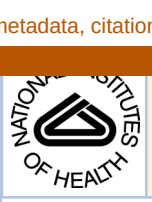

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The Shifting Subtypes of ADHD: Classification depends on how symptom reports are combined

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Abstract

Research on the correlates of ADHD subtypes has yielded inconsistent findings, perhaps because the procedures used to define subtypes vary across studies. We examined this possibility by investigating whether the ADHD subtype distribution in a community sample was sensitive to different methods for combining informant data. We conducted a study to screen all children in grades 1–5 (N=7847) in a North Carolina County for ADHD. Teachers completed a DSM-IV behavior rating scale and parents completed a structured telephone interview. We found substantial differences in the distribution of ADHD subtypes depending on whether one or both sources were used to define the subtypes. When parent and teacher data were combined, the procedures used substantially influenced subtype distribution. We conclude the ADHD subtype distribution is sensitive to how symptom information is combined and that standardization of the subtyping process is required to advance our understanding of the correlates of different ADHD subtypes.

Keywords

Attention-Deficit Hyperactivity Disorder; ADHD; Classification; Subtypes; Epidemiology

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Introduction

The American Psychiatric Association lists three subtypes of attention-deficit/hyperactivity disorder (ADHD) in DSM-IV(American Psychiatric Association, 2000). These are a Predominantly Inattentive Type (ADHD-PI), a Predominantly Hyperactive-Impulsive Type (ADHD-PH), and a Combined Type (ADHD-C) for those with both inattentive and hyperactive/impulsive symptoms.

The subtype classification system for ADHD is used extensively by clinicians and researchers. Clinicians are interested in knowing whether patterns of comorbidity and treatment efficacy differ by subtype (Jensen, Martin, & Cantwell, 1997). Youth with ADHD-PH and ADHD-C are believed to be at higher risk for conduct problems (Milich, 2001) while those with ADHD-PI are at higher risk for learning disabilities, anxiety, and depression (Gaub & Carlson, 1997; Gaub & Carlson, 1997). Girls with ADHD are believed to have higher rates of ADHD-PI than ADHD-C (Biederman et al., 2002; Carlson, Tamm, & Gaub, 1997) although some carefully screened samples did not replicate this finding (Hinshaw, 2002; McBurnett et al., 1999). Researchers are actively investigating neuropsychological and genetic profiles of the subtypes (Castellanos & Tannock, 2002; Larsson, Lichtenstein, & Larsson, 2006; Stawicki, Nigg, & Von Eye, 2006; Stefanatos & Baron, 2007). However, these efforts have yielded inconsistent results; in many studies correlates of ADHD-PI and ADHD-C do not differ as much as originally predicted (Biederman et al., 1997; Hinshaw, 2001). Although some authors have argued that the differences between the subtypes are clear and that ADHD-C and ADHD-PI should be classified as entirely different disorders because of differences in prevalence, gender, age of onset and comorbidity of externalizing disorders (Milich, 2001), others, particularly those who have tried to validate the subtypes using neuropsychological or laboratory measures, have had difficulty replicating consistent differences (Chhabildas, Pennington, & Willcutt, 2001; Nigg, Blaskey, Stawicki, & Sachek, 2004).

Several explanations have been offered for why it has been difficult to identify consistent differences between the ADHD subtypes. One explanation is that the ADHD-PI group is heterogeneous and only a subset, those with a “sluggish cognitive tempo,” differ from children with the Combined Type (McBurnett et al., 1999). This viewpoint suggests that youth classified with ADHD-PI without a slow cognitive tempo might be better classified as ADHD-C. However, the evidence supporting the sluggish cognitive tempo hypothesis has been mixed (Carlson & Mann, 2002; Hinshaw, Carte, Sami, Treuting, & Zupan, 2002). Others argue that the DSM-IV subtype criteria are not developmentally sensitive. In general, hyperactive-impulsive symptoms tend to decline as children age (although feelings of restlessness may persist), but inattentive symptoms remain relatively constant (Hart, Lahey, Loeber, Applegate, & Frick, 1995; Weyandt et al., 2003). In cross-sectional studies the proportion of children with ADHD-C is higher in studies of young children and lower in studies of adolescents (Barkley, 1998; Bolfek, 2004; Hart et al., 1995). Because the ADHD subtype criteria are the same for 6 years olds and for 15 years olds, the subtype distribution might differ across two cross-sectional samples simply because the age distributions are different. The decline in hyperactive symptoms as children age suggests that if a group of children were followed prospectively, the subtype distribution would tend to shift away from the Combined Type and toward the Predominantly Inattentive Type. Another explanation for why it has been difficult to find consistent differences between the subtypes is methodologic; research groups may be applying the subtype criteria differently. In this paper, we explore this methodologic explanation.

Large differences in the estimates of the DSM-IV ADHD subtype distribution have been reported. In some studies ADHD-PI occurs most often, but in others ADHD-C predominates

(Table 1). In the literature, the proportion of the Predominantly Inattentive Type varies from a low of 3% (Mitsis, Mckay, Schulz, Newcorn, & Halperin, 2000) to a high of 78% (Weiler, Bellinger, Marmor, Rancier, & Waber, 1999); the Combined Type varies from 19% (Weiler et al., 1999) to 93% (Mitsis et al., 2000), and the Predominantly Hyperactive-impulsive Type ranges from 2% (Rowland et al., 2001) to 53% (Pineda et al., 1999). Some of this variability could be attributable to chance or to differences in the specific populations studied. Nevertheless, from an epidemiologic perspective, the large variability in the estimates is disconcerting and raises the question of whether methodological differences in how researchers are defining ADHD subtypes has contributed to this variability.

An extensive literature exists on the use of different informants in child psychiatry (Jensen et al., 1999; Offord et al., 1996); (Piacentini, Cohen, & Cohen, 1992; Stanger & Lewis, 1993). The consensus among most researchers is that youth self-report is of limited use in assessing ADHD but both teacher and parent reports are crucial (American Academy of Pediatrics, 2000; Dulcan, 1997). DSM-IV was the first version of the DSM to require evidence of impairment in two settings (American Psychiatric Association, 1994). This criterion suggests that having data from two or more informants in different settings is important for establishing a diagnosis of ADHD. Thus DSM-IV raised the stakes around how informant information is used.

Some evidence suggests that the distribution of the ADHD Types is influenced by the type of informant reports used; teacher ratings only, parent ratings only, or multiple informants (Table 1). If only teacher-rating scales were used, ADHD-PI predominated in 8/9 samples (Baumgaertel, Wolraich, & Dietrich, 1995; Carlson et al., 1997; Gomez, Harvey, Quick, Scharer, & Harris, 1999; Mitsis et al., 2000; Nolan, Gadow, & Sprafkin, 2001; Weiler et al., 2000; Wolraich, Hannah, Baumgaertel, & Feurer, 1998; Wolraich, Hannah, Pinnock, Baumgaertel, & Brown, 1996). If only parent rating scales were used, ADHD-PI predominated in 6/8 studies (Gomez et al., 1999; Graetz, Sawyer, Hazell, Arney, & Baghurst, 2001; Mitsis et al., 2000; Pineda et al., 1999; Rasmussen et al., 2002; Weiler et al., 1999). However, in studies where teacher and parent data were combined, ADHD-C predominated in 9/13[9] samples (Counts, Nigg, Stawicki, Rappley, & Von Eye, 2005; Eiraldi, Power, & Nezu, 1997; Faraone, Biederman, Weber, & Russell, 1998; Hinshaw, 2002; Lahey et al., 1994; McBurnett et al., 1999; Mitsis et al., 2000; Murphy, Barkley, & Bush, 2002; Rowland et al., 2001). However, some studies excluded participants with ADHD-PH because it is common only among preschool children. If one separates the studies this way, ADHD-C predominated in 5/9 studies that combined parent and teacher report and included all three subtypes (Faraone et al., 1998; Lahey et al., 1994; McBurnett et al., 1999; Mitsis et al., 2000; Rowland et al., 2001) and in 4/4 studies that only included ADHD-PI and ADHD-C (Counts et al., 2005; Eiraldi et al., 1997; Hinshaw, 2002; Murphy et al., 2002).

Most of the studies that used only parent ratings or that used only teacher ratings used checklists and most of the studies that combined ratings used both checklists and structured interviews (Table 1). Therefore, the differences in the subtype distributions in these studies may be related to their instrumentation and not to the methods they used to combine information. For example, among studies that used teachers as informants, the study by Mitsis et al. (Mitsis et al., 2000) was the only one to use a structured interview rather than rating scales to collect symptom information, and they reported higher rates of ADHD-C and lower rates of ADHD-PI than any other study. Nevertheless, we think it is unlikely that instrumentation explains most of the differences in Table 1 because the one study that carefully compared the performance, discrimination, and predictive validity of rating scales

[9]The study by Weiler in Table 1 reported on a referred sample and a community samples; we are counting these as two samples.

versus structured interview for classifying psychiatric disorders including ADHD, concluded that there was little difference (Boyle et al., 1997).

In this paper, we used data from a population-based study of ADHD to evaluate the impact of variations in how informant information is used on the subtype distribution. First, we evaluated whether we could replicate the finding that ADHD-PI predominates in studies with only one informant. Next, we examined how the ADHD subtype distribution may be affected by both the manner of combining data from different informants, and the symptom threshold required to define the different subtypes. In epidemiologic studies there are two general approaches for combining informant data. Some studies use lenient OR rules which simply combine the reported symptoms from two or more informants (Lahey et al., 1994; Mitsis et al., 2000). Other studies use AND rules that combine symptoms and impose additional informant-specific criteria (Mill et al., 2006; Mota & Schachar, 2000; Schachar et al., 2007; Weiler et al., 1999). For example, under an AND rule a participant might need to show 6 or more combined symptoms of inattention or hyperactivity/impulsiveness in addition to having at least four symptoms reported by each informant. Because they add additional criteria, AND rules are more restrictive than OR rules and may thus alter the subtype distribution. Another way to conceptualize the difference between AND rules and OR rules is that under AND rules both informants must endorse some level of symptoms to meet criteria but under OR rules the report of one informant alone may be sufficient to meet criteria. Our underlying assumption for all comparisons was that the methods used to combine informant data might shift the distribution of the ADHD subtypes, and that varying methods used to assign subtypes may thus contribute to the inconsistent findings on the correlates of different ADHD subtypes that have been reported.

Methods

Population

In 1998 and 1999, we screened children in grades 1–5 who were enrolled in one of 17 public elementary schools in Johnston County, North Carolina for ADHD. During this time period, Johnston County was predominantly rural, but rapidly growing and becoming more suburban; the population grew 50% between 1990 and 2000. The county was about 16% African American, 8% Hispanic and the median household income in 1999 was about $41,000 (U.S. Census Bureau, 2000).

We screened children for ADHD in two phases. In Phase 1, we sent parents a letter of support from the superintendent of schools, a consent letter, and a brief form about past diagnosis of ADHD and medication treatment in their child. We also asked teachers to complete a DSM-IV behavior rating scale on each participant. In Phase 2, we interviewed parents of potential ADHD cases (defined below) using a structured telephone interview.

Instruments

Teacher report of ADHD symptoms—We developed the NIEHS Teacher Rating Scale (NTRS). This instrument had wording similar or identical to most other DSM-IV scales but used response categories of “Never, Hardly ever, Some of the time, and Often.” We made “Often” the most severe category, to make the scale more compatible with the ADHD module of the Diagnostic Interview Schedule for Children (DISC), Version 4, which we used to interview parents (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000). We considered a symptom positive if it was rated “Often”.

The scale had good psychometric properties, comparable to those of other DSM-IV rating scales (Rowland, Umbach, Bohlig, Stallone, & Sandler, 2007). The internal consistency of

the NTRS for inattentive and hyperactive-impulsive items was 0.97 (Cronbach's α) for an ADHD symptom severity score (four-point scale) and 0.94 when we dichotomized symptoms as often/not often. The test-retest reliability of the NTRS (Pearson correlation coefficient of symptom severity scores) was 0.94 for the Inattentive subscale and 0.90 for the Hyperactive/Impulsive subscale (mean time between ratings was 4 weeks, range 2 weeks-13 weeks). We assessed convergent validity by asking the teacher who completed the NTRS to complete a CAP rating scale or a Conners rating scale on the same child. The two subscales of the CAP scale, "inattention" and "hyperactive/impulsive," were highly correlated (0.90, 0.89) with the NTRS's similarly named subscales. The Conners' ADHD index had a correlation of 0.91 with the NTRS ADHD Combined subscale and the Conner's Hyperactivity Scale had a correlation of 0.89 with the NTRS Hyperactive/impulsive subscale. Confirmatory factor analyses strongly support the construct validity of the NTRS (Rowland et al., 2007).

Parent report of ADHD symptoms—We administered a modified ADHD module of the DISC to parents or guardians by telephone. We modified the DISC by not asking parents about their child's symptoms at school because we collected this information directly from the child's teacher. Some data suggest parent ratings of their child's behavior at school correlates better with their ratings of the child's behavior at home than with teacher reports (Mitsis et al., 2000).

Teacher report of impairment—We assessed school impairment with a modified Vanderbilt AD/HD Diagnostic Teacher Rating Scale (Wolraich, Feurer, Hannah, Baumgaertel, & Pinnock, 1998). The Vanderbilt scale asks a teacher to rate a child's school performance as problematic, average, or above average using a 5 point Likert scale. We modified this procedure to ask whether a "child had a problem in any of the following areas" and if so, to rate the severity of the problem as "mild, moderate, or severe." We asked about academic performance in four subjects; reading, arithmetic, writing, and spelling instead of "reading, mathematics, or written expression" on the original scale and asked about "relationships with other children at school, relationships with teachers and other adults at school, disruptive classroom behavior, self esteem, assignment completion, and organizational skills" instead of "relationships with peers, following directions/rules, disrupting class, assignment completion, and organizational skills" on the original scale. Children were considered impaired at school if the teacher rated them "below grade level" in an academic subject or if they had moderate or severe problems in any of the other impairment areas.

Parent report of impairment—Impairment at home was assessed with the DISC questions about relationships with family and peers. These questions ask whether the child's problems caused the parent to get annoyed or upset, made it difficult for them to do things as a family or for the child to spend time with friends, made it difficult for the child to complete homework, or made the child feel "bad or very bad". Moderate impairment was defined as having a problem "some of the time ", or if the child felt "bad". Severe impairment was defined as having a problem "a lot of the time" or if the child felt "very bad."

Sampling

The study protocol was approved by the NIEHS IRB. There were 7,847 children in grades 1–5. We excluded children with severe developmental disabilities in self-contained classrooms (N=146), and children with special education designations for autism, mental handicap (IQ<70) or severe health disabilities (such as traumatic head injury or childhood cancer) (N=114). Children with learning disabilities or behavioral problems were included

regardless of classroom placement. Seven thousand five hundred eighty seven children were initially targeted but one child died and we had to exclude children who subsequently left the school system before contact was initiated (N=254). Thus, 7,332 children were eligible for screening after exclusions. (Figure 1)

Parents or guardians of 6,139 of the 7,332 eligible children (84%) gave written permission to have their child's teacher complete the screening questionnaire. The consent form included a question about whether the child had ever been diagnosed with ADHD and whether he or she was taking medication to treat ADHD.

Teachers completed screening forms (NTRS) on 6,072 of the 6,139 (99.9%) children whose parents gave permission for an overall Phase 1 completion rate of 83% (6,072/7,332). Four hundred eleven children were excluded from the subsequent telephone interview because they had a severe medical disability, had been in class too briefly (<9 weeks), or had parents with low English proficiency. Therefore, 5,661 children were eligible for the Phase 2 parent telephone interview.

If parents reported a child was taking medication to treat ADHD, the child was considered a potential case. A child not taking ADHD medication was considered a potential case if the teacher indicated that the child often exhibited at least 3 of 9 DSM-IV hyperactive/impulsive symptoms or at least 3 of 9 inattentive symptoms, and was impaired in either behavior or academic performance at school.

In Phase 2, we interviewed the parents or guardians of two groups, a random sample of all eligible children (N=706) and a group of all remaining potential cases who were not in the random sample (N=1,246). The purpose of the random sample was to create a group that was representative of the whole population and was not enriched for cases. We used computer generated random numbers to select a random sub-sample from all eligible students who had parental consent. This sample yielded 169 potential ADHD cases and 537 who were not potential cases. Budget constraints prevented us from interviewing parents of all 1,246 potential ADHD cases not in the random sample, so we selected 913 of them at random (using a similar process) for parental interview. Therefore, there were 1,619 parents/guardians eligible for the interview (706 from the random sample and 913 other potential cases). 1,160/1,619 parents/guardians completed telephone interviews (72%)(Figure 1).

Assignment of ADHD Types

Children were assigned an ADHD Type using a two-step procedure; (1) we decided if each child met criteria as an ADHD Case and (2) for children who were classified as cases we assigned one of three subtypes (ADHD-C, ADHD-PI, or ADHD-PH). In Step 1, if a child met case criteria for either inattentive symptoms or hyperactive-impulsive symptoms (or both), he or she was declared a case. Moderate or severe impairment from these symptoms in each setting was also required for all case definitions.

For this paper, we adopted the following notation to summarize inattentive and hyperactive/impulsive symptom counts by informants. The numbers of symptoms required to meet criteria are denoted by N_1- N_2- N_3 where N_1 is the number of symptoms endorsed by one informant; N_2 is the number of symptoms endorsed by a second informant; and N_3 is the number of unduplicated symptoms. To determine the number of unduplicated symptoms, symptoms that are reported by both informants are only counted once. For example, if a parent reported 4 inattentive symptoms and a teacher reported 3 of the same inattentive symptoms, that would count as 4 unduplicated symptoms, not as 7. However, if 2 of the 3 symptoms reported by the teacher were different from the symptoms reported by the parent, there would be 6 unduplicated symptoms. The DSM-IV ADHD-Criteria require six or more

inattentive symptoms or six or more hyperactive-impulsive symptoms, so we required at least 6 unduplicated symptoms ($N_3 = 6$) for all case definitions.

As noted above, there are two types of procedures for combining informant data, AND rules and OR rules. The main difference between the two methods is that OR rules combine symptoms from both informants but do not impose specific requirements on each informant. That is, they only use N_3, the number of unduplicated symptoms. AND rules also combine symptoms but, in addition, include informant-specific requirements. They use N_1, N_2, and N_3. We will use X/Y to denote whether AND or OR rules were used to combine symptoms in Step 1 (case determination) and in Step 2 (subtype determination), respectively. For example the notation AND/OR means that the AND rule was used for case determination and the OR rule was used to determine the subtype.

An OR rule was used in the DSM-IV ADHD field trials (Lahey et al., 1994) and subsequently by others (Mitsis et al., 2000). AND rules also have been used by several investigators to define cases (Mill et al., 2006; Mota & Schachar, 2000; Schachar et al., 2007; Weiler et al., 1999).

The difference between AND rules and OR rules has important implications for subtyping as illustrated in the following example comparing subtype determination under a 6-4-6 AND/AND rule and a 6-4-6 AND/OR rule. Suppose that the parent of an elementary school girl reported 6 inattentive symptoms and 4 hyperactive-impulsive symptoms; her teacher reported 7 inattentive symptoms and 2 hyperactive-impulsive symptoms; and after combining parent and teacher reports, there were 7 unduplicated inattentive symptoms and 6 unduplicated hyperactive-impulsive symptoms. The symptom counts for this child are 6-7-7 for inattentive symptoms and 4-2-6 for hyperactive-impulsive symptoms. These symptom counts meet 6-4-6 AND case criteria for inattentive symptoms, but not for hyperactive-impulsive symptoms. Consequently, the girl would be classified as a case in Step 1. If an AND rule was used to determine subtype in Step 2 (6-4-6 AND/AND), the girl would be classified as ADHD-PI since she meets the AND criteria for inattentive symptoms but does not meet the AND criteria for hyperactive-impulsive symptoms. In contrast, if the subtype was based on OR criteria (6-4-6 AND/OR), she would be classified as ADHD-C since she meets OR criteria for both types of symptoms. As shown in this example, it is possible for a child who is classified as ADHD-C by the less restrictive OR rule to be classified as ADHD-PI or ADHD-PH when the more restrictive AND rule is used. A child who is classified as ADHD-C by the AND rule will always be classified as ADHD-C by the OR rule.

Data Analysis

Our goal was to explore how sensitive the subtype distribution was to changes in the methods used to combine symptoms across informants. We first examined the subtype distribution using symptom-reports from only one informant (either teacher or parent). Cases had to have at least 6 inattentive or 6 hyperactive-impulsive symptoms. Because an AND rule or an OR rule could be used at either step, there are four possible combinations – OR/OR, OR/AND, AND/OR, and AND/AND. However, one combination OR/AND, while theoretically possible, probably would never be used because if one uses a lenient definition for defining cases and a restrictive definition for defining subtype, this creates a group of cases who do not meet the restrictive criteria and cannot be subtyped. We therefore evaluated the impact of the other three rule combinations on the ADHD subtype distribution. Most of these case-definitions were taken from published reports but a few combinations we had not seen were included for illustration purposes. Finally we looked within each AND/OR and AND/AND combination to see whether the subtype distribution differed by symptom threshold used.

Some analyses could only be done in a random sample of study participants, not the whole population. A chi-square test was used to test subtype distributions for teacher ratings in the random sample compared to those who were not in the random sample in order to evaluate the validity of this approach.

The binomial distribution was used to calculate 95% confidence limits for percentages changing from ADHD-C to ADHD-PI or to ADHD-PH when the subtype rule was changed from OR to AND.

Results

Table 2 presents the demographic composition of the potential case pool in our population. Almost three quarters of the potential cases were male, and about a third were non-white. About two thirds were in grades 1–3.

Table 3 shows the distribution of the three subtypes (ADHD-C, ADHD-PI, and ADHD-PH) in our data using different rules for combining symptom reports from parents and teachers to assign case status and subtype. When we only used teacher data (Table 3, line A1), ADHD-PI occurred most often, which replicated the pattern we observed in the literature. Almost 60% of the cases were ADHD-PI. Because we used a two-step sampling procedure that required at least 3 inattentive or 3 hyperactive-impulsive symptoms at school for children who were not in the random sample and who were not taking medication we could only examine the distribution of ADHD Types using parent data in the random sample (among 82 cases from the 509 participants) (Figure 1). Using parent data from the random sample, ADHD-C and ADHD-PI occurred in about equal proportions (Line A2). This pattern was different from what we found in the teacher-only data and did not replicate the pattern we observed in the literature for parent-only studies (Table 1). We also checked the subtype distribution for teacher data using only the random sample. There were 50 cases with 24% classified as ADHD-C; 64% classified as ADHD-PI; and 12% classified as ADHD-PH. This distribution was not significantly different from the distribution of the 299 cases who were not included in the random sample (p=0.56).[10]

Using the OR rule to assign case status and to assign subtypes (as was done in the DSM-IV field trials) created almost an equal distribution of ADHD-C and ADHD-PI and a relatively large proportion of ADHD-PH (14%) (line B1, Table 3). This subtype distribution, like the parent-only distribution, had to be based on the random sample which is why the number of cases is only 100.

We initially used a 3-3-6 AND rule to assign case status and an OR rule to assign subtype (3-3-6 AND/OR). Using this approach (line C1) ADHD-C predominated (66%), ADHD-PI occurred in almost a third of the cases, and ADHD-PH became rare. If, for exactly the same cases, we used an AND rule to define case status and an AND rule to define subtype (3-3-6 AND/AND), the distribution shifted, ADHD-PI predominated (53%), ADHD-C became less common (36%) and ADHD-PH increased to 10% (line D1). Table 4 rearranges some information in Table 3 to show the subtype shifts between AND/OR and AND/AND procedures for three different case definitions. Under a 3-3-6 case definition, 36% (100/275) (95% CI: 31% to 42%) of the 275 children who were classified as ADHD-C when subtyped by OR were reclassified as ADHD-PI when subtyped by AND (Table 4). An additional 8%

[10]In the single informant analyses, most of the children who were identified as cases for parents were not the same children identified as cases by teachers. Out of the 509 children in the random sample who had parent interviews, 35 were cases by teacher only, 67 were cases by parent only, and 15 were cases by both. Of those 15 cases, parents and teachers agreed on the subtype for only 3 children.

(23/275) (95% CI: 5% to 12%) who were classified as ADHD-C under the OR subtype rule were re-classified as ADHD-PH under the AND subtype rule.

Similarly, when we used a 6-4-6 AND rule for case determination and an OR rule for subtype determination (6-4-6 AND/OR), there was a preponderance of ADHD-C (72%) with lower percentages of ADHD-PI (26%) and ADHD-PH (2%) (Table 3, Line C2). Under a 6-4-6 AND/AND rule, the subtype distribution shifted toward ADHD-PI (59%) with an increase in the percentage of ADHD-PH (13%) and a decrease in the percentage of ADHD-C (29%) (Line D2). This shift occurs because 46% (109/239) (95% CI: 39% to 52%) of those who were classified as ADHD-C by the OR criterion were classified as ADHD-PI by the AND criterion, and 14% of the ADHD-C cases (34/239) (95% CI: 10% to 19%) changed to ADHD-PH when the subtype rule was changed from OR to AND (Table 4).

Under a 6-6-6 AND/OR definition, ADHD-C predominated (75%) with lower frequencies for ADHD-PI (22%) and ADHD-PH (2%) (Table 3, Line C3). When the subtype rule was changed from OR to AND, the frequency for ADHD-C decreased substantially (21%) and the frequencies for ADHD-PI (62%) and ADHD-PH (17%) increased (Line D3). This shift occurred because 53% of the ADHD-C cases (84/159) (95% CI: 45% to 61%) changed to ADHD-PI and 19% of ADHD-C (30/159) (95% CI: 13% to 26%) changed to ADHD-PH (Table 4).

In sum, a substantial percentage (45% (95 CI: 39% to 51%) for 3-3-6, 60% (53%–66%) for 6-4-6, and 72% (64% to 79%) for 6-6-6) of those who are classified as ADHD-C by OR rules become ADHD-PI or ADHD-PH when AND rules are applied during the subtyping step (Table 4). The subtyping rules are deterministic. Logically only some changes are possible because AND rules are more stringent than OR rules. Participants who are classified as ADHD-C under AND/OR rules can be ADHD-C, ADHD-PI, or ADHD-PH under AND/AND. Participants who are classified as ADHD-PI or ADHD-PH under AND/OR rules will remain the same subtype under AND/AND rules (Table 4).

When we looked at different symptom cutoffs within each AND/OR combination, the subtype distributions were relatively constant (Table 3, lines C1–C3 and lines D1–D3). This result suggests that how AND and OR rules are used is more important in shaping the subtype distribution than the symptom threshold used to define ADHD cases.

Discussion

In a seminal paper, Mitis et al (Mitsis et al., 2000) reported that using reports from one informant to assign ADHD subtypes yielded a different subtype distribution than when both parent and teacher data were utilized. To our knowledge this finding in a clinical sample has not previously been demonstrated in a population-based sample, although epidemiologists studying ADHD are well aware that prevalence estimates can shift markedly depending on the case definition of ADHD (Boyle et al., 1996; Cohen, Riccio, & Gonzalez, 1994; Lambert, Sandoval, & Sassone, 1978).

In this community-based epidemiologic study, we estimated the distribution of the three ADHD subtypes under various scenarios. We found that the relative distribution of the three Types shifted – sometimes dramatically - depending on how informant information was used and combined. The subtype distribution shifted markedly depending on how AND or OR rules were paired to define cases and subtype. In contrast, within a set of rules, increasing the number of symptoms required to become a case had less impact on the distribution. The subtype distribution when the teacher was the only informant was closer to the AND/AND rules for two informants than to the AND/OR rules.

Our results are consistent with two previous studies that reported differences in the distribution of the subtypes based on the rules used to define the Types. Weiler et al. suggested that the prevalence of the ADHD Types might differ depending on how parent or teacher data were used (Weiler et al., 1999). Mitsis et al demonstrated in a clinic sample of 74 children that the distribution of the ADHD Types depended on whether informant symptom reports were combined (Mitsis et al., 2000). They noted that "compared with diagnoses based on reports from a single informant, combining information across informants greatly increased the rate of ADHD-C, while substantially diminishing the rate of non-diagnosis. Furthermore, when parent and teacher reports are combined…ADHD-I (PI) and ADHD-H (PH) become relatively rare."

Interpreting the subtype literature is presently difficult because the methods sections of many papers do not distinguish whether an OR or an AND method was used to define cases or to assign subtypes. The methods that authors have used to define cases and to assign subtypes need to become more explicit if we are going to make progress understanding the ADHD subtypes.

It is widely appreciated that subtle changes in case definition can have a major impact on prevalence estimates (Boyle et al., 1996; Cohen et al., 1994; Lambert et al., 1978). It seems less widely appreciated that the methods used to combine symptom reports by different informants can influence the subtype distribution.

Our results suggest that there may be problems with current estimates of the ADHD subtype distribution. Many published reports are limited by reliance on only one informant. Because DSM-IV stipulates that symptoms causing impairment must be present in two or more settings, studies that only used one informant and did not include information about symptoms and impairment in different settings should receive less credence than studies that followed the DSM-IV criteria more closely by using multiple informants to provide information about the child's behavior in those settings. In addition, because our results suggest that how symptoms are combined is crucial in understanding the subtype distribution, calculating the distribution based only on teacher reports or only on parent reports may be misleading.

To understand the true ADHD subtype distribution, as well as the important correlates and outcomes associated with the different subtypes, we need more studies that integrate information from both parents and teachers and which are explicit about the methods used to combine informant information. Because referral patterns make clinic populations subject to complex biases (Goodman et al., 1997), more population-based studies are needed. The ADHD field trials relied on a clinic sample (Lahey et al., 1994); it is not clear how the sampling strategy that they used may have influenced the subtype distribution that they observed.

In addition to generating more reliable estimates of the distribution of the three subtypes, standardizing the methods used to assign subtypes would have other benefits because a major source of variability between studies would have been eliminated. The ADHD literature has not been able to identify a consistent set of neuropsychological or genetic correlates for the three subtypes. Standardizing the methods used to assign subtypes will reduce some of the variability between studies and may reveal important differences and new insights.

Limitations

We collected data about hyperactive-impulsive and inattentive symptoms among elementary school students in one North Carolina County. It is not clear how well the results of this

study would apply to other U.S. populations. In our population, a substantial proportion of ADHD-C under OR rules became ADHD-PI or ADHD-PH under AND rules. We think that this general pattern is likely to be repeated in any other populations being studied because OR rules are less stringent than AND rules. Replication in other populations, however, would verify whether the magnitude of change we observed occurs in most other situations. For this reason, we hope other investigators will try to replicate these findings in other samples.

It is also important to recognize that we examined a series of epidemiologic case definitions of ADHD in this study. Although all case definitions required at least 6 hyperactive-impulsive symptoms or at least 6 inattentive symptoms and evidence of impairment from these symptoms, these epidemiologic case definitions are not identical to a clinical diagnosis of ADHD. For example, we did not interview the children in our study, apply the age-at-onset criteria or rule out other competing conditions. Although we do not believe that the basic findings of this study would change if a complete diagnostic workup were used to identify cases instead of our epidemiologic methods, this would be important to confirm in subsequent research.

Conclusion

Of the different combinations of approaches used to define ADHD cases and subtypes, no method is inherently “correct”. Although the “OR” method was used in the DSM-IV field trials and is the simplest rule for combining informant information in epidemiologic studies, many researchers prefer more restrictive AND rules that require some concordance in observer’s reports. Among study populations that receive the most careful screening, several levels of screening procedures are typical, that is participants must meet criteria on multiple measures (Hinshaw, 2002; Hinshaw et al., 1997; Stawicki et al., 2006). How does this selection process influence the subtype distributions of these studies? Do the participants in these study populations more closely resemble epidemiologic samples that have been screened by the AND Method, the OR method, or neither?

Given the wide fluctuations in the subtype distribution that are possible when the rules are vague, it would be desirable to standardize procedures for assigning ADHD subtypes or, at least, to urge authors to make their methods for combining informant reports explicit. Otherwise, it is difficult to compare results across studies. In the meantime, the subtype literature should be read with caution; in particular, studies that used OR rules to define case status and subtype should not be compared to studies that used AND rules to determine case status and subtype.

Which of the approaches to combining symptoms is best is not clear, although the implications are important. Additional research is needed to determine which subtype distribution and methods for creating it seems to best fit the underlying biologic (genetic, neuropsychological, etiologic and treatment) models of the subtypes. In the DSM-IV field trials, Lahey et al wrote that “Taken together, these findings suggest that the DSM-IV types of attention deficit hyperactivity disorder are distinct in a number of ways, but tests are needed in future studies of possible differences in etiology, clinical course, and response to treatment among the three types” (Lahey et al., 1994). Thirteen years later, this picture has not changed much. We propose that methodologic differences in how research groups combined informant reports may have muddied the waters and contributed to the slow progress in differentiating the subtypes in their etiology, clinical course, and response to treatment.

In the meantime, we suggest that the DSM-V workgroups address the variability in the ADHD subtypes by proposing more explicit and detailed guidelines about how symptom and impairment information from different informants should be combined. Standardized criteria for assigning ADHD subtypes would have important implications for treatment, research, and prevention.

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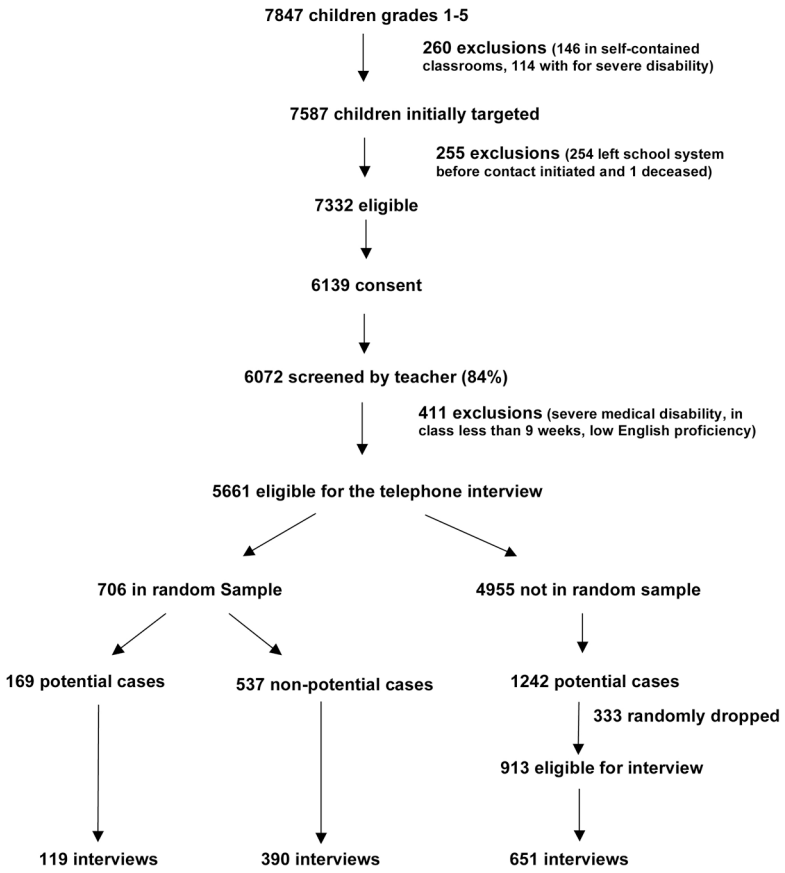

Figure 1.

Table 1

Distribution of the Three ADHD Subtypes in the Literature, by Informant and Type of Instrument

Study	Total ADHD cases	ADHD-C		ADHD-PI		ADHD-PH		Diagnostic instruments
		N	%	N	%	N	%	
Teacher only								
(Wolraich et al., 1998)	698	205	29	380	54	113	16	Rating scales
(Nolan et al., 2001)	476	109	23	296	62	71	15	Rating scales
(Gomez et al., 1999)	112	27	24	74	66	11	10	Rating scales
(Gaub and Carlson, 1997)	221	51	23	123	56	47	21	Rating scales
(Wolraich et al., 1996)	943	300	32	447	47	196	21	Rating scales
(Baumgaertel et al., 1995)	192	52	27	97	51	43	22	Rating scales
(Weiler et al., 2000)								
refered sample	94	25	27	59	63	10	11	Rating scales
community sample	30	8	27	21	70	1	3	Rating scales
(Mitsis et al., 2000)	56	27	48	15	27	14	25	structured interview (DISC)
Parent only								
(Pineda et al., 1999)	87	18	21	23	26	46	53	Rating scales, structured interview (by authors)
(Gomez et al., 1999)	126	37	29	54	43	35	28	rating scales
(Graetz et al., 2001)	268	67	25	133	50	68	25	structured interview (DISC)
(Mitsis et al., 2000)	63	45	71	7	11	11	18	structured interview (DISC)
(Weiler et al., 1999)								
refered sample	109	36	33	68	62	5	5	Rating scales
community sample	25	10	40	13	52	2	8	Rating scales
(Rasmussen et al., 2002)								
Australia cohort	161	76	47	61	38	24	15	Rating scales
Missouri cohort	239	60	25	150	63	29	12	structured interview (DICA)
Parent and Teacher								
(Weiler et al., 1999)								
referred sample	54	10	19	42	78	2	4	Rating scales
community sample	12	3	25	9	75	0	0	Rating scales

Study	Total ADHD cases	ADHD-C		ADHD-PI		ADHD-PH		Diagnostic instruments
		N	%	N	%	N	%	
(Gomez et al., 1999)	30	7	23	21	70	2	7	Rating scales
(McBurnett et al., 1999)	656	425	65	184	28	48	7	Rating scales
(Lahey et al., 1994)	276	152	55	74	27	50	18	structured interview (DISC)
(Chhabildas et al., 2001)	114	33	29	67	59	14	12	Rating scale
(Rowland et al., 2001)	46	33	72	12	26	1	2	structured interview (DISC) and rating scales
(Faraone et al., 1998)	301	185	61	89	30	27	9	structured interview (KSADS) and rating scales
(Mitsis et al., 2000)	69	64	93	2	3	3	4	Structured interview (DISC)
(Hinshaw, 2002) *	140	93	66	47	34			structured inteview (DISC), rating scales and direct observation
(Murphy et al., 2002) *	96	60	63	36	38			Rating scales, structured interview (DSM-IV based), expert clinical diagnosis
(Eiraldi et al., 1997) *	53	27	51	26	49			Rating scales, structured interview (DICA-R)
(Counts et al., 2005) *	134	96	72	38	28			Rating scales, structured interview (DISC-IV)

* These studies only included children who were either ADHD-C or ADHD-PI. Children with ADHD-PH were not included.

Table 2

Demographic Characteristics of Potential Cases

	Total pop
Variable	**N (%)**
Gender	
Male	1,022 (72%)
Female	389 (28%)
Race	
White	966 (68%)
Non-white	445 (32%)
Grade	
1–3	943 (67%)
4–5	468 (33%)
Age	
5–6	93 (7%)
7–8	545 (39%)
9–10	548 (39%)
11+	225 (16%)

Table 3

Distribution of ADHD Subtypes by Subtyping Method for Different Case Definitions[1]

	All Cases N[2] (%)	Combined ADHD-C N (%)	Inattentive ADHD-PI N (%)	Hyperactive ADHD-PH N (%)
A. Using Data from Only a SINGLE INFORMANT				
1. Teacher data only with cases and subtypes defined as 6 or more inattentive symptoms and/or 6 or more hyperactive-impulsive symptoms.	349 (100%)	101 (29%)	199 (57%)	49 (14%)
2. Parent data only with cases and subtypes defined as 6 or more inattentive symptoms and/or 6 or more hyperactive-impulsive symptoms.	82[3] (100%)	33(40%)	32 (39%)	17 (21%)
B. OR rule for case definition and OR rule for subtyping (Two Informants)				
1. 0-0-6 case definition. For cases and subtypes: No requirements on teacher or parent report. At least 6 unduplicated symptoms when data are combined.	100[3] (100%)	44 (44%)	42 (42%)	14 (14%)
C. AND rule for case definition and OR rule for subtyping (Two Informants)				
1. 3-3-6 case definition. For cases: 3 or more symptoms by teacher report, 3 or more symptoms by parent report, and at least 6 unduplicated symptoms when data are combined. For subtypes: at least 6 unduplicated symptoms.	417 (100%)	275 (66%)	122 (29%)	20 (5%)
2. 6-4-6 case definition. For cases: 6 or more symptoms by either teacher or parent report, at least 4 symptoms by the other informant, and at least 6 unduplicated symptoms when data are combined. For subtypes: at least 6 unduplicated symptoms.	334 (100%)	239 (72%)	87 (26%)	8 (2%)
3. 6-6-6 case definition. For cases: 6 or more symptoms by teacher report and 6 or more symptoms by parent report, and at least 6 unduplicated symptoms when data are combined. For subtypes: at least 6 unduplicated symptoms.	211 (100%)	159 (75%)	47 (22%)	5 (2%)
D. AND rule for case definition and AND rule for subtyping (Two Informants)				
1 3-3-6 case definition. For cases: 3 or more symptoms by either teacher or parent report and at least 3 symptoms by other informant and at least 6 unduplicated symptoms when data are combined. For subtypes: 3 or more symptoms by teacher and 3 or more symptoms by parent, and at least 6 unduplicated symptoms.	417 (100%)	152 (36%)	222 (53%)	43 (10%)
2. 6-4-6 case definition. For cases: 6 or more symptoms by either teacher or parent report and at least 4 symptoms by the other informant and at least 6 unduplicated symptoms when data are combined. For subtypes: 6 or more symptoms by either teacher or parent report and at least 4 symptoms by other informant and at least 6 unduplicated symptoms.	334 (100%)	96 (29%)	196 (59%)	42(13%)
3. 6-6-6 case definition. For cases: 6 or more Inattentive and 6 or more Hyperactive/Impulsive symptoms reported by both teacher and parent and at least 6 unduplicated symptoms. For subtypes: 6 or more symptoms by teacher and 6 or more symptoms by parent and at least 6 unduplicated symptoms.	211 (100%)	45 (21%)	131 (62%)	35 (17%)

[1] All symptom combinations were also required to be associated with moderate or severe impairment in each setting.

[2] The N is the number of cases that were positive for step 1 (case determination) according to the rules in each line.

[3] Because we used a two-step sampling procedure that used a 3-3-6 algorithm and began with the teachers screen, we could only calculate a 0-0-6 or a parent only definition in a random sub-sample of participants who had teacher screening data and parent questionnaire data regardless of whether they were a potential case.

Table 4

How subtypes shifted when an AND rule rather than an OR rule was used for subtyping under 3 different Case Definitions

3-3-6 AND/AND	3-3-6 AND/OR			
	ADHD-C	ADHD-PI	ADHD-PH	Total
ADHD-C	152	0	0	152
ADHD-PI	100	122	0	222
ADHD-PH	23	0	20	43
Total	275	122	20	417

6-4-6 AND/AND	6-4-6 AND/OR			
	ADHD-C	ADHD-PI	ADHD-PH	Total
ADHD-C	96	0	0	96
ADHD-PI	109	87	0	196
ADHD-PH	34	0	8	42
Total	239	87	8	334

6-6-6 AND/AND	6-6-6 AND/OR			
	ADHD-C	ADHD-PI	ADHD-PH	Total
ADHD-C	45	0	0	45
ADHD-PI	84	47	0	131
ADHD-PH	30	0	5	35
Total	159	47	5	211

Note: Participants who are classified ADHD-C under AND/OR rules can be classified ADHD-C, ADHD-PI, or ADHD-PH under AND/AND rules. Participants who are ADHD-PI or ADHD-PH under AND/OR rules will be the same classification under AND/AND rules. **Zero in these tables must be zeros; no other value is logically possible in those cells.**