

RESEARCH REPORT

A latent class analysis of antisocial personality disorder symptom data from a multi-centre family study of alcoholism

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Abstract

Aims. To determine if there are subtypes of Antisocial Personality Disorder (ASPD), as manifested by distinctive symptom profiles or by associations with alcohol, other drug dependence or other psychiatric disorders. **Methods.** Data on 38 symptoms of ASPD (including childhood conduct disorder) obtained from probands, their relatives and controls (2834 females and 3488 males) recruited for the Collaborative Study on the Genetics of Alcoholism (COGA) were analyzed using latent class analysis. Associations of the resulting latent classes with alcohol dependence (AD) and other psychiatric disorders were examined. **Findings.** Among women, a 4-class solution was obtained in which conduct disorder and ASPD were found almost exclusively in the most severely affected class with two additional classes with mild and moderate behavior problems also identified. A strong linear trend ($p < 0.001$) for AD was observed, with each successive class manifesting a higher prevalence than the previous class. Milestones of drinking careers and dependence on other drugs also showed a strong association with class severity. Among men, a 5-class solution was obtained and, like women, the highest prevalence of ASPD (74.6%) was found in the most severely affected class. Somewhat unexpected was the observation that prevalence of AD was equivalent in the two most severe classes. The data for men indicated a class with a milder spectrum of childhood misbehaviors but with an adult ASPD profile—as well as other psychiatric co-morbidity—that was comparable to the most severe class. **Conclusions.** Overall, findings from both men and women did not support the existence of subtypes of ASPD, but rather indicated a disorder distributed on a severity spectrum.

Introduction

The association of Antisocial Personality Disorder (ASPD) with alcohol dependence has been established in both clinical and general population samples (Lewis *et al.*, 1983; Hesselbrock,

Hesselbrock & Stabenau, 1985; Helzer & Przybeck, 1988; Lewis, 1990; Hesselbrock, Meyer & Hesselbrock, 1992; Kessler *et al.*, 1997). This association has been observed in both directions: that is, markedly increased rates

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of ASPD have been observed in alcoholic populations (Helzer & Przybeck 1988; Kessler *et al.*, 1997), and higher than expected rates of alcoholism have been reported among criminals (Guze *et al.*, 1969) (who presumably would qualify for an ASPD diagnosis) as well as among those with an actual ASPD diagnosis (Lewis *et al.*, 1983).

The co-morbidity of the two disorders has both clinical and etiologic significance. A substantial body of research has documented the poorer prognosis of antisocial alcoholics in treatment (Hesselbrock *et al.*, 1984; Hesselbrock, Hesselbrock & Workman-Daniels, 1986; Lewis *et al.*, 1987; Kadden *et al.*, 1989; Cooney *et al.*, 1991, Liskow *et al.*, 1991; Litt *et al.*, 1992). However, some research groups have documented successful outcomes of treated ASPD substance abusers (Longabaugh *et al.*, 1994; Brooner *et al.*, 1998), challenging the belief of their treatment intractability. Further investigation of treatment efficacy for alcoholic individuals with co-morbid ASPD is included as an objective of Project MATCH, a multi-site alcoholism treatment-matching protocol funded by NIAAA (Donovan & Mattson, 1994).

From an etiological perspective, features of ASPD and of childhood conduct disorder are important elements in two well-known subtypes of alcoholism: Type II (identified by Cloninger, Bohman & Sigvardsson, 1981) and Type B (Babor *et al.*, 1992), both of which have been claimed to be more familial than their non-ASPD counterparts. Cloninger *et al.* reported a more heritable form of alcohol dependence that was characterized by earlier onset (before age of 25) and an inability to abstain among male alcoholics, which they labeled Type II alcoholism. The applicability of such types to female alcoholism has, however, been unclear. Babor *et al.* distinguished a Type B alcoholic with characteristics in common with those of Type II, namely higher density of alcoholism in relatives, more childhood conduct problems and earlier onset of problem drinking. However, the two-cluster model did not appear to be the best solution for females, as attested to in a re-analysis of those data in which a 4-cluster solution was identified as a better solution for women (Del Boca & Hesselbrock, 1995). Recently, however, data from a large national sample of twins provided firm evidence of a substantial genetic influence common to both alcohol dependence and the

precursor to ASPD—conduct disorder—in both men and women, in which 11% and 23% of the total phenotypic variation in men and women, respectively, was due to genetic influences that were common to conduct disorder and alcohol dependence (Slutske *et al.*, 1998).

Thus far, the literature has been silent on whether certain clusters of ASPD symptoms might be more strongly associated with alcohol and other substance dependence disorders than other ASPD symptoms. Data on specific adult antisocial behaviors have either been unavailable or unanalyzed in studies. In the Babor *et al.* (1992) elaboration, only aggregate ASPD symptomatology was presented; this was significantly elevated, as expected among Type B alcoholics, but patterns of specific antisocial symptomatology in the sample were not investigated. Thus, questions remain regarding whether subtypes of ASPD exist that may be fruitful in refining alcoholism phenotypes. To this end, data from a multi-site family study of alcoholism were analyzed to address the following questions: (a) do subtypes of ASPD symptoms exist? (b) are some ASPD symptom patterns more associated with alcohol dependence than others? and (c) does psychiatric co-morbidity distinguish certain ASPD symptom profiles?

Methods

COGA study

Data were collected from alcoholic probands, their relatives and controls who participated in the multi-site Collaborative Study on the Genetics of Alcoholism (COGA). Briefly, COGA is a multi-center family study of alcoholism in which probands ascertained from treatment facilities at six centers in the United States and their family members are interviewed with a comprehensive psychiatric instrument. Probands must meet lifetime criteria for both DSM-III-R alcohol dependence (APA, 1987) and Feighner alcoholism at the definite level (Feighner *et al.*, 1972). Families with at least three alcoholic first-degree relatives are studied further with a more extensive protocol that includes neurophysiological testing, biochemistry analysis and (in a subset of most informative families) genotyping. In addition, control families are selected from a variety of sources at different sites, including drivers' license records, individuals attending medical/dental clinics and advertisements and questionnaires mailed to random subjects at a

university. The COGA protocol was approved by IRBs at all six COGA centers, and informed consent was obtained from all subjects prior to administering the protocol.

Assessment

The COGA assessment interview, the Semi-structured Assessment for the Genetics of Alcoholism (SSAGA), is a reliable and valid interview that elicits both life-time and current information for a comprehensive range of psychiatric disorders (Bucholz *et al.*, 1994, 1995; Hesselbrock *et al.*, 1999b). DSM-III-R is the classification system on which the SSAGA is based, although other classification systems are covered for some diagnoses. Test-retest reliability data from COGA centers indicated excellent reliability of the SSAGA ASPD section, with a kappa of 0.70 (95% CI 0.54–0.87) (Bucholz *et al.*, 1994) and, more recently, a kappa of 0.71 (95% CI 0.49–0.93) obtained from a test-retest of the SSAGA and the SCID interviews (Hesselbrock *et al.*, 1999b). Reliability data for other diagnoses, including alcohol dependence, other drug dependence and depression have also indicated good to excellent reliability, with kappas exceeding 0.60 for most diagnoses (Bucholz *et al.*, 1994; Hesselbrock *et al.*, 1999b).

To qualify for a diagnosis of ASPD in the DSM-III-R classification system, an individual must meet criteria for both childhood conduct disorder and adult antisocial behaviors. A minimum of three of 12 behaviors occurring before the age of 15 satisfies the DSM-III-R Conduct Disorder criterion, while four of 10 behaviors occurring repeatedly since the age of 15 are required to satisfy the adult antisocial behavior criterion. However, because ages of onset for each childhood symptom were obtained, conduct symptoms may be scored as occurring before age 15 as well as by the more liberal measure of before age 18.

The diagnosis-orientated ASPD section of the SSAGA was structured for efficiency, allowing individuals who had fewer than two childhood symptoms to skip out of the adult section. This skip was instituted since these individuals would not qualify for the full diagnosis of DSM-III-R ASPD. However, excluded from this skip-out were individuals who reported more than one alcohol or other drug problem (not necessarily diagnostic). The ASPD section was structured

similar to the version of ASPD used at two sites in the Epidemiologic Catchment Area study in the early 1980s (Robins *et al.*, 1991). For the analyses reported here, only individuals who were asked about both childhood and adult symptomatology were included.

Furthermore, childhood and adult misbehaviors attributed exclusively to substance use were not considered in these analyses. To rate symptom attribution interviewers probed in a systematic way, similar to probing patterns used in other structured psychiatric diagnostic interviews such as the DIS (Robins *et al.*, 1985).

The total number of individuals analyzed here included 2834 women and 3488 men, who represented 63% of females and 89% of males in the complete COGA Master File at the time of analysis (MF55). Alcoholic probands comprised 19.4% of the sample analyzed here, while relatives of the probands constituted 71.1%, and controls completed the remaining 9.5%. Table 1 presents the symptoms that were included in the analyses, along with their prevalence by gender in this sample. Latent class analysis (LCA) was applied to 38 items (13 childhood conduct symptoms and 25 adult misbehaviors) to identify subtypes of ASPD with distinct symptom profiles that could be used to advance efforts for phenotyping alcohol dependence.

Latent class analysis

LCA is a statistical method that is based on the assumption that the frequencies with which different symptom endorsement profiles occur in a dataset can be explained by the existence of a small number of mutually exclusive respondent classes or subtypes, m , with each class having a distinctive "profile" of symptom endorsement probabilities that is constant for all members of that class (McCutcheon, 1987). This technique has been used to study subtypes for a wide variety of psychiatric and medical illnesses and syndromes, including attention deficit-hyperactivity disorder (Hudziak *et al.*, 1998; Neuman *et al.*, 1999); depression (Eaton *et al.*, 1989); alcohol dependence (Heath *et al.*, 1994; Bucholz *et al.*, 1996); schizophrenia (Kendler, Karkowski & Walsh, 1998), conduct disorder (Eaves *et al.*, 1993), myocardial infarction (Rindskopf & Rindskopf, 1986) and nicotine withdrawal (Madden *et al.*, 1997).

A critical assumption of LCA is that within a

Table 1. Prevalence of items used in latent class analyses (LCA)

	Prevalence (%)	
	Females	Males
Childhood behaviors		
Truant	25.2	34.4
Ran away from home	4.3	4.9
Started fights as a child	4.6	13.4
Used a weapon in a fight	1.0	3.3
Raped someone	0.1	0.1
Hurt animals on purpose	2.3	10.0
Deliberately injured someone	1.0	2.2
Vandalized	3.6	12.1
Burglarized	2.3	9.8
Set fires	5.1	20.3
Lied often	7.2	10.7
Stole things/forged name	25.9	39.8
Mugged someone	0.2	0.9
Adult behaviors		
Unemployed but able to work	9.6	11.2
Work tardiness or frequently absent	4.9	4.0
Quit jobs often	14.0	17.4
Stole as an adult	21.5	34.6
Vandalized as an adult	8.0	22.0
Arrested	10.3	28.7
Arson	1.1	5.6
Burglarized	3.8	17.6
Mugged	0.7	5.3
Illegal activities	21.8	45.5
Raped	0.1	0.7
Fighting	24.6	49.8
Weapon use	3.1	7.9
Deliberately injured someone	2.3	4.8
Hit spouse, offspring	9.8	6.0
Defaulted on debts	20.3	26.5
Defaulted on family support	0.8	3.8
No fixed address	4.3	5.9
Lied	10.0	15.9
Conned people	7.0	16.8
Reckless behavior	23.4	55.7
DWIs	16.1	44.2
Serious neglect of children	1.5	1.0
Never faithful	1.7	7.3
Lack of remorse	12.1	22.2

class, the probabilities of endorsing different symptoms are statistically independent (Clogg, 1995). This is the principle of local independence; that is, the relationships between two variables are predicated on a third, unobserved—“latent”—variable, so that once this latent variable is taken into account, the observed measures are no longer related.

To select a model, an *m*-class solution was compared to an *m* + 1-class solution by a likelihood ratio χ^2 test with degrees of freedom equal to *r* + 1, where *r* is the number of items used in

the analysis. We have based our selection of a model on parsimony, adequacy of the model with respect to the research questions being posed, generalizability of the model to other samples and sample size. More conventional global goodness-of-fit tests are difficult to interpret in data such as these; this is because the large number of items produce somewhat sparse tables so that the distribution of the fit statistics is not well known. Therefore, our model selection was not based on an overall goodness-of-fit test.

For a given model, parameter estimates in-

clude: (1) class membership probabilities (which may be thought of as class prevalence estimates) and (2) class-specific symptom endorsement probabilities (SEP). SEPs reflect the probability that an individual will have a given response on an item, conditional on being in that class. In the case of psychiatric data, where symptoms are typically dichotomized as present or absent, these parameters reflect the probability that the symptom is endorsed by the individual, given membership in that class. Classes are characterized by the SEPs for each item, as well as by their estimated prevalence.

Assignment of individuals to classes was based on a probabilistic method, not most likely class (Clogg, 1995). To do this, the conditional probabilities of membership in each class were computed for each symptom profile. For an n -class solution, n duplicate observations for each subject were created, but with different class memberships 1 to n assigned to different observations, using as a data weight for a given observation the corresponding conditional class membership probability, given the symptom profile. This multiple imputation approach avoids the problem of biased estimates that can arise if class membership assignment is based solely on the most likely class membership for a given symptom profile (Clogg, 1995). In analyses reported here, the non-independence of observations on family members was ignored which, although possibly overestimating the significance of parameter estimates, ensures that results can be compared meaningfully to findings on samples of unrelated individuals (Bucholz *et al.*, 1996).

Results

Sample description

The average age of the women in the sample was 36.0 (SD \pm 5.9 years), with a median age of 34. They had a mean of 12.8 (SD \pm 1.1) years of schooling, with 16.1% having 4 years or more of college. The majority were white (75.4%), 15.8% were black, and the remainder were Hispanic (6.0%), Native American (1.1%) or other (1.5%). Nearly half (49.1%) were currently married, 26.8% had never been married, 15.3% were divorced, 6.2% were separated and 2.7% were widowed. Most (52.2%) worked all 12 months in the last year, with 77.5% of the sample having worked for at least 1 month. The median grouped family income was \$30 000–

39 999. In this alcoholic family study, 41.3% met life-time criteria for DSM-III-R alcohol dependence, 25.7% met criteria for life-time DSM-III-R depression and 3.9% qualified for a life-time diagnosis of DSM-III-R ASPD. Prevalence of other substance dependence ranged from 3.9% (opiate) to 15.6% (for cocaine and marijuana). Of this sample, 22.4% reported having ever received treatment in a chemical dependency or psychiatric unit. The mean Global Assessment of Functioning (GAF) score (Endicott *et al.*, 1976), assigned by the interviewer at the time of interview, was 74.1 (SD \pm 6.5), indicative of slight impairment in functioning.

Men in the sample were on average 38.3 (SD \pm 16.2) years of age, with a median age of 35. They averaged 12.8 (SD \pm 1.1) years of schooling, with 19.1% reporting 4 years or more of college. The majority were white (75.2%), 16.4% were black and the remainder were Hispanic (5.7%), Native American (0.9%) or other (1.8%). Nearly half (44.9%) were currently married, 34.9% had never been married, 14% were divorced, 5.5% were separated and 0.8% were widowed. A majority (52.4%) had worked all 12 months in the last year, with 83% of the sample reporting having worked for at least 1 month in the last year. In these men from this family study of alcoholism, of whom 10% were controls, 64.8% met life-time criteria for DSM-III-R alcohol dependence and 14.8% qualified for a life-time diagnosis of ASPD. The prevalence of other substance dependence ranged from 6.2% (for sedatives) to 27.8% (for marijuana). Eleven per cent (11.2%) met life-time criteria for a major depressive episode, and about 2% qualified for life-time diagnoses of social phobia and of panic disorder. Nearly 39% reported having been treated in a psychiatric or chemical dependency unit. Mean GAF score was 72.7 (SD \pm 6.3) which, as for women, indicated slight impairment.

Latent class analyses

Two to six class solutions were estimated for women and men. While the statistical evidence did not unequivocally point to the 4-class over the 5-class solution for women, inspection of the classes revealed a very rare class that was idiosyncratic in nature in the 5-class solution, leading to selection of the 4-class for women. A 5-class solution adequately fit the data from

Table 2. Summary of results of latent class analysis

	- 2 ln likelihood	χ^2	p^*
<i>Females</i>			
No. of classes			
2	47974.790	—	—
3	47243.593	731.197	0.000
4	46838.846	404.747	0.000
5	46442.267	396.579	0.000
6	46189.204	253.063	0.000
<i>Males</i>			
No. of classes			
2	88542.427	—	—
3	87137.077	1405.35	0.000
4	86521.757	615.32	0.000
5	86089.345	432.41	0.000
6	85741.494	347.85	0.000

* χ^2 distributed with 39 degrees of freedom. Degrees of freedom between an m-class and m + 1-class model are calculated as follows: 38 for the items estimated in the additional class and 1 for the estimate of the extra class prevalence, for a total of 39 degrees of freedom.

men. The results of the latent class models, comparison of models and associated statistics, and significance levels are displayed in Table 2. Figures 1 and 2 graph individual symptom endorsement probabilities (SEPs) by class separately for women and men.

For women, Class A comprised nearly half the sample (48.4%), with negligible SEPs for most childhood (mean SEP 0.02) and adult behaviors (mean SEP 0.02). Class B (23.4% of the female sample) had similarly negligible SEPs for childhood behaviors (mean 0.05), but differed from Class A with respect to adult behaviors, as may be detected in the overall mean SEP for adult behaviors of 0.14. Among Class B, SEPs for aggressive behaviors were sharply elevated, with an SEP for fighting close to 0.6. SEPs for irresponsible and unlawful behaviors (e.g. quitting jobs, speeding tickets) were modestly elevated, ranging from 0.2 to 0.4.

Unlike Classes A and B, Class C (20.3%) had modestly elevated SEPs for several childhood behaviors, with SEPs for truancy and stealing most pronounced. The mean SEP for childhood behaviors was 0.11. SEPs ranged from 0.2 to 0.6 for a variety of adult behaviors, including stealing, engaging in illegal activities, defaulting on debts, lying and recklessness (speeding tickets, drinking-driving difficulties); the mean SEP for adult behaviors was 0.12, slightly lower than that observed for Class B.

Finally, Class D (7.9% of the sample) had substantially elevated SEPs (most exceeding 0.2, with six exceeding 0.6) for misbehaviors in both childhood and adulthood, indicative of a severely affected group. Childhood items with the highest SEPs in this class included truancy, initiating fights, lying and stealing; the overall mean SEP for childhood behaviors was 0.22. Adult behaviors that were most pronounced (SEPs greater than 0.6) included stealing, engaging in illegal activities, fighting and defaulting on debts. The mean SEP for adult antisocial behaviors was 0.32. Across all classes, however, many of the symptoms of childhood conduct disorder were rare in these women, even in the severely affected class.

Figure 2 displays class-specific SEPs for the 5-class solution for men. In general, class-specific mean SEPs were higher in men than in women, although characterization of the classes was similar. Class A (24.9%) was comprised of unaffected individuals, with very low SEPs for both childhood and adult misbehaviors. Mean SEP was 0.04 for childhood and 0.05 for adult misbehaviors. Class B (25.9% of the sample) was distinguished by the childhood misbehavior of truancy; all other childhood behaviors had modest SEPs, with an overall mean SEP for childhood misbehaviors of 0.07, only slightly higher than that for Class A. Adult misbehaviors prominent in this class included being arrested, engag-

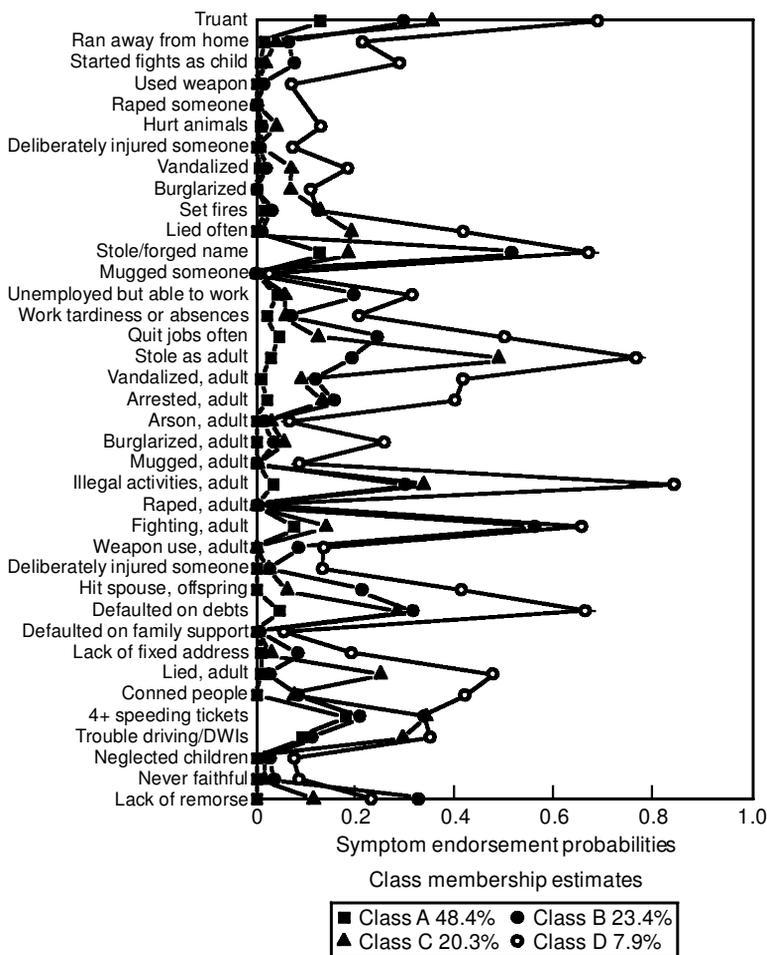


Figure 1. 4-class solution: females.

ing in illegal activities, fighting, speeding tickets and driving difficulties (recklessness) and absence of remorse. The average SEP for adult behaviors was 0.15, considerably higher than that for childhood behaviors.

Class C (18.3% of the sample) showed more evidence of childhood misbehaviors than either Classes A or B, including aggressive behaviors (vandalism, arson), as well as a very high SEP for non-confrontational stealing; the mean SEP for childhood behaviors for this class was 0.17. However, the mean SEP for adult behaviors of 0.16 was only slightly higher than that of Class B. Adult behaviors with elevated SEPs in this class included stealing, vandalism and engaging in illegal activities. Class D (18.5% of the sample) had a childhood profile similar to that of

Class C, but with a slightly higher SEP for lying and lower SEPs for stealing and arson. Overall, the mean SEP for childhood items for this class was 0.14, slightly lower than that observed for Class C. In contrast, the adult profile for Class D differed markedly from that of Class C, with elevated SEPs for illegal behaviors and burglary and irresponsible behaviors in several domains; the average SEP for adult behaviors was 0.29, considerably higher than that observed for Class C.

Alone of the five classes, Class E (constituting 12.4% of males) had large SEPs for many childhood behaviors, as reflected in a mean SEP of 0.34. SEPs for adult behaviors were similarly elevated, with an overall mean of 0.42, and particularly high (well over 0.6) for aggressive,

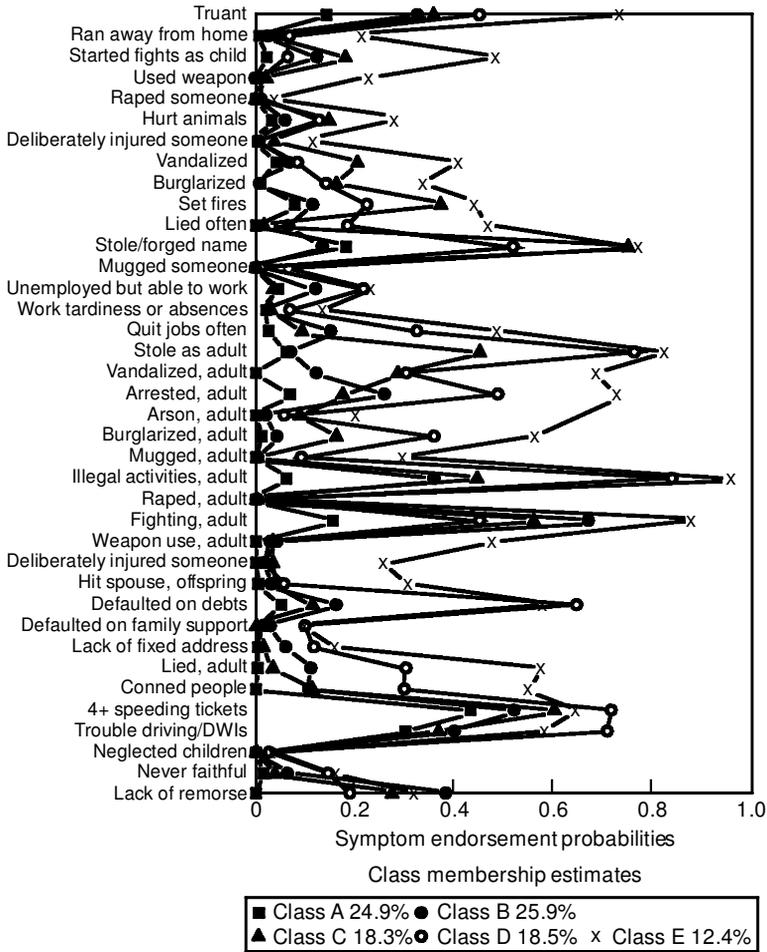


Figure 2. 5-class solution: males.

illegal and reckless activities. This class had the most severe symptom profile.

Class membership, childhood conduct disorder and ASPD

The classes were cross-tabulated with DSM-III-R life-time criteria for childhood conduct disorder and the full and partial diagnoses of ASPD (Table 3).

For women, childhood conduct disorder, using the DSM-III-R requirement of three or more symptoms occurring before the age of 15, was prevalent only in Class D, where 58.9% met criteria, compared to only 13.2%, 2.4% and 0.4% of Classes C, B and A, respectively. Results were similar when the more liberal age

cut-off of 18 was used. Prevalence was substantial only in Class D, where 78.9% met this criterion, compared to 28.6%, 11.3% and 1.2% in Classes C, B and A, respectively. Consistent with these data, DSM-III-R ASPD was common only in Class D, where 45.3% met life-time criteria; only 2% of Class C, a negligible percentage of Class B, and none in Class A, met full criteria for ASPD. Results were similar when behaviors that were attributed solely to substances were included in the diagnostic algorithm. When the childhood conduct criterion for ASPD was ignored, the same pattern persisted: four or more adult misbehavior groups were present in 83.9% of Class D, but only in a minority of women in Classes B and C (25.4%

Table 3. Class membership and childhood conduct and adult ASPD symptom prevalence

	A	B	C	D	<i>p</i>	
<i>Females</i>						
Childhood conduct						
3 + symptoms before age 15	0.37	2.45	13.67	59.09	0.001	
3 + symptoms before age 18	1.25	11.30	28.64	78.93	0.001	
DSM-III-R ASPD, excluding exclusively substance- related symptoms	0	0.32	1.41	45.26	0.000	
DSM-III-R ASPD, including all symptoms	0	0.77	3.66	49.83	0.000	
4 + Adult ASPD symptoms, ignoring childhood criterion	0.06	25.38	19.87	83.92	0.001	
	A	B	C	D	E	<i>p</i>
<i>Males</i>						
Childhood conduct						
3 + symptoms before age 15	1.34	5.66	38.16	28.54	84.11	0.001
3 + symptoms before age 18	3.04	14.52	59.31	56.26	96.96	0.001
DSM-III-R ASPD, excluding exclusively substance- related symptoms	0	2.14	7.18	19.85	74.63	0.000
DSM-III-R ASPD, including all symptoms	0.02	2.75	11.54	26.46	77.84	0.000
4 + Adult ASPD symptoms, ignoring childhood criterion	0.87	29.09	27.41	80.63	90.14	0.001

and 19.9%, respectively), and were virtually absent in Class A.

Among men, the majority in Class E (84%) met criteria for childhood conduct disorder, compared to only 28.3% of Class D, 37.2% of Class C, 5.6% of Class B and 1.3% of Class A. When the more liberal age criterion of 18 was used, results resembled those for the more stringent age criterion. Nearly all in Class E (96.9%) were observed to satisfy this criterion, compared to about half in Classes D and C, and 14.5% and 3.0% in Classes B and A, respectively. For the full diagnosis of ASPD, Class E manifested the highest prevalence, with 74.6% meeting life-time criteria; this compares to 19.9% of Class D, 7.2% of Class C, 2.1% of Class B and 0 in Class A. Results were similar when symptoms attributed solely to substance involvement were counted towards diagnosis. When the childhood criterion was ignored, equally high proportions of men in Classes D and E met the criterion for four or more adult misbehaviors (80.6% of Class D and 90.1% of Class E).

Drinking milestones, alcohol symptomatology and dependence

Differences among the classes in age of reaching

several milestones in drinking careers were investigated. Table 4 displays the mean ages of onset of regular drinking and of first intoxication by class for females and males. ("Regular drinking" was defined as drinking at least once a month for 6 months or more.) The onset age decreased significantly as class assignment increased in severity. Each successive class had a significantly earlier age of onset of the milestone than the class before it. Earliest onsets of regular drinking and intoxication were observed in the most affected classes, D for women and E for men. Life-time maximum number of drinks in a day significantly increased as class assignment progressed from the least to the most affected. Only Classes B and C for females and males did not differ statistically in the life-time maximum drinks consumed.

When specific alcohol symptoms were examined across classes, there was an increase in the proportion with the given symptom as class severity escalated and a marked excess of severe alcohol symptoms such as withdrawal, morning drinking, binge drinking and being unable to stop drinking in the most severe classes (Table 4).

Class membership was cross-tabulated with

Table 4. Age of onset of drinking milestones and % with alcohol symptoms by class

	A	B	C	D	
<i>Females</i>					
Milestone					
Age of regular drinking +	20.5 _{abc}	19.5 _{ade}	18.5 _{bdf}	16.5 _{cef}	
Age of 1st intoxication	18.8 _{abc}	17.9 _{ade}	16.5 _{bdf}	14.9 _{cef}	
Maximum number of drinks in 24 hours	10.0 _{abc}	14.2 _{ad}	14.6 _{bc}	24.9 _{cde}	
Alcohol symptoms (% having)					
Binge drinking*	5.4%	15.8%	20.2%	45.2%	
Unable to stop*	11.2%	18.3%	26.6%	45.3%	
Morning drinking*	5.1%	10.6%	14.1%	28.4%	
Fighting*	7.0%	25.4%	23.1%	52.6%	
Depressed*	8.5%	17.6%	26.5%	43.5%	
Withdrawal*	8.7%	18.7%	23.3%	47.3%	
	A	B	C	D	E
<i>Males</i>					
Milestone					
Age of regular drinking +	19.1 _{abcd}	18.1 _{aefg}	17.5 _{behi}	16.4 _{cfhj}	15.1 _{dgiij}
Age of 1st intoxication	17.8 _{abcd}	16.7 _{aefg}	15.8 _{behi}	14.7 _{cfhj}	13.6 _{dgiij}
Maximum number of drinks in 24 hours	17.8 _{abcd}	23.1 _{aef}	23.2 _{bgh}	34.2 _{cegi}	38.0 _{dghi}
Alcohol symptoms (% having)					
Binge drinking*	15.8%	23.5%	21.4%	60.6%	59.1%
Unable to stop*	18.7%	24.7%	24.5%	56.8%	50.3%
Morning drinking*	13.6%	18.6%	14.8%	43.9%	38.4%
Fighting*	21.6%	42.8%	43.4%	63.8%	80.7%
Depressed*	10.7%	18.4%	18.1%	52.0%	48.3%
Withdrawal*	16.2%	23.1%	21.6%	55.5%	53.8%

Items with letters in common are statistically different ($p < 0.05$). * $p < 0.001$. + “Regular drinking” defined as drinking a least once a month for 6 months or more.

four diagnostic classifications of alcohol dependence, including DSM-III-R, DSM-IV, ICD-10 and Feighner (definite). There was a strong linear relationship ($p < 0.0001$) between class assignment and life-time prevalence of alcohol dependence for all classifications for women. However, for men, while there was a significant association between class and alcohol dependence, life-time prevalence did not increase with each successive class. Rather, life-time prevalence was similar for Classes D and E, and in Classes B and C (as evaluated by *post hoc* contrasts of all pairs of classes), using a Wald statistic ($p > 0.36$ for all D vs. E comparisons, and $p > 0.29$ for all B vs. C comparisons).

Class membership and other psychiatric co-morbidity
The life-time prevalence of other psychiatric dis-

orders by class and gender is displayed in Table 5. For females, the prevalence of other substance dependence disorders increased linearly with each class. Exceptions to this pattern were observed for cocaine dependence, where Classes B and C were similar ($p = 0.06$) and for sedative dependence, where no differences among the classes were observed ($p = 0.11$). The relationship with other psychiatric disorders followed no pattern. For panic disorder, while Class D had a significant excess compared to Classes C ($p = 0.03$), B ($p = 0.0005$) and A ($p = 0.0001$), Classes B and C were similar ($p = 0.12$) as were Classes A and B ($p = 0.16$). For social phobia, the statistical evidence pointed only to significant differences between Class A and each of the other classes ($p > 0.89$ for all comparisons). Evidence from the Mantel-Haenszel test for trend

Table 5. Prevalence of psychiatric disorder and general psychosocial functioning by class

Diagnosis	A	B	C	D	<i>p</i> *	
<i>Females</i>						
Dependence on						
Cocaine	5.7	18.5	22.8	49.9	0.000	
Marijuana	5.9	16.4	24.1	50.4	0.000	
Opiate	0.8	3.6	6.0	18.4	0.000	
Sedative	1.4	4.9	7.0	20.0	0.000	
Stimulants	3.5	8.4	14.5	25.2	0.000	
Depression	23.3	26.8	29.1	28.5	0.005	
Social phobia	2.4	5.3	5.2	5.7	0.001	
Panic	4.1	5.5	7.8	12.8	0.000	
Mean GAF score +	77.7	71.4	72.6	63.0	0.0001	
	A	B	C	D	E	<i>p</i> *
<i>Males</i>						
Dependence on						
Cocaine	4.7	11.4	14.5	46.1	56.2	0.000
Marijuana	7.8	16.2	24.4	52.5	60.6	0.000
Opiate	1.0	3.0	3.6	14.9	22.4	0.000
Sedative	0.9	2.3	4.1	12.9	18.1	0.000
Stimulants	1.5	5.4	8.7	22.3	26.8	0.000
Depression	10.8	10.0	11.0	12.2	13.2	0.082
Social phobia	1.2	2.1	1.4	2.7	3.5	0.011
Panic	1.2	1.6	2.0	3.7	4.7	0.000
Mean GAF score +	78.0	74.2	75.8	66.4	63.9	0.0001

* Mantel-Haenszel χ^2 test for linear trend. + *F* test from ANOVA.

for depression indicated significance at the 0.005 level, but *post hoc* comparisons of prevalences between the classes revealed that only Classes A and C were significantly different ($p = 0.006$); there was no evidence for increased prevalence with each successive class ($p > 0.11$ for all other comparisons).

Results were different for men. Unlike the data for alcohol dependence, where life-time prevalence was similar for Classes D and E, and for B and C, for dependence on other substances a general pattern of significantly increasing prevalence with each successive class was observed. The exceptions to this were no difference between Classes D and E for stimulant dependence, and between Classes B and C for opiate and cocaine dependence.

For other psychiatric disorders the evidence pointed to differences between the extreme classes (e.g. Classes A vs. E), with little evidence for statistical differences in life-time prevalence for the other classes for both panic disorder and social phobia. There were no significant differences in life-time prevalence of major depression among the classes, either from the Mantel-Haenszel trend analysis ($p = 0.08$) or the *post hoc*

individual prevalence comparisons ($p > 0.09$ in all comparisons).

GAF ratings at the time of interview decreased significantly as class profiles increased in severity for both women and men, ranging from a high of nearly 78 for both women and men in the least severe class, representing transient stressors and mild current impairment, to a low of about 63 for the most severe class, indicative of moderate difficulties in current functioning.

Discussion

Three questions have spurred the analyses in this report. The first asked whether there were subtypes of ASPD differing in symptom profiles in these data. In this large sample of alcoholic probands, their relatives and controls, subtypes of ASPD based on latent class analysis of conduct and ASPD symptoms were not observed. Endorsement of different subgroups of items by different classes was not observed. There was no evidence, for example, of a class with only child conduct problems but few adult problems, as has

been reported by others, such as Hesselbrock & Hesselbrock (1994) in their sample of treated alcoholics (although this was a rare subtype comprising only 10% of their sample.) Rather, each successive class appeared to be more severe than the preceding one, as attested to by the increase in SEPs with each more severe class. This was true for both men and women.

Evidence was found for an adult ASPD problem group in men. This class (Class D in the male sample) had a mild symptom profile for childhood behaviors, but a severe profile for adult behaviors. This inference was supported by the results of latent class and the cross-tabulation of the classes with a variable reflecting four or more adult antisocial behaviors in which marked elevation of adult behaviors was observed for Class D, even though a small percentage of Class D met criteria for full ASPD. Our findings confirm earlier reports of a subtype of individuals with primarily adult antisocial behaviors (Brooner *et al.*, 1992; Hesselbrock & Hesselbrock, 1994; Cottler *et al.*, 1995) based on drug-abusing populations in treatment. Our data from a primarily untreated sample of individuals with substantial substance abuse pathology are more generalizable and support the subdiagnostic category of "adult antisocial behaviors" in the current nosology.

The second question related to the association between the identified latent classes and the diagnosis of alcohol dependence. This association was found to be strong and to increase with class severity. This was particularly evident among women, not only for alcohol dependence but also for drinking milestones and for alcohol symptom prevalence. These findings suggest the importance of childhood conduct/adult misbehaviors in the pathway to alcohol dependence for women.

Patterns for men followed those observed for women in terms of more pathological drinking careers across, and greater prevalence of alcohol dependence and of specific alcohol symptoms with, class severity. However in men, unlike in their female counterparts, neither prevalence of alcohol dependence nor of alcohol symptoms was significantly different in the two most severe classes (D and E), despite differences in the childhood conduct symptom profile in these two classes. Also, these two classes had similar prevalence of adult antisocial behaviors, despite marked differences in the childhood profile. This

finding is indicative of a route to alcohol dependence in men that is not so grounded upon childhood misbehaviors.

The third question concerned the association of other psychiatric co-morbidity with the classes. Here as elsewhere the severity interpretation applied. Findings were consistent with those from other studies reporting that individuals with ASPD were observed to have higher prevalence of alcohol and other substance dependence compared to their non-ASPD counterparts (Hesselbrock & Hesselbrock, 1994; Hesselbrock *et al.*, 1985). Our data indicate that these associations were not limited to a diagnosis of ASPD, since psychopathology increased with each more severe class of antisocial symptomatology, not just in those classes in which ASPD was especially prevalent. This pattern held for both men and women. Interestingly, when the class was held constant, we did not observe gender differences in prevalence: that is, the prevalence of cocaine dependence was equivalent in the most severe classes for both males and females. This may reflect the structure of the ASPD diagnostic section of the SSAGA, in which individuals who completed the full section all had more than one substance problem. This finding may not hold in subsequent analyses based on the follow-up data where all individuals, regardless of their history of substance problems, completed the section.

Patterns for other psychiatric disorders were less clear. In women, the statistical evidence for association of the classes with depression and social phobia was equivocal. *Post hoc* analyses indicated that significant differences existed only between Class A and each of the other classes. The prevalence rates in the other classes were statistically similar. It may be that the χ^2 test is heavily influenced by the end points and not as sensitive to the points in the middle. Rates appeared to flatten for both depression and social phobia in Classes B, C and D for women. Evidence for panic disorder deviated from this pattern; both χ^2 and *post hoc* Wald tests indicated significant differences between the less severe classes (A and B) and the more severe classes (C and D), with the latter classes having higher prevalence.

In men, findings for other psychiatric disorders were more clear-cut. Modest linear trends were observed for depression and social phobia. The interpretation of the data for panic disorder,

with its clear association with class severity, suggested an interplay among ASPD, substance dependence and anxiety that would merit future investigation. Although the possibility that the association is due to self-medication (Schuckit *et al.*, 1997) may not be definitively excluded, in the analyses reported here only panic disorder independent of substance use was considered.

Our findings indicated that in only the most severe classes (Class D for women, class E for men) was the prevalence of full-blown ASPD high, yet classes other than this most severe one for men evidenced serious co-morbidity. Is this indicative of the need for a nosological change? Similar findings in other datasets would be needed before recommending amendments to diagnostic criteria.

Our analyses are not without limitations. These data are from an extremely high-risk sample of probands and their relatives, and may not reflect other populations. The sample is primarily white; nevertheless, there is a substantial proportion of African-Americans and Hispanics, but other analyses of COGA data did not identify differences in the prevalence of ASPD among alcoholics by ethnicity (Hesselbrock *et al.*, 1999a). A second limitation is that, given the need for family data for the genetic linkage study, exceptionally co-operative families may have been recruited leading to an undersampling of ASPD, or selection of milder forms of ASPD. The latter point is supported by the GAF data, which suggest that participants were only mildly impaired, although overestimation of GAF scores may not be ruled out as an explanation. In addition, as with other studies in which the primary source of data is self-report with no collateral information, recall bias may have led to under-reporting of childhood symptomatology. Also, our data did not permit determining pervasiveness or density of the ASPD symptoms, since neither the number of times a behavior had occurred nor age of onset of each behavior were routinely collected. Our inference that certain classes evinced similar SEP profiles might not hold when persistence and density of behaviors are taken into account. The reliability of the attribution of substance behaviors is unknown. Finally, the structure of the ASPD section in the SSAGA—specifically, its mandated inclusion of those with only alcohol or other drug problems—may have led to an overstatement of the association with alcohol and drug dependence.

Taken as a whole, our findings do not suggest subtypes of ASPD symptom profiles but rather indicate that ASPD symptomatology is on a spectrum of severity. Our data agree with the assertion of Robins (1966) that it is the number of conduct and antisocial symptoms, along with their persistence over time, rather than any particular behavior or cluster of behaviors that indicate severity and are linked to poor outcomes. From a phenotyping perspective, as the data for men indicated, mild childhood behavior patterns may separate out a group of alcohol dependent men who otherwise could not be distinguished from their counterparts with full ASPD. However, because our sample is drawn from a very high-risk family study of alcohol dependence, its generalizability may be in question. Confirming these findings in a representative sample is a necessary next step.

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