

## **Cognitive Dysfunction and the Inherited Predisposition to Alcoholism:**

**NOTE:** There are three abstracts attached to this paper -- each describing a study which demonstrates the utility of the neuropsychological battery compiled for the original study.

## Provocation, Acute Alcohol Intoxication, Cognitive Performance, and Aggression

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This study investigated the relationships between provocation, acute alcohol intoxication, impaired frontal-lobe function, and aggressive behavior. The authors ranked 114 men according to their performance on two neuropsychological tests associated with frontal-lobe function. Forty-eight men (24 with scores in the upper and 24 with scores in the lower performance quartiles) participated in the full study. Half completed an aggression task while intoxicated, the remainder while sober. Aggression was defined as shock intensity delivered to a sham opponent. Shock intensity significantly increased as a main effect of provocation, alcohol intoxication, and lower cognitive performance. Furthermore, provocation interacted significantly with test performance such that individuals in the lower cognitive performance quartile responded to increased provocation with heightened aggression.

Violence presents a serious and growing challenge to North American society. More than a million and a half individuals are victims of violent crime each year (U.S. Bureau of the Census, 1991); 20,000 are murdered (Prothrow-Stith, 1990). Aggression can be defined as any behavior directed toward the goal of harming another living being who is motivated to avoid such treatment (Baron & Richardson, 1994). Various antecedents to aggressive behavior have been implicated, including social, situational, and individual determinants. A major social determinant of aggression is provocation, in the form of verbal insult, physical attack, or other noxious stimuli (Hammock & Richardson, 1992).

One of the most important situational determinants of aggression is acute alcohol intoxication, which is associated with more than half of all homicides, assaults, rapes, and cases of family violence (Murdoch, Pihl, & Ross, 1990). Bushman and Cooper's (1990) meta-analytic review of over 30 controlled laboratory studies concluded that alcohol-intoxicated individuals are significantly more verbally and physically aggressive. However, every one who drinks does not become aggressive, and the study of characteristics of predispositions to aggressive responses becomes particularly relevant.

Many individual determinants including personality traits, attitudes, genetic factors, and sex differences have been implicated in aggressive behavior (Baron & Richardson, 1994; Wood, Wong, & Chachere, 1991). The occurrence of a violent act in

response to external factors is thought to require the interaction of various cognitive processes, including planning of behavior and consciousness of the act and its consequences (Tancred Volkow, 1988). As the frontal cortices are thought to be involved in the highest level of goal-directed activity, including organization and planning of behavior (Damasio, 1979; Lu, 1980), the present study focused on individual differences in performance on neuropsychological tests of frontal-lobe function.

Some neuropsychological evidence associates frontal-lobe deficits with poorer regulation of human social behavior. Individuals with frontal-lobe damage often exhibit a "disinhibition syndrome" characterized generally by impulsivity and socially inappropriate behavior (Hecaen & Albert, 1978; Miller, 1979). If damage occurs early enough in life, it can result in the development of pervasive abnormalities of affective and social behavior (Eslinger & Damasio, 1986) and the inability to accommodate social impulses into the total personality structure (Ack & Benton, 1948).

Furthermore, some research links various forms of antisocial behavior with poor performance on putative frontal-lobe function measures (Buikhuisen, 1987; Lueger & Gill, 1990; Moore, 1990). However, one review concluded that despite the evidence supporting a specific relationship between violent criminal behavior and frontal-lobe dysfunction, alternative explanations could not be ruled out (Kandel & Freed, 1989).

A theoretical explanation for how impaired frontal-lobe function might lead to impaired regulation of social behavior is that there is a disturbance of the synthesis of external and internal cues underlying the regulation of complex behavior (Luria, 1980). As a consequence, behavior is governed more by impulse, current focus of attention, or salient stimulus cues than by rules or plans (Luria, 1980). Although this condition would not necessarily lead to increased aggression under normal circumstances, it might in situations where the salient cue is provocation and where peripheral or less contingent cues that inhibit aggression, such as fear of violence-related consequences

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## Cognitive Function, Cardiovascular Reactivity, and Behavior in Boys at High Risk for Alcoholism

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Boys (average age = 12.1 years) from families with an extensive history of paternal alcoholism differed from controls of similar age and IQ on measures of cognitive function, cardiovascular reactivity, and parent-rated conduct problems. High-risk boys performed most poorly on neuropsychological tests of frontal lobe function. According to tests of temporal organization and conditional-associate learning, control over working memory was the frontal subfunction primarily affected. A mental arithmetic task also elicited greater heart rate increases and peripheral vasoconstriction among high-risk boys than among controls. After controlling for group status, significant correlations remained between frontal lobe test scores and disruptive behavior and between cardiovascular hyperreactivity and anxiety levels. The possible contribution of these findings to alcohol abuse was discussed.

Behavioral genetic methods have been used to identify individuals with a predisposition to develop alcoholism (Goodwin, 1984) and have spurred attempts to identify characteristics, either biological or environmental, that distinguish them from the general population. Empirically derived markers observed prior to the onset of alcoholism may reflect underlying etiologic mechanisms. However, it is widely accepted that the causes of alcoholism are multidetermined and that alcoholics and their vulnerable family members form a heterogeneous population (Pihl, Peterson, & Finn, 1990; Sher, 1991). The specific effect of any single marker will probably not be as important to etiology as the total number of operative risk factors (Tarter, 1988). Research into vulnerability for alcoholism should benefit, then, from diverse approaches to identifying the most probable set of risks.

We examined two sets of characteristics associated with paternal alcoholism that may contribute to both the onset and advancement of alcoholism (Peterson, Finn, & Pihl, 1992; Pihl & Peterson, 1992). The first of these concerns the stress-dampening response to alcohol. Autonomic nervous system reactivity, particularly cardiovascular response to aversive and nonaversive stimuli, has distinguished the at-risk group from normal controls and offspring from families where alcoholism is limited to a single member (Finn & Pihl, 1987, 1988). This autonomic hyperreactivity is moderated by alcohol. Daughters of male multigenerational alcoholics have also exhibited electrodermal reactivity to novelty that was normalized by a moderate dose of

alcohol (Stewart, Finn, Peterson, & Pihl, 1994). Drinking may serve the function of normalizing states of hyperarousal in these individuals, and their informal attempts to self-medicate could develop into alcohol dependence over time.

If hyperreactivity is associated with etiology, then it should predate experimentation with alcohol and correlate with behaviors or traits related to alcohol use, such as conduct disorder, extroversion, or anxiety. In previous studies with adults, cardiovascular response was induced by the threat of electric shock. Research with children presented an opportunity to evaluate autonomic nervous system response to less aversive stimuli. If alternative induction procedures are successful, the generality of the hyperreactivity phenomenon would be enhanced. During mental stress, heart rate reactivity occurs independently of somatic activity and metabolic demand. Cardiac response to laboratory stressors is also fairly representative of heart rate response to a number of naturalistic, "real-world" challenges, especially in cardiovascularly hyperreactive individuals (Turner, 1989). Enhanced cardiovascular arousal during a competitive mental arithmetic task was therefore expected to characterize the high-risk group.

The second characteristic is a profile of cognitive dysfunction drawn from neuropsychological tests designed to test the functional integrity of the frontal lobes (Peterson et al., 1992). Several research groups attempted to delineate patterns of cognitive functioning that represent the at-risk population and obtained mixed results. This had led some to discount cognitive impairment as an etiological factor in alcoholism (Alterman & Hall, 1989). However, variable methodologies may have contributed to this confusion. Studies have not always screened for potential confounds of cognitive ability such as craniocerebral injury, birth trauma, febrile seizures, and fetal alcohol syndrome (West & Prinz, 1987). The definition of high risk has sometimes permitted the inclusion of participants with limited genetic predisposition. Results have also differed according to the battery of tests administered. Comprehensive neuropsychological test batteries were typically designed to localize lesions

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## Cognitive and Neuropsychological Characteristics of Physically Aggressive Boys

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Cognitive-neuropsychological tests were given to adolescent boys ( $N = 177$ ) to investigate processes associated with physical aggression. Factor analysis yielded 4 factors representing verbal learning, incidental spatial learning, tactile-lateral ability, and executive functions. Physical aggression was assessed at ages 6, 10, 11, and 12, and 3 groups were created: stable aggressive, unstable aggressive, and nonaggressive. The authors found main effects for only the executive functions factor even when other factors were used as additional covariates in a step-down analysis; nonaggressive boys performed better than stable and unstable aggressive boys. The covariates family adversity and anxiety were both related only to the verbal learning factor. This study highlights the importance of deficits in executive function in the expression of physical aggression relative to other cognitive-neuropsychological functions.

The likelihood of expressing violent behavior is multifactorial (Raine, 1993) and probably interactive (Pennington & Benvenuto, 1993), thus making the delineation of mechanisms of this complex behavior obscure. Attention has been given to social factors (Haapasalo & Tremblay, 1994; G. R. Patterson & Yoerger, 1992); personality in adolescence (Tremblay, 1992) and adulthood (Sigvardsson, Bohman, & Cloninger, 1987); psychophysiological profiles (Raine, Venables, & Williams, 1990); hormonal profiles (Dabbs, Jurkovic, & Frady, 1991); genetic background (Morell, 1993); and neuropsychological motivational processes (C. M. Patterson & Newman, 1993). Regarding the latter approach, deficits in cognitive-neuropsychological abilities early in life, the focus of this study, have been viewed as contributing to an impulsive behavioral style in a brain-environment interaction (Moffitt, 1993b) and to transactionally affect social maturity (Buikhuisen, 1987) and consequent likelihood of aggressive responding.

Both cognitive and behavioral similarities have been noted between individuals who have had frontal lobe damage, some-

times called the *pseudopsychopathic syndrome* (Moffitt, 1990; Stuss & Benson, 1984) or *acquired sociopathy* (Eslinger & Damasio, 1985), and those who show characteristics of antisocial behavior (Price, Daffner, Stowe, & Mesulam, 1990; Weiger & Bear, 1988). This observation has been a major impetus for the research of neuropsychological abnormalities in antisocial individuals. The authors of recent literature reviews (Buikhuisen 1987; Kandel & Freed, 1989; Moffitt, 1990, 1993a; Pennington & Benvenuto, 1993; see also reviews in J. S. Milner, 1991) and several other studies (e.g., Hurt & Naglieri, 1992; Lueger & Gill 1990; Moffitt, Lynam, & Silva, 1994) unanimously conclude that impairments in cognitive functions are implicated in the regulation of aggressive behavior.

Three major classes of cognitive impairment seemingly associated with aggressive behavior are those affecting executive functions, verbal abilities, and abnormalities in cerebral dominance. *Executive functions* (also called *conative* or *control functions*) describe capacities for the initiation and maintenance of efficient attainment of goals (Lezak, 1985). They are typically derived from tests that assess primarily programming and planning of goal-oriented motor behavior skills, modulation of behavior in light of expected future consequences, anticipation of events in the regulation of behavior, learning of contingency rules and the ability to use feedback cues, inhibition of response set and flexibility (vs. perseveration), abstract reasoning, problem solving, sustained attention, and concentration. These abilities require active monitoring, operate within working memory (Petrides, Alivisatos, Evans, & Meyer, 1993), and have been associated with frontal lobe activity (Lezak, 1980; Welsh & Pennington, 1988). These important functions, historically overshadowed by a focus on more easily managed abilities related to speech, perception, and memory, have been more extensively studied in the past 20 years (Benton, 1994).

Weaknesses in verbal skills affect language-based performance in areas such as receptive listening and reading, expressive speech and writing, and memory for verbal material.

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# Cognitive Dysfunction and the Inherited Predisposition to Alcoholism\*

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**ABSTRACT.** A battery of neuropsychological tests was administered to 22 nonalcoholic sons of male alcoholics (SOMAs) from families with extensive histories of male alcoholism and to 22 nonalcoholic controls with no history of familial alcoholism. In each group 11 subjects were tested while sober and 11 were tested while alcohol-intoxicated. Analyses of the results of this battery suggested (1) that SOMAs may be characterized by comparative decrements in those cognitive functions associated with the organization of novel information, dependent in theory upon the prefrontal cortex; and (2) that alcohol detrimentally affects delayed memory, associated with the

temporal cortex, equally across groups. Of these SOMAs 20 had previously participated in one of two studies that demonstrated their cardiovascular hyper-reactivity to threat/stress and their increased sensitivity to the reactivity-dampening effects of alcohol intoxication. Correlational analyses of the results of the present and previous studies demonstrated the existence of a highly significant relationship between cognitive impairment, cardiovascular hyper-reactivity and susceptibility to the reactivity-dampening effects of alcohol. (*J. Stud. Alcohol* 53: 154-160, 1992)

**A** VARIETY of studies have demonstrated that the sons of male alcoholics (SOMAs) are at heightened genetic risk for the development of alcoholism. None of these studies are above reproach methodologically (Lester, 1988; Murray et al., 1983; Searles, 1988), but taken collectively they suggest that SOMAs are three to nine times more likely to become alcoholic than are the sons of non-alcoholics (Cloninger et al., 1988; Goodwin, 1985). The precise nature of this increased risk remains unknown, but in recent years a number of markers that appear in association with it have been tentatively identified (Begleiter and Porjesz, 1988). These markers have been described critically, in detail, by Pihl et al. (1990).

A number of studies have demonstrated that SOMAs perform more poorly than controls on tests of linguistic ability, abstraction and problem solving (Drejer et al., 1985; Gabrielli and Mednick, 1983; Whipple et al., 1988). Additional evidence exists suggesting that SOMAs hyper-react psychophysiologically to threat and novelty (Finn and Pihl, 1987, 1988; Finn et al., 1990). Tarter et al. (1985, 1988) have drawn a parallel between the cognitive and behavioral styles of SOMAs and of those with minor prefrontal cortical trauma. Gray (1982, 1987), Luria (1980), Vinogradova (1975), Nauta (1974), Sokolov (1969) and

Granit (1977) reviewed general neuropsychological information suggesting (1) that the prefrontal cortex provide the physiological substrate for the cognitive functions associated with abstract classification and planning; (2) that the prefrontal cortex serves to inhibit or modulate the function of various subcortical structures, including those governing threat or novelty response; (3) that the hippocampus and hypothalamus are critically involved in this threat response; and (4) that alcohol intoxication might interfere with hippocampal function.

Peterson and Pihl (1990), integrating these sources of information, have hypothesized that SOMAs have difficulty in abstractly classifying and/or in modulating their reaction to threatening or novel information, perhaps because of mild decrements in prefrontal function. They suggest alcohol consumption might ameliorate the negative subjective consequences of this difficulty—associated with increased physiological reactivity—by interfering with the function of the novelty/threat response system.

Three primary hypotheses were derived from this theory, for the purposes of the present study. It was predicted that (1) sober SOMAs would perform more poorly than controls on cognitive tests of classification and planning generally associated with prefrontal function; (2) alcohol intoxication would interfere with the performance of both groups on those neuropsychological tests that putatively assess transfer of information into long-term memory, as associated with the hippocampus; (3) decrements in prefrontal function among SOMAs would be correlated with their cardiovascular hyper-reactivity to threat. These hypotheses

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were to be tested in three parts. The first part involved assessment of the neuropsychological function of stringently selected sober SOMAs and controls, in order to help determine if and in what manner their cognitive abilities differed. The second part involved a similar assessment, conducted upon intoxicated SOMAs and controls, in order to help determine primarily what neuropsychological functions alcohol intoxication impairs per se and, further, to investigate whether SOMAs and controls differ in their susceptibility to alcohol's effect on cognition. The third part of the study involved investigation of the relationship between the cognitive functioning of these SOMAs and their previously reported (Finn and Pihl, 1987, 1988) cardiovascular reactivity, and sensitivity to dampening (Finn and Pihl, 1987, 1988) of that reactivity by alcohol consumption.

### Method

#### *Subjects*

Two groups of 22 ( $N = 44$ ) nonalcoholic men participated in this study. All subjects scored 5 or less on the Michigan Alcoholism Screening Test (MAST) (Selzer, 1971) and none could be characterized as alcohol dependent or abusing by the criteria set forth in the DSM-III (American Psychiatric Association, 1980). Subjects younger than 18 and older than 30 years of age were excluded from participation. Those who completed the study had a mean age, equivalent across groups, of approximately 24 years. All subjects were raised by their biological parents; all were white.

In the first of these two groups were SOMAs who had at minimum, in addition to their father, a paternal grandfather and brother or paternal uncle who were alcoholic according to diagnoses made at a major Montreal psychiatric institution, where families of alcoholics are screened, interviewed, referred for counseling and recruited as potential subjects for a number of interdisciplinary research efforts. At this institution, extensive family histories are taken from as many family members as possible. Diagnoses for the interviewed members are based on the MAST and DSM-III criteria. Unavailable family members are diagnosed according to the Family History Research Diagnostic Criteria (FH-RDC) (Endicott et al., 1975). Subjects are selected according to these stringent criteria in order to increase the likelihood that they truly are at increased genetic risk for the inheritance of alcoholism. This increased risk is reflected in the fact that 76% of the first- and second-degree male relatives of subjects selected in this fashion are alcoholic (Finn and Pihl, 1987). SOMAs had an average of 13.4 years of education and drank between 5 and 15 drinks a week. Mean age of onset of paternal alcoholism was 20 years. Probands with alcoholic mothers, with mothers who drank during pregnancy or with psychotic relatives were excluded.

In the second group were 22 men recruited by newspaper advertisement as paid controls. Healthy nonalcoholic moderate social drinkers (between 5 and 15 drinks/week) with between 13 and 14 years of education were selected for participation. Control subjects had no identifiable alcoholism (MAST and DSM-III criteria) in the past two generations of their pedigree. Control subjects familiar with psychological experimentation or who had psychotic relatives were excluded from participation. An augmented group of these subjects also served as controls in the concurrently run Peterson et al. (1990) study.

All subjects were asked to refrain from the consumption of alcohol for 24 hours and from food for 4 hours before the experimental session. Subjects were paid \$5 per hour for their participation.

#### *Design and procedure: Parts 1 and 2*

Upon arrival at the laboratory subjects were familiarized with the experimental procedure and were required to sign an informed consent form. Each subject was then randomly assigned to receive either 1.32 ml/kg of 95% pharmaceutical alcohol mixed 5:1 in orange juice or to receive an equivalent amount of juice by body weight and 0.132 ml/kg pharmaceutical alcohol, to provide "active placebo" (Ross and Pihl, 1989) control for subject and experimenter expectancy. All subjects were then submitted to a battery of neuropsychological tests. An independent-groups design with random group assignment was chosen specifically to control for the effect of practice on the neuropsychological test battery.

It should be noted additionally that, although expectancy and dose generally confound the effects of a drug (Marlatt and Rohsenow, 1980), previous experience with the test battery used in this study, within the confines of a multiple-dose balanced-placebo design, indicated that it was insensitive to the effects of expectancy and sensitive to the pharmacological effects of a 1.32 ml/kg dose of 95% pure pharmaceutical alcohol (Peterson et al., 1990).

Each subject was given three drinks and was asked to finish them within 20 minutes. After a 15-minute waiting period, each subject was given the first of three subjective intoxication scales and the first of three breathalyzer tests. The former were completed privately to control for the effects of experimenter demand. Subjects were then taken to a separate testing area where they were administered the following tests in random order by three experimenters blind to the subject's risk status and assigned condition. These tests were chosen for heuristic purposes, and were classified accordingly, because the cognitive abilities they test have been experimentally associated with the function of relatively specific cortical areas. It should be noted, however, that there is no simple one-to-one relationship

between cortical locale and cognitive function. Nonetheless, since the neuropsychological approach allows in part for analysis of cognitive functioning per se, and, further, provides for the possibility of clarifying the nature of the relationship between cognition and cortical functioning, its utility outweighs the inherent risk of oversimplification.

*Tests of cognitive function often associated with the prefrontal cortex*

*Porteus Maze (extension series).* Subjects are required to complete a series of mazes ranked according to difficulty. Individuals with lesions of the frontal lobes demonstrate impairments in their ability to correctly complete this test (Crown, 1952; Malmö, 1948; Mettler, 1952) which was designed to measure planning and foresight (Porteus, 1959).

*Rey-Osterreith Complex Figure: Copy.* Subjects are required to copy a complex spatial figure from an original. Individuals with prefrontal damage copy this figure (Lezak, 1976) and complex figures in general (Luria, 1980) poorly, although parietal damage may also produce performance deficits (Lezak, 1976) of a more severe sort.

*Thurstone Word Fluency.* Subjects are required to write as many words beginning with "S" as possible in 5 minutes. Individuals with left frontal damage consistently demonstrate impairments in word fluency (Benton, 1968; Ramier and Hecaen, 1970) which measures the ability to generate words according to an abstract conceptual category.

*Self-Ordered Pointing (SOP): 12 representational drawings.* Subjects must point to a different one of 12 pictures of familiar objects, presented in 12 different arrays. Individuals with frontal damage consistently manifest deficits in performance on this task, which requires the ability to organize information conceptually. Individuals with temporal damage also manifest deficits that vary with the severity of their lesion (Petrides and Milner, 1982), although temporally damaged individuals also tend to suffer from severe memory loss.

*Wisconsin Card Sort Test (WCST).* Subjects are presented sequentially with 64 cards, and are required to categorize them according to feedback provided by an investigator. Individuals suffering from dorso-lateral frontal lesions perform poorly on this test, which is sensitive to perseveration (Grant and Berg, 1948; Milner, 1964).

*Tests of memory often associated with the temporal cortex*

*Wechsler Logical Memory: Immediate and 25-minute delay.* Subjects are required to repeat two stories, in sequence, once immediately after presentation and once (unknown to them a priori) 25 minutes later, after completion of a number of other tasks. Individuals with temporal (particularly hippocampal) damage perform poorly on these tests, especially after a delay (Milner, 1975).

*Wechsler Paired Associates: Difficult and easy pair.* Subjects are orally presented three times with 10 word pairs and are required to remember the second word in each pair. Six pairs are easy and four difficult to associate. Individuals with left temporal (particularly hippocampal) damage have difficulty in completing this test, and there is additional evidence that organic brain damage particularly impairs recall of the difficult pairs (Walsh, 1978).

*Rey-Osterreith Figure: Reproduction from memory.* Subjects are required to redraw the figure they copied 2 minutes earlier, with no a priori knowledge that they are to do so, after completing several other tasks. Patients with right temporal (particularly hippocampal) damage have difficulty in completing this task (Milner, 1975).

*Tests of cognitive function often associated with the parietal-occipital cortex*

*Albert's Test of Visual Neglect.* Subjects are given pencil and a sheet of paper with a number of short lines printed on it, and are asked to bisect each line with another short line. Subjects who suffer from parietal damage perform particularly poorly on this test (Albert, 1973).

*Apraxia questionnaire.* Subjects are required to originate and/or duplicate a number of simple motor operations. This questionnaire provides a general measure of ideomotor, ideational and buccofacial apraxia, which has been operationally defined by exclusion as a disorder of skilled movement not caused by weakness, deafferentation, abnormal tone or posture, movement disorder, intellectual deterioration, poor comprehension or lack of cooperation (Heilman and Valenstein, 1985).

*Miscellaneous tests*

The Information subtest of the Revised Wechsler Adult Intelligence Scale (WAIS-R) provided a measure of accumulated verbal knowledge. The Digit Symbol WAIS-I subtest was included because it is sensitive to variation in motivation (Lezak, 1976) and as a measure of performance IQ. A Reaction Time Test, with three subtests of increasing complexity, was included to assess motor speed.

Tests were completed within 1.5 hours. Subjects were given a breath-analyzer test and a subjective intoxication scale half-way through and at the end of the test session debriefed and, upon regaining sobriety (BAC < .04) were paid \$25 and allowed to leave.

*Part 3*

Twenty of the 22 SOMAs who volunteered for the present study had previously participated in one of two projects that demonstrated their augmented cardiovascular hyper-reactivity to threat/stress and their increased sensi-

tivity to the reactivity-dampening effects of alcohol, in comparison to matched controls (Finn and Pihl, 1987, 1988). Participants in these studies were subjected to a number of successive electric shocks (1.85 mA for 0.25 seconds), whose onset was signaled by a 10-second count-down, once while sober and once under the influence of either 1.00 or 1.32 ml of 95% pure pharmaceutical alcohol per kg of body weight, in counterbalanced order. In these studies, sober SOMAs from families with extensive male familial alcoholism reacted to the shock procedure with significant increases in heart rate (HR) and significant decreases in digital blood volume amplitude (DBVA) (cardiovascular reactivity) in comparison to controls, whereas when these subjects were alcohol-intoxicated this characteristic cardiovascular hyper-reactivity was essentially eliminated (cardiovascular reactivity dampening).

The theory presented by Peterson and Pihl (1990) and discussed earlier predicts that deficits in the cognitive functions associated with the prefrontal cortex should be accompanied by increased cardiovascular reactivity to threat and that alcohol intoxication should eliminate that reactivity. Exploratory correlational analyses comparing prefrontal function, cardiovascular reactivity and alcohol-induced reduction of reactivity were therefore completed.

## Results

### Parts 1 and 2

The nature of the relationship between risk, alcohol intoxication and neuropsychological performance was explored statistically by 2 (SOMA/Control)  $\times$  2 (Alcohol/No-Alcohol) analyses of variance (ANOVA), employed separately for each measure. Post hoc tests of simple

main effects were employed in the single case of the Thurstone Word Fluency Test, where interaction effects reached significance.

Subjects of each risk status maintained equivalent mean blood alcohol concentrations of approximately .10 for the duration of the test period and rated themselves as equally intoxicated on all three scales of subjective intoxication. No subjects in either group or condition made any errors while carrying out the tasks associated with Albert's Test of Visual Neglect or the apraxia questionnaire. Nevertheless, the analyses demonstrated two primary effects (Table 1). One can be attributed to risk status, the other to the consequences of intoxication.

With regards solely to risk status: SOMAs manifested comparative decrements in performance on the Rey-Osterreith (copy) ( $F = 5.2$ , 1/40 df,  $p < .05$ ), Self-Ordered Pointing ( $F = 11.3$ , 1/40 df,  $p < .001$ ), Difficult Paired Associates ( $F = 5.87$ , 1/40 df,  $p < .05$ ) and Information tests ( $F = 4.8$ , 1/40 df,  $p < .05$ ). With regards solely to intoxication: Alcohol consumption impaired the performance of individuals in both risk categories, on the Porteus Maze ( $F = 4.1$ , 1/40 df,  $p < .05$ ), Rey-Osterreith (copy) ( $F = 5.2$ , 1/40 df,  $p < .05$ ), Wisconsin Card Sort ( $F = 4.1$ , 1/40 df,  $p < .05$ ), Easy Paired Associates ( $F = 5.3$ , 1/40 df,  $p < .05$ ), Difficult Paired Associates ( $F = 8.2$ , 1/40 df,  $p < .01$ ), Delayed Rey-Osterreith Figure ( $F = 24.7$ , 1/40 df,  $p < .001$ ) and Delayed Logical Memory ( $F = 15.6$ , 1.40 df,  $p < .001$ ) tests. Additionally, SOMAs and controls were differentially affected by alcohol while completing the Thurstone Word Fluency Test ( $F = 5.5$ , 1/40 df,  $p < .05$ ), in that the controls were significantly impaired ( $F = 6.3$ , 1/40 df,  $p < .05$ ) while the SOMAs were not.

TABLE 1. Tests of cognitive function mean ( $\pm$  SD) scores

	Sons of alcoholics		Controls	
	No Alcohol	Alcohol	No Alcohol	Alcohol
<b>Tests associated with the prefrontal cortex</b>				
Porteus Maze Age	13.9 $\pm$ 3.4	<sup>1</sup> 12.7 $\pm$ 3.1	14.9 $\pm$ 1.3	<sup>1</sup> 13.0 $\pm$ 1.8
Rey-Osterreith Copy	<sup>*</sup> 31.7 $\pm$ 4.6	<sup>*</sup> 26.9 $\pm$ 6.2	32.7 $\pm$ 3.3	<sup>1</sup> 31.9 $\pm$ 2.4
Thurstone Fluency	<sup>3</sup> 38.4 $\pm$ 13.1	<sup>2</sup> 42.1 $\pm$ 10.7	<sup>2</sup> 50.0 $\pm$ 9.3	<sup>3</sup> 39.0 $\pm$ 8.2
Self-Ordered Pointing	<sup>*</sup> 5.4 $\pm$ 1.4	<sup>*</sup> 5.8 $\pm$ 3.8	3.3 $\pm$ 1.9	3.2 $\pm$ 1.4
Wisconsin Card Sort	20.4 $\pm$ 9.5	<sup>1</sup> 23.7 $\pm$ 6.7	14.9 $\pm$ 7.7	<sup>1</sup> 22.9 $\pm$ 11.4
<b>Tests associated with the temporal cortex</b>				
Logical Memory	9.4 $\pm$ 2.8	8.0 $\pm$ 3.1	10.6 $\pm$ 3.6	8.9 $\pm$ 2.7
Logical Memory Delay	8.9 $\pm$ 3.2	<sup>1</sup> 4.7 $\pm$ 2.4	9.4 $\pm$ 3.1	<sup>1</sup> 6.6 $\pm$ 2.9
Paired Associate (E)	17.0 $\pm$ 1.5	<sup>1</sup> 15.4 $\pm$ 2.0	17.0 $\pm$ 1.5	<sup>1</sup> 16.1 $\pm$ 2.2
Paired Associate (D)	<sup>*</sup> 7.1 $\pm$ 1.5	<sup>*</sup> 4.7 $\pm$ 3.3	8.9 $\pm$ 2.1	<sup>1</sup> 6.7 $\pm$ 3.2
Rey-Osterreith Delay	20.2 $\pm$ 6.6	<sup>1</sup> 13.0 $\pm$ 5.9	22.1 $\pm$ 5.8	<sup>1</sup> 12.4 $\pm$ 3.8
<b>Miscellaneous tests</b>				
Information	<sup>*</sup> 20.5 $\pm$ 4.7	<sup>*</sup> 20.7 $\pm$ 4.3	22.8 $\pm$ 3.3	23.4 $\pm$ 2.2
Digit Symbol	59.9 $\pm$ 9.6	54.4 $\pm$ 6.4	59.3 $\pm$ 7.4	60.0 $\pm$ 8.0
Reaction Time	34.7 $\pm$ 5.8	37.7 $\pm$ 5.8	34.8 $\pm$ 6.7	33.5 $\pm$ 5.7

Risk effect: <sup>\*</sup> $p < .05$ . Drug effect: <sup>1</sup> $p < .05$ . Interaction: <sup>3</sup> $p < .05$ .

Note: Scores for the Self-Ordered Pointing are reported as total errors in three trials of 12. Scores for the Wisconsin Card Sort are reported as total errors in 64 trials.

TABLE 2. Correlation matrix

	Pearson correlation coefficients ( <i>N</i> = 20)					
	HR Increase	HR Dampen	DBVA Decrease	DBVA Dampen	Self-Ordered Pointing	Wisconsin Card Sort
HR Increase	.86	.83	.73	.57	.69	
	.0001	.0001	.0002	.0082	.0007	
HR Dampen		.79	.73	.77	.54	
		.0001	.0003	.0001	.0137	
DBVA Decrease			.88	.52	.69	
			.0001	.0192	.0010	
DBVA Dampen				.42	.54	
				.0673	.0140	
Self-Ordered Pointing					.53	
					.0169	

### Part 3

In order to examine the relationship between prefrontal function/planning and cardiac hyper-reactivity/alcohol dampening, scores on the five tests associated with the prefrontal cortex (Porteus Maze, Rey-Osterreith (copy), Self-Ordered Pointing, Wisconsin Card Sort and Thurstone Word Fluency) were included in a Pearson product-moment correlation matrix along with two indices of sober stress/threat reactivity (HR increase and DBVA decrease) and two indices of alcohol-intoxication-induced stress/threat reactivity dampening (HR increase reduction and DBVA decrease reduction). A number of correlation coefficients in this matrix approximated or exceeded the alpha 0.0025, determined by Bonferroni correction for matrix size (alpha (0.05) divided by the number of correlations of interest (20)). These correlations are presented in Table 2. It is of interest to note that the correlation between WCST performance and HR increase improves when only those who completed the WCST sober ( $n = 11$ ) are considered ( $r = 0.75$ ,  $p < .009$ ) and falls for those who took the test drunk ( $r = 0.49$ ,  $p < .18$ ). This is an important consideration from the methodological viewpoint, because alcohol detrimentally affected WCST scores for both groups. It is also interesting to note that HR reactivity (increase) is highly correlated with HR ( $r = 0.86$ ,  $p < .0001$ ) and DBVA ( $r = 0.73$ ,  $p < .0002$ ) dampening, and that DBVA reactivity (decrease) is highly correlated with DBVA ( $r = 0.88$ ,  $p < .0001$ ) and HR ( $r = 0.79$ ,  $p < .0001$ ) dampening.

Two separate canonical correlation analyses were also conducted to further aid in exploring the nature of the relationship between neuropsychological performance and cardiovascular reactivity and to provisionally determine how much of the variance in the latter could be accounted for by the former. The first of these analyses examined the relationship between the neuropsychological variables SOP and WCST and HR and DBVA reactivity; the second examined the relationship between SOP/WCST and HR/DBVA dampening. Significant correlations emerged in the

former case (1st canonical correlation  $r = 0.75$ ;  $R^2 = 0.57$ ; Wilks' lambda  $F = 4.2$ , 4/32 df;  $p < .008$ ) and in the latter (1st canonical correlation  $r = 0.81$ ;  $R^2 = 0.65$ ; Wilks' lambda  $F = 6.4$ , 4/32 df;  $p < .0004$ ).

### Discussion

#### Parts 1 and 2

Sober SOMAs could be distinguished from controls by their performance on four cognitive tasks: the Self Ordered Pointing, Rey-Osterreith (copy), Difficult Pairs Associates and WAIS-R Information tests. Successful completion of the Self-Ordered Pointing Test requires the generation of a workable strategy for memory and intact memory itself (Petrides and Milner, 1982). Although temporal damage, and subsequent memory loss, can interfere per se with performance on this test, tests most sensitive to temporal damage (delayed recall) did not distinguish SOMAs from controls. This suggests that comparative lack of organization accounts for their poorer performance. Accurate copying of the Rey-Osterreith figure requires intact spatial perception, a putative function of the parietal cortex (Luria, 1980) and the ability to organize complex novel nonverbal visual information into logical subgroups (Lezak, 1976; Luria, 1980). Although both parietal and frontal damage can interfere with performance on this test (Lezak, 1976), the fact that SOMAs performed well on the tests for apraxia and neglect, but comparatively poorly on other frontal tests, suggests that lack of organization, rather than impairment in spatial perception, accounted for their minor, but statistically significant, performance decrement.

The development of a mnemonic device or another similar strategy for aiding memory also seems crucial to success on the Difficult Paired Associates subtest, although obviously also involves recall per se. The easy word pairs are matched according to inherent association (e.g., baby cries), and one word serves as a cue for the other during memory trials. No inherently meaningful associations exist for the difficult pairs (e.g., crush-dark) and must then

fore be invented. The fact that SOMAs performed at par with regards to the easy pairs, but comparatively poorly on the difficult pairs, suggests once again that SOMAs are characterized by decrements in the ability to organize or categorize information. Although none of these individual tests can be considered conclusive in isolation, the overall pattern of results suggests that sober SOMAs may be characterized by deficits in the ability to organize and categorize novel information. This ability has been most commonly associated with the function of the prefrontal cortex (Luria, 1980). The deficit in accumulated knowledge, demonstrated by the Information subtest of the WAIS-R, is a possible consequence of this primary dysfunction, which may well have existed in some form since birth.

Three tests of those cognitive abilities associated with the prefrontal cortex proved mildly sensitive to the debilitating effects of alcohol intoxication (Porteus Maze, Rey-Osterreith copy and Wisconsin Card Sort Test). However, those cognitive abilities associated with the functions of the temporal cortex—particularly of the hippocampus—were even more severely affected. Subjects who had consumed alcohol were impaired in their recall of word pairs (Easy and Difficult Paired Associates), in delayed recall for a narrative (Delayed Logical Memory) and for nonverbal information (Delayed Rey-Osterreith Figure). This pattern of results, equal for both groups, is in keeping with that suggested/reported by Gray (1982). Direct evidence supporting the contention that alcohol interferes with hippocampal function has also recently been reported (Lovinger et al., 1989).

The single interaction effect detected by the Thurstone Word Fluency Test is interesting and suggests perhaps that SOMAs are less sensitive to the detrimental effects of alcohol on word fluency than are controls. It is not unreasonable to suppose that those who are predisposed to abuse alcohol benefit maximally from its positive attributes and suffer minimally from its drawbacks, at least in the short term.

### Part 3

Two particularly interesting patterns of correlations emerged with regards to the theoretical relationship between cognitive performance and cardiovascular reactivity: scores on the Wisconsin Card Sort Test (WCST) were highly correlated with sober HR increase and DBVA decrease to signalled shock. This means that those who made the most errors during the WCST were most reactive to the signalled shock. Scores on the Self-Ordered Pointing Test (SOP) were correlated similarly with sober HR increase and DBVA decrease, although not as strongly. Performance on both tests was also correlated with alcohol-induced HR and DBVA reactivity dampening, most significantly for SOP and HR dampening.

This means that those who made the most errors during the SOP were most susceptible to the HR reactivity-dampening effect of alcohol. This general line of reasoning is supported by the results of the canonical correlation analysis. Although this analysis should be considered exploratory because of the small sample size involved, it adds credence to the notion that poorer cognitive performance and increased cardiovascular reactivity/alcohol dampening are significantly related in multi-generational SOMAs.

With respect to the relationship between general cardiovascular reactivity and cardiovascular reactivity dampening, sober HR increase was highly correlated with alcohol dampening of that increase and, similarly, sober DBVA decrease was highly correlated with alcohol dampening of that decrease. Sober HR increase was also highly correlated with DBVA dampening and, likewise, sober DBVA decrease was highly correlated with HR dampening. This combination of results suggests that alcohol intoxication essentially eliminates reactivity within the confines of the present paradigm.

### Conclusion

This study provides tentative support for the hypothesis that sober SOMAs from families with extensive multi-generational male alcoholism are characterized by comparative decrements in the ability to classify or to attribute meaning to novel information. This ability has been classically associated with prefrontal cortical function. This study also demonstrates the existence of a significant relationship between certain aspects of this cognitive deficit and the cardiovascular hyper-reactivity and alcohol-reactivity-dampening characteristic of such SOMAs and that such reactivity and dampening are integrally related. In addition, demonstration that alcohol intoxication severely impairs the transfer of information from short-term storage into permanent memory in SOMAs and controls lends additional credence to Gray's (1982, 1987) report that alcohol intoxication particularly impairs hippocampal function.

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