calcium groups on mood was significant ($F = 4.85$; $df = 1,45$; $p = .03$). The effects of frequency and amount of alcohol consumption were also significant in this sub-sample. The demographics-partialled correlations of amount ($b = .557$; $F = 11.83$; $p < .01$) and frequency ($b = .394$; $F = 6.6$; $p < .05$) of alcohol use remained significant when the effects of the biochemical factors were also partialled out (for amount: $b = .574$; $F = 13.7$; $p < .001$; for frequency: $b = .429$; $F = 7.3$; $p < .01$). Again, the effect of alcohol use on mood is equally strong in the "biochemical sub-group". This association appears to be mediated, to some extent, by the effects of calcium.

Wisconsin Card Sort Test. Neither the perseverative error rate, nor mean trials to criterion measure was significantly influenced by the biochemical factors.

Rigidity. When the effect of the demographic variables was accounted for ($F = 5.91$; $df = 3,38$; $p < .01$), the inclusion of the biochemical factors in the equation was found to have a significant influence on the rigidity factor ($F = 3.62$; $df = 7,34$; $p < .01$). This was due to the inverse effect of the potassium factor on rigidity ($F = 2.75$; $p < .05$).

Attention. The general attention factor also was affected significantly by the inclusion of the biochemical factors in

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Figure 5

The Relationship between the Serum Calcium Factor and Mood
Disturbance*

*The Mood disturbance variable is the standardized POMS (Total Mood Disturbance Score) residual value, after age, sex, and education are partialled out.

Third Multiple Regressions:- Neuroanatomy

The third set of multiple regressions was, again, similar to the first two. However, the neuroanatomical factors were entered into the equation on the second step, after the demographic variables had been entered. Dietary and alcohol variables were entered on the third step. Listwise deletion was used resulting in a sample size of 51.

General neuropsychological performance. The demographic variables ($F = 6.99$; $df = 3,47$; $p < .001$), and especially education ($F = 16.06$; $p < .001$) were related significantly to general performance. When the CAT-scan factors were entered into the equation on the second step, the influence on neuropsychological performance remained significant ($F = 3.82$; $df = 8,42$; $p < .01$). This was due primarily to the effect of the factor representing the density of the corona radiata ($F = 5.24$; $p < .05$). Figure 6 demonstrates this relationship. The analyses of variance of neuropsychological performance revealed a significant effect of the four corona radiata density groups ($F = 3.08$; $df = 3,58$; $p < .02$) which was primarily linear ($F = 7.1$; $df = 1,58$; $p < .01$). However the non-linear trend approached significance ($F = 2.5$; $df = 2,58$; $p < .07$). Thus, when the density of the white matter exceeded mean or normal limits an inverse effect on performance was seen.

Figure 6

The Relationship between Corona Radiata Density and General Neuropsychological Performance*

*The neuropsychological performance variable is the residual value, when age, sex, and education are partialled out of the standardized factor score. Corona radiata density units are standardized factor scores.

One standard deviation above the mean for the corona radiata ($\bar{x} = 31.9$ H.U.) would result in a mean value of 34.8 H.U. This latter value approximates that of the unmyelinated thalamic region ($\bar{x} = 34.5$ H.U.). Again, the effect of diet remained significant in this second sub-sample. The partial correlation of dietary quality with performance was $b = .356$ ($F = 6.67$; $p < .05$) when only the demographic variables were controlled, and $b = .335$ ($F = 5.2$; $p < .05$) after the CAT-scan factors were partialled out.

Mood disturbance. Although the demographic variables were not related to mood, there was a borderline effect for the addition of CAT-scan factors to the equation predicting mood ($F = 1.33$; $df = 8, 42$; $p < .20$). This was due to the influence of frontal density on mood disturbance ($F = 3.59$, $p < .05$). Figure 7 represents this relationship. The analysis of variance of mood disturbance does not reveal a significant linear effect of the four frontal density groups. However, the non-linear trend approaches significant ($F = 2.2$; $df = 2, 58$; $p < .1$). Thus it appears that both low density values and high values directly influence mood disturbance. The demographics partialled correlation of amount of alcohol with mood ($b = .503$; $F = 15.59$; $p < .001$) prior to entering in the CAT-scan factors remained significant when CAT-scan factors were partialled out as well ($b = .484$; $F = 12.59$; $p < .001$). Similarly, the partial correlation of alcohol frequency with mood prior to controlling for CAT-scan factors ($b = .38$; $F = 7.79$; $p < .01$) remained significant when they were partialled

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Figure 7

The Relationship Between Frontal Lobe Density and Mood
Disturbance*

*The Mood disturbance variable is the standardized POMS (Total Mood Disturbance Score) residual value, after age, sex, and education are partialled out.

out ($b = .39$, $F = 7.2$, $p < .05$).

Wisconsin Card Sort Test: Trials to Criterion. Although Trials to Criterion was not significantly affected by the multiple regression equation of demographic variables and CAT-scan factors, it is interesting to note that it was positively related to the univariate factor of sulcal size ($b = .322$; $F = 3.94$; $p < .05$) when the demographic variables were partialled out.

General attention. This factor tended to be affected by the inclusion of CAT-scan measures to the equation ($F = 1.67$, $df = 8, 39$; $p < .1$). Attention was inversely affected by sulcal size ($b = -.294$; $F = 3.89$; $p < .05$) when the demographic variables were partialled out.

Path Analyses

The multiple regressions revealed two major patterns in the data. First, general neuropsychological performance was found to be associated with dietary quality, biochemical factor potassium, and the neuroanatomical factor of corona radiata density. Second, mood was associated with alcohol use, the biochemical factor calcium, and the neuroanatomical factor frontal lobe density. In order to describe the nature of the associations in these two sets of variables, path analyses were performed. Path analysis is a descriptive statistical tool which enables the researcher to apply causal models to a given data set. It does not enable one to test a causal hypothesis but, rather, allows one to examine the appropriateness of "fit" of a causal model for the specific data set to which it is applied.

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The path analysis method requires one to make assumptions regarding the causal ordering of variables, based on previous research or on "common sense". For example, it was assumed that nutritional status exerted an effect on neuropsychological functioning, rather than vice versa, as the results of several experimental studies of vitamin, mineral and general nutrient supplementation have reported consistently a direct effect on psychological performance (Coleman et al., 1978; Gowans, 1980; Hall, 1980; Merzbacher, 1979; Rimland et al., 1978). Similarly, nutritional status was assumed to affect biochemical and neuroanatomical indices, rather than vice versa, as previous research has documented the effects of dietary factors on biochemical (Hall, 1980, neurophysiological (Tucker & Sandstead, 1981), and neuroanatomical measures (Strom, 1978). It was also assumed that, on a chronic basis, alcohol use was more apt to affect mood disturbance than vice versa. This assumption was based, in part, on the work of Parker and associates (personal communication, 1982) which showed that female social drinkers in an outpatient treatment program who complied in cessation of alcohol use, showed significantly greater improvement of depressive symptoms than did matched controls. Alcohol use is known to disrupt a variety of limbic hormonal systems which are involved in mood regulation (Tabakoff et al., 1978). The causal nature of the relation between biochemical and neuroanatomical measures is unspecified in these models. The research in this area is scant; however, it was assumed that

NUTRITIONAL STATUS

biochemical and electrolyte variation may be more likely to influence tissue density than vice versa. The assumption that both of these factors affect psychological performance appears justified on the basis of previous research (Bergman, 1980; Hall, 1980).

With these assumptions in mind, a causal model for the nutritional biochemical and neuroanatomical indices of neuropsychological performance was developed and is presented in Figure 8. Table IX is a Decomposition Table for the path analysis of factors influencing general neuropsychological performance. This decomposes the total covariance between each pair of variables in the model into variance which is considered, (on the basis of the a priori assumptions by which the model was developed) to be causal and that which is non-causal. The causal variance involves the direct covariance (i.e., the partial correlation between each pair of variables, after variance attributable to the other variables in the model has been partialled out), and indirect covariance, (the sum of the products of partial correlations through non-direct causal pathways as indicated by the path analysis model). The sum of the direct and indirect variance is the total causal covariance. The difference between the total covariance and causal covariance, then, is assumed to be the non-causal covariance, or covariance which cannot be explained by the model as it was conceived.

The decomposition table (Table 9) clearly illustrates a number of interesting findings. First, the inverse effect of

CAUSAL INFLUENCE

Figure 8

Path Analysis Model of the Nutritional, Biochemical and Neuro-anatomical Indices of Neuropsychological Performance*

*Neuropsychological performance, in this context, is the residual performance score after age, sex, and education have been partialled out.

Table 9

Decomposition Table of Indices of Neuropsychological Performance

Bivariate Relationship	Total Covariance	Causal		Non-Causal
		Direct	Indirect	
$(X_1 X_2)$ General nutrition x potassium	.04	.04	None	None
$(X_1 X_3)$ General nutrition x corona radiata density	-.39	.40	$(P_{12})(P_{23})$ = .016	.006
$(X_2 X_3)$ Potassium x corona radiata density	.39	.41	None	-.02
$(X_1 X_4)$ General nutrition x general neuropsych performance	.31	.13	$(P_{12})(P_{24})$ = .015 $(P_{12})(P_{23})(P_{34})$ = .007 $(P_{13})(P_{34})$ = .168 Total = .180	None
$(X_2 X_4)$ Potassium x general Neuropsych. Perf.	.21	.37	$(P_{23})(P_{34})$ = -.17	.01
$(X_3 X_4)$ Corona Radiata Dens x General neuropsych performance	-.33	-.42	None	.09

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diet on corona radiata density is primarily direct, and not mediated by its effect on potassium. Second, the direct effect of potassium on performance ($b = .37$) is counteracted by the indirect pathway through corona radiata (C.R.) density: although potassium is positively related to C.R. density, this factor is related inversely to performance. Thus, the total covariance between potassium and performance ($b = .21$) is substantially smaller than the direct relationship ($b = .37$). Similarly, the direct negative effect of CR density on performance ($b = -.42$) is counteracted by the positive relationship of potassium to both, so that the total covariance between CR density and performance is reduced ($b = -.33$). Finally, of major interest, is the nature of the effect of diet on neuropsychological performance. Of the total covariance between these two factors, ($b = .31$) approximately 42% ($b = .13$) is attributable to the direct effect of nutrition on performance. The remaining 58% is indirect, primarily through the inverse effect of nutrition on CR density, and its negative effect on performance.

Two path analyses were performed with the alcohol-related data, since amount of alcohol consumption appeared to affect the biochemical, neuroanatomical and mood disturbance factors differently than did frequency of alcohol consumption. Figure 2 illustrates the model which was developed to examine these relationships with mean amount of alcohol consumed per occasion. The counteracting effects of biochemical and neuroanatomical factors on psychological measures, seen in Figure 8,

Figure 9

Path Analysis Model of Alcohol Consumption (Amount) Biochemical
and Neuroanatomical Indices of Mood Disturbance*

*Mood disturbance in this context is the residual mood disturbance score, after the effects of age, sex, and education have been partialled out.

Non-Causal

Bivariate Relationship	Total Covariance	Causal Direct	Indirect	Total	Non-Causal
$X_1 X_2$ Amt./Occ. x Calcium	.037	.037	None	.037	0
$X_1 X_3$ Amt./Occ. x Frontal Density	-.137	-.15	$(P_1 P_2) (P_2 P_3) = .013$	.137	0
$X_2 X_3$ Calcium x Frontal Density	.339	.344	None	.344	-.005
$X_1 X_4$ Amt./Occ. x Mood Disturbance	.399	.471	$(P_1 P_2) (P_2 P_3) (P_3 P_4) = .005$ $(P_1 P_3) (P_3 P_4) = -.06$ $(P_1 P_2) (P_2 P_4) = -.017$ $= -.072$	.399	0
$X_2 X_4$ Calcium x Mood Disturbance	-.319	-.472	$(P_2 P_3) (P_3 P_4) = .137$	-.355	.016
$X_3 X_4$ Frontal Density x Mood Disturbance	.175	.399		.399	-.224

is also seen in this model. That is, although calcium and frontal density are positively related to each other, calcium exerts a negative effect on mood disturbance while frontal density enhances it. Thus, in both cases, the direct effect is stronger than the total covariance, as the indirect association attenuates the direct effect. The direct effect of alcohol on mood is, again, stronger than the total covariance. The indirect pathway, through frontal density has an attenuating effect, thereby reducing the total covariance between alcohol and mood.

The decomposition table provides an excellent illustration of the complexity of the association between frontal density and mood disturbance. That is, there is a strong direct effect of tissue density, accounting for over 15% of the variance in mood disturbance. However, there is also a fairly strong counteracting, negative effect, which accounts for approximately 8% of the mood variance. Interpretation of this relationship may be facilitated by referring back to Figure 7 which illustrates the association between frontal density and mood. There is a curvilinear relationship whereby, below the mean for frontal density there tends to be a negative effect on mood disturbance; whereas above the mean for frontal density the effect on mood disturbance is positive.

With frequency of alcohol consumption, a slightly different picture emerges. Frequency of consumption is related positively to mood disturbance ($r = .379$) and 95% of the effect is direct, i.e., it is not mediated by the effects of calcium and/or

frontal density on mood. The remaining 5% is attributable to the indirect effect of consumption frequency through calcium. The relation of consumption frequency to frontal lobe density ($r = -.122$) is, in part, direct (57.4%), while 43.6% of the relation may be attributed to the indirect pathway through calcium. Again, the decomposition table provides a clearer picture of complex associations of frontal lobe density with serum calcium levels and mood disturbance. There is a strong direct effect of frontal density which accounts for more than 10% of the variance in mood disturbance. However, there is also a negative effect, not explained by this model, which accounts for 3% of the variance in mood disturbance. This curvilinear effect of frontal density on mood (similar to that seen in the model for amount of alcohol consumed per occasion) probably accounts for the fact that, although calcium levels and frontal density are positively related, their overall effects on mood disturbance are opposite in direction.

In summary, the path analyses illustrate the following points regarding the major results of this study: (1) although biochemical measures of serum minerals are positively related to measures of neuroanatomical density, the former have beneficial effects on neuropsychological performance and mood, while the latter adversely affect these factors. This pattern may be best understood in light of the curvilinear nature of the effect of tissue density on the psychological measures; (2) the effect of nutrition on neuropsychological performance is largely (42%) direct, but also (58%) due to the indirect pathway

Figure 10

Path Analysis Model of Alcohol Consumption (Frequency), Biochemical and Neuroanatomical Indices of Mood Disturbance*

*Mood disturbance in this context is the residual score, after the effects of age, sex and education have been partialled out.

Table 1. Bivariate Correlations of Frequency of Sleep Disturbance with Frequency of Frontal Density

Bivariate Relationship	Total Covariance	Causal Direct	Indirect	Total	Non-Causal
$X_1 X_2$					
Alc. Frequency x Calcium	-.158	-.158	None	-.158	0
$X_1 X_3$					
Alc. Frequency x Frontal Density	-.122	-.07	$(P_1 P_2) (P_2 P_3) = -.052$	-.122	0
$X_2 X_3$					
Calcium x Frontal Dens.	.339	.327	None	.327	.012
$X_1 X_4$					
Alc. Frequency x Mood Disturbance	.379	.361	$(P_1 P_2) (P_2 P_3) (P_3 P_4) = -.018$ $(P_1 P_2) (P_2 P_4) = +.06$ $(P_1 P_3) (P_3 P_4) = -.024$ $-.018$	.379	0
$X_2 X_4$					
Calcium x Mood Disturbance	-.319	-.38	$(P_2 P_3) (P_3 P_4) = .113$	-.267	-.052
$X_3 X_4$					
Frontal Density x Mood Disturbance	.175	.347		.347	-.172

through corona radiata density; (3) the total effect of amount of alcohol consumed per occasion on mood is less than the direct effect, since the indirect effect through frontal lobe density attenuates the relation by 15.3%; (4) the effect of alcohol consumption frequency is 95% direct, and 5% may be attributed to the indirect pathway, through calcium.

Summary of Statistical Highlights

The major statistical results of this study may be summarized as follows:

(1) Alcohol use did not influence neuropsychological performance but was strongly related to mood disturbance when age, sex, and education were controlled;

(2) General dietary quality was related to general neuropsychological performance with the demographic variables controlled;

(3) The factor representing serum levels of potassium, sodium and alkaline phosphatase was predictive of general neuropsychological performance, rigidity, and Wisconsin Card Sort Test performance;

(4) The factor representing serum calcium and phosphorous was related to mood disturbance;

(5) Corona radiata tissue density was predictive of general neuropsychological performance and exerted a strong mediating effect in the association of diet with neuropsychological performance.

(6) Frontal lobe tissue density was related to mood disturbance in a curvilinear fashion. The complex nature of this

association precluded the clear interpretation of its role in mediating the effects of alcohol consumption on mood in this study.

7

XI

DISCUSSIONValidity and Reliability of Self-Reported Alcohol Consumption

The correlations of biochemical indices of alcoholism (Ryback et al., 1978) with amount and frequency of alcohol use did provide evidence of concurrent validity of reported frequency of alcohol consumption in that 4 of the 7 measures were related significantly to drinking frequency. These indices are successfully used in clinical settings with alcoholics, and are known to return to normal with periods of one to two weeks abstinence from alcohol (personal communication from Dr. N. Nayar, Chief of the Alcohol Addiction Unit, Royal Ottawa Hospital, Ottawa, Canada). Since frequency and recency of consumption are generally thought to be associated more closely with these biochemical parameters than is amount consumed per occasion, it is not surprising that frequency of drinking was associated with 4 of these 7 indices, while amount per occasion was not. This does not reflect on the absence of validity of reported amount of alcohol consumption, but rather indicates that the validating criterion (i.e., the biochemical profile) itself is of limited utility as a measure of alcohol use since it is highly dependent on relatively acute (i.e., within one to two weeks) effects of alcohol use.

The test-retest reliability assessment confirmed that reported frequency of alcohol use is, indeed, highly reliable. However, the reliability coefficient for amount of alcohol

consumed per occasion was somewhat lower.

One reason for the relatively low reliability for amount consumed per occasion is that the inventories given during the testing session were often completed incorrectly with respect to that item. That is, many subjects perceived the 10-point scale of relative frequency for each amount (i.e., "not at all" through "always") as an absolute frequency of consumption scale rather than a question of how often they drank that much when they did drink. Although Parker and Noble (1980) have derived a correction procedure for this error, the investigator informed the subjects of the error when they had made it and they then responded differently on the questionnaire completed at home. Thus, the at-home response to this item was used in subsequent analyses.

Relationship of Nutritional Status and Dietary Intake

The only nutrients for which both serum and dietary measures were available were calcium and phosphorous. It was not expected that there should be a direct correspondence between dietary intake and serum concentration of calcium and phosphorous since their levels in blood are so tightly controlled by hormonal mechanisms. The result of this hormonal activity is that calcium and phosphorous levels are altered by dietary intake only in relatively extreme cases of hypocalcemia and hypophosphatemia, or when the ratio of calcium to phosphorous intake differs markedly from 1:1. Parathormone operates to increase serum calcium levels and decrease the concentration of inorganic phosphorous. Thus, they are normally inversely

related. Indeed, this is the case in the present sample ($r = -.541$; $p < .001$). However, there are some dietary factors which are known to affect calcium absorption, and thus influence serum calcium levels. For example, diets rich in protein tend to facilitate calcium retention. In the present sample, the percentage of Recommended Dietary Allowance (RDA) for protein was positively related to serum calcium levels ($r = .255$; $p < .05$). Conversely, ingestion of foods such as cereal seeds which contain phytic acid and, incidentally, abundant supplies of the B-complex vitamins have been found to be related inversely to serum calcium levels. In the present study, calcium levels were found to be inversely related to the percentage RDA of thiamine ($r = -.36$; $p < .01$), riboflavin ($r = -.36$; $p < .01$), niacin ($r = -.41$; $p < .003$), vitamin B6 ($r = -.42$, $p < .002$) and vitamin B12 ($r = -.49$; $p < .001$). Conversely, ingestion of these B vitamins was related positively to serum inorganic phosphorous. Beyond these relatively subtle effects, however, the associations between dietary intake of the essential vitamins and minerals and serum levels of calcium, phosphorous, glucose, sodium, potassium and hemoglobin are not strong.

Relationship of Neuroanatomical and Neuropsychological Measures

Only one neuropsychological measure, Wisconsin Card Sort Test performance, was related significantly ($p < .05$) to the multiple regression of the neuroanatomical indices. This was primarily the result of its strong association with the following linear measures of frontal lobe status: Wisconsin performance

declined as the width of the interhemispheric fissure and of the subdural space between the left frontal cortex and skull increased. In addition, performance on this test was related inversely to the density of the left corona radiata, the white matter ascending from subcortical structures to all areas of the cortex. Thus, the Wisconsin Card Sort test does appear to be sensitive specifically to the degree of sulcal enlargement in the left frontal lobe and to the density of left ascending white matter.

Three other tests, the Shipley Abstraction index, Block Design test, and the Design Fluency measure were associated significantly with the multiple regression of the neuroanatomical measures at the $p < .1$ level of significance. Because the relatively small sample size and large number of dependent measures resulted in a substantial loss of power for these regressions, the $p < .1$ level was accepted as significant. Performance on all three of these tests was most strongly and inversely influenced by the width of the interhemispheric fissure. Like Wisconsin Card sort performance, the Design Fluency measure also was related inversely to the width of the subdural space between the frontal cortex and skull. However, for the Wisconsin Card Sort test, this effect was maximal on the left side, while it was greatest on the right side for design fluency. The Shipley Abstraction index was related inversely to the density of the right thalamus. Thus, the data tend to confirm the classical neuropsychological literature concerning the lateralization of performance on the

Wisconsin Card Sort test as being dependent on the left frontal cortex (Milner, 1964). In addition, support is provided for the involvement of the frontal cortex in performance on tests of visual-spatial (Block Design) and abstraction (Shipley Abstraction) abilities. In particular these data are the first to corroborate the conclusion of Jones-Gotman and Milner (1979) that Design Fluency performance is mediated specifically by the right frontal cortex.

The verbal tests, Shipley Verbal Index and Verbal Fluency test, and the Attentional measure (number of correct responses on the A:Dynamic phase of the CPT) were not related to the multiple regression of the neuroanatomical measures. However, it is worth noting that attention was related inversely to sulcal enlargement, and that performance on the verbal tests, especially verbal fluency, was related inversely to the density of the frontal white matter, thalamic nuclei, and corona radiata. The density of the corona radiata also was related inversely to performance on Shipley Abstraction, Block Design, and Wisconsin Card Sort tests. In other words, the more dense this white matter, the poorer was neuropsychological performance. Debilitating increases in tissue density may be attributed to a loss of myelin, dehydration due to electrolyte imbalances, or vascular edema. Since vascular edema is more likely to be associated with an increase in cortical rather than subcortical density, the explanations of myelin loss and dehydration appear more plausible. At present, there is no justification for choosing one of these hypotheses over the other. This matter will be discussed again at a later point.

Finally, it should be noted that there were no gender effects

an lateralization of neuropsychological performance or neuro-anatomical structure.

Factor Analyses

The factor analysis of the psychological data did not reveal trends towards lateralized superiorities or deficits. This was not unexpected in a non-lesion group. Generally, those subjects who performed well on the verbal and sorting tasks, also did well on the spatial and design tasks. However, separate factors for rigidity (associated with age), Wisconsin Card Sort test performance, attentional performance on the CPT, and mood state were obtained. In order to enable the comparison of these results to those of previous studies and to facilitate replication of the present study, two of the Wisconsin Card Sort scores, the CPT score, X:Dynamic Pace correct responses, and the POMS:Total Mood Disturbance score were used in the analyses, rather than the actual factors obtained. The general neuropsychological performance factor then, which was found later to be highly sensitive to diet and neuro-anatomical status, was derived in such a way that it was not related (i.e., orthogonal) to the factors representing mood state, general attention, and motor abilities. Although this factor also was independent of the obtained Wisconsin Card Sort factor, it was moderately but significantly related to the two Wisconsin variables, Trials-to-criterion and perseverative ratio, used in this analysis. Again, it is not surprising that subjects who function well generally perform well on the Wisconsin test.

The same pattern was obtained from the factor analysis of

the nutritional data, in that only two factors were obtained. The general nutrition factor reflected the fact that subjects whose diets were rich in certain nutrients tended to have high levels of all nutrients. Calories also loaded highly on the general nutrition factor indicating that, in this upper-class socioeconomic group, total intake reflected highly nutritious intake, with a minimal ingestion of "empty", or "junk-food" calories. Intake of vitamins, and especially the B-vitamins factored out separately from the general nutrition factor. This may be due to the fact that approximately 14 of the subjects were taking multivitamin and B-complex vitamin pills on a self-prescribed basis.

Three biochemical factors were obtained, and named for the variable which loaded most heavily on each; thus the factors labelled hemoglobin, potassium, and calcium were used in later analyses. In addition, glucose also was used in subsequent analyses as it had failed to load significantly on any of the obtained factors. Normally, hormonal mechanisms operate to produce inverse relationships between potassium and sodium, and between calcium and inorganic phosphorous. However, the hormonal regulation of potassium and sodium is less effective than is the case with calcium and phosphorous. The positive relationship between sodium and potassium indicates that, in all likelihood, variation on that factor is due less to hormonal than to dietary mechanisms. Conversely, the inverse relationship between calcium and phosphorous indicates

that that factor is strongly affected by hormonal activity (i.e., parathormone).

Five neuroanatomical factors were obtained (from the 19 measures taken by the radiologist) which were anatomically quite specific. All linear measures of ventricular size (i.e., Huxman's measure, 3rd ventricle size, global assessment of ventricular size) loaded onto one factor, which correlated quite highly (sharing 50% of common variance) with the VBR measure done by the author. Similarly, a single factor reflecting sulcal size, or cortical shrinkage, was obtained, representing the linear and global measurements of sulcal size and width of the space between frontal cortex and skull. Three factors were obtained from the tissue-density measurements, reflecting (a) frontal grey- and white-matter density, (b) subcortical (corona radiata) white-matter density, and (c) subcortical (thalamic) grey-matter density. In all cases the factors obtained represented bilateral measurements, so that asymmetrical or lateralized neuroanatomical factors could not be distinguished.

Effects of Diet and Alcohol Use on Psychological Performance

Perhaps the most interesting finding of this study is the effect of dietary quality on general neuropsychological performance when effects of demographic variables (age, sex and education) were controlled. This relation is linear, and accounts for over 9% of the variance in neuropsychological performance. While 9% is not an overwhelming proportion of variance, it is quite a substantial effect in view of the fact

that none of the subjects were malnourished, and they were from upper-middle-class backgrounds. It is also quite noteworthy that the effect obtained in a neuro-radiological outpatient sample. In such a sample one might expect a fair amount of extraneous variance in neuropsychological performance associated with the neurological symptoms which led to the radiological referral. This characteristic of the sample may be a major reason why the subtle effects of non-alcoholic drinking on neuropsychological performance were not replicated in the present study. At the same time, however, it renders the dietary effect all the more noteworthy.

In the present study, alcohol use and dietary quality were not related. This finding may be due to the fact that the sample was generally well-educated and of high socio-economic status. It is quite possible that in a less well-educated and wealthy sample, subjects who drink more heavily would have poorer diets. This confound may have contributed to the alcohol effect documented in social drinkers by previous research (e.g., Parker & Parker, 1982; Parker et al., 1980).

There are possible explanations, other than the non-normal population characteristics of the present sample, for the absence of the alcohol-use effect in this study. The most obvious and overwhelming "effect" of alcohol consumption was on mood disturbance. This critical factor has not been controlled in previous studies of social drinkers. In other studies, including the present one, mood disturbance is related inversely to performance on specific neuropsychological

tests. In the present study, mood disturbance was significantly and inversely related to performance on the Shipley, Verbal and Abstraction indices, Block Design, Digit Symbol, and the Wisconsin Card Sort test, but was of course orthogonal to the General Neuropsychological Performance factor and the Rigidity factor. Thus, the effect of social drinking and alcohol use on cognitive performance in other studies was, in all likelihood, secondary to the effect of depressed mood. Indeed, mood disturbance may have caused both increased alcohol use and decreased quality of neuropsychological performance. We will return to the issues of causality later in this discussion.

There are several ways besides being neurological referrals in which the present sample differed from that of Parker and Noble (1977; 1980). They originally documented the social drinking effect in college students and later replicated the finding with businessmen. Compared to their sample of businessmen (Parker & Noble, 1980), the present sample was 48% female (vs. 0%), had a slightly higher income (\$30,000/yr. vs. \$25,500/yr.), drank less frequently (158 times/yr. vs. 204 times/yr.) and was probably more frequently on medication (69.8% vs. unknown). In order to attempt to replicate the results of Parker and Noble (1980), the following subsamples were examined for the relationship between alcohol use and neuropsychological performance: (1) subjects not on medication, (2) subjects with referrals for headache only, (3) moderate and heavy drinkers (i.e., no abstainers), (4) males only.

In none of these subsamples were the results of Parker and Noble (1980) replicated nor was any effect of alcohol use on neuropsychological performance obtained. When the sample was divided by age, there were significant correlations between amount of alcohol consumed per occasion and performance on the Shipley Abstraction and Block Design tests ($r = -.33$; $r = -.28$ respectively) in subjects over 45. However, when the effects of sex and education are partialled out, these correlations are no longer significant. In summary, although alcohol consumption was unrelated to neuropsychological performance in this study, it was strongly and positively related to mood disturbance. Amount and frequency of alcohol use together account for more than 20% of the variance in mood disturbance, and the effect has both significant linear and curvilinear trends. This latter effect is due to the fact that, like heavy drinkers, abstainers tend to have greater mood disturbance than light drinkers.

Neither the rigidity factor nor the perseverative error ratio was affected by diet and alcohol use, but both were strongly positively related to age. Thus older subjects were more rigid and perseverative in their responses. This type of error is a classic age-related cognitive deficit, generally associated with the onset of cortical atrophy, predominantly in the frontal lobe (Luria, 1966).

It had been expected that general dietary quality would have a positive effect on attentional processes, but this hypothesis was not supported in the present study. Previous

research documenting this effect was conducted primarily with malnourished children, rather than well-nourished adults. This major discrepancy provides the most obvious explanation for the failure to replicate this finding. It is possible that, in children, the most basic cognitive functions such as attention are adversely affected by malnutrition, whereas in adults the effects of lower dietary quality are more subtle and neuropsychologically specific. This does not exclude the possibility that the effects of diet are, indeed, mediated more by subcortical than by cortical impairment. However, these deficits may be more obviously manifested in children by gross attentional disorders, and in adults by subtle neuropsychological decrements.

The Role of Biochemical Factors

The General Neuropsychological performance, Attention, and Rigidity factors were directly associated with the biochemical factor, potassium. Although both potassium and sodium (which loaded most highly on this factor) were related significantly to reported dietary intake of iron and magnesium, the potassium factor was not related to the general nutrition factor. Thus, its relationship to the dietary measures used in this study (which did not include potassium and sodium) is unclear. However, other studies have demonstrated an inverse relation between adult dietary restriction and serum potassium levels (Webb & Gehl, 1980). Potassium is known to play a major role in maintaining the neuronal membrane potential, and hypokalemia has been implicated in psychiatric symptoms of

nervousness, irritability, headaches and depression. Cognitive symptoms include diminished concentration, attention span, memory, and abstracting abilities (Webb & Gehl, 1980). The psychiatric and cognitive sequelae of hypokalemia are more well-documented than is the case for any other mineral or electrolyte. Thus, it is not surprising that serum potassium levels should play such a central role in general neuro-psychological performance, cognitive rigidity, and general attention. However, it is highly noteworthy that such a robust effect, on a variety of uncorrelated cognitive factors, should be obtained in a sample with a normal distribution of serum potassium levels.

The biochemical factor most strongly associated with mood was calcium. Mood disturbance declined significantly and linearly as serum calcium levels increased; calcium level accounted for approximately 10% of the variance in mood. Serum calcium showed a moderate but significant inverse association with frequency of alcohol consumption. This effect has been documented by others (e.g., Tabakoff et al., 1979), but the precise mechanism underlying this relation is unknown. It is possible that heavy alcohol use may disrupt hormonal systems (for example, parathormone), which regulate serum levels of calcium and inorganic phosphorous. Calcium is critical for the stabilization and regulation of membrane permeability, and thus for impulse initiation and propagation. It plays an equally important role in the release of neurotransmitters such as norepinephrine and acetylcholine. Hypocalcemia has

been found to result in profound symptoms of emotional lability (Webb & Gehl, 1980) and anxiety attacks (Pitts & McClure, 1967). The present study thus provides additional support to the association of calcium and mood, but in a non-deficient population. This relationship has not been documented previously in a non-hypocalcemic population.

The Role of Neuroanatomical Factors

The general neuropsychological performance factor was significantly affected by the neuroanatomical factor representing the density of the ascending white matter of the corona radiata. When the normal density value for this region was exceeded, general neuropsychological performance declined. The adverse effects of increased white matter density may be attributable either to (a) loss of myelin or (b) dehydration. The density of the corona radiata was associated strongly and inversely with general nutritional quality. Thus, as previous research suggests, dietary insufficiency may have led to subcortical myelin loss (thus increased density of the white matter), which subsequently resulted in decrements in general neuropsychological performance. If the increased tissue density was attributable to dehydration, one might expect an association of greater tissue density with reduced ventricular and/or sulcal size. That is, diffuse reduction in CSF would manifest itself in increased tissue density and decreased ventricular and sulcal size. In fact, this association is upheld: the measures of (a) sum of 4 largest sulcal widths, and (b) width of the frontal lobes have negative loadings of $-.32$ and $-.38$

respectively on the corona radiata density factor. Thus dehydration remains a very plausible alternative explanation.

There was a strong and positive relation between the serum potassium factor and corona radiata density. This result may appear somewhat confusing, as serum potassium was positively related to neuropsychological performance, while tissue density was inversely related to tissue density. However, there was a non-linear trend, of borderline significance, in the association of corona radiata density with neuropsychological performance. Thus, increases in the serum potassium factor may have been associated more with increasing tissue density below the mean (normal) value than above the mean. Below the mean, corona radiata density tended to be positively related to neuropsychological performance, as was serum potassium level. Thus the positive relation between tissue density and potassium levels may reflect a neuropsychologically healthy state of densely packed neuronal tissue in association with the necessarily abundant supply of intracellular potassium. However, as the density value of the corona radiata increases beyond normal values, and approaches and exceeds the value of subcortical grey matter, it becomes obvious that the neuropsychologically debilitating processes of myelin loss and/or dehydration are operative.

Mood was related significantly to the frontal-lobe density factor, again in a curvilinear manner. That is mood disturbance is enhanced by both low (less than one standard deviation below the mean) and high (more than .5 standard

deviation above the mean) frontal lobe density values. This tissue density factor represented the density of both white and grey matter in the frontal lobes. Thus, while low values probably reflect neuronal loss (but quite possibly edema or vasoconstriction), very high values may reflect myelin loss in white matter, dehydration throughout the frontal lobe, or hyperemia in frontal cortex. Unfortunately, there are no data which would enable one to choose among these alternative explanations.

Frontal lobe density was related positively to serum calcium levels. This is similar to the case with potassium and corona radiata density. That is, the positive association between calcium and frontal lobe density may reflect the fact that general neuropsychological performance is enhanced by normal (as opposed to subnormal) frontal neuronal density and necessary supplies of abundant calcium for the regulation of neuronal transmission.

Both amount and frequency of alcohol consumption were related inversely to frontal density, but this effect just failed to reach significance. Frequency of alcohol consumption was related positively and significantly to ventricular size, and inversely related to density of the corona radiata. Thus the notion that the effects of alcohol use are neuroanatomically restricted to the frontal lobes is not supported in this study.

Path Analyses

The major finding of the dietary path analysis is the mediating role played by corona radiata density in the

relationship between diet and general neuropsychological performance. When demographic variables are partialled out, diet accounts for approximately 10% of the variance in neuropsychological measures. Approximately 42% of this explained variance cannot be attributed to factors other than diet in the path analysis model, and is therefore termed direct. However, 58% of the diet-related variance in general neuropsychological performance can be attributed to the indirect effect of diet on corona radiata density and its effect on performance. Thus, 58% of the dietary effect is mediated by the effects of lower tissue density in the corona radiata.

The path analyses of the alcohol data are far less clear-cut regarding the mediating roles of biochemical and neuro-anatomical factors. The direct effect of amount of alcohol consumed per occasion on mood disturbance does not appear to be mediated by the effects of serum calcium, and is, in fact, attenuated or counteracted by its relation to frontal lobe density, i.e., amount of alcohol use is related to frontal lobe density, but frontal density is positively related to mood disturbance. A plausible explanation for this complex pattern lies in the curvilinear trend in the relationship between frontal density and mood. The decomposition tables for the alcohol use path analyses demonstrated that although the effect of frontal tissue density on mood disturbance was primarily positive, there was also a strong negative effect which was not explained by the model. The most compelling explanation for this is that frontal tissue density tends to inversely affect

mood disturbance at sub-normal values but that as density exceeds the norm, mood disturbance increases. Nonetheless, the role of biochemical and neuroanatomical factors in the relationship between amount of alcohol use and mood remains unclear.

The picture is somewhat clearer with frequency of alcohol consumption. It appears that, while 95% of the relationship between frequency of alcohol use and mood cannot be attributed to indirect effects in the model, 5% of the explained variance may be attributed to the indirect, or mediating effects of the serum calcium factor. Similarly, the inverse effect of frequency of alcohol use on frontal lobe density is 57% direct, and 43% of the relationship is attributable to the indirect, or mediating role of the calcium factor. This pattern of results (that is, the inverse effects of alcohol use on calcium levels and frontal density) may be a factor in the inverse part of the effect of frontal density on mood disturbance. However the trend analysis necessary to confirm this notion required a greater sample size than was available in the present study.

Conclusion

How do these results address the major objectives of this study? To summarize briefly, the present study was designed to address the following major issue: are alcohol-related psychological deficits apparent in relatively affluent, social-drinking, adults when diet, mood and other potentially confounding variables are controlled? Corollary hypotheses were (1)

Does dietary quality influence psychological performance in well-nourished, well-educated, upper socioeconomic status adults?; (2). How specific are these alcohol- and diet-related impairments with respect to psychological functioning?; (3) What are the mediating roles played by biochemical and neuro-anatomical factors in this relationship?

This study has demonstrated that mood disturbance is strongly associated with alcohol use in well-nourished, non-alcoholic adults. However, the expected association of alcohol use on neuropsychological performance was not obtained. This discrepancy from previous research on social drinking may be attributable to any one, or a combination of the following explanations: (1) in previous research, alcohol use was confounded with diet; (2) neuropsychological performance was confounded with mood in previous studies; (3) the nature of this sample (i.e., neuroradiological referrals) precluded replicating the very subtle effects of social drinking.

Factors of neurological and psychiatric disorder, acute intoxication and hunger, and withdrawal were controlled through the elimination from the study of subjects with these symptoms. The extraneous variables age, sex, and education were statistically controlled. Subsequently it was found that general dietary quality (protein-calorie and mineral intake) was significantly related to general neuropsychological performance. This study is the first to demonstrate diet-related neuropsychological deficits which are independent of socioeconomic status and age, in an affluent adult group.

Another issue addressed by this research involves the specificity of alcohol- and diet-related effects. Previous research has supported the notion that alcohol-related impairment is mediated primarily by frontal lobe dysfunction. The present study does not confirm this hypothesis. Alcohol use was more strongly related to neuroanatomical changes in ventricular size and corona radiata density than to frontal lobe alterations. On the other hand, the mood disturbance so strongly associated with both amount and frequency of alcohol use showed a strong curvilinear association with frontal lobe density. Thus, the involvement of the frontal lobes in alcohol-related dysfunction should not be discounted. Although Parker and Noble (1977; 1980) had found amount of alcohol consumed per occasion to be a more reliable predictor of alcohol-related impairment than was frequency of consumption, the present study failed to confirm this notion. Both frequency and amount of alcohol use were related to mood disturbance - frequency of consumption was significantly related to biochemical predictors of alcoholism, while amount of alcohol use was not.

The data concerning the neuroanatomical specificity of the effects of dietary insufficiency do provide some support for the notion that subcortical structures may be most affected. Previous studies have noted that the primary changes attributable to dietary restriction are subcortical myelin loss, and attentional deficits (which are classically believed to be mediated by subcortical mechanisms). The neuroanatomical factor

most affected by general dietary quality was the white matter of the corona radiata. While these changes cannot be attributed definitively to myelin loss (e.g., as opposed to dehydration), such a mechanism is highly plausible. Indeed, the mediating effects of corona radiata density appear to account for more than half of the 10% in general neuropsychological variance attributable to dietary quality. The specific roles played by different dietary nutrients could not be clearly established in this study, as subjects tended to be either generally well-nourished, or slightly lacking in all nutrients. Nevertheless, an examination of the zero-order correlations reveals that the nutrients having the strongest associations with neuropsychological performance appear to be the minerals phosphorous, magnesium, and iron.

This study also investigated the extent of the mediating roles of biochemical and neuroanatomical factors in the effects of diet and alcohol use on psychological measures. The effects of dietary quality on neuropsychological performance definitely appear to be fairly strongly mediated by the neuroanatomical density of the corona radiata. The most compelling explanation is that more than half of this relationship is due to the adverse effect of poor dietary quality on myelin formation and/or hydration in the corona radiata which, in turn, results in impaired neuropsychological functioning. There also appears to be a mediating role for serum potassium in this relationship, but its influence is less clear.

The effect of frequency of alcohol use on mood disturbance

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appears to be mediated to a small extent (5%) by serum calcium levels. The neuroanatomical measure of frontal lobe density may also play a strong mediating role in the association of alcohol use with mood, but the curvilinear nature of the relationship between frontal density and mood renders the mediating role of frontal lobe dysfunction a complex issue which must await further research for clarification.

While the present study provides very interesting and suggestive results concerning the issues it was designed to address, it has indicated a number of important questions which require further investigation. First, the effect of dietary quality on neuropsychological and neuroanatomical measures must be replicated, as this is the first study to yield such results in a well-nourished adult sample. Second, the attempt to replicate Parker and Noble's (1977; 1980) work should also be repeated in a way that controls for mood disturbance and diet, but in another (i.e., not neurological referrals) sample. Finally, dietary and alcohol use manipulations should be carried out in an experimental setting. The present study was, of course, correlational and while many exciting results were obtained, experimental manipulations of diet and alcohol use are required before one can validly discuss their neuropsychological, biochemical, and neuroanatomical effects.

TIGHT BINDING
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Appendix I

- a) Parker Alcohol Inventory: long form
- b) Parker Alcohol Inventory: short form

TIGHT BINDING
Reliure trop rigide

page 1

The following questions are concerned with your use of alcohol-containing beverages, both past and present. It is extremely important for you to answer each question as accurately as possible. It does not matter whether you never drink alcohol or whether you drink quite frequently - we need your answers to these questions.

We will follow strict guidelines to insure the complete confidentiality of your responses. Throughout the study, your responses will be identified by a number only. At no time will your name appear on your questionnaire. Please try to answer as honestly as possible.

Please take this page and put it in front of you while you complete the questionnaire. You may need to refer to it as you answer the questions.

Thank you for your cooperation.

KIND OF ALCOHOLIC BEVERAGES:

BEERS: Lager, Malt Liquor, Stout, Ale, Porter, etc.

TABLE WINES: Red, White, Rose, Sparkling wines (not fortified wines)

SPIRITS: Whiskey, Scotch, Bourbon, Rye, Gin, Rum, Vodka, Tequila

OTHERS: Fortified wines such as desert or cocktail wines, Sherry, Port, Madera, Vermouth, Muscatel, Liqueurs, Cordials, etc.

ONE DRINK:

12 oz. can of BEER (regular size)

4 oz. glass of TABLE WINES(regular size)

1 1/2 oz. of SPIRITS either mixed or straight
(regular bar drink)

2 oz. glass of OTHER BEVERAGE (cordial size)

TIGHT BINDING
Reliure trop rigide

Now we are going to ask about your use of alcohol.

200

1. How often do you usually drink alcoholic beverages (beer, wine, spirits or others)

check one

☐ 3 times a day or more

☐ 2 times a day

☐ 1 time a day

☐ nearly every day

☐ 3 to 4 times a week

☐ 1 to 2 times a week

☐ 2 to 3 times a month

☐ 1 time a month

☐ less than once a month, but at least once a year

☐ less than once a year

☐ never (If you have not had any alcohol in the past few months SKIP to Question 16)

TIGHT BINDING
Reliure trop rigide

2. What is your favorite alcoholic drink? _____

3. When you drink alcoholic beverages, how often do you drink BEER?

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

4. When you drink alcoholic beverages, how often do you drink TABLE WINES?

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

5. When you drink alcoholic beverages, how often do you drink SPIRITS?

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

6. When you drink alcoholic beverages, how often do you drink OTHER BEVERAGES?

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

Think back over the past few months.

7. How many drinks do you usually have when you drink (in the past few months)?

check one

_____ 20 or more drinks

_____ 11 - 19 drinks

_____ 9 - 10 drinks

_____ 7 - 8 drinks

_____ 5 - 6 drinks

_____ 3 - 4 drinks

_____ 1 - 2 drinks

TIGHT BINDING
Reliure trop rigide

Remember these questions are about your drinking over the past few months.

8. When you drink how often do you have 20 or more drinks at a time?

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

9. When you drink how often do you have 11 to 19 drinks at a time and no more?

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

10. When you drink how often do you have 9 or 10 drinks at a time and no more?

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

11. When you drink how often do you have 7 or 8 drinks at a time and no more?

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

12. When you drink how often do you have 5 or 6 drinks at a time and no more?

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

13. When you drink how often do you have 3 or 4 drinks at a time and no more?

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

14. When you drink how often do you have 1 or 2 drinks at a time and no more?

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

15. During the past few months, what is the most you have drunk at any one occasion?

check one

_____ 20 or more drinks

_____ 11 - 19 drinks

_____ 9 - 10 drinks

_____ 7 - 8 drinks

_____ 5 - 6 drinks

_____ 3 - 4 drinks

_____ 1 - 2 drinks

TIGHT BINDING
Reliure trop rigide

16. How long has it been since you last had a drink containing alcohol?

check one

_____ Within the past 6 hours

_____ Between 6 and 12 hours ago

_____ Between 12 and 24 hours ago

_____ Between 1 and 4 days ago

_____ Between 4 and 7 days ago

_____ 1 to 3 weeks ago

_____ Longer ago than that

17. When you last had a drink containing alcohol, how many drinks did you have?

check one

_____ 20 or more drinks

_____ 11 - 19 drinks

_____ 9 - 10 drinks

_____ 7 - 8 drinks

_____ 5 - 6 drinks

_____ 3 - 4 drinks

_____ 1 - 2 drinks

18. About how old were you when you first started drinking, disregarding small tastes of alcoholic beverages?

_____ age

19. Since you first started drinking, has there ever been a time when you drank noticeably more than you drank during the past several months?

_____ Yes

_____ No

If you answered NO please skip to Question 23.

20. How old were you when you drank more?

Age _____ to _____

21. For how long were you a heavier drinker?

_____ years _____ months

TIGHT BINDING
Reliure trop rigide

22. When you drank more than you do now, approximately how often did you usually drink alcoholic beverages?

check one

_____ 3 times a day or more

_____ 2 times a day

_____ 1 time a day

_____ nearly every day

_____ 3 to 4 times a week

_____ 1 to 2 times a week

_____ 2 to 3 times a month

_____ 1 time a month

_____ less than once a month, but at least once a year

_____ less than once a year

23. When you drank more, how many drinks did you usually have when you drank?

check one

_____ 20 or more drinks

_____ 11 - 19 drinks

_____ 9 - 10 drinks

_____ 7 - 8 drinks

_____ 5 - 6 drinks

_____ 3 - 4 drinks

_____ 1 - 2 drinks

TIGHT BINDING
Reliure trop rigide

24. Since you first started drinking, has there ever been a time when you drank noticeably less than you drank during the past several months?

_____ Yes _____ No

If you answered NO please skip to Question 29.

25. How old were you when you drank less?

Age _____ to _____

26. For how long were you a lighter drinker than you are now?

_____ years _____ months

27. When you drank less than you do now, approximately how often did you usually drink alcoholic beverages?

check one

_____ 3 times a day or more

_____ 2 times a day

_____ 1 time a day

_____ nearly every day

_____ 3 to 4 times a week

_____ 1 to 2 times a week

_____ 2 to 3 times a month

_____ 1 time a month

_____ less than once a month, but at least
once a year

_____ less than once a year

_____ never

28. When you drank less, how many drinks did you usually have on each occasion?

check one

_____ 11 drinks or more

_____ 9 - 10 drinks

_____ 7 - 8 drinks

_____ 5 - 6 drinks

_____ 3 - 4 drinks

_____ 1 - 2 drinks

_____ 0 drinks

TIGHT BINDING
Reliure trop rigide

Please answer with a check the word that best describes:

	Nondrinker	Light Drinker	Moderate Drinker	Heavy Drinker	Very Heavy Drinker	Alcoholic
29. You						
30. Your spouse, if you are currently married						
31. Your father						
32. Your mother						
33. Most of your friends						

34. Have you ever had or do you now have any of the following?

	Have you ever had		Were you treated	
	Yes	No	Yes	No
alcoholism	—	—	—	—
diabetes	—	—	—	—
headaches, frequent or severe	—	—	—	—
dizziness or fainting spells	—	—	—	—
severe head injury	—	—	—	—
been knocked unconscious	—	—	—	—
convulsions or epilepsy	—	—	—	—
severe anxiety	—	—	—	—
severe depression	—	—	—	—
excessive elation	—	—	—	—
difficulty in concentration	—	—	—	—
loss of memory (abnormally severe)	—	—	—	—
illness due wholly or in part to nervousness	—	—	—	—

TIGHT BINDING
Reluctant to rigide

Have you ever had or do you now have any of the following?

	Have you ever had		Were you treated	
	Yes	No	Yes	No
excessive sleepiness	—	—	—	—
meningitis	—	—	—	—
stroke	—	—	—	—
abnormal blood pressure	—	—	—	—
heart disease	—	—	—	—

If you answered yes to any of the above, please elaborate (how long ago, treatment of illness- if any, present condition)
Please list any medication currently used, dosage and the frequency used.

35. Do you smoke cigarettes?

Yes No

TIGHT BINDING
Reliure trop rigide

If Yes, indicate how many cigarettes you usually smoke each day.

_____ cigarettes

36. How many cups of coffee do you usually drink each day? _____ (fill in)

37. How many cups of tea do you usually drink each day? _____ (fill in)

38. How many can of cola (Coke, Pepsi, Diet Rite, Royal Crown) do you usually drink each day? _____ (fill in)

39. What was your age at your last birthday? _____

40. What is your height? _____

41. What is your present weight? _____

42. Please indicate your sex Male _____ Female _____

43. How much formal education have you had?

check nearest answer

_____ some grade school

_____ finished grade school

_____ some high school

_____ finished high school

_____ some college

_____ finished college

_____ attended graduate school or professional school
after college

44. How much formal education did your father have?

check nearest answer

_____ some grade school

_____ finished grade school

_____ some high school

_____ finished high school

_____ some college

_____ finished college

_____ attended graduate school or professional school
after college

45. Are you presently employed?

_____ Yes

_____ No, but I usually am

_____ No

_____ Retired and not presently employed

Please describe your present job. (If you are retired describe the last job you held)

46. Type of Industry _____

47. Nature of Job _____

48. How long have you had this job? _____

49. Have you ever held a job other than the one you now have?

_____ Yes _____ No

If Yes, what was the job you held for the longest time?

50. Type of Industry _____

51. Nature of Job _____

52. How long did you have this job? _____

53. Will you please indicate your present marital status

_____ married and living with spouse

_____ married and living separately from spouse

_____ common-law

_____ widowed

_____ divorced

_____ single

54. How many times have you been married? _____

0 1 2 3 4 or more

55. What is your present religious affiliation? _____

56. Mother's religion? _____

57. Father's religion? _____

58. Is English your native language?

 Yes No

59. What is your race? _____

60. Check the figure that comes closest to your present yearly family income (before taxes).

<u> </u> less than \$5,000	<u> </u> 16,000 - 20,000	<u> </u> 41,000 - 50,000
<u> </u> 6,000 - 10,000	<u> </u> 21,000 - 30,000	<u> </u> 51,000 - 60,000
<u> </u> 11,000 - 15,000	<u> </u> 31,000 - 40,000	<u> </u> more than 60,000

Parker Alcohol Inventory

- short form -

Now we are going to ask about your use of alcohol.

1. How often do you usually drink alcoholic beverages (beer, wine, spirits or others)

check one

- ☐ 3 times a day or more
- ☐ 2 times a day
- ☐ 1 time a day
- ☐ nearly every day
- ☐ 3 to 4 times a week
- ☐ 1 to 2 times a week
- ☐ 2 to 3 times a month
- ☐ 1 time a month
- ☐ less than once a month, but at least once a year
- ☐ less than once a year
- ☐ never (If you have not had any alcohol in the past few months SKIP to Question 11)

Think back over the past few months.

2. How many drinks do you usually have when you drink (in the past few months)? (7)

check one

- ☐ 20 or more drinks
- ☐ 11 - 19 drinks
- ☐ 9 - 10 drinks
- ☐ 7 - 8 drinks
- ☐ 5 - 6 drinks
- ☐ 3 - 4 drinks
- ☐ 1 - 2 drinks

Remember these questions are about your drinking over the past few months.

3. When you drink how often do you have 20 or more drinks at a time? (8)

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

4. When you drink how often do you have 11 to 19 drinks at a time and no more? (9)

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

5. When you drink how often do you have 9 or 10 drinks at a time and no more? (10)

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

6. When you drink how often do you have 7 or 8 drinks at a time and no more? (11)

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

7. When you drink how often do you have 5 or 6 drinks at a time and no more? (12)

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

8. When you drink how often do you have 3 or 4 drinks at a time and no more? (13)

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

9. When you drink how often do you have 1 or 2 drinks at a time and no more? (14)

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
never rarely half the time usually always

10. During the past few months, what is the most you have drunk at any one occasion? (15)

check one

_____ 20 or more drinks

_____ 11 - 19 drinks

_____ 9 - 10 drinks

_____ 7 - 8 drinks

_____ 5 - 6 drinks

_____ 3 - 4 drinks

_____ 1 - 2 drinks

11. How long has it been since you last had a drink containing alcohol?

(16)

check one

_____ Within the past 6 hours

_____ Between 6 and 12 hours ago

_____ Between 12 and 24 hours ago

_____ Between 1 and 4 days ago

_____ Between 4 and 7 days ago

_____ 1 to 3 weeks ago

_____ Longer ago than that

12. When you last had a drink containing alcohol, how many drinks did you have?

(17)

check one

_____ 20 or more drinks

_____ 11 - 19 drinks

_____ 9 - 10 drinks

_____ 7 - 8 drinks

_____ 5 - 6 drinks

_____ 3 - 4 drinks

_____ 1 - 2 drinks

Appendix III
Three-Day Diet Diary

Directions for Food Diary

1. Keep a record of everything you eat and drink.
2. Write down all foods and beverages consumed; eg: don't forget to mention butter on toast and vegetables, milk or cream and sugar in coffee, toppings on dessert, sauces on meat, etc.
3. For dishes containing more than one ingredient, such as sandwiches or casseroles, try to record each ingredient separately. Be as specific as possible
4. Record brand names of food, liquor etc. where applicable.
5. Try to be specific in recording amounts consumed. If unsure of ounces, for example, of meat or cheese consumed, you may draw the size and width of the serving on the back of the sheet.
6. Include all nutrient supplements and vitamin pills.
7. Be honest : Do not change your eating habits while you are keeping this diary, unless directed by physician (Please indicate if you are on a special diet and if so, the reason and period of time of the diet.)

PLEASE TRY TO RECORD YOUR FOOD
INTAKE IN THE FOLLOWING MANNER:

217

BY OUNCES

Meat - cooked weight
Cheese - ounces or slices
Lunchmeat & bacon slices

BY FLUID OUNCES

Soup, juice, milk
Beer, wine, soft drinks
Mixed drinks breakdown
of ingredients

BY CUP

Cooked vegetables
Cereals
Desserts, ice cream
Canned fruits
Salads

BY TEASPOON OR TABLESPOON

Sugar
Butter or oleo - or by pat
Salad dressing, gravy
Syrup, jam, jelly
Creaming product in coffee
or tea

BY SLICE

Cake, pie
Bread
Tomato slices

BY COUNT

Crackers, cookies, nuts
Eggs, hot dogs
Fresh fruit

Date:

Amount

Amount²¹⁸

Breakfast: Place:
Time:

Snack: Place:
Time:

Snack: Place:
Time:

Dinner: Place:
Time:

Lunch: Place:
Time:

Snack: Place:
Time:

Date:

Amount

Amount 219

Breakfast: Place:
Time:

Snack: Place:
Time:

Snack: Place:
Time:

Dinner: Place:
Time:

Lunch: Place:
Time:

Snack: Place:
Time:

Date:

Amount

Amount 220

Breakfast: Place:
Time:

Snack: Place:
Time:

Snack: Place:
Time:

Dinner: Place:
Time:

Lunch: Place:
Time:

Snack: Place:
Time:

Appendix III

Psychological Tests: Instructions for Administration and
Scoring, and Test Forms Used

- A) Continuous Performance Test
- B) Psychiatric Interview Schedules (Research Diagnostic Criteria) for Psychotic Symptoms and Alcoholism
- C) Profile of Mood States
- D) Shipley Institute of Living Scale
- E) Wechsler Adult Intelligence Scale: Block Design and Digit Symbol Subtests
- F) Wisconsin Card Sort Test
- G) Verbal Fluency Test
- H) Design Fluency Test

CPT

NAME: _____

DATE: _____

PHASE I/X - FP

PHASE II/AX - FP

PHASE III/X - DP

	PHASE I/X - FP	PHASE II/AX - FP	PHASE III/X - DP
CHAS.			
LINE			
INC.			
COST			
ACC. PL.			
ET.			
TOTAL			
CPT			
ACC CPT			
MTTR			
WASTE.			

Research Diagnostic Criteria
Psychiatric Interview Schedule

Patient: _____ Location & No.: _____

Completed by: _____ Date: _____ Dx: _____

NO	PROBABLE	YES (DEFINITE)
----	----------	----------------

1. SCHIZOPHRENIA. A through C required for period being considered.....

A. During active illness: 2 of following for definite; 1 for probable.#...

- *1. Thought broadcasting, insertion or withdrawal *
2. Delusions of control (influence) or bizarre or multiple del.*.....
3. Other delusions (cf manual) except persecutory or jealous; 1 wk...
4. Delusions of any type if accomp. by halluc. for 1+ wk.....
- * 5. Audit. hall. voices commenting on pt. or 2 voices conversing.....
6. Non-affective verbal halluc. * spoken to pt.....
7. Halluc. any type thru day for sev. days or interm. 1 month.....
- > 8. Def. inst. marked formal thought disorder* accomp. by either: bl. or inappr. affect, del. or halluc. any type, grossly disorg. behav.

B. Signs of illness lasting at least 2 wks from onset (current may be res.)

C. Criteria 5A, 5B, 9A & 9B not met during active period illness.....

2. SCHIZO-AFFECTIVE DISORDER, MANIC TYPE. A through E required.....

A. Criteria 5A met.....

B. Criteria 5B met.....

C. At least one of following during active illness.....

1. Criteria 1A1 met.....
2. Criteria 1A6 thru day for sev days or interm. 1 wk period.....
3. Criteria 1A5 met.....
4. 1 week with no prom. depressive or manic Sx but had del. or hall..
5. Criteria 1A8 met more than 1 wk in absence of prom. manic Sx.....

D. Signs of illness lasting at least 1 week from onset (current may be res)

E. Affective Sx overlap to some degree with schiz Sx.....

3. SCHIZO-AFFECTIVE DISORDER, DEPRESSED TYPE. A through E required.....

A. Criteria 9A met.....

B. Criteria 9B met.....

C. At least one of the following is present.....

1. Delusions of being controlled or meets criteria 1A1.....
2. Criteria 1A6 thru day for sev. days or interm. thru 1 week.....
3. Criteria 1A5 met.....
4. More than 1 month with del. or hall. (not depr rel) & no prom a...
5. Preocc. with a del or hall to rel exclusion of other Sx (not dep)...
6. Criteria 1A8 met.....

D. Signs of illness lasting at least 1 wk from onset (current may be res.)

E. Affective Sx overlap to some degree with active schiz Sx.....

NOTES: * If Sx in this group only assoc. with drug or alcohol, Dx = 22.0

* Use definition provided in full manual.

DEPRESSIVE SYNDROME SUPERIMPOSED ON RESIDUAL SCHIZOPHRENIA. A through C required ☐ ☐ ☐

A. Meets criteria for Residual Schizophrenia (see schiz. subtypes, p).. ☐ ☐ ☐

B. Meets criteria 9A and 9B..... ☐ ☐ ☐

C. The depressive syndrome is prominent & relatively persistent 1+ weeks... ☐ ☐ ☐

MANIC DISORDER. (May precede or follow Dx9.) A through E required..... ☐ ☐ ☐

A. Period(s) w. predominant elevated, expansive or irritable mood @..... ☐ ☐ ☐

B. If mood elev. or xpansive 3 of following; if irritable only, than 4 @.. ☐ ☐ ☐

1. Increased activity socially, work, sexually, home or phys. restl.. ☐ ☐ ☐

2. More talkative than usual or felt pressure to keep talking.... ☐ ☐ ☐

3. Flight of ideas* or subjective experience that thots are racing... ☐ ☐ ☐

4. Inflated self esteem (grandiosity, which may be delusional)..... ☐ ☐ ☐

5. Decreased need for sleep..... ☐ ☐ ☐

6. Distractibility - attn. too easily drawn to trivial ext. stimuli.. ☐ ☐ ☐

7. Xs involvement in activities w/o recognizing poss. painful conseq. ☐ ☐ ☐

C. At least 1 of the following..... ☐ ☐ ☐

1. Meaningful conversation impossible..... ☐ ☐ ☐

2. Serious impairment socially, family, home, school or work..... ☐ ☐ ☐

3. In absence of 1 or 2, hospitalization..... ☐ ☐ ☐

D. Duration of manic features 1+ week or any duration if hospitalized..... ☐ ☐ ☐

E. None of the following present (do not include if due to drug or EtOH).. ☐ ☐ ☐

1. Criteria 1A1..... ☐ ☐ ☐

2. Criteria 1A6 thru day for sev. days or interm. 1 week..... ☐ ☐ ☐

3. Criteria 1A5..... ☐ ☐ ☐

4. More than 1 wk with del or halluc. and no prom. manic or depr. Sx. ☐ ☐ ☐

5. More than 1 wk meeting criteria 1A8 with no prominent manic Sx... ☐ ☐ ☐

HYPMANIC DISORDER. (May precede or follow Dx 9.) A through D required.... ☐ ☐ ☐

A. Distinct period with predom. elevated, xpansive or irritable mood..... ☐ ☐ ☐

B. If mood elev. or xpansive 2 signs from 5B; if only irritable 3 from 5B. ☐ ☐ ☐

C. Duration 2-6 days = probable; duration 1 week = definite..... ☐ ☐ ☐

D. Does not meet criteria for Dx 1, 2, 3 or 5..... ☐ ☐ ☐

BIPOLAR DEPRESSION WITH MANIA (BIPOLAR 1) At some time in his life has met criteria for 5 and 9, 10, or 11. Prob. if manic diagnosis only prob..... ☐ ☐ ☐

BIPOLAR DEPRESSION WITH HYPOMANIA (BIPOLAR 2). At some time in his life has met criteria for 6 and 9, 10 or 11. Has never met criteria for 5. Prob. if Dx of 6 only probable..... ☐ ☐ ☐

NO
PROBABLE
DEFINITE

226

MAJOR DEPRESSIVE DISORDER (may precede or follow Dxd) A through F required.

A. Distinct period of dysphoric mood or loss of int. or pleasure.....

B. 5 of following for definite; 4 for prob. (prev. episode 4 & 3 resp.)...

1. Poor appetite or st. loss or incr. appetite or wt. gain: change of 1 lb. a wk for several wks or 10 lbs a yr. when no diet.....
2. Sleep difficulty or sleeping too much.....
3. Loss of energy, fatigability or tiredness.....
4. Psychomotor agitation or retardation - not subjective.....
5. Loss of interest in usual activities incl. soc & sex (not if del)..
6. Self reproach, excessive or inappr. guilt - may be delusional.....
7. c/o or shows decr. concentration or indecisive (not if frm thot d)
8. Recurrent thoughts of death or suicide or any suicidal behavior...

C. Duration 1 - 2 wks = Prob.; more than 2 wks = Definite.....

D. Sought or was sent to help, took meds or impaired in home, work or soc.

E. None of the following suggesting schizophrenia are present.....

1. Criteria 1A1.....
2. Criteria 1A6 for several days or intermittent for 1 week.....
3. Criteria 1A5.....
4. Del. or halluc other than depr. related for 1 mo. w/o prom. depr..
5. Preoccupation with del or halluc other than depr to exclusion oSx..
6. Criteria 1A8.....

F. Does not meet criteria for Dx of (Schizophrenia, residual subtype.....

UNSPECIFIED FUNCTIONAL PSYCHOSIS. A and B required.....

A. Does not meet criteria for 1, 2, 3, 5 or 9.....

B. One of the following.....

1. Delusions.....
2. Hallucinations.....
3. Incoherence.....
4. Grossly bizarre behavior (e.g. disrobing in public, unprovoked shouting & yelling at passers-by).....

OTHER PSYCHIATRIC DISORDER. Cannot fit any other Dx. A and B required.....

A. One of the following.....

1. Picture not suggestive of RDC Dx but does suggest known disorder..
2. 1 or more RDC Dx suspected but Sx too minimal to meet criteria....
3. Cannot determine chronology of Sx. e.g. Ethanol & hallucinations..
4. Inadequate information to establish a definitive diagnosis.....
5. Likely known organic etiology such as alcohol, drug abuse, fever..

B. If a disturbance in mood, thinking or behavior 1 of the following req..

1. Sought or was referred for help from someone.....
2. Took medication other than occas h.s. hypnotic for insomnia.....
3. Impairment in functioning with family, home, work, school or soci.

NO
PROBABLE
DEFINITE

A. Based on the course of the present period of schizophrenia.

- [illegible]

--	--	--

NO
PROBABLE
DEFINITE

SAMPLES OF SCHIZO-AFFECTIVE DISORDERS

A. Based on the course of the present period of schizo-affective dis.

1. Acute schizo-affective disorder. A through C required.....
 - a. Sudden onset: less than 3 mos to Sx in 2C or 3C.....
 - b. Short course: cont. ill w significant signs schiz less t 3 mo
 - c. Full recovery from any previous episode.....
2. Subacute schizo-affective disorder. Course closer to acute than ch
3. Subchronic schiz-aff disorder. Course closer to chronic than acute
4. Chronic schiz-aff disorder. Sig. signs schiz cont. pres 2 yrs.....

B. Temporal relationship of affective and schizophrenic-like features.

1. Mainly schizophrenic. A or B required.....
 - a. Core Sx in 2C or 3C present 1+ wk in absence of manic or depr
 - b. Prior to affective Sx had features assoc w schiz: soc w'd'r'l impaired occup. f'n., eccentric, blunted, unusual thots perc
2. Mainly affective. A and B required.....
 - a. Sx in 2C or 3C followed manic or depr Sx & were never present for more than 1 wk in absence of manic or depr. Sx.....
 - b. Good premorbid social and occupational adjustment.....
3. Other: Does not clearly fit either 1 or 2.....

C. Length of time from 1st signs incr. pathol. to any core Sx from 2C or 3C.

1. Less than 2 days.....
2. Less than 1 week.....
3. Less than 1 month.....
4. Less than 2 months.....
5. More than 2 months.....

"Significant signs of schizophrenia" are any signs listed in 1A when considering schizophrenia or the signs in 2C or 3C when considering schizo-affective disorders AND: "other delusions or hallucinations, extreme social withdrawal, mild formal thought disorder, or unusual thoughts or perceptual experiences."

Research Diagnostic Criteria
Alcoholism Interview Schedule

Yes

No

1. Has your family ever objected to your drinking? — —
2. Did you ever think you drank too much in general? — —
- 3. Have others ever said you drink too much for your own good?
(such as friends, physicians, clergymen, etc) — —
4. Have you ever felt guilty about drinking? — —
5. Have you ever lost friends because of drinking? — —
6. Did you ever get into trouble at work because of drinking? — —
7. Did you ever lose a job on account of drinking? — —
8. Did you ever have trouble with auto driving (speeding, accident, etc) because of drinking? — —
9. Have you ever been arrested, even for a few hours, because of drinking and/or disturbing the peace? — —
10. Have you ever gotten into fights when drinking? — —
11. have you ever gone on benders? (48 hours of drinking associated with default of usual obligations: must have occurred more than once). — —
12. Have you ever wanted to stop drinking and couldn't? — —
13. have you ever tried to control your drinking by trying to drink only under certain circumstances (time of day, places, associates)? — —
14. Did you ever drink before breakfast? — —
15. Did you ever drink unusual things such as hair tonic, paint solvent, rubbing alcohol? — —
16. Have you ever had memory losses when drinking? (Blackouts) — —
17. Have you ever experienced impotence associated with drinking? — —
18. St's, shakes, liver disease, or other medical complications? — —

Profile of Mood States

Shipley Institute of Living Scale

At 1 below, the first word in each line is printed in capital letters.
The first word are four other words. Draw a line under the one word
meaning the same thing, or most nearly the same thing, as the first word.
If you are not sure, guess. A sample has been worked out for you.

BOOK 22
07-08/
09-10/
11-12/

SAMPLE

LARGE red big silent wet

are to underline the one word in each line that means the same thing as
the first word.

BEGIN HERE

VA —
AA —
CQ —

(1) TALK	draw	eat	speak	sleep
(2) PERMIT	allow	sew	cut	drive
(3) PARDON	forgive	pound	divide	tell
(4) COUGH	pin	eraser	sofa	glass
(5) REMEMBER	swim	recall	number	defy
(6) TUMBLE	drink	dress	fall	think
(7) HIDEOUS	silvery	titled	young	dreadful
(8) CORDIAL	swift	muddy	leafy	heartly
(9) EVIDENT	green	obvious	skeptical	afraid
(10) IMPOSITOR	conductor	officer	book	pretender
(11) MERIT	deserve	distrust	fight	separate
(12) FASCINATE	welcome	fix	stir	enchant
(13) INDICATE	defy	excite	signify	bicker
(14) IGNORANT	red	sharp	uninformed	precise
(15) FORTIFY	submerge	strengthen	vent	deadend
(16) RENOWN	length	head	fame	loyalty
(17) NARRATE	yield	buy	associate	teal
(18) MASSIVE	bright	large	speedy	low
(19) HILARITY	laughter	speed	grace	malice
(20) SPURCHED	stolen	pointed	remade	soiled

(21) SQUANDER	tease	belittle	cut	waste
(22) CAPTION	drum	ballast	heading	ape
(23) FACILITATE	help	turn	strip	bewilder
(24) JOCOSE	humorous	paltry	fervid	plain
(25) APPRISE	reduce	strew	inform	delight
(26) RUE	eat	lament	dominate	cure
(27) DENIZEN	senator	inhabitant	fish	atom
(28) DIVEST	dispossess	intrude	rally	pledge
(29) AMULET	charm	orphan	dingo	pond
(30) INEXORABLE	untidy	involatile	rigid	sparse
(31) SERRATED	dried	notched	armed	blunt
(32) LISSOM	moldy	loose	supple	convex
(33) MOLLIFY	mitigate	direct	pertain	abuse
(34) PLAGIARIZE	appropriate	intend	revoke	maintain
(35) ORIFICE	brush	hole	building	lute
(36) QUERULOUS	maniacal	curious	devout	complaining
(37) PARIAH	outcast	priest	lentil	locker
(38) APET	waken	ensue	incite	placate
(39) TEMERITY	rashness	timidity	desire	kindness
(40) PRISTINE	vain	sound	first	level

OFFICE
USE ONLY

DECK 42

13-14/

15-16/

17-18/

PART II

Complete the following. Each dash () calls for either a number or a letter to be filled in. Every line is a separate item. Take the items in order, but don't spend too much time on any one.

START HERE

- 1) 1 2 3 4 5 _
- 2) white black short long down _ _
- 3) A3 BC CD D _
- 4) 2 Y X W V U _
- 5) 1 2 3 2 1 2 3 4 3 2 3 4 5 4 3 4 5 6 _ _
- 6) NE/SW SE/NW E/W N/ _
- 7) escape scape cape _ _ _
- 8) oh ho rat tar mood _ _ _
- 9) A Z B Y C X D _
- 10) tot tot bard drab 537 _ _ _
- 11) mist is wasp as pint in tone _ _
- 12) 5 7 3 2 6 7 3 2 6 5 3 2 6 5 7 2 6 5 7 3 _ _ _ _
- 13) knit in spud up both to stay _ _
- 14) Scotland landscape scapegoat _ _ _ _ ee
- 15) surgeon 1234567 snore 17635 rogue _ _ _ _
- 16) tan tan rib rid rat raw hip _ _ _
- 17) tar pitch throw saloon bar rod fee tip end plank _ _ _ _ meals
- 18) 3124 82 73 46 13 _
- 19) lag leg pen pin big bog rob _ _ _
- 20) two w four r three _

ages 237 - 241.

are not to be
filmed due to

Copyright Material

Wisconsin Card Sort Test

WISCONSIN CARD SORT

4 Cards

1. Ask patient to tell what he sees -
 Patient tells you what he sees -
 if not, correct, or add adjective
 (make sure not color blind)

2. Now this stack of cards is for you - what I would like you to do is
 take these cards one at a time and match them with one of these four
 cards(point)according to some characteristic.

I can't tell you what that character is, but I will tell you after
 you sort each card whether you have done it correctly or incorrectly.

What you can do is make little piles under the stim cards and once
 you put a card down you have to leave it there - I will tell you
 whether you are correct or incorrect. Use that to help you to figure
 out how to sort the next card.

10 correct in a row: Switch categories

60 incorrect, stop test

Do 6 categories or 128 cards, whichever comes first.

When the subject has made 10 responses, the cards are placed on
 a tray, the tray is shifted to the next set of cards. The testing is
 continued until the subject has completed ³ sets of 10 or has used more
 than 60 cards in a single set.

When testing is completed, tally the total number of trials
 in which the subject has responded correctly. Count the number of trials in which
 the subject has responded incorrectly. Count the number of trials in which the
 subject has responded correctly ¹⁻⁶ ~~1-6~~ ¹⁻⁶ ~~1-6~~.

Verbal Fluency Test

Design Fluency Test

1) VERBAL FLUENCY

In the next 5 minutes write down as many words as you can think of beginning with the letter S

They can't be common names like Sam or Suzy but must be common words that you might find in a dictionary.

2) DESIGN FLUENCY

A/ In the next five minutes I would like you to draw as many different designs as you can think of. These drawings cannot represent any real or actual objects. Also they must be very different from one another.

Try not to scribble because scribbles look so much alike.

1. Warning - I can name that it looks like a

That one looks very much like this one.

unacceptable

acceptable

Appendix IV
CAT-Scan Scoring Form

NAME _____

X-Ray No. _____

Date _____

Run No. _____

Contrast _____

Non-Contrast _____

A. Clinical Ratings:

1. Global Assessment of Sulci _____

2. Global Assessment of Ventricles _____

B. Linear Measurement

1. Cortical

- a. Sum of width of 4 largest sulci _____
- b. Width of Interhemispheric fissure _____
- c. Width of innertable of skull to frontal lobe
 1. Right _____
- 2. Left _____
- d. Width of frontal lobes _____

2. Ventricular

- a. Width of 3rd ventricle-level of thalmus _____
- b. Width of lateral ventricles at frontal
 horns (A) and width of caudate nucleus (B)

A= _____

B= _____

$$A + B = C$$

C= _____

(Single Measure of Ventricular Size)

C. Region of Interest

- 1. Frontal Lobes (Areas 9, 10, 11 and 12)
 - a. Right _____
 - b. Left _____
- 2. Frontal lobes (Anterior to Frontal Horns)
 - a. Right _____
 - b. Left _____
- 3. Thalmus
 - a. Right _____
 - b. Left _____
- 4. Corona Radiata
 - a. Right, _____
 - b. Left _____
- 5. Brain stem _____

Slice 3

Slice 5

Slice 6

Slice 8

Slide Two

UNCUS

Amygdala

Margie 496-4588

- Dr Charks Office

- describe validity amendment to protocol
- study of normal volunteers
- how to amend ; due date ; processes

CARLETON UNIVERSITY

Appendix V

Zero-Order Correlations of Diet, Alcohol Use and Serum Nutrients
with Psychological Measures*

- A) Dietary Nutrients and Psychological Measures
- B) Alcohol Use and Psychological Measures
- C) Serum Nutrients and Psychological Measures
- D) Alcohol Use and Dietary Nutrients
- E) Alcohol Use and Serum Nutrients
- F) Serum Nutrients and CAT-Scan Measures

*Only correlations significant at $p < .05$ are reported.

Appendix 5A

Dietary Nutrients and Psychological Measures

	Poms Total	Block Des	Drg Syn	SILS AA	Verb Flu	Des Flu	WCTS TTC	WCS: PE
Calories		.398	.297	.258	.259	.266		
Carbo's		.287	.244			.306		
Protein		.264	.254	.234	.275			
Fats		.213	.247					
Vit. A								-.211
Thiamine								
Riboflav.								
Phosph.		.331	.186	.213	.190	.20	-.228	
Iron		.304	.261		.273			
Magnes.		.278			.226	.245	-.178	
Calc.								
Vit. B6								
Vit. B12								
Niacin	.273							

Appendix 5B

Alcohol Use and Psychological Measures

	<u>Amt/Occasion</u>	<u>Frequency of Alc. Use</u>
POMS:Total	.436	.354
Block Des		
Digit Sym		
SILS VA		
SILS AA		
Verbal Flu.		
Verbal Persev		
Design Flu		.239
Design Persev		
WCST:TTC		
WCST:PE		
Attention	.185	

Appendix 5C

Serum Nutrients and Psychological Measures

	Calc.	Inorg. Phos.	Gluc.	Alk Phos	Na	K	Hgb	RBC
POMS:Tot	-.302					-.235		
Bi. Design						.322		
Big Sym	.303					.299		
SILS:VA								
SILS:AA	.237							
Verb. Flu								
Verb. Persev		-.225				-.212		
Des. Flu			.248					
Des. Persev					.361			-.281
WCST:TTC	-.295		-.298			-.23		
WCST:PE								

Appendix 5D

Alcohol Use and Dietary Nutrients

	Amt./Occ.	Frequency
Calories		
Carbo's		
Protein		
Fats		
Vit. A		
Thiamine		
Riboflavin		
Phosphorous		
Iron		
Magnesium	.217	.204
Calcium	.237	
Vit. B6		
Vit. B12	.193	
Niacin		

III

The Relation of Amount of Alcohol Use with Mood Disturbance

Appendix 5F

Serum Nutrients and CAT-Scan Measures

	Calc.	In. Phos.	Gluc	Alk. Phos.	Na	K	Hct	RBC
Global:								
1) Sulci				-.284				
2) Ventricles	-.446							
Linear:								
3) Sulci				-.343				
4) Int. Hem. Fis	-.405		-.501	-.428		-.428		
5) Rt. Fr. Subdur					.399			
6) Lt. Fr. Subdur								
7) Width Fr. L.				-.406	-.345			
8) 3rd Vent.	-.487			-.313		-.337	-.353	
9) Ant. Horns	-.414	.310						
10) Lat. Vent.	-.473							
Density:								
11) Rt. Fr. Grey	.421							
12) Lt. Fr. Grey	.462							
13) Rt. Fr. White	.375	-.289				.275		
14) Lt. Fr. White	.305					.302		-.325
15) Rt. Thal				.331				
16) Lt. Thal				.377				
17) Rt. Cor. R.				.470				
18) Lt. Cor. R.				.328				
19) Br. Stem				.292				

Appendix VI

Scattergrams for Figures I to VII

I

The Relation of Diet with Neuropsychological Performance

24/09/81

PAGE

(C) 1981

NO. 1000 OF THE 1000000000

SECTION 1000

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SECTION 1000

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SECTION 1000

SECTION 1000

SECTION 1000

04/08/00

II

The Relation of Frequency of Alcohol Use with Mood Disturbance

STATISTICS OF AGE, SEX, RACE

STATISTICS

POPULATION (84)

POP. AGE OF 15+

POP. AGE OF 15+

137858

192716

102

6.00000

1.00000 (10)

EXTRACTED VALUES

1.1112

1.1112

0

0.00000

0.1111

0.00000

0.00004

0.00154

8

***** IS RELATED TO A CORRELATION COEFFICIENT *****

III

The Relation of Amount of Alcohol Use with Mood Disturbance

STATION

STATION (18)

EST -

VALUES -

1980

1981

1982

107

IV

Relation of Potassium with Neuropsychological Performance

STATISTICS OF SIX NATION DATA

FILE SYSTEM (CREATION DATE = 08/02/83)

SCATTERGRAM OF (DEEN) NEURON

STATISTICS OF AGE N. PSY DATA

STATISTICS..

CORRELATION (R) -

STD ERR OF EST -

PLOTTED VALUES -

0.20000

0.20000

0.20000

R SQUARED

INTERCEPT (A)

ADJUSTED VALUES

0.160

0.160

0.160

0.160

0.160

0.160

0.160

0.160

0.160

***** IS OBTAINED IF A CORRELATION COEFFICIENT IS OBTAINED

V

Relation of Calcium with Mood Disturbance

SCATTERS OF AGE DATA

STATISTICS

CORRELATION (R)

STD ERR OF EST

PLOTTED VALUES

INTERCEPT

CALCULATED VALUES

STATISTICS IS PRINTED IF A

VI

Relation of Corona Radiata Density with Neuropsychological
Performance

SCATTERING OF WAVE NUMBER DATA
 FILE: SYSPLE (CREATION DATE = 04/02/91)
 SCATTERING OF (DOWN) NUMBER

3.41

2.84

2.27

1.69

1.12

.54

-.03

-.61

-1.13

-1.75

-2.37

0.4

-1.17

-1.36

-2.03

-1.13

-2.37

STATISTICS
 CORRELATION (R) - .7701
 COR. ERR OF EST - .0004
 EXCLUDED VALUES - 62
 IS POINTED TO A CORRELATION ANALYSIS

VHI

Relation of Frontal Lobe Density With Mood Disturbance

CONTENTS OF NSL R-55V DATA

FILE SYSTEM: ACQUISITION DATE = 04/09/93

CONTENTS OF (P140) TOMS101M

CONTENTS OF (P140) TOMS101M

CONTENTS OF (P140) TOMS101M

CONTENTS OF (P140) TOMS101M

CONTENTS OF (P140) TOMS101M

CONTENTS OF (P140) TOMS101M

CONTENTS OF (P140) TOMS101M

CONTENTS OF (P140) TOMS101M

CONTENTS OF (P140) TOMS101M

CONTENTS OF (P140) TOMS101M

3.79

2.99

2.40

1.90

1.41

.91

.42

-.08

-.57

-1.07

-1.56

-1.99

1.40

2.09

2.40

2.90

1.41

.91

.42

-.08

-.57

-1.07

-1.56

-1.99

-1.99

-1.72

-1.45

-.99

-.52

-.05

.41

.80

1.01

1.40

1.90

2.40

2.90

1.41

.91

.42

-.08

-.57

-1.07

-1.56

-1.99

4 4

OF / DE

Variable	Mean	Standard Deviation
Alcohol Use		
a) no. drinks/occasion	3.37	3.69
b) frequency/year	161.49	264.05
Dietary Intake (% RDA)		
a) Calories	81.25 (1746.3 kcal)	29.6
b) Protein	141.80	52.5
c) Carbohydrates	59.38	21.8
d) Fats	95.27	50.6
e) Vitamin A	211.55	155.8
f) Vitamin C	351.59	444.1
g) Thiamin	347.70	1047.4
h) Niacin	188.50	175.1
i) Riboflavin	326.01	919.9
j) Vitamin B6	263.41	824.4
k) Vitamin B12	272.87	593.0
l) Phosphorous	133.79	49.6
m) Iron	109.69	57.3
n) Magnesium	82.15	30.3
o) Calcium	82.09	42.8
Psychological Performance		
a) SIIS: Verbal	32.14	6.14
b) SIIS: Abstraction	25.71	8.71
c) POMS: Total Mood Disturbance	151.58	37.69
d) CPT: XDP: no. correct	53.84	5.52
e) Verbal Fluency Quantity	37.68	13.6
f) Verbal Fluency % Persev.	2.53	3.36
g) Design Fluency Quantity	18.2	10.79
h) Design Fluency % Persev.	8.88	9.79
i) WCST: Trials to Criterion		
j) WCST: Perseverative Ratio		
k) WAIS: Block Design (Adj.)	12.16	3.115
l) WAIS: Digit Symbol (Adj.)	12.53	2.85

END

1 1.0 4 8 6

FIN