STATIC ATAXIA AS A PSYCHOBIOLOGICAL MARKER FOR ALCOHOLISM

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Supported by Grant AA05909 from the National Institute on Alcohol Abuse and Alcoholism

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ABSTRACT

Sons and daughters of male alcoholics were compared to the sons and daughters of controls on two measures of static ataxia. Increased sway was seen in the children of the alcoholic fathers who had an average of 3.7 first and second degree relatives meeting criteria for alcoholism. The possibility that static ataxia may be a psychobiological marker for the more genetically mediated variant of alcoholism is discussed.
Vulnerability for developing alcoholism undoubtedly involves the interaction of both genetic and environmental factors. The evidence for genetic mediation includes a higher incidence of alcoholism in biological relatives of alcoholic probands as contrasted with the incidence of other psychiatric disorders in these relatives as well as predictable increases in the incidence of the disorder with increases in the proportion of shared genes. Studies of monozygotic and dizygotic twins, half-siblings reared apart, and parents and offspring separated by adoption all point to genetic factors contributing to the familial aggregation of alcoholism.

When alcoholism is considered to be a unitary trait, then its inheritance is compatible with multifactorial inheritance. However, recent findings from studies ongoing in St. Louis and Sweden indicate that alcoholism cannot be considered a homogeneous, discrete disorder. Cloninger and colleagues have proposed two genetically distinct forms of alcoholism, a "milieu-limited" form and a "male-limited" form. The former is characterized by milder alcohol use in parents of the proband alcoholic, minimal criminality, and greater variation in the expression of the disorder with varying environments. The latter, which tends to be transmitted primarily from father to son, includes familial criminality, and tends to be expressed independent of environmental conditions. Recognition of the heterogeneous nature of alcoholism may facilitate the search for psychobiological markers for increased risk to developing alcoholism.

One potential psychobiological marker, static ataxia, has shown great promise as a marker, because it has now been replicated in three previous studies. Lipscomb and colleagues, studying blood alcohol discrimination in family history positive and family history negative college students, were the first to observe that those with a family history of alcoholism exhibited more sway than those without such a history, both in the sober
condition and while drinking. Measuring the body sway of children using an apparatus patterned after Lipscomb, Hegedus and colleagues found increased sway in the offspring of alcoholic fathers as contrasted with offspring of normal fathers. Moreover, the children of alcoholic fathers proved to have more sway than children whose fathers met Research Diagnostic Criteria (RDC) for major depressive disorder. Lester and Carpenter reported that children of alcoholic fathers could be distinguished from children of normal fathers, taking into account a number of variables such as height, weight, and sex and including a broader range of ages of offspring. The results obtained in their study are even more persuasive that static ataxia may be a useful psychobiological marker in that the phenomenon is sufficiently robust to be detected using a different measurement technique. Lester and Carpenter used a movement platform rather than the harness technique used in previous studies.

The present study was undertaken to determine if similar results could be obtained using children of alcoholic probands who are part of a larger ongoing study of highly selected families in which multiple measures of potential markers are recorded. Because of the selection criteria which are used, the resulting families may be said to be high density families. Families are selected if there are two adult male alcoholic sibs and one non-affected sib. Their parents are included in the assessments as well, many of whom are alcoholic. Thus, the children for whom static ataxia measures were conducted are the third generation for whom marker data is being collected in our laboratory. Using the distinction between milieu and male-limited subtypes of alcoholism, the present children are most probably those at risk for developing what Cloninger and colleagues term the male-limited form of the disorder. The male-limited form appears to be more strongly transmitted by factors that are genetically mediated. While the transmission of this form appears to be primarily from father to son, the risk for transmission from fathers to daughters
is currently less well known. Goodwin et al. (15) studying female adoptees, some of whom had biological fathers who were alcoholic and some of whom did not, found too few cases within the entire sample (2 each) to determine if transmission of alcoholism is greater in daughters of male alcoholic probands. Because this more genetically mediated form has been better characterized for male-male transmission, it has been termed "male-limited." However, if in fact this more genetically mediated form occurs in women as well as men, then daughters of male alcoholics (particularly those with multiple affected relatives) may have an increased genetic risk. Therefore, daughters might be expected to show similar deviations on this psychobiological marker as has been reported for male children who are at risk (12,13).

SUBJECTS AND METHODS

Subjects

Children whose fathers were either alcoholic or free of all psychopathology (normal fathers) and who had participated in other research in our laboratories, were invited, with the parents' consent, to participate in the present study. Presence of alcoholism or other psychopathology was diagnosed in the fathers and other relatives using a structured interview (Diagnostic Interview Schedule) supplemented by questions from the Renard Diagnostic Interview concerning alcohol use. Only those meeting Feighner' (16) criteria for definite alcoholism (three out of four categories with a positive symptom) as well as DSM III criteria were included. Control fathers were social drinkers recruited through advertising, who were screened using the same structured interviews and found to be free of all psychopathology (lifetime diagnosis) including neither probable (two out of three categories) or definite alcoholism. Control fathers had been selected for the larger study because they were free of psychopathology including alcoholism, and additionally had no first degree relative with psychopathology.
All of the mothers (affected and control groups) were free of psychopathology including alcoholism by family report. The mothers were not interviewed directly as they were not part of the ongoing larger study as were the fathers, for whom structured (Renard Diagnostic Interview) psychiatric interviews were completed. The alcoholic fathers were free of other psychopathology (e.g., depression, schizophrenia, anxiety disorders).

Nineteen Caucasian children between the ages of 8 and 14 participated in the research (fourteen females and five males). The affected group was comprised of nine children, the controls ten. Seven families provided two sibs for assessment; additionally, one control family provided a cousin as well. None of the subjects had any history of psychiatric treatment or neurological disorder. All of the subjects were living in intact families with the biological parents. The mean ages of the two groups were quite similar for the affected and controls (mean ± standard error = 10.7 ± .66 and 11.0 ± .80, respectively). The educational levels of fathers were also quite similar (13.3 ± .24 and 14.8 ± .61 years for children of alcoholics and controls, respectively).

Procedure

Static ataxia was measured using an apparatus patterned after that used by Lipscomb et al. and previously used in the study by Hegedus and colleagues. Subjects were asked to stand as stationary as possible on a designated spot on the floor within a quiet room with only the experimenter present. Attached around the child’s thorax and over the upper arm was a harness which was connected by nylon line to two wall-mounted photoelectric counters designed to detect movement in either the anterior-posterior or lateral directions. A movement of 1.28 cm in either direction can be detected with this apparatus. In the first series of trials, subjects were asked to stand with hands folded across the chest and with their feet side by side at a distance
of approximately 4-6 inches (subject's feet were positioned with respect to floor reference lines). All subjects completed the trials with their shoes removed. The stance with the children took in this condition was patterned after that used by Lipscomb (personal communication) and will be referred to in subsequent analyses as "Lipscomb method." The children were asked to complete 5 one minute trials with 30 seconds of rest in between trials. Eyes were open or closed on alternate trials starting with an eyes open trial. Motion for the three eyes open trials (first, third and fifth trials in the series) and the two eyes closed trials (second and fourth) may be seen in Figures 1 and 2.

In the second series of trials, subjects were asked to stand with heel to toe and with hands clasped (elbows up) and away from the body. This stance is a modified Romberg method used in neurological assessments and is generally considered more difficult to complete than the former task. Our goal was to make the task more difficult to determine if group differences would be manifest only when task difficulty was enhanced. Previous studies had shown that group differences were most apparent in the eyes closed condition, which is a more difficult task to complete than is the eyes open condition. Therefore, this series of three trials was completed in the eyes closed condition only.

RESULTS

Analyses of variance were performed to determine if children of alcoholics differed from children of controls on the two conditions employed, the "Lipscomb method" and the modified Romberg. For the "Lipscomb method" in the eyes open condition, a $2 \times 2 \times 3$ ANOVA--group x direction of sway (AP versus lateral) x trials--was performed. Significant main effects were found for group ($F=4.79$, df=1,17, $p=.042$) and trial ($F=5.58$, df=2,34, $p=.008$) factors. A parallel analysis was performed for the eyes closed condition revealing a significant group effect ($F=8.08$, df=1,17, $p=.011$). No significant dif-
STATIC ATAXIA MOTION COUNTS
ANTERIOR–POSTERIOR

TRIALS by CONDITION

Legend

- AFF
- CONTRC
STATIC ATAXIA MOTION COUNTS

LATERAL

Legend
☐ AFF
☒ CONTROL

TRIALS by CONDITION
ferences were noted for the trial factor in this condition. Similar analyses were performed for the more difficult task, the modified Romberg stance. No significant differences were found for either the eyes open or eyes closed conditions for the modified Romberg stance.

[Place Figures 1 and 2 about here]

DISCUSSION

The present study investigated three variables found in previous studies to affect the likelihood of detecting sway: the direction of sway (anterior-posterior versus lateral), eyes open or closed, and trials. While Lester and Carpenter\textsuperscript{14} have found greater sway in the lateral direction for children of alcoholics when compared to control children, the present findings do not suggest any difference as a function of direction of sway. However, it should be noted that the Lester and Carpenter study used a movement platform technique that might have been more sensitive to lateral displacements than is the harness technique used in this and other\textsuperscript{12,13} studies.

Consistent with previous findings\textsuperscript{12,14} greater sway was found in the eyes closed than in the eyes open condition. Only one previous study\textsuperscript{13} has failed to find significant group differences for children of alcoholics and controls in the eyes closed condition.

Two previous studies have employed multiple trials to assess sway\textsuperscript{12,14} though in one\textsuperscript{12} subjects were at varying blood alcohol levels as repeated trials were performed. In contrast to previous reports indicating no effect of either trials or the interaction of trials with a family history of alcoholism, the present study did find significant effects of repeated trials. Subjects showed increased sway across trials. Whether this was due to fatigue, decreased attention, or loss of motivation to remain steady with time
is uncertain at present. It is of interest to note that there was no interaction between trials and group membership—the children of alcoholics showed no greater tendency to sway with repeated trials than did the controls.

Finally, the present study utilized two postures for eliciting sway, one of which was chosen because it was presumed to be a more difficult task (modified Romberg). As expected, greater sway was noted in all subjects when performing this task. However, when sway was measured with the Romberg modification the groups were not found to be significantly different. These results are somewhat unexpected in view of the significant differences obtained using the Lipscomb method, a task which is clearly less difficult.

The present results confirm the earlier reports of Lipscomb et al.,¹² Hegedus et al.,¹³ and Lester and Carpenter,¹⁴ all of whom have found children of alcoholics to sway more than control children. These results extend the observation to include children of alcoholics who were, because of the design of the larger study, also the nieces and nephews of alcoholics. Many had grandparents and/or great aunts and uncles who were alcoholic as well. Analysis of the extended pedigrees indicated an average of 3.3 male and .33 female first or second degree relatives who were alcoholic. Thus, it would appear that the subtype of alcoholism exhibited in fathers of the high risk children assessed here is a more genetically mediated form termed "male-limited" by Cloninger. It is of interest to note that the majority of our subjects were female, suggesting that sway may be a useful psychobiological marker, even among females, who are selected from families in which there is a heavy loading of this more genetically mediated form of alcoholism.
REFERENCES


Figure 1 - Motion counts of children of alcoholic fathers (affected) and control fathers in the anterior-posterior direction, employing the "Lipscomb" procedure for measuring sway. Both eyes open and eyes closed conditions were assessed. The numbers refer to repeated trials in the same condition. Results are mean values (± SE) for each group.

Figure 2 - Motion counts of children of alcoholic fathers (affected) and control fathers in the lateral direction, employing the "Lipscomb" procedure for measuring sway. Both eyes open and eyes closed conditions were assessed. The numbers refer to repeated trials in the same condition. Results are mean values (± SE) for each group.
ACKNOWLEDGMENTS

We wish to thank Marilyn Glick for her usual excellent editorial assistance. We greatly appreciate the help of the parents of these children who permitted them to take part in the study, transported them to our laboratory, and patiently waited for them to complete the assessments. A special thanks to the children for volunteering to be in our study.