The Latent Class Structure of ADHD Is Stable Across Informants

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Previous studies have looked at the structure of attention-deficit/hyperactivity disorder (ADHD) using latent class analysis (LCA) of Child Behavior Checklist (CBCL) or Diagnostic and Statistical Manual of Mental Disorders (DSM) symptom structure. These studies have identified distinct classes of children with inattentive, hyperactive, or combined subtypes and have used these classes to refine genetic analyses. The objective of the current report is to determine if the latent class structure of ADHD subtypes is consistent across informant using the Conners' Rating Scales (CRS). LCA was applied to CRS forms from mother, father, and teacher reports of 1837, 1329 and 1048 latency aged Dutch twins, respectively. The optimal solution for boys was a 5-class solution for mothers, a 3-class solution for fathers, and a 4-class solution for teachers. For girls, a 4-class solution for mothers and a 3-class for fathers and teachers was optimal. Children placed into a class by one informant had markedly increased odds ratio of being placed into the same or similar class by the other informants. Results from LCA using Dutch twins with the CRS show stability across informants suggesting that more stable phenotypes may be accessible for genotyping using a multi-informant approach.

Attention-deficit/hyperactivity disorder (ADHD) has been the focus of multiple twin, family, adoption and molecular genetic studies(DiMaio et al., 2003; Faraone & Doyle, 2001). The aggregate aim of these studies has been to determine if ADHD is influenced by genetic factors and then to begin the difficult task of identifying the genes that place an individual at risk for the disorder.

Latent class analysis (LCA) allows the investigator to examine the structure underlying a set of symptoms to help identify phenotypes that can be used for later genetic studies (Hudziak et al., 1998). Using this strategy, a classification scheme slightly different from the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) categorical approach has been proposed by our group and others where response profiles tend to fall into 6- to 8-class solutions rather than a 3-class (inattention, hyperactive, or combined type) solution (Hudziak et al., 1998; Neuman et al., 2001; Neuman et al., 1999; Rasmussen et al., 2004; Rasmussen, Neuman, et al., 2002; Todd et al., 2001). Todd and his colleagues have demonstrated via molecular genetic studies, that different genotypes are associated with different discrete latent classes (Todd et al., 2003). Specifically, they found association between a single nucleotide polymorphism in the nicotinic acetylcholine receptor alpha 4 subunit gene and the latent-class defined inattentive subtype of ADHD that was not present when using DSM-interview defined ADHD. They recommended that work that has been conducted looking at trials with nicotine and nicotinic agonists specifically investigate their use in inattentive symptoms of ADHD. This work has yet to be replicated, but raises the prospect that via phenotypic refinement gene discoveries will be realized.

LCA classes of attention problem items have been shown to be similar across cultures including American, Brazilian, and Australian (Rasmussen, Neuman, et al., 2002; Rasmussen, Todd, et al., 2002; Rohde et al., 2001) when using DSM items. Additionally, LCA investigations of the Attention Problems (AP) scale of the Child Behavior Checklist (CBCL) have also been completed (Hudziak et al., 1999). The LCA classes have been shown to be relatively consistent regardless of whether DSM ADHD symptoms or CBCL Attention Problems items have been analyzed. However, all previous LCA analyses of attention problems have used parental (most often maternal) and/or adolescent self-reports for the identification of symptoms. There has been no evaluation of the latent structure of ADHD using

Received 22 July, 2005; accepted 20 April, 2006.

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multiple informants. While it is not required by DSM to have the evaluation of outside care providers and/or teachers to the make the diagnosis of ADHD, these opinions may be quite important to confirm impairment in multiple settings. Certainly, obtaining the opinions of teachers is encouraged in clinical practice (Dulcan, 1997) and the use of teacher reports has been associated with less rater bias (Power et al., 1998) and has been informative to genetic studies of ADHD (Nadder et al., 2002). Moreover, work by Martin and Curran has been instrumental in taking evaluations by multiple informants to the next level. They have shown that there are methods by which information can be combined and used in a genetically informative fashion (Curran et al., 2003; Martin et al., 2002). In order to proceed in a similar fashion, the requisite first step is to show that the latent structure of attention problems in children is the same or similar regardless of informant. This is what this article intends to examine. Phenotypic refinement using multiple informant approaches can guide molecular genetic studies on two levels. First, to consider and control for variance across informants typically seen in DSM approaches and, second, to determine if different informants yield different latent class membership which would then necessitate a different approach to selecting subjects for molecular genetic analyses. Thus the potential contribution of this approach is to further phenotype refinement, using an alternative to DSM approaches, for further twin and molecular genetic studies, many of which are already being done using the single informant latent class approach.

It has been proposed that using a DSM categorical approach diminishes statistical power, results in rater bias confounds, and can lead to case misidentification. The CBCL AP, which has the advantage of normative data for multiple informants across multiple ages, has been criticized because it does not contain the majority of the DSM ADHD symptoms and although highly correlated with ADHD (Biederman et al., 1993; Chen et al., 1994; Hudziak et al., 2004), it does not necessarily identify children who meet criteria for ADHD. Additionally, it is not the 'clinical taxonomy' used to identify and treat children with ADHD (Hudziak et al., 2004). A middle of the road strategy is to use a well-characterized and often used set of instruments, the Conners' Rating Scales (CRS), which we have been shown to be a useful and genetically informative measure of attentional problems and oppositional behavior (Hudziak et al., 2005a, 2005b). The advantage of this approach is that the CRS contains many of the DSM criteria, but provides separate norms by gender and informant.

The intent of this study was to perform LCA on the CRS data from multiple informants (mothers, fathers, and teachers) in order to identify genetically meaningful phenotypes which may be more generalizable than on a single informant. We sought to replicate the latent class structure of CBCL and DSM attention problems using the CRS and to compare it across informants. This work represents the first systematic study of similarities and differences in latent class structure of ADHD symptoms across different informants. We predicted that the class structure for mother reports on the CRS would be similar to what we have seen for DSM-IV maternal reports (Hudziak et al., 1998; Rasmussen, Neuman, et al., 2002; Todd et al., 2001) and CBCL AP (Hudziak et al., 1999). Because differences in agreement between parents are often less than differences between teachers and parents (Achenbach et al., 1987) and because the Conners' Teachers forms are slightly different than the Conners' Parent forms, we further predicted the latent class structure would be reasonably similar between mothers and fathers, but might differ between parents and teachers.

Materials and Methods

Participants

The study was part of an ongoing twin-family study of health-related characteristics, personality, and behavior in the Netherlands. The subjects were all part of the Netherlands Twin Registry (NTR; Boomsma et al., 2002). For this study, we assessed a cohort of Dutch twins born between the years of 1989 and 1992 whose parents reported on their behavior when they were 10 years old. Socioeconomic status (SES) was derived from the level of parental occupation as reported by the parents and was assessed when the twins were 10 years old. Occupation was coded using a 5-point scale and was based on the mental complexity of the work and ranged from elementary to scientific work. When the occupation information was present for both parents, the highest level was used. The distribution of SES in the present sample was 3% (elementary), 16% (lower), 42% (middle), 26% (higher), and 12% (scientific). The comparison of the observed distribution with that of the general Dutch population revealed a small discrepancy (Rietveld et al., 2003). The level of occupation of the parents of the twins were higher than the level in the general population.

For the LCA, 2160 participants had mother, father, and/or teacher ratings on the CRS. Participants were excluded from the analysis if any of the CRS ADHD-related items were left unanswered. This left 1837 participants with mother ratings, 1329 participants with father ratings and 1048 participants with teacher ratings available for analysis. For cross-informant analyses, only those participants who had information from both (for the between-parent analysis) or all three (for the parent–teacher analysis) informants were included in the analyses. There were 1219 participants with mother and father ratings and 598 participants with mother, father, and teacher ratings.

https://doi.org/10.1375/twin.9.4.507 Published online by Cambridge University Press

Procedure

The assessment procedures at each age have been described in detail elsewhere (Boomsma et al., 2002). Parents received a Conners' Parent Rating Scale–Revised: Short Form (CPRS-R:S) by mail. Parents who did not return the forms within 2 months received a reminder. For the collection of teacher information, parents were asked permission to approach the teacher of their twins. Parents who gave their consent were also asked for the names of the teachers and the addresses off the schools. Teachers were then contacted and received a Conners' Teacher Rating Scale–Revised: Short Form (CTRS-R:S) by mail. Teachers who did not return the form within 2 months received a reminder by mail. This resulted in an average participation rate of 62.3% for mothers, 49.9% for fathers and 79.1% for teachers of the first-born child and 78.3% for teachers of the second-born child.

Measures

Mothers and fathers completed the CPRS-R:S (Connors, 2001). The questionnaire consists of 27 items, given in Table 1, rated on a 4-point Likert scale for symptom severity (i.e., 0 = *Not true at all*; 1 = *Just a little true*; 2 = *Pretty much true*; 3 = *Very much true*). The items are summarized on four scales: Oppositional (six items); Cognitive Problems/ Inattention (CP/IN; six items); Hyperactivity (six items); and ADHD Index (ADHDi; 12 items) with three items overlapping on two scales. The derivation of these scales is described in detail elsewhere (Connors, 2001). Three of these scales, Oppositional, CP/IN, and Hyperactivity, were originally derived for the Conners' Rating Form: Long Form. To provide brief versions of these scales for the CPRS-R:S, only items loading the highest from an exploratory factor analysis of the factor-scale items on the long form were used (loadings ≥ .40). The ADHDi was developed specifically to discriminate children with ADHD from matched controls. The scales are known to have good reliability and internal consistency. (In the original norming study, the ADHDi displayed a kappa of .904, internal consistency coefficients for all four scales were above .81 for males and females, and test-retest reliability coefficients for the scales were between .62 and .85 over a period of 6 to 8 weeks.) As the current study was interested in ADHD-type items, the items from the Oppositional scale were omitted from the analyses, leaving 21 items. For the purposes of the current study, scores on each of the items included in the analyses were truncated to create a dichotomous value (e.g., presence vs. absence) for each item. Items with a score of 0 or 1 were scored as absent and scores of 2 or 3 scored as present.[1]

Teachers completed the CTRS-R:S (Connors, 2001), which was similar, although not identical, to the CPRS-R:S. The questionnaire consists of 28 items rated on the same 4-point Likert scale for symptom severity used on the CPRS-R:S. The items are summarized on four scales: Oppositional (five items); CP/IN (five items); Hyperactivity (seven items); and ADHDi (12 items) with one item loading on two scales. Three of these scales, Oppositional, CP/IN, and Hyperactivity, were originally derived for the Conners' Teacher Rating Scale — Revised: Long Form. The derivation of these scales was similar to the CPRS-R:S and is described in detail elsewhere (Connors, 2001). These scales show similarly good reliability and consistency. (The ADHDi displayed a kappa of .807. Internal consistency coefficients for all four scales are above .88 for males and females. Test-retest reliability coefficients for scales were between .72 and .92 over a period of 6 to 8 weeks.) Again, the items from the Oppositional scale were omitted from the analyses, leaving total of 22 items. Scores on each of the items included in the analyses were truncated as they were for the parent analysis.

Any comparisons between boys and girls or between informants in the scores on the CPRS-R:S or CTRS-R:S were performed by using average item scores (to account for different number of items on the CPRS-R:S and the CTRS-R:S) in two-tailed repeated measures ANOVAs using the program SPSS (2001).

Latent Class Analysis

LCA is a form of categorical data analysis which hypothesizes that it is possible to account for the observed symptom (or item) endorsement profiles of respondents in terms of some small number of mutually exclusive respondent classes (M), with each class having its own set of symptom endorsement probabilities. LCA presupposes the existence of discrete latent categories or classes which distinguishes it from factor analysis which assumes continuous latent variables are present. Local independence is assumed; that is, that under an M-class solution, the conditional probabilities of endorsing a set of items are statistically independent for a given class (Goodman, 1974). For example, under a 1-class model, which does not distinguish between those subjects with ADHD problems versus those without, this assumption is clearly false. An individual who reports a history of one or more ADHD symptoms is much more likely to report other ADHD symptoms than one who does not. A 2-class model also is not likely to fulfill the assumption of local independence. Subjects who report few ADHD symptoms almost surely will be different from subjects who report many ADHD symptoms. However, as the number of latent classes estimate increases, it is assumed that homogenous classes or types will be defined such that individuals within a class will differ in symptom endorsement profiles only because of measurement error or stochastic factors. If the underlying latent variable is continuous rather than categorical, then the LCA-derived classes will reflect differences in severity. The resulting parameter estimates are (1) probabilities of class membership assignment for individuals and (2) symptom endorsement probabilities for each class.

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Table 1

Items from CTRS-R:S and CPRS-R:S

LCA item	Teacher item	CTRS-R:S subscale	Parent item	CPRS-R:S subscale	Parent and teacher items match
1	Poor in arithmetic	CP/IN			
2	Poor in spelling	CP/IN			
3	Not reading up to par	CP/IN			
4	Forgets things he/she has already learned	CP/IN	Gets distracted when given instructions to do something	ADHDi	
5	Lacks interest in schoolwork	CP/IN	Messy or disorganized at home or school	ADHDi	
6	Inattentive, easily distracted	ADHDi	Inattentive, easily distracted	ADHDi	*
7	Short attention span	ADHDi	Short attention span	ADHDi	*
8	Only pays attention to things he/she is really interested in	ADHDi	Only attends if it is something he/she is very interested in	ADHDi	*
9	Distractibility or attention span a problem	ADHDi	Distractibility or attention span a problem	ADHDi	*
10	Fails to finish things he/she starts	ADHDi	Fails to complete assignments	CP/IN	*
11	Does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand directions)	ADHDi	Does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand directions)	CP/IN and ADHDi	*
12			Has trouble concentrating in class	CP/IN and ADHDi	
13			Avoids, expresses reluctance about, or has difficulties engaging in tasks that require sustained mental effort (such as schoolwork or homework)	CP/IN and ADHDi	
14			Needs close supervision to get through assignments	CP/IN	
15			Difficulty doing or completing homework	CP/IN	
16	Fidgets with hands or feet or squirms in seat	ADHDi	Fidgets with hands or feet or squirms in seat	ADHDi	*
17	Has difficulty playing or engaging in leisure activities quietly	HI	Has difficulty playing or engaging in leisure activities quietly	HI	*
18	Restless in the 'squirmy' sense	HI	Restless in the 'squirmy' sense	HI	*
19	Is always 'on the go' or acts as if driven by a motor	HI	Is always 'on the go' or acts as if driven by a motor	HI	*
20	Has difficulty waiting his/her turn	HI	Has difficulty waiting in lines or awaiting turn in games or group situation	HI	*
21	Disturbs other children	ADHDi	Hard to control in malls or while grocery shopping	HI	
22	Cannot remain still	ADHDi	Easily frustrated in efforts	ADHDi	
23	Leaves seat in classroom or in other situations in which remaining seated is expected	HI	Leaves seat in classroom or in other situations in which remaining seated is expected	ADHDi	*
24	Runs about or climbs excessively in situations where it is inappropriate	HI	Runs about or climbs excessively in situations where it is inappropriate	HI	*
25	Interrupts or intrudes on others (e.g., butts into others' conversations or games)	ADHDi			
26	Excitable, impulsive	HI and ADHDi			
27	Restless, always up and on the go	ADHDi			

Note: CTRS-R:S = Conners' Teacher Rating Scale — Revised: Short Form; CPRS-R:S= Conners' Parent Rating Scale — Revised: Short Form; LCA = Latent Class Analysis; CP/IN = Cognitive Problems/Inattention scale; ADHDi = ADHD index; HI = Hyperactive-Impulsive scale.

Latent class models were fitted by means of an expectation maximization algorithm (Dempster et al., 1977), using the program LCAP (Neuman et al., 1999). Models estimating 1-class through 9-class solutions were compared. To calculate the best fitting model, we compared the change in the Bayesian Information Criterion (BIC), a goodness-of-fit index that considers the rule of parsimony, when moving from an M to an M+1 class solution.

LCA was performed on mother, father, and teacher report data for boys and girls separately using all of the completed reports available for the

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Table 2

Means and Standard Deviations of Average Item Scores for Participants for Whom Data were Available from All Three Informants

	Male (n = 287)		Female (n = 311)	
	Mean	*SD*	Mean	*SD*
ADHD Index				
Mother	.797	.697	.506	.532
Father	.726	.630	.467	.502
Teacher	.551	.617	.264	.390
Hyperactivity Index				
Mother	.587	.641	.300	.452
Father	.553	.593	.311	.427
Teacher	.429	.580	.165	.310
Cognitive-Inattention Index				
Mother	.765	.745	.488	.571
Father	.711	.696	.448	.565
Teacher	.625	.711	.465	.590

given informant. Once the optimal solution was chosen and class assignments were made, comparisons between informants were considered. Thus, class assignment was performed first using all available data for each informant. Participants were dropped in the cross-informant analysis if they did not have ratings from one or more informant. Across informant class assignments were made by calculating the Euclidean distance between item endorsement probabilities and choosing as equivalent classes the classes that were closest in Euclidean distance by taking the minimum of the square root of the squared differences between each corresponding point between curves (Rasmussen et al., 2004). We computed odds ratios for all comparisons between classes by looking at the probability of being in a particular class by one informant given that the child was classified into that class by another informant (versus the probability of being placed into any of the other classes).

Results

Average item scores for the three subscales used in the analysis are given in Table 2. As could be predicted from previous findings, boys scored higher than girls on all scales of the CPRS-R:S and the CTRS-R:S. A repeated measures ANOVA with between-item factor of sex and within-item factor of informant demonstrated a significant main effect ($p \leq .001$) for informant (F = 96.14, 36.3, and 10.45 for ADHDi, HI, and CP/IN, respectively) and for sex (F = 43.88, 486.27, 606.00 for ADHDi, HI, and CP/IN, respectively) for all three subscales with boys consistently showing higher scores than girls and parents rating the children as having more symptoms than teachers. For only the CP/IN subscale, there was also a significant interaction of informant by sex with teachers consistently rating boys lower on the CP/IN scale than either mother or father (F = 7.40, p = .007).

Latent Class Analysis Results

Turning to the results from the LCA, nine latent class models were fit to the data, representing a 1-class through a 9-class solution. As the number of classes increased, improvements were made in the goodness-of-fit, as evidenced by a decrease in the BIC. For boys, additional classes failed to result in meaningful, more parsimonious solutions at the point of a 5-class solution for mothers, 3-class solution for fathers, and 4-class solution for teachers. For girls, optimal solutions included four classes for mothers, three for fathers, and three for teachers.

The class solution information including prevalence of assignment of individuals to each class are presented in Table 3 and are presented graphically in Figure 1. Figure 1 shows the probability of item endorsement plotted versus item number. Since there were different items included on the CTRS and the CPRS, there are 27 total items on each graph, only a subset of which is plotted for each informant. The item number scheme is provided in Table 1.

We chose names for these classes on the basis of the pattern of symptom endorsement within the response profile and the apparent 'strength' of the symptom endorsement. As would be predicted, the majority of 10-year-old children, both boys and girls, were assigned to a class in which very few items were endorsed. The class solutions were similar but not identical between boys and girls and across informants. We first describe the classes by informant and then discuss the across-informant information.

Maternal Classes

For females, the solution led to two mild and two severe classes. For males the solution led to two mild, two severe and one moderate class. The least severe of these classes was a 'no or mild symptoms' group into

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Table 3

Mother, Father, and Teacher Classes Compared to ADHDi, HI, and CP/IN Clinical and Borderline Clinical Cutpoints

		Total	ADHDi > 5%	ADHDi > 10%	HI > 5%	HI > 10%	CP/IN > 5%	CP/IN > 10%
Mother classes								
Male	No or mild symptoms	510 (60.8%)	0 (0%)	0 (0%)	1 (0.2%)	25 (4.9%)	0 (0%)	0 (0%)
	Mild inattentive	108 (12.9%)	0 (0%)	0 (0%)	1 (0.9%)	16 (14.8%)	0 (0%)	4 (3.7%)
	Severe inattentive	101 (12.0%)	6 (5.9%)	44 (43.6%)	14 (13.9%)	57 (56.4%)	13 (12.9%)	54 (53.5%)
	Hyperactive-impulsive	55 (6.6%)	2 (3.6%)	3 (5.5%)	29 (52.7%)	49 (89.1%)	0 (0%)	2 (3.6%)
	Severe combined	65 (7.7%)	44 (67.7%)	62 (95.4%)	60 (92.3%)	65 (100%)	19 (29.2%)	52 (80%)
	Total maternal males	839 (100%)	52 (6.2%)	109 (13.0%)	105 (12.5%)	212 (25.3%)	32 (3.8%)	112 (13.3%)
Female	No or mild symptoms	744 (74.5%)	0 (0%)	1 (0.1%)	24 (3.2%)	86 (11.6%)	0 (0%)	1 (0.1%)
	Mild combined	156 (15.6%)	0 (0%)	27 (17.3%)	51 (32.7%)	92 (59%)	1 (0.6%)	45 (28.8%)
	Severe inattentive	57 (5.7%)	28 (49.1%)	49 (86%)	12 (21.1%)	29 (50.9%)	31 (54.4%)	54 (94.7%)
	Severe combined	41 (4.1%)	36 (87.8%)	41 (100%)	41 (100%)	41 (100%)	24 (58.5%)	34 (82.9%)
	Total maternal females	998 (100%)	66 (6.6%)	124 (12.4%)	138 (13.8%)	266 (26.7%)	59 (5.9%)	143 (14.3%)
Father classes								
Male	No or mild symptoms	440 (69.7%)	0 (0%)	0 (0%)	1 (0.2%)	21 (4.8%)	0 (0%)	0 (0%)
	Mild inattentive	123 (19.5%)	0 (0%)	4 (3.3%)	22 (17.9%)	61 (49.6%)	0 (0%)	12 (9.8%)
	Severe combined	68 (10.8%)	23 (33.8%)	57 (83.8%)	39 (57.4%)	55 (57.4%)	21 (30.9%)	57 (83.8%)
	Total paternal males	631 (100%)	23 (3.6%)	61 (9.7%)	64 (10.1%)	142 (10.1%)	21 (3.3%)	70 (11.1%)
Female	No or mild symptoms	531 (76.1%)	0 (0%)	2 (0.4%)	24 (4.5%)	68 (12.8%)	0 (0%)	0 (0%)
	Mild combined	122 (17.5%)	5 (4.1%)	27 (22.1%)	47 (38.5%)	82 (67.2%)	7 (5.7%)	47 (38.5%)
	Severe inattentive	45 (6.4%)	37 (82.2%)	44 (97.8%)	30 (66.7%)	38 (84.4%)	27 (60.0%)	45 (100%)
	Total paternal females	698 (100%)	42 (6.0%)	73 (10.5%)	106 (15.2%)	201 (28.8%)	34 (4.9%)	93 (13.3%)
Teacher classes								
Male	No or mild symptoms	333 (68.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Severe inattentive	67 (13.8%)	0 (0%)	1 (1.5%)	0 (0%)	0 (0%)	16 (23.9%)	28 (41.8%)
	Hyperactive-impulsive	45 (9.3%)	0 (0%)	0 (0%)	0 (0%)	4 (8.9%)	0 (0%)	0 (0%)
	Severe combined	40 (8.2%)	10 (25.0%)	18 (45.0%)	7 (17.5%)	25 (62.5%)	2 (5.0%)	10 (25.0%)
	Total teacher males	485 (100%)	11 (2.3%)	22 (4.5%)	7 (1.4%)	30 (6.2%)	20 (4.1%)	40 (8.2%)
Female	No or mild symptoms	424 (75.3%)	0 (0%)	2 (0.5%)	3 (0.7%)	34 (8.0%)	0 (0%)	0 (0%)
	Mild combined	104 (18.5%)	1 (1.0%)	16 (15.4%)	13 (12.5%)	31 (29.8%)	12 (11.5%)	32 (30.8%)
	Severe inattentive	35 (6.2%)	25 (71.4%)	32 (91.4%)	25 (71.4%)	33 (94.3%)	6 (17.1%)	12 (34.3%)
	Total teacher females	563 (100%)	28 (5.0%)	53 (9.4%)	48 (8.5%)	113 (20.1%)	21 (3.7%)	48 (8.5%)

which the majority of the samples, female or male, were classified (74.5% and 60.8%, respectively).

For females, the next highest percentage was placed into a mild combined class that consisted of a profile with relatively low endorsement probability of both inattentive and hyperactive-impulsive (HI) items. This comprised 16.9% of the sample. In all, the percentage of girls that fell into one of the no or mild symptoms classes was 77.7%. The next highest level of assigned class membership for females was a severe inattentive class with 5.7% of girls being assigned to this class. The final class, which comprised 4.1% of the girls, was a severe combined class that had a similar inattentive profile to the severe inattentive class, but also included high endorsement probabilities on the HI items. Together, the severe inattentive and severe combined classes comprised 9.8% of the girls in the sample.

For males, classes were similar, although a separate HI class emerged. After the 'no or mild symptoms' class, a mild inattentive class was identified with 12.9% of the sample. Together, these no or mild symptoms classes comprised 73.7% of the sample. A severe inattentive class comprised 12% of the sample and a severe HI class comprised 6.6% of the sample. Finally, 7.7% of the sample was classified into a severe combined class. Overall, the three severe, more symptomatic classes made up 26.3% of the sample.

Paternal Classes

The latent classes that emerged from the father's reports included three classes for both boys and girls. For girls, the fathers identified a no or mild symptoms

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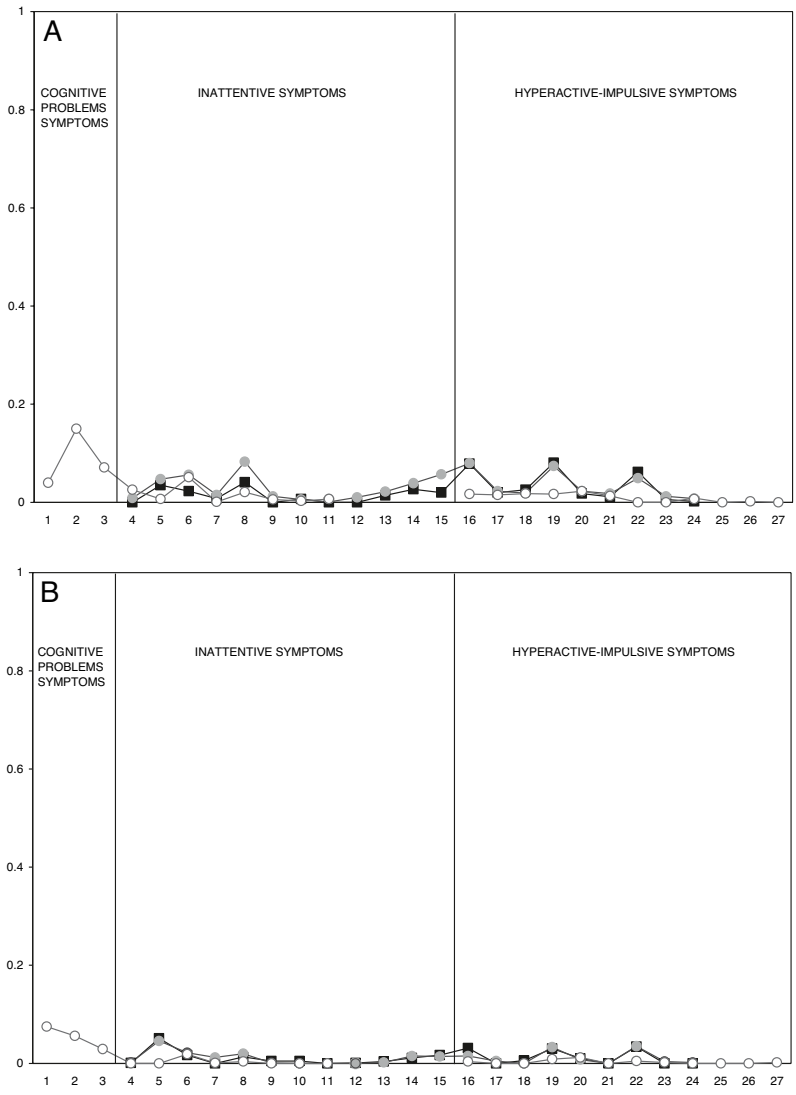

Figure 1 (continued over)

Latent class symptom endorsement profiles for mother (■) father (●) and teacher (○) solutions for males (left column) and females (right column).

Note: Probability of item endorsement is plotted versus items. The items are listed in Table 1. Panels A and B show the male and female no or mild symptoms classes. Panel C shows the male mild inattentive class. Panel D shows the female mild combined class. Panels E and F show the male and female severe inattentive classes. Panels G and H show the male and female severe combined classes. Panel I shows the male hyperactive-impulsive class.

class, a mild combined class, and a severe inattentive class that captured 76.1%, 17.5%, and 6.4%, respectively. In boys, the fathers identified a no or mild symptoms class, a mild inattentive class and a severe combined class which captured 69.7%, 19.5%, and 10.8% of the sample, respectively. These classes mapped very well onto the maternal classes; although, as one might expect, in the mild inattentive class in the boys, there were higher symptom endorsement probabilities for inattentive items (likely reflecting those boys who may have been classified into a severe inattentive class if a higher number of classes were fit) and in the severe inattentive class in girls there were higher symptom endorsement probabilities for the hyperactive items (likely reflecting those girls who may have been classified into the severe combined class, had it come out of the modeling). Similar to the mother report, more boys than girls were classified into the more severe classes.

Teacher classes

The teacher classes mapped very well onto the parental classes. For girls, the teachers identified a no or mild symptoms class, a mild combined class, and a severe inattentive class which captured 75.3%, 18.5%, and 6.4%, respectively. For boys, the teachers identified a no or mild symptoms class, a severe inattentive class, a severe combined class, and a HI class. These captured 68.7%, 13.8%, 8.2% and 9.3% of the sample, respectively. In girls, the mild combined class had slightly lower HI item endorsement probabilities and the severe inattentive class had slightly higher HI symptom probabilities than parent reports.

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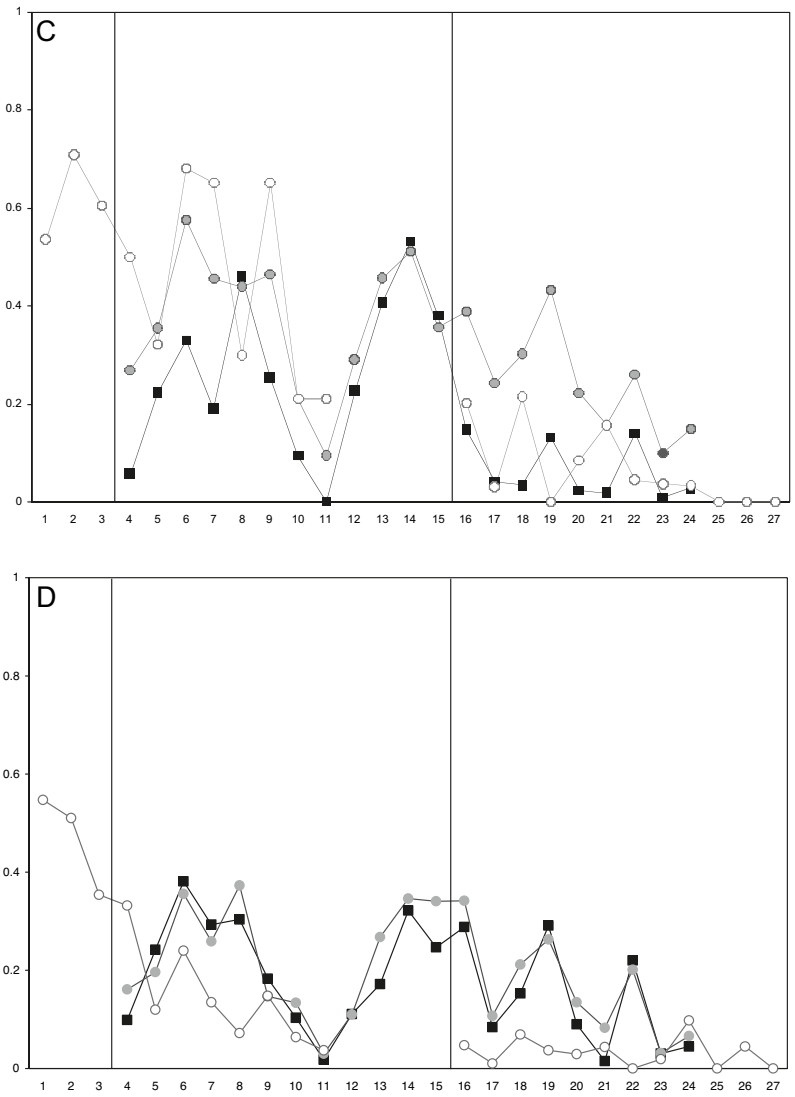

Figure 1 (continued)

Latent class symptom endorsement profiles for mother (■) father (●) and teacher (○) solutions for males (left column) and females (right column).

Note: Probability of item endorsement is plotted versus items. The items are listed in Table 1. Panels A and B show the male and female no or mild symptoms classes. Panel C shows the male mild inattentive class. Panel D shows the female mild combined class. Panels E and F show the male and female severe inattentive classes. Panels G and H show the male and female severe combined classes. Panel I shows the male hyperactive-impulsive class.

This suggests that teachers identified girls as having either mild inattentive symptoms in isolation or severe inattentive symptoms with hyperactivity. This later group is similar to a combined type and it mapped closely in Euclidean distance to the severe combined type, despite being closest to the severe inattentive type. Again, more boys than girls were classified into the severe symptom classes.

Comparing Class Assignment to Symptom Severity

The cross-tabulation between the CRS and the LCA classes are given in Table 3. This table contains class membership as it compares to the 95 percentile and 90 percentile Conners' cutpoints that have been suggested as 'clinical' or 'borderline clinical'. Here, maternal classes are compared to the cutpoints for maternal ADHDi, CP/IN, and HI, the paternal classes to paternal cutpoints, and the teacher classes to teacher cutpoints. Very few children scored in the borderline or clinical range on the ADHDi, HI, or CP/IN if they had been classified into the no or mild symptoms class category, regardless of informant. As the severity of the classes increased, more children were identified as falling into the borderline clinical, or clinical range. Most of the children in the 'severe combined' category, regardless of informant, were in the clinical range on the HI and the ADHDi and almost all were in the borderline clinical range. The CP/IN seemed to mainly capture children placed into the more severe classes and identified fewer children as clinical or borderline clinical by teacher report than by parent report.

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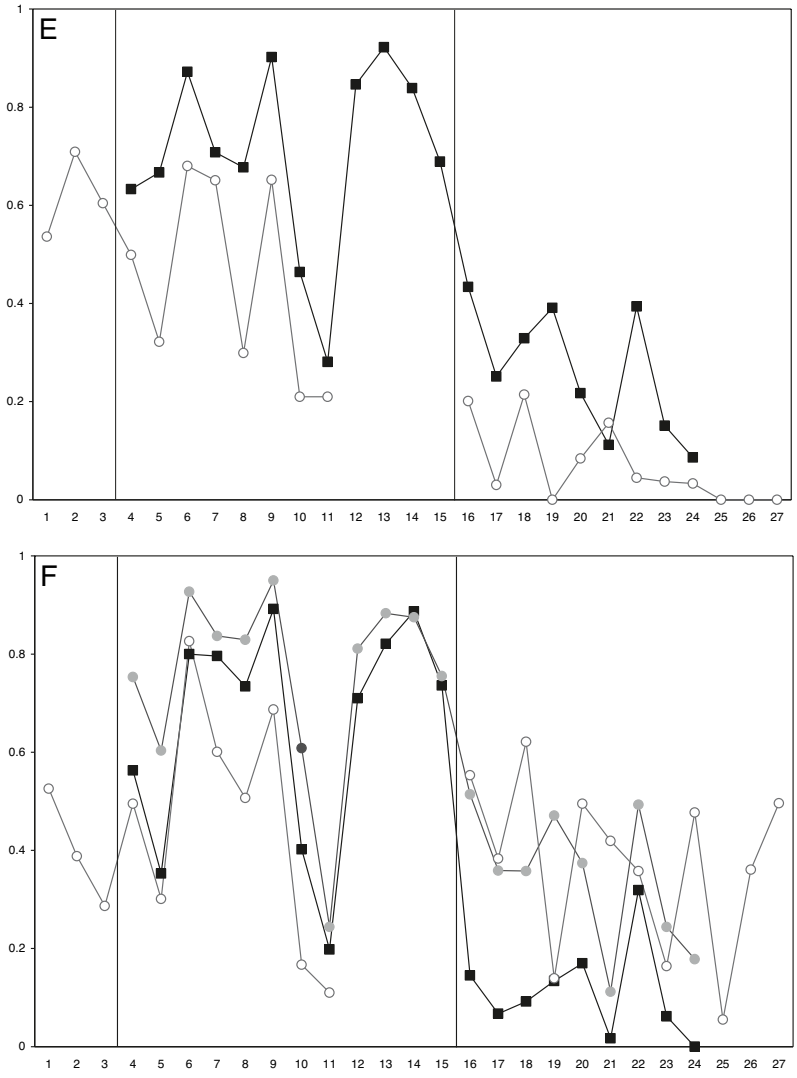

Figure 1 (continued)

Latent class symptom endorsement profiles for mother (■) father (●) and teacher (○) solutions for males (left column) and females (right column).

Note: Probability of item endorsement is plotted versus items. The items are listed in Table 1. Panels A and B show the male and female no or mild symptoms classes. Panel C shows the male mild inattentive class. Panel D shows the female mild combined class. Panels E and F show the male and female severe inattentive classes. Panels G and H show the male and female severe combined classes. Panel I shows the male hyperactive-impulsive class.

Boys who fell into the 'mild inattentive' classes by paternal or maternal report were not well identified by either the ADHDi or the CP/IN.

Comparing Class Assignment Across Informants

The cross-tabulation of class assignment across informants and the corresponding odds ratios are presented in Tables 4 to 6. Looking first at parental agreement, the odds ratio of being placed into the no or mild symptoms class for fathers given that the child was classified into the no or mild symptoms class by the mother report was 17 to 19 for boys and girls. Boys classified by their mothers as having mild or severe inattentive problems had a high probability of being placed into the mild inattentive class by paternal report, and for girls there was a high likelihood of being placed into the mild combined category for fathers, given that was also the class for mothers. There was an especially high likelihood of being classified into the severe combined class for fathers, given that was also the class for mothers, with odds ratios of 38.02 and 42.62 for boys and girls, respectively. These relations held also with the mother to teacher and father to teacher agreement, albeit at a lower level. One exception was that girls classified by fathers as severe inattentive had almost equal likelihood of being classified by teachers as mild combined or severe inattentive, and girls classified by fathers as mild combined had higher odds ratio of being classified as severe inattentive than mild combined by teachers.

We examined the possibility that there may be a bias on the placement into latent classes on the basis

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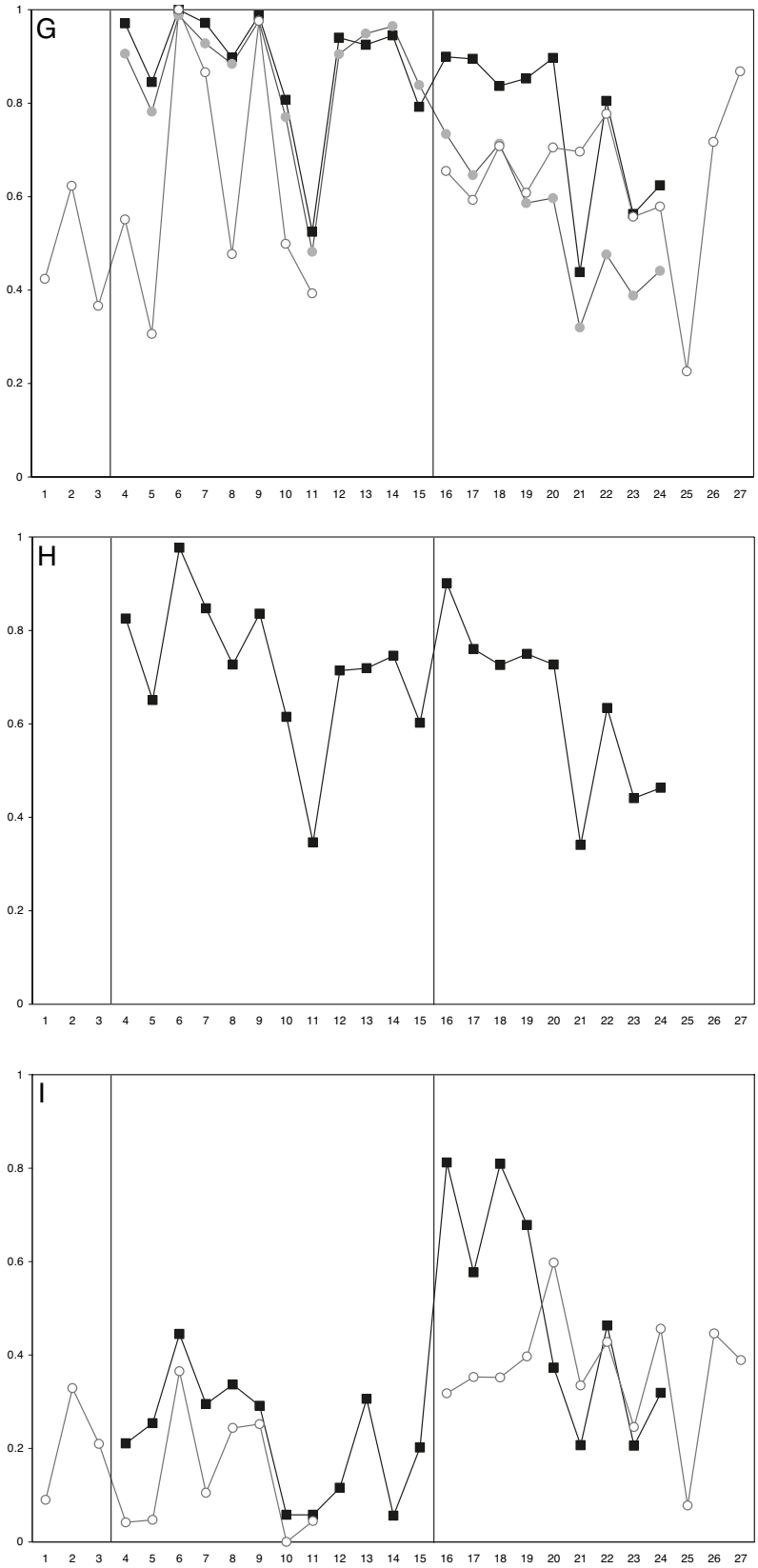

Figure 1 (continued)

Latent class symptom endorsement profiles for mother (■) father (●) and teacher (○) solutions for males (left column) and females (right column).

Note: Probability of item endorsement is plotted versus items. The items are listed in Table 1. Panels A and B show the male and female no or mild symptoms classes. Panel C shows the male mild inattentive class. Panel D shows the female mild combined class. Panels E and F show the male and female severe inattentive classes. Panels G and H show the male and female severe combined classes. Panel I shows the male hyperactive-impulsive class.

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Table 4a

Mother Classes Compared to Father Classes

		Male		
Father class	No or mild symptoms	Mild inattentive	Severe combined	Total
Mother class				
No or mild symptoms	332	32	4	368
Mild inattentive	44	18	3	65
Severe inattentive	9	34	18	61
Hyperactive-impulsive	15	17	3	35
Severe combined	6	10	34	50
Total	406	111	62	579
		Female		
Father class	No or mild symptoms	Mild combined	Severe inattentive	Total
Mother class				
No or mild symptoms	435	44	5	484
Mild combined	41	52	7	100
Severe inattentive	7	12	14	33
Severe combined	1	7	15	23
Total	484	115	41	640

of responding, given that far fewer individuals had data from all three informants. We were interested in whether adults were more likely to respond about children whose behaviour was of concern and consequently would have a higher percentage of children placed into severe latent classes when all three informants were available. This did not appear to be the case. For example, for males in the maternal-paternal comparison where 579 responses were available, 62 (10.5%) children were placed into the severe combined latent class by maternal report. For males in the maternal-teacher comparison where 287 responses were available for males, 22 (8%) children were place into the severe combined latent class by maternal report.

Discussion

Use of LCA of the CPRS-R:S and CTRS-R:S demonstrates similar, although not identical latent classes for attention problems, impulsivity, and hyperactivity as those which have been identified previously. What is evident from these analyses is that there is an underlying structure of inattention and hyperactivity in the general population that is identified regardless of the taxonomy employed and regardless of informant. Does this represent only that the questions being

Table 4b

Odds Ratios (with 95% Confidence Intervals) of Mother to Father Comparisons

		Male	
Father class	No or mild symptoms	Mild inattentive	Severe combined
Mother class			
No or mild symptoms	17.07 (10.94–26.65)	0.16 (0.10–0.25)	0.03 (0.01–0.08)
Mild inattentive	0.88 (0.51–1.53)	1.73 (0.96–3.12)	0.37 (0.11–1.23)
Severe inattentive	0.05 (0.03–0.11)	7.21 (4.12–12.63)	4.51 (2.40–8.48)
Hyperactive-impulsive	0.29 (0.15–0.59)	4.52 (2.25–9.10)	0.77 (0.23–2.59)
Severe combined	0.04 (0.02–0.11)	1.06 (0.51–2.19)	38.02 (18.77–77.0)
		Female	
Father class	No or mild symptoms	Mild combined	Severe inattentive
Mother class			
No or mild symptoms	19.39 (12.37–30.37)	0.12 (0.08–0.19)	0.03 (0.01–0.09)
Mild combined	0.15 (0.10–0.24)	8.20 (5.12–13.15)	1.12 (0.48–2.60)
Severe inattentive	0.07 (0.03–0.17)	2.80 (1.33–5.86)	15.83 (7.18–34.91)
Severe combined	0.01 (0.00–0.09)	2.06 (0.83–5.13)	42.62 (16.59–109.51)

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Table 5a

Mother Classes Compared to Teacher Classes

			Male		
Teacher class	No or mild symptoms	Severe inattentive	Hyperactive–impulsive	Severe combined	Total
Mother class					
No or mild symptoms	166	12	10	3	191
Mild inattentive	18	7	2	2	29
Severe inattentive	9	8	2	9	28
Hyperactive-impulsive	10	0	4	3	17
Severe combined	8	3	5	6	22
Total	211	30	23	23	287
			Female		
Teacher class	No or mild symptoms	Mild combined	Severe inattentive		Total
Mother class					
No or mild symptoms	205	33	7		245
Mild combined	33	7	6		46
Severe inattentive	3	5	2		10
Severe combined	2	3	5		10
Total	243	48	20		311

asked in any of the instruments (CBCL, DSM-IV checklist, CPRS-R:S, CTRS-R:S) are simply sampling the same dimension or is it possible that these symptoms are consistent regardless of the instrument used? One of the arguments against the use of the CBCL as a measure of attention problems has been that it does not contain all of the DSM-IV items that can be used for definitive diagnosis. Interestingly, when using an instrument that contains some of the DSM-IV items (CPRS-R:S, CTRS-R:S), few of the DSM-IV items (CBCL) or the DSM-IV items itself there is similar latent class structure. What is notable here is that the numbers of classes that are identified using LCA of the Conners' forms is lower than the numbers identified previously using DSM items (Hudziak et al., 1998; Neuman et al., 2001; Neuman et al., 1999; Rasmussen, Neuman, et al., 2002; Rasmussen, Todd, et al., 2002; Todd et al., 2001) and is somewhat intermediate between the 6- and 8-class solutions that have been seen using the DSM and the 3-class solution that was found using the CBCL (Hudziak et al., 1999). This may be due to the items sampled on the CPRS-R:S and the CTRS-R:S. For example, there are few impulsive items on either scale, making it unlikely, for

Table 5b

Odds Ratios (with 95% Confidence Intervals) of Mother to Teacher Comparisons

			Male	
Teacher Class	No or mild symptoms	Severe inattentive	Hyperactive–impulsive	Severe combined
Mother class				
No or mild symptoms	7.53 (4.21–13.45)	0.29 (0.13–0.63)	0.35 (0.15–0.84)	0.06 (0.02–0.21)
Mild inattentive	0.55 (0.25–1.23)	3.25 (1.25–8.43)	0.84 (0.19–3.76)	0.84 (0.19–3.76)
Severe inattentive	0.13 (0.06–0.31)	4.31 (1.70–10.91)	0.87 (0.19–3.93)	8.29 (3.18–21.62)
Hyperactive-impulsive	0.49 (0.18–1.34)	0.00 (—)	4.06 (1.21–13.68)	2.68 (0.71–10.10)
Severe combined	0.17 (0.07–0.44)	1.39 (0.39–5.01)	4.04 (1.34–12.2)	5.47 (1.90–15.78)
			Female	
Teacher class	No or mild symptoms	Mild combined		Severe inattentive
Mother class				
No or mild symptoms	3.78 (2.08–6.84)	0.53 (0.27–1.05)		0.12 (0.05–0.32)
Mild combined	0.66 (0.33–1.35)	0.98 (0.41–2.34)		2.69 (0.98–7.41)
Severe inattentive	0.11 (0.03–0.43)	6.00 (1.67–21.60)		3.93 (0.78–19.88)
Severe combined	0.06 (0.01–0.30)	2.44 (0.61–9.78)		19.07 (4.97–73.10)

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Table 6a

Father Classes Compared to Teacher Classes

			Male		
Teacher class	No or mild symptoms	Severe inattentive	Hyperactive–impulsive	Severe combined	Total
Father class					
No or mild symptoms	168	16	14	7	205
Mild inattentive	31	9	3	9	52
Severe combined	12	5	6	7	30
Total	211	30	23	23	287
			Female		
Teacher class	No or mild symptoms	Mild combined	Severe inattentive		Total
Father class					
No or mild symptoms	212	33	7		252
Mild combined	30	10	10		50
Severe inattentive	1	5	3		9
Total	243	48	20		311

example, that the talkative-impulsive class seen by Rasmussen, Neuman, et al. (2002) would be replicated here.

The data presented here also show that the class structure is quite similar regardless of informant, with a few exceptions. What does differ is the proportion of children who are in each latent class as a function of informant. Teachers tend to report fewer symptoms in general, classifying fewer children as deviant on the subscales (which may represent a cultural difference between American and Dutch teachers) and, especially for girls, their responses correspond to less severe symptom classes. The consistency of the class assignment between parents is markedly better than that between parents and teachers. This could mean either that the parent is more aware of the child's behavior or that the child is behaving markedly different in the classroom setting. It is possible that the reason for the low corroboration of symptom endorsement typically seen across informants (Achenbach et al., 1987) is a function less of reporter bias than of differential responding of the child. However, the general latent class structure of the teachers, regardless of the differences in symptom endorsement appears to be very similar to latent class structure on the basis of parental report. A finding immediately obvious is that a purely HI subtype does not emerge from father data alone. The pure HI subtype has been the topic of much interest since it occurs less frequently and may have a different neuropsychological profile than either the combined or inattentive subtypes. From these data it appears that paternal report is not enough to identify this subtype. Certainly of note is that the majority of the teachers in this sample were female. Is there something about the hyperactive boy in the context of being examined by a female that makes it more likely that he will be identified? Conversely, is there something about the hyperactive

Table 6b

Odds Ratios (with 95% Confidence Intervals) of Father to Teacher Comparisons

			Male	
Teacher Class	No or mild symptoms	Severe inattentive	Hyperactive–impulsive	Severe combined
Father class				
No or mild symptoms	4.12 (2.35–7.22)	0.41 (0.19–0.89)	0.59 (0.25–1.43)	0.15 (0.06–0.37)
Mild inattentive	0.45 (0.24–0.85)	2.13 (0.91–4.97)	0.66 (0.19–2.30)	3.30 (1.34–8.12)
Severe combined	0.19 (0.09–0.43)	1.86 (0.65–5.28)	3.53 (1.27–9.80)	4.58 (1.71–12.29)
			Female	
Teacher class	No or mild symptoms	Mild combined		Severe inattentive
Father class				
No or mild symptoms	4.79 (2.59–8.83)	0.44 (0.22–0.88)		0.10 (0.04–0.27)
Mild combined	0.34 (0.18–0.65)	1.47 (0.68–3.18)		6.28 (2.46–16.03)
Severe inattentive	0.03 (0.00–0.25)	7.53 (1.94–29.15)		8.38 (1.93–36.45)

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boy that makes fathers less likely to identify those symptoms? Fathers appear to identify children as falling into one of three classes — severe, mild, or nothing. Certainly the most complete picture of the latent structure comes from the maternal report, and this has been the most extensively studied. However, the work here falls prey to the fact that maternal report contained the highest numbers of responses in the dataset. Thus, the increased information in the latent structure by maternal report may simply be a reflection of improved power.

One important observation is the high numbers of children classified into some latent class other than 'no symptoms'. Clearly we cannot make the argument that more than 20% of the sample has clinical ADHD. Rather, when looking only at children who were classified as being in a severe latent class by more than one informant, these numbers decrease to numbers that approximate the estimates from epidemiological samples. For example, the percentage of children placed into one of the severe latent classes by both maternal and paternal report was 6.6%.

Interestingly, one latent class subtype that emerges across the reports of all informants with only one exception (fathers' rating of boys) is the severe inattentive subtype. This is the subtype that has been shown by Todd and colleagues (Todd et al., 2003) to be related to the acetylcholine receptor alpha 4 subunit gene. It would be intriguing to look at the possibility of further refinement of this subclass using multi-informant information. One could classify those children who fall into the severe inattentive class across multiple informants and subsequently use this information to identify a more extreme phenotype for use in gene finding experiments.

Limitations

Like other approaches the CPRS-R:S and CTRS-R:S do not include all 18 items of the DSM-IV, thus use of these scales is not a direct test of DSM-IV ADHD. However, the CPRS-R:S and CTRS-R:S are closer in content to DSM than other quantitative measures of ADHD like the CBCL.

Second, our data on a large set of 10-year-old twins may not generalize to children of older ages or to self-reports. However, we are investigating the stability of the latent class structure for maternal reports across age groups of 7-, 10-, and 12-year-olds and the results suggest that it is stable across ages (Copeland et al., unpublished data). We will be examining the data further to determine if the cross-informant information corresponds in the same fashion across age.

Third, the low numbers of participants who have data from all three informants is potentially limiting. The possibility of ascertainment bias is certainly present here in that it may be that the teachers most involved with the parents (and, therefore most likely to agree with the parents on symptoms) may have been the most likely to participate.

Finally, at this point we can not present data on the number of children who exceeded CPRS-R:S or CTRS-R:S cutpoints who also met DSM-IV diagnostic criteria for ADHD. In order to test these relations, our group is currently interviewing a subset of this sample and analyzing these data in order to determine those relations.

Acknowledgments

The authors would like to thank Jeri Ogle for her help in the preparation of this manuscript. This research was supported by grants NIMH MH58799, NWO 904-57-94, NWO 575-25-006 and the Centre for Neurogenomics and Cognition Research (CNCR).

Endnote

1 While truncation of ordinal scales for the purposes of LCA is well established, it is not beyond reproach. We have additionally performed LCA on several other possible truncations of the CTRS and CPRS and have found that the optimal solutions and the class characteristics remain the same while the proportions of the sample placed into the classes changes with varying methods of truncation.

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