Relationship of Age of First Drink to Child Behavioral Problems and Family Psychopathology

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The Collaborative Study on the Genetics of Alcoholism (COGA) (Principal Investigator: H. Begleiter; Co-Principal Investigators: L. Bierut, H. Edenberg, V. Hesselbrock, Bernice Porjesz) includes nine different centers where data collection, analysis, and storage take place. The nine sites and Principal Investigators and Co-Investigators are: University of Connecticut[3] (V. Hesselbrock); Indiana University[4] (H. Edenberg, J. Nurnberger Jr., P.M. Conneally, T. Foroud); University of Iowa[1] (S. Kuperman, R. Crowe); SUNY HSCB (B. Porjesz, H. Begleiter); Washington University in St. Louis[2] (L. Bierut, J. Rice, A. Goate); University of California at San Diego[5] (M. Schuckit); Howard University (R. Taylor); Rutgers University (J. Tischfield); Southwest Foundation (L. Almasy). Lisa Neuhold serves as the NIAAA Staff Collaborator. This national collaborative study is supported by the NIH Grant U10AA08403 from the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

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ABSTRACT

Background: An early age of first drink (AFD) has been implicated in a variety of negative outcomes in adolescence and early adulthood. Studies involving AFD have often focused on these negative outcomes, but rarely have addressed the additional presence of: existing child problematic behavioral symptoms, multigenerational familial alcohol dependence (AD), or multigenerational familial antisocial personality disorder (ASPD).

Methods: Using data from a multi-center genetic study on alcoholism, we investigated the differences between two groups of children, one coming from families heavily loaded for alcohol dependence and the other from population controls. A multilevel, multi-step regression model using child characteristics (gender and years of alcohol exposure), family characteristics (income, living arrangement, parental AD, parental ASPD, adult siblings with AD or ASPD, and extended family members with either AD or ASPD) and child problematic behavior variables (grade retention, externalizing and internalizing behavioral scale scores, and substance use) was performed to predict age of first drink.

Results: The final model indicated that 4 variables contributed significantly to the model's ability to predict age of first drink. The most important variable was "years of alcohol exposure" which explained 43.5% of the variance, followed by "marijuana use" (2.7% of the variance), "maternal AD" (2.2% of the variance), and "paternal ASPD" (2.1% of the variance). Family density of AD (or ASPD) did not contribute to the model.

Conclusions: The study suggests that age of first drink, while related to maternal AD, is not as strongly associated with a "loaded" family history of alcohol dependence (or ASPD) as is problematic alcohol use. Other potential factors such as peer influences or accessibility of alcohol may play a stronger role in the initiation of alcohol use.

Keywords: Age of First Drink, Alcoholism, Externalizing Disorders, Childhood Psychopathology, Family Factors

INTRODUCTION

Alcohol use in late childhood/early adolescence is a common event. Johnston et al. (2003) reports that over 50% of surveyed 8th graders (typical age of 14) have already used alcohol and that approximately half of these have already had at least one episode of being "drunk." This information is significant due to the fact that recent studies have suggested that early use of alcohol predicts alcohol diagnoses in children (DeWit et al., 2000) and adults (York, 1999). Additional negative outcomes of early drinking include increased rates of childhood psychiatric disorders, lowered success in school and extracurricular activities, increased criminal behavior, and lowered overall life satisfaction and productivity (DeWit et al., 2000; Guo et al., 2000; Kuperman et al., 2001a; Legrand et al., 1999; McGue et al., 2001b; McGue et al., 2001a; Prescott and Kendler, 1999; York, 1999). As they enter their adult years, children with a history of early use of alcohol continue to experience increased rates of psychiatric problems as well as increased health risks related to substance abuse, less stability of employment and committed relationships, and increased criminal behavior (Sussman et al., 2000; York, 1999).

However, the majority of children who drink alcohol by 8th grade do not go on to have significant problems, and studies differ in their findings. Some of these discrepancies may be due to differences in definitions. The majority of studies use a dichotomous split to define age of first drink; this has varied from preadolescence (DeWit et al., 2000; Hawkins et al., 1997) to early adolescence, with the most common dichotomy being younger than 15 compared to 15 years or older (DeWit et al., 2000; Grant and Dawson, 1997; Legrand et al., 1999; McGue et al., 2001b; McGue et al., 2001a). A more important difference may be the definition of what actually constitutes a first drink. This has ranged from any use of alcohol (Johnston et al., 2003) to a sip of alcohol (Guo et al., 2000), to a full drink of beer, wine, or hard liquor (DeWit et al., 2000; Grant and Dawson, 1997; McGue et al., 2001b; McGue et al., 2001a; York, 1999).

A more complex problem is many of the studies only examine the outcomes of early AFD but not its antecedents and do not incorporate data about the child or the child's family. Some of the hypothesized individual early AFD risk factors include being male (Dawson and Grant, 1998; Disney et al., 1999), having parents with alcohol dependence or antisocial personality disorder (Assanangkornchai et al., 2002; Kuperman et al., 1999; Legrand et al., 1999), having a childhood diagnosis of a disruptive disorder (Assanangkornchai et al., 2002; Disney et al., 1999; Kuperman et al., 2001a; Kuperman et al., 2001b), positive peer attitudes towards substance use (Botvin et al., 1998; Hawkins et al., 1997; Mcculler et al., 2001) and parenting and other home environmental factors

(Griffin et al., 2000; Kuperman et al., 2001b). However, many of these co-occurring antecedents may also predict these same negative outcomes of AFD as previously listed (Garmezy and Masten 1994; Patterson et al., 1989; Patterson and Stouhamer-Loeber, 1984).

Since early AFD is related to so many negative outcomes, it is important to fully understand why some children who begin drinking at a young age go on to have problems later in life and others do not. Our hypothesis is that early AFD is not a primary causal predictor of poor outcome, as measured by more problematic alcohol and substance use in later adolescence, but instead represents a marker for the presence of other risk factors which themselves are more directly related to such outcomes. If this is the case, recognition and potential treatment of these other markers maybe a more effective method of decreasing alcohol and substance use in adolescence then simply delaying a child's age of first drink. The Collaborative Study on the Genetics of Alcoholism (COGA) provides an opportunity to disentangle these factors since it incorporates detailed data on children ages 7 to 17, including information about their psychiatric symptoms, their onset and ongoing use of alcohol and other substances, their parental psychiatric symptoms, and their home environment. Using this population, the current study will explore the relationships among AFD, parental diagnoses of alcohol dependence and antisocial personality disorder, and family history of multigenerational problematic drinking and antisocial personality, on the other hand, symptom count scales measuring problem behaviors associated with attention deficit hyperactivity, oppositional defiant, conduct problems, and problematic substance use (tobacco, marijuana, and other street drugs).

METHODS

The subjects in this study were all participants in the Collaborative Study on the Genetics of Alcoholism (COGA). COGA is a multi-center, longitudinal project comprised of six subject collection centers located in California, Connecticut, Indiana, Iowa, Missouri, and New York. The goal of COGA is to study various behavioral, biochemical, genetic, neuropsychological, and neurophysiologic phenomena related to alcoholism. Institutional Review Boards at all sites reviewed and approved the study design and procedures. Parents and their children provided informed consent and assent, respectively, for participation in this study.

SUBJECTS. Two types of families make up the COGA database; those defined as COGA families and control families. The COGA families were chosen by first inviting an adult who was receiving treatment for alcoholism to enter the study. A trained research assistant using the Semi-Structured Assessment for the Genetics of

Alcoholism (SSAGA) (Bucholz et al., 1995) interviewed this person. Individuals fulfilling criteria for both a DSM-III-R diagnosis of alcohol dependence (AD) as well as a Feighner diagnosis of definite alcoholism (Feighner et al., 1972) were then diagnosed as a COGA alcoholic and were asked permission to interview other adult first-degree family members. If at least two more of these relatives were also COGA alcoholics, then all available relatives (including children and extended family members) were interviewed. During the interview process, all adult family members provided family history psychiatric data about other adults in the extended family. Control families were recruited from dental and family practice clinics, businesses, churches, and driver's license renewal centers and received the same assessment battery. Control families were not selected with respect to the presence or absence of any psychiatric disorder; alcohol dependence was present in approximately 30% of these families. The recruitment procedure has been more fully detailed by Begleiter et al. (1995).

In the first phase of the COGA project, trained research assistants interviewed a total of 1333 children, age 7 to 17,using age appropriate versions of the Child Semi-Structured Assessment for the Genetics of Alcoholism (C-SSAGA) (Kuperman et al., 1999). In addition, a guardian (usually the mother) was given a version of the C-SSAGA (C-SSAGA-P) to obtain corroborative data. All versions of the C-SSAGA used in this study allowed a diagnosis to be made for most DSM-III-R childhood disorders.

The subgroup of children included in this study had to have: a) a reported age of first drink (AFD) between 5 and 17 and b) a completed parental C-SSAGA-P. AFD was determined through the use of the C-SSAGA question "How old were you when you had your very first whole drink?" This definition was used because it indicated a substantial amount of alcohol ingestion; it was more than that used in religious ceremonies and more than a taste that parents might offer to a child at a family meal. Of the original 1333 children, 440 had a reported AFD along with a completed C-SSAGA-P, 1 had a reported AFD on the C-SSAGA but had no completed C-SSAGA-P, and 892 denied any exposure to alcohol (of the latter, 60.0% were under the age of 12). The 440 children in the final sample consisted of 339 (77.0%) offspring from COGA families and 101 (23.0%) from control families.

The characteristics of these two groups were compared across of a number of measures. The first set of measures included the following variables selected from the literature as being important to age of AFD: gender, age of the child at interview, the child's length of exposure to alcohol (defined as the age of interview minus the age of reported first drink in years), parental ages at interview, family composition (defined as the child living with either biological mom, biological dad, both biological parents, or no biological parents), family income (defined as

whether the family in which the child resided was above or below the median yearly income of $30,000 for the 440 children), paternal or maternal diagnosis of alcohol dependence, paternal or maternal diagnosis of antisocial personality disorder (ASPD), and the presence of academic difficulties (defined as being held back a grade in school).

The second set of comparison measures consisted of the variables used to define various behavioral problems, including problematic alcohol use and the use of tobacco and marijuana. Since we desired to explore the range of behavioral problems, symptom scales were used instead of the absence or presence of a full DSM-III-R diagnosis. Combining both child and parent C-SSAGA-data, scales were created such that information from either interview resulted in a positive symptom endorsement for a particular question (Bird et al., 1992). In general, the behavioral scales consisted of behavioral items presented in the part "A" section of the DSM-III-R for a given child psychiatric diagnosis. The first scale consisted of the first 8 symptoms of attention deficit hyperactivity disorder (ADHD) since these were asked of all children (children without a positive response to at least one of these symptoms "skipped out" of the rest of the ADHD section). The second scale consisted of the first 5 symptoms in part "A" for the diagnosis of oppositional defiant disorder (ODD); children skipped to the next section if there were no positive responses to any of these symptoms. The third scale comprised all 13 symptoms in the part "A" section of conduct disorder (no skip outs in this section). The fourth scale was developed as a composite measure of internalizing symptoms from three different DSM-III-R disorders: the first 2 symptoms in the part "A" section of the DSM-III-R for major depressive disorder, the first 4 symptoms in the part "A" section for separation anxiety disorder, and the first symptom in the part "A" section for overanxious disorder. These symptoms were included because they were asked of all children in the sample; children who did not give a positive response to items early on in one of these sections (or parents who were reporting on their child) moved on to the next section of the C-SSAGA. (Cronbach's α score was 0.65 for this composite scale and indicated sufficient item consistency). The alcohol problematic use scale was derived from summing the number of positive responses to the first 9 symptoms in the part "A" section of the DSM-III-R for psychoactive substance dependence (there were no missing data in this section since all subjects endorsed a history of at least one full drink of alcohol).

While both COGA and control children indicated some use of either marijuana or other street drugs (defined as cocaine, speed, opiates, hallucinogens, downers, and/or inhalants), problematic use as defined by the presence of even a single DSM-III-R symptom of abuse or dependence was rare in both groups. Tobacco use was

ascertained by asking the child (and his/her guardian) if he/she "had ever used tobacco by smoking cigarettes or by chewing", problematic use could not be determined due to the limited number of questions concerning tobacco contained in this version of the C-SSAGA. Therefore three dichotomous variables were created indicating whether a child had used tobacco, marijuana, or other street drugs.

Since the COGA study contained family history data, the final set of variables were used to quantify the differences in familial rates of AD and ASPD. Whenever possible, a parental diagnosis of AD or ASPD was directly made from the parent's SSAGA interview. If the parent did not have a SSAGA interview, and in the case of all other adult family members, the family history method of Rice et al. (1995) was used to impute psychiatric diagnoses. Familial AD and ASPD were examined in three different ways across COGA and control families. The first was to examine the percentages of children that had a specified relative class with a diagnosis of AD or ASPD. The second method calculated the average number of adult siblings or second-degree relatives with a diagnosis of AD or ASPD. Because the number of relatives in the family history database was greater for the COGA than for control children, the third method attempted to standardize this data by employing percentages (e.g. the number of adult relatives per family class with an alcohol dependence diagnosis was divided by the total number of unique adult relatives in that class contained in the family history database). The same procedure was then repeated for ASPD. These percentages were then compared across family relative class (either just first-degree, second-degree, or both) for alcohol dependence or ASPD.

Statistical Analyses. The relationships between family type (COGA and control) and variables of interest were examined using Chi-square Test of independence, Fisher's Exact Test of independence, and two independent samples T-Test. These variables included gender; family composition; child's age, age of first drink, and years of alcohol exposure; parents' ages; family income; the presence of a parent(s), adult sibling(s), and second-degree relatives with AD or ASPD; the number of adult siblings and second-degree relatives with AD or ASPD; and the average percentages of first- and second-degree relatives with AD or ASPD.

Finally, a three-level regression analysis was performed on AFD. At each step in the model, homoscedasticity (an assumption for the regression tests) was verified. The explanatory variables used here were determined by results from the preliminary analyses. In Level 1, only two child characteristic variables (gender and years of alcohol exposure) were considered. In Level 2, thirteen family characteristic variables were considered. These 13 variables were subdivided into seven categories: 1) Family variables: family annual income below

$30,000, and child's living arrangement with respect to his/her biological parents; 2) Parental AD diagnosis (diagnosis of each parent used separately); 3) Parental ASPD diagnosis (diagnosis of each parent used separately); 4) Number of adult sibling with AD or ASPD diagnoses (diagnoses entered separately); 5) Number of adult second-degree relatives with AD or ASPD diagnoses (diagnoses entered separately); 6) Proportion of second-degree relatives with AD or ASPD diagnoses (diagnoses entered separately); 7) Family type variable (COGA or Control). Family variables numbered 4 and 5 above were entered into the model to determine whether there existed a threshold effect (i.e. a minimum number) of alcoholic/ASPD family members in a given class of relatives to predicted AFD. Variables 6 and 7 were entered into the model as a proxy for indicating the strength of genetic loading for alcoholism/ASPD to predicted AFD.

In the final level, eight child problematic behavior variables were considered. These were divided into four categories: 1) School problem variable (has been retained a grade in school); 2) Externalizing behavioral scale scores (scale score entered individually for attention-deficit/hyperactivity, oppositional defiant, conduct, and their sum described as a total external behavior scale); 3) Substance use scores (use of tobacco and marijuana entered individually); and 4) Internalizing scale score.

RESULTS

Demographic findings of the COGA and control children are shown in Table 1. At the time of interview, age was significantly different between the two groups; COGA children were on average 0.8 years younger than control children. Though mean age of first drink did not differentiate COGA from control children, “years of alcohol exposure” was marginally significant (p=0.04). Both COGA mothers and fathers were on average approximately 5 years younger than control mothers and fathers. In general COGA children appeared to have more nonspecific difficulties/stressors. The rate of COGA children being held back a year in school was almost 2.5 times higher than their control counterparts. COGA children were almost 3 times less likely to live in homes with both biological parents present. The child’s family income also appeared to be affected by family type; COGA children were 2.5 times more likely to reside in homes with an annual income less than $30,000).

[Insert Table 1 about here]

Table 2 shows the mean and standard deviation of the scores derived for behavioral scales. As a group, COGA children had elevated scale scores compared to controls for all of the behavioral scale scores though these

were significant only for attention deficit hyperactivity, opposition defiant, conduct, total externalizing, and internalizing behavioral scales but not for problematic alcohol use. The rate of marijuana use was higher in COGA children but did not differ for use of tobacco or other street drugs.

[Insert Table 2 about here]

As shown in the first part of Table 3, the percentages of COGA children who had an alcoholic mother or father were much higher than the percentages of control children. The COGA rate was increased approximately 9 fold for mothers and approximately 2 fold for fathers compared to controls. COGA children had higher rates of AD in second-degree family members as well; increased rates were significant for maternal grandfathers (1.8 fold), paternal aunts/uncles (3.5 fold) and maternal aunts/uncles (2.3 fold).

[Insert Table 3 about here]

The same set of analyses was performed for an ASPD diagnosis. As shown in the second part of Table 3, the percentages of COGA children with an ASPD mother or father were much higher than the percentages of controls. Among COGA children, 7.1% of them had mothers with a diagnosis of ASPD versus none of the control mothers. A diagnosis of ASPD in fathers was 4 times more common among COGA children than controls. The percent of COGA children with known a maternal or paternal aunt or uncle with ASPD was approximately 10 times greater than the percent for controls.

Table 4 presents this data looking at the average number of adult siblings and second-degree relatives with diagnoses of AD or ASPD. Though the average numbers of adult siblings with AD or ASPD were relatively small for both COGA and control children, they was increased 2.5 times for AD and 3.6 times for ASPD in COGA families. Similarly, the average number of second-degree relatives with ASPD was 28 times greater for COGA versus control families.

[Insert Table 4 about here]

Table 5 shows that on average, COGA children had a 3 fold higher rate of AD first-degree adult relatives; a 1.5 fold higher rate of AD second-degree adult relatives; and a rate that was 2.2 fold higher for combined first- and second-degree relatives compared to the appropriate relative class of control children. Similar findings were found for the rates of adult relatives with a diagnosis of ASPD; COGA children, on average, had a 4.9 fold increase in first-degree relatives, a 14.6 fold increase in second-degree relatives, and a 5.5 fold increase in combined first- and second-degree relatives compared to control children.

[Insert Table 5 about here]

A three-level regression approach was used with the above variables to predict the age of first drink. At each level (and each step) there was no significant evidence to reject the common variance assumption. Variables examined in the first level consisted of child characteristics and included gender and the number of years of alcohol exposure. Using this model in which there was "0" years of alcohol exposure, baseline AFD was 14.8 years. Gender did not significantly contribute to this model while predicted AFD decreased by approximately 0.83 years for each year of alcohol exposure ($p<0.0001$).

The second regression level consisted of 7 steps. In the first step, family variables of income and living arrangement were added to years of alcohol exposure. Both of these additional variables were significant. Baseline AFD (defined as the child having "0" years of alcohol exposure, family income $\geq$\$30,000 per year, and living with no biological parents) was 15.2 years. Predicted AFD decreased by approximately 1 year for each year of alcohol exposure ($p<0.0001$), by 0.5 years if the family yearly income was less than \$30,000 ($p=0.0333$) and had a variable relationship depending upon the family living arrangement ($p=0.0427$). This varied from a decrease of 0.5 years if the child lived just with his/her biological mom to no change in baseline if the child did not live with either biological parent.

Step 2 involved adding the variables of maternal and paternal AD to years of alcohol exposure, income, and living arrangement. This model resulted in a baseline AFD (defined as the child having "0" years of alcohol exposure, family income $\geq$\$30,000 per year, and not having an AD mom) of 15.2 years. Predicted AFD decrease by 0.5 years for family income less than \$30,000 ($p=0.0046$), by 0.8 years for each year of alcohol exposure ($p<0.0001$), and by 0.5 years for a mother with alcohol dependence ($p=0.0031$). In this step the presence of an AD father and family living arrangement lost their significance in predicting AFD and were both removed from the model.

Step 3 added the variables of maternal and paternal ASPD to the results of the previous step. AFD baseline was 15.2 years and was defined as the child having "0" years of alcohol exposure, not having an AD mom, and not having an ASPD father. Predicted AFD decreased by approximately 0.8 year for each year of alcohol exposure ($p<0.0001$), by approximately 0.7 years if mom was AD ($p=0.0001$), and by 0.9 years if dad was ASPD ($p<0.0001$). Maternal ASPD was not related to AFD and family income no longer remained significant; both were dropped from the model.

Step 4 added the variables number of adult siblings with alcohol dependence or ASPD to the previous model. AFD baseline was 15.2 years and was defined as the child having "0" years of alcohol exposure, not having an AD mom, not having an ASPD father, and not having any adult siblings with AD. Predicted AFD decreased by approximately 0.8 years for each year of alcohol exposure ($p<0.0001$), by approximately 0.7 years if mom was AD ($p=0.0001$), and by 0.9 years if dad was ASPD ($p<0.0001$). AFD increased by 0.3 years for each adult sibling with alcohol dependence ($p=0.0416$). The number of adult siblings with ASPD did not relate to AFD.

Steps 5 through 7 sequentially tested the relationships of the number of second-degree relatives with alcohol dependence or ASPD, the percent of second-degree relatives with alcohol dependence or ASPD, and membership in a COGA family. None of these variables were related to AFD and the model remained the same as at the end of step 4.

Level three of this regression series consisted of 4 steps that examined variables that appeared directly related to the child's behavioral problems. The first step added the single variable "held back a grade in school", while step two sequentially added the scores for attention deficit hyperactivity, oppositional defiant, conduct, and total externalizing behavioral scales to the four variables that remained significant from before. Again none of these variables were significantly related to AFD. The third step added the variables of "used marijuana" and "used tobacco" to the above 4 variables. (The variable "used other street drugs" was not used because of its relative rarity.) The fourth step added the variable internalizing scale score. In this level, only marijuana use was significantly related to predicted AFD while the "number of adult AD siblings" lost its relationship. The remaining model consisted of a baseline AFD of 14.9 years defined as occurring in a child having "0" years of alcohol exposure, not having an AD mom, not having an ASPD father, and a child who did not *use* marijuana. Predicted AFD decreased by approximately 0.9 years for each year of alcohol exposure ($p<0.0001$), by approximately 0.8 years for an AD mom ($p<0.0001$), by 1 year for an ASPD dad ($p<0.0001$), and increased by 0.9 years if the child used marijuana ($p<0.0001$). This overall model explained 50.5% of the variance of predicted AFD; duration of alcohol exposure accounted for the majority of the variance at 43.5%; marijuana use accounted for 2.7% of the variance; an AD mother accounted for 2.2%; and an ASPD father accounted for 2.1%.

The finding that predicted AFD was increased with marijuana use was further explored. The average age of reported AFD in the 201 children who used marijuana (12.9±2.1 years) was not different than the 239 children (12.8±2.6 years) who did not ($t=0.43$, $p<0.6709$). In these 201 children, age of marijuana initiation was 13.8±2.2

years and was greater than their reported AFD ($t=4.3$, $p<0.0001$). This demonstrates that reported AFD actually occurs after the initiation of marijuana use and suggests that the contribution of this variable may be influenced by the variables of maternal AD and paternal ASPD.

DISCUSSION

This study explored the relationships between age of first drink and a number of variables described in the literature as being significantly associated with an early age of first drink. Two groups of children were compared in this study, the first were the offspring of families with a high loading for alcoholism while the second consisted of offspring from population based control families. Similar to the report by Johnston et al. (2003), the average age of first drink for these study subjects began during late childhood/early adolescence, and alcohol use was relatively common regardless of whether the children were from high risk or control families.

As the literature and our own ascertainment procedures would suggest, the two groups of children varied across several different measures. The high-risk "COGA" children appeared to have significantly more stressors than controls. They were held back a grade more often at school, resided more often in homes missing one or both biological parents, resided in homes with lower yearly incomes, and secondary to the COGA selection process had higher rates of first- and second-degree relatives with AD. In addition COGA children had more first- and second-degree relatives with a diagnosis of ASPD. COGA children also scored higher on measures related to externalizing and internalizing behavioral difficulties and were more likely to have tried marijuana. Neither COGA nor control children experienced frequent problematic drinking symptoms, though COGA children scores were marginally higher on this scale. Similarly, the rates of tobacco use and other street drug use were modestly higher in COGA versus control children

The important new methodological contribution of this study was the combining of associated variables in a multilevel, multi-step regression to determine which contributed the most to the prediction of AFD. In the first level regression, gender was not a significant factor, though length of alcohol exposure was and remained throughout. In the next level, maternal AD and paternal ASPD were significantly related to predicted AFD. Adult siblings with AD, yearly family income, and living arrangement were initially related to predicted AFD but dropped out when other variables were entered. Furthermore, maternal ASPD, paternal AD, the number of adult siblings with ASPD, and all the various measures used to quantify the *loading of family history* for alcohol dependence or

antisocial personality disorder did not contribute to the prediction of AFD. The last level of the regression analyses added child variables and except for marijuana use none of these variables were related to the prediction of AFD. The final model consisted of the variables "years of alcohol exposure", "maternal AD", "paternal ASPD", and "use of marijuana" and these variables accounted for over 50% of the variance in the model's prediction of AFD.

There are four main findings from this study. First, despite the many differences between the COGA and control samples in direct comparisons of the child's behavioral scale scores and variables assigned to quantify the density of family history of alcohol dependence (or ASPD), none of these entered in the final regression model to predict AFD.

Second, each year of alcohol exposure decreased predicted AFD by 0.9 years and this variable accounted for the overwhelming majority of the variance (43.5%). From a logical standpoint, this is a "confounded" relationship since years of alcohol exposure is derived by directly comparing a child's age at interview with his/her actual reported age of first drink.

Third, family history of alcohol dependence (or ASPD) as measured by the number or percent of first-degree relatives, second-degree relatives, the sum of both, or just being a member of a COGA family, was not related to predicted age of first drink. This appears to be in line with recent studies that suggest age of first drink is less heritable than alcohol problem use and may be the result of a number of environmental factors including peer influences, accessibility of substances, and sibling interactions as well as family history (Rhee et al., 2003; Prescot and Kendler, 1999).

Fourth, the *protective* nature of marijuana use appears to be a spurious finding: initiation age of marijuana use occurred after reported AFD in the children who reported using both, and the actual contribution of marijuana use to the final model's ability to predict AFD is less than 3% of the variance.

There are many strengths to this study. Data was collected through the use of trained interviewers in a methodical fashion with both COGA and control family members receiving the same measures including those for collecting data on both immediate and extended family members. On average the interviews were performed less than three years after the child's actual reported age of first drink, minimizing the retrospective nature of the data. We purposely chose to use symptom counts instead of psychiatric diagnoses in order to cast the widest possible net to determine relationships between various symptoms and predicted AFD. This is also the only study to our knowledge that directly looked at the effect of parental and familial ASPD in predicting AFD.

This paper has several limitations. First, the majority of study subjects came from families with multiple alcohol dependent adults, and these were combined with a smaller number of "natura'' controls. Thus the ability to generalize the findings to other populations in which there is not an extensive family history of alcoholism may be impaired (though no measure of the density of familial alcoholism had a relationship to predicted AFD). The second limitation is that 60% of the children who did not report an actual AFD were under the age of 12 and thus likely to have limited access to alcohol. Perhaps as these children age, and begin to drink they may contribute additional data and affect our model's prediction of AFD.

There are several questions this study does not answer. Because of the limited age range of the subjects in this study (all were under the age of 18) it does not provide information as to whether these children, or a subset of these children, are more likely to develop alcohol, psychiatric, legal, job, or other life problems as they age. In this study, the reported age of first drink on average occurred approximately 2 1/2 years prior to their interview age. Despite this interval of alcohol exposure, 247 children (56.1%) indicated that they had no problematic alcohol use symptoms. At first glance this suggests that in at least the short term, there may not be any relationship between age of first drink and early onset of alcohol related problems. A different perspective would suggests that 193 of the children (43.9%) have at least one alcohol related problem and perhaps it is this subgroup that is at risk for the development of the negative outcomes associated with an early age of first drink. Since the COGA study is designed to be longitudinal in nature, many of the children have been or will be re-interviewed when they are an adolescent and/or when they are a young adult. This will allow additional children an opportunity to report "age of first drink" and allow determination of whether the findings presented here still hold, and more importantly may allow us to tease out the contributions of each of the proposed variables to the risk of a negative outcome in young adulthood.

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Table 1: Child and Family Characteristics

Variable	COGA	Control	Statistic (p-value), df
	N (%)	N (%)	
Child Family Type	339 (77.0)	101 (23.0)	
Child Gender			0.1~ (0.7223), 1
Male	161 (47.5)	50 (49.5)	
Female	178 (52.5)	51 (50.5)	
Child Held Back a Grade	110 (32.4)	13 (12.9)	14.8~ (<0.0001), 1
Family Composition			115.4~ (<0.0001), 3
Both Biologic Parents	105 (31.0)	93 (92.1)	
Only Biologic Mom	183 (54.0)	6 (5.9)	
Only Biologic Dad	22 (6.5)	2 (2.0)	
Neither Biologic Parent	29 (8.5)	0 (0.0)	
Family Income < $30,000/Yr	195 (57.5)	23 (22.8)	37.6~ (<0.0001), 1
Age	Mean (SD)	Mean (SD)	
Child	N=339	N=101	
Interview (C-SSAGA)	15.0 (1.9)	15.8 (1.5)	4.2^ (<0.0001), 209
First Drink	12.7 (2.3)	13.1 (1.9)	1.1* (0.2598), 438
Alcohol Exposure (difference)	2.3 (1.9)	2.7 (2.1)	2.2* (0.0403), 438
Mother	N=299	N=101	
Interview (SSAGA)	39.3 (5.8)	44.3 (5.1)	7.6* (<0.0001), 398
Father	N=213	N=95	
Interview (SSAGA)	42.1 (6.8)	47.0 (4.9)	7.2^ (<0.0001), 245

~ Chisq Test for Independence
* T-Test (equal variances)
^ T-Test (unequal variances)

Table 2: Child Behavioral and Substance Use Scale Scores by Family Type

	COGA	Control	Statistic (p-value), df
Behavior Scale Score:	Mean (SD)	Mean (SD)	
Attention Deficit Hyperactivity (Max=8)	2.6 (2.4)	1.9 (2.3)	2.6* (0.0092), 438
Oppositional Defiant (Max=5)	1.3 (1.6)	0.8 (1.3)	3.6^ (0.0004), 201
Conduct Behavior (Max=13)	3.1 (2.5)	2.3 (2.3)	2.8* (0.0050), 438
Total Externalizing (Max=26)	8.9 (6.0)	6.4 (6.0)	3.7* (0.0002), 438
Internalizing (Max=7)	2.2 (1.5)	1.7 (1.5)	2.7* (0.0067), 438
Problematic Alcohol Use (Max=9)	1.4 (2.2)	1.1 (1.7)	1.2^ (0.2509), 207
Positive Substance Use	N (%)	N (%)	
Marijuana	167 (49.3)	34 (33.7)	7.6~ (0.0057), 1
Tobacco	121 (35.7)	34 (33.7)	0.1~ (0.7078), 1
Street Drug (any cocaine, speed, opiates, hallucinogens, downers, and/or inhalants)	59 (17.4)	15 (14.9)	0.4~ (0.5472), 1

~ Chisq Test for Independence
* T-Test (equal variances)
^ T-Test (unequal variances)

Table 3: Percentage of Biological Adult Family Member Diagnosed as Alcohol Dependent or Antisocial Personality Disorder in 339 COGA and 101 Control Children

Diagnosis of	COGA Family	Control Family	Chisq (p-value)~
Alcohol Dependence	N (%)	N (%)	
1° Adult Relatives			
Mother	151 (44.5)	5 (5.0)	53.3 (<0.0001)
Father	204 (60.2)	30 (29.5)	29.0 (<0.0001)
Adult Sibling (At least 1)	50 (14.8)	8 (7.9)	3.2 (0.0750)
2° Adult Relatives			
Paternal Grandfather	94 (27.7)	19 (18.8)	3.2 (0.0728)
Maternal Grandfather	129 (38.1)	21 (20.8)	10.3 (0.0013)
Paternal Grandmother	28 (8.3)	4 (4.0)	2.1 (0.1442)
Maternal Grandmother	37 (10.9)	6 (5.9)	2.2 (0.1395)
At least 1 Paternal Avuncular	128 (37.8)	11 (10.9)	26.0 (<0.0001)
At least 1 Maternal Avuncular	154 (45.4)	20 (19.8)	21.4 (0.0001)
Antisocial Personality Disorder	N (%)	N (%)	
1° Adult Relatives			
Mother	24 (7.1)	0 (0.0)	7.6 (0.0060)
Father	81 (23.9)	6 (6.0)	15.8 (<0.0001)
Adult Sibling (At least 1)	17 (5.0)	3 (3.0)	1.8 (0.3866)
2° Adult Relatives			
Paternal Grandfather	6 (1.8)	0 (0.0)	108 (0.1782)
Maternal Grandfather	6 (1.8)	0 (0.0)	108 (0.1782)
Paternal Grandmother	0 (0.0)	0 (0.0)	Not Applicable
Maternal Grandmother	3 (0.9)	0 (0.0)	0.9 (0.3428)
At least 1 Paternal Avuncular	54 (15.9)	0 (0.0)	18.3 (<0.0001)
At least 1 Maternal Avuncular	74 (21.8)	2 (2.0)	21.5 (<0.0001)

~ 1 df

Table 4: Average Number of Biological Adult Siblings and Second-degree Relatives with a Diagnosis of Alcohol Dependence or Antisocial Personality Disorder in 339 COGA and 101 Control Children

Diagnosis of	COGA Family Mean (SD)	Control Family Mean (SD)	Statistic (p-value), df
Adult Siblings			
Alcohol Dependence	0.20 (0.59)	0.08 (0.27)	3.0^ (p=0.0032), 365
Antisocial Personality Disorder	0.05 (0.24)	0.03 (0.17)	1.1^ (p=0.2736), 226
2° Adult Relatives			
Alcohol Dependence	3.03 (2.34)	0.85 (1.23)	12.4^ (p<0.0001), 322
2° Adult Relatives	0.56 (0.92)	0.02 (0.14)	10.5^ (p<0.0001), 385

^ T-Test (unequal variances)

Table 5: Mean Percent of Biological Adult Relatives with a Diagnosis of Alcohol Dependence or Antisocial Personality Disorder in 339 COGA and 101 Control Children

Diagnosis of	COGA Family Mean (SD)	Control Family Mean (SD)	Chisq (p-value) df
Alcohol Dependence			
1° Adult Relatives	49.7 (26.6)	16.6 (25.7)	11.0* (<0.0001), 438
2° Adult Relatives	51.6 (28.3)	34.5 (37.8)	3.9^ (0.0002), 109
1° & 2° Adult Relatives	51.0 (20.8)	23.2 (26.2)	9.8^ (<0.0001), 140
Antisocial Personality Disorder			
1° Adult Relatives	14.7 (22.4)	3.0 (10.1)	7.5^ (<0.0001), 371
2° Adult Relatives	10.2 (17.3)	0.7 (4.5)	8.8^ (<0.0001), 404
1° & 2° Adult Relatives	11.3 (13.5)	2.0 (6.4)	9.6^ (<0.0001), 117

* T-Test (equal variances)
^ T-Test (unequal variances)