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Validity of DSM-IV attention–deficit/hyperactivity disorder symptom dimensions and subtypes

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Abstract

DSM-IV criteria for ADHD specify two dimensions of inattention and hyperactivity-impulsivity symptoms that are used to define three nominal subtypes: predominantly hyperactive-impulsive type (ADHD-H), predominantly inattentive type (ADHD-I), and combined type (ADHD-C). To aid decision-making for DSM-5 and other future diagnostic systems, a comprehensive literature review and meta-analysis of 546 studies was completed to evaluate the validity of the DSM-IV model of ADHD. Results indicated that DSM-IV criteria identify individuals with significant and persistent impairment in social, academic, occupational, and adaptive functioning when intelligence, demographic factors, and concurrent psychopathology are controlled. Available data overwhelmingly support the concurrent, predictive, and discriminant validity of the distinction between inattention and hyperactivity-impulsivity symptoms, and indicate that nearly all differences among the nominal subtypes are consistent with the relative levels of inattention and hyperactivity-impulsivity symptoms that define the subtypes. In contrast, the validity of the DSM-IV subtype model is compromised by weak evidence for the validity of ADHD-H after first grade, minimal support for the distinction between ADHD-I and ADHD-C in studies of etiological

influences, academic and cognitive functioning, and treatment response, and the marked longitudinal instability of all three subtypes. Overall, it is concluded that the DSM-IV ADHD subtypes provide a convenient clinical shorthand to describe the functional and behavioral correlates of current levels of inattention and hyperactivity-impulsivity symptoms, but do not identify discrete subgroups with sufficient long-term stability to justify the classification of distinct forms of the disorder. Empirical support is stronger for an alternative model that would replace the subtypes with dimensional modifiers that reflect the number of inattention and hyperactivity-impulsivity symptoms at the time of assessment.

Keywords

ADHD; DSM-IV; DSM-5; validity; subtypes; symptoms

Despite over 30 years of research since subtypes of attention-deficit/hyperactivity disorder (ADHD) were first specified in the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III; American Psychiatric Association, 1980), the optimal approach to describe heterogeneity among individuals with ADHD remains unclear. Diagnostic criteria for ADHD in the fourth edition of the DSM (DSM-IV; American Psychiatric Association, 1994) defined three nominal subtypes based on differential elevations on two dimensions of nine symptoms of inattention and nine symptoms of hyperactivity-impulsivity. The Predominantly Inattentive Type (ADHD-I) includes individuals with six or more symptoms of inattention and fewer than six symptoms of hyperactivity-impulsivity, the Predominantly Hyperactive-Impulsive Type (ADHD-H) includes individuals with six or more symptoms of hyperactivity-impulsivity and fewer than six symptoms of inattention, and the Combined Type (ADHD-C) is defined by six or more symptoms on both dimensions.

This paper describes the results of a comprehensive literature review and meta-analysis that was conducted to critically evaluate the validity of the DSM-IV model of ADHD. We also review the much smaller group of studies that tested the validity of several alternative approaches to subtype classification, and conclude with recommendations for future diagnostic models of ADHD. Several factors suggest that a comprehensive review of the DSM-IV ADHD symptom dimensions and subtypes is needed to aid decision-making for DSM-5 and other future diagnostic systems:

1. The literature search for the present review identified over 450 relevant papers that were not included in previous systematic reviews of ADHD subtypes (e.g., Lahey & Willcutt, 2002; Milich, Balentine, & Lynam, 2001; Woo & Rey, 2005).
2. No previous empirical reviews have systematically evaluated whether the distinction between inattention and hyperactivity-impulsivity symptoms is internally and externally valid and should be retained in future diagnostic systems.
3. ADHD-H emerged unexpectedly for the first time as a result of the DSM-IV field trials (Lahey et al., 1994), and the validity of this new subtype has never been comprehensively evaluated.
4. Previous reviews based on a small subset of the studies included in the current review reached different conclusions regarding the validity of the distinction between ADHD-C and ADHD-I. Several authors concluded that ADHD-C and ADHD-I are valid subtypes within the overarching ADHD diagnosis (e.g., Carlson & Mann, 2000; Lahey & Willcutt, 2002). In contrast, others argued that ADHD-I should be reconceptualized as a separate disorder that is distinct from ADHD-C and ADHD-H (e.g., Barkley, 2006; Milich et al., 2001), and questioned whether

DSM-IV criteria for ADHD-I effectively capture an hypothesized inattentive group without hyperactivity that may be distinct from ADHD (e.g., McBurnett, Pfiffner, & Frick, 2001; Milich et al., 2001).

5. A final important overarching question is whether the nominal DSM-IV subtypes provide any unique information that is not conveyed by the differential elevations of the subtypes on the two symptom dimensions (e.g., McBurnett et al., 1999). If the clinical correlates of the subtypes are fully explained by the relative levels of inattention and hyperactivity-impulsivity symptoms at the time of diagnosis, categorical diagnostic subtypes may not be necessary to describe heterogeneity in ADHD (e.g., Lahey & Willcutt, 2010).

Levels of analysis for the evaluation of the validity of a mental disorder

The criteria which must be met for a mental disorder to be considered valid have been the focus of considerable debate in the literature. Because space constraints for the current paper preclude a comprehensive discussion, several benchmark papers that discuss these issues are listed in Section 3.1 of the online supplemental materials. These papers consider a range of important considerations, including the role of theory in the development of diagnostic criteria, the extent to which the definition of a mental disorder is influenced by social values, and the utility of a dimensional versus categorical conceptualization of mental disorders. For the current review we focus on the criteria for the validation of a mental disorder that were initially proposed by Robins and Guze (e.g., Robins & Guze, 1970) and later expanded for childhood disorders (Cantwell, 1980).

Internal validity and longitudinal stability

Before testing the external validity of ADHD, the DSM-IV symptom dimensions and subtypes must be shown to have adequate internal and inter-rater reliability. In addition, because ADHD is defined as a chronic condition that is expected to be relatively stable across development (American Psychiatric Association, 1994), results regarding the short-term and long-term stability of the ADHD symptom dimensions and subtypes provide another key criterion to evaluate the validity of the DSM-IV model.

Criterion and predictive validity

Concurrent and future functional impairment—Criterion validity refers to a significant association between a construct and an important independent external criterion (Cronbach & Meehl, 1955). Under the prevailing model that informs the DSM enterprise (e.g., Spitzer & Wakefield, 1999), a foundational aspect of criterion validity for a mental disorder is evidence that the disorder is associated with distress or functional impairment that is sufficiently severe to warrant intervention. For this reason, the inclusion criteria for many studies required documentation of impairment for an individual to be included in a group with ADHD. As a result, care must be taken to avoid a tautology in which the same measures of impairment are used to both define and externally validate the disorder.

Despite this caveat, previous studies provide important information regarding this essential criterion in several ways. A number of studies defined groups with ADHD based on DSM-IV symptom criteria only, then tested whether each symptom dimension or subtype was associated with significant functional impairment (e.g., Gaub & Carlson, 1997; Lahey et al., 1994; Lahey et al., 1998). Further, most studies that used full DSM-IV criteria to define ADHD assessed impairment as part of an initial structured interview, then administered a separate battery of measures of specific aspects of functional impairment that were not used to assign participants to groups with and without ADHD. Finally, several longitudinal studies examined the predictive validity of DSM-IV ADHD by testing whether the number

of inattention or hyperactivity-impulsivity symptoms or the nominal ADHD subtype at baseline predicted future negative outcomes (e.g., Hinshaw, Owens, Sami, & Fargeon, 2006; Lahey & Willcutt, 2010).

Confounding factors—It is often unclear whether functional impairment or other external measures are associated with ADHD per se or with other factors that are often correlated with ADHD, such as lower intelligence, other concurrent disorders, and low socioeconomic status or other demographic variables. Therefore, some researchers argue that these variables should always be controlled in statistical analyses to ensure that impairment associated with ADHD cannot be explained more parsimoniously by group differences on these correlated variables (Lahey et al., 1998). Alternatively, it is possible that ADHD symptoms may directly cause group differences on measures such as tests of intelligence (Barkley, 1997), and covariance between ADHD and other disorders may be attributable to a third factor such as shared genetic or environmental susceptibility (e.g., Thapar, Harrington, & McGuffin, 2001; Willcutt et al., 2007). In these latter cases controlling for these correlated variables may remove meaningful variance in ADHD symptoms. Therefore, to provide a comprehensive summary of the literature on ADHD we included all relevant studies in the review whether or not these potential confounds were controlled, then examined whether the pattern of results changed in studies that controlled one or more of these variables.

Discriminant validity

Evidence regarding discriminant validity provides one of the most decisive tests of the validity of the DSM-IV model of ADHD. To justify their distinction, the DSM-IV dimensions and subtypes must be shown to have differential associations with important external variables such as measures of functional impairment, developmental course, etiological influences, pathophysiology, or treatment response. If the symptom dimensions and subtypes are associated with identical external correlates, it would be most parsimonious for future diagnostic criteria to collapse the symptom dimensions and subtypes to form a single disorder without subtypes. In contrast, if the external correlates of the dimensions or subtypes are completely different the subtypes may be best conceptualized as distinct and unrelated disorders.

The most compelling support for the DSM-IV model would be provided by a more nuanced pattern in which some key correlates are shared across dimensions and subtypes, whereas other important criterion measures are uniquely associated with each symptom dimension and subtype. For example, the distinction between DSM-IV ADHD-C and ADHD-I would be validated if ADHD-C was more strongly associated with weak response inhibition, whereas ADHD-I was characterized by a more pronounced weakness in sustained attention.

METHODS

Due to space constraints, this section provides a brief overview of the review procedures, and a comprehensive description of the literature search and methodology of the meta-analysis is provided in section 1 of the online supplemental materials. Supplement section 1 includes specific information regarding the statistical power of the meta-analysis and the procedures that were used to test and correct for any significant publication bias or heterogeneity among the effects.

Literature search

A comprehensive search of the relevant literature was completed to identify all published studies that included data relevant to the internal or external validity of the DSM-IV ADHD

symptom dimensions or subtypes. Studies across the developmental spectrum were included in the review, but studies of children and adolescents were analyzed separately from studies of adults to evaluate potential developmental differences in the validity of the dimensions or subtypes. The literature search identified 546 papers based on 386 independent samples that met inclusion and exclusion criteria for the review.

A meta-analysis was completed for each criterion measure if data were available from multiple studies that used designs and measures that were sufficiently similar to justify pooled analyses (e.g., reliability and developmental course of the dimensions and subtypes, functional impairment, comorbidity, and neuropsychological functioning). A formal meta-analysis was not completed for several other validity criteria because the specific methods of the available studies were not sufficiently similar to allow effects to be combined across studies (e.g., studies using electrophysiological and neuroimaging methods, studies of specific candidate gene polymorphisms, and treatment studies). Instead, a qualitative review of each of these domains is provided in the body of the manuscript, and a comprehensive list of studies of each criterion is included in section 3 of the supplemental materials.

Presentation of results

The results of the meta-analyses are summarized in Tables 1 - 8, and parallel tables in the supplemental materials list the individual effect sizes that are included in the overall effect size. Notes in Tables 1 - 8 indicate any overall effects with significant evidence of heterogeneity or publication bias, and the details of these analyses are provided in the corresponding Supplement table. Zero-order correlations (r) were analyzed for correlational analyses of continuous measures. If a study reported means and standard deviations for groups with the nominal DSM-IV ADHD subtypes and/or a comparison group without ADHD, the effect size of each group difference was estimated by calculating Hedges' g , the difference between the group means divided by the pooled standard deviation (e.g., Hedges & Olkin, 1985). Hedges' g is similar to Cohen's d (Cohen, 1988), a widely-used effect size measure, but corrects for a small bias in d that leads to a slight overestimation of the effect size (e.g., Borenstein, 2009). Subtype comparisons that reported rates of categorical outcomes on dichotomous dependent measures were converted to odds ratios for the meta-analysis.

RESULTS

Internal validity, reliability, and symptom utility

Factor analyses—Exploratory and confirmatory factor analyses have been conducted on parent, teacher, and self-report ratings of over 60,000 children and adolescents (Supplement Table 2). These studies consistently support the distinction between symptoms of inattention and symptoms of hyperactivity-impulsivity. Estimates of internal consistency are high for both symptom dimensions (mean $\alpha = .89 - .92$ in studies of children and adolescents and $.82 - .86$ in studies of adults; Supplement Tables 3 and 4), and correlations between inattention and hyperactivity-impulsivity symptoms are moderate to high but less than unity ($r = .63 - .75$; Supplement Tables 3 and 4). These converging results suggest that DSM-IV inattention and hyperactivity-impulsivity are distinguishable but substantially correlated dimensions.

Results were less clear when confirmatory factor analyses were conducted to test whether symptoms of impulsivity and hyperactivity should be separated. Some studies suggested that a three-factor model with separate impulsivity and hyperactivity factors provided a small but significant improvement in fit over the two-factor DSM-IV model (studies are listed in the notes for Supplement Table 2), but correlations between hyperactivity and impulsivity symptoms were extremely high ($r = .80 - .90$) and close to the maximum possible correlation

based on the reliability of the two dimensions. This pattern of results led most authors to conclude that the two-dimension DSM-IV model was more parsimonious than a three-factor model with a separate impulsivity dimension (e.g., Gomez, Burns, Walsh, & Hafetz, 2005; Wolraich et al., 2003). However, the small number of impulsivity items in the DSM-IV symptom list may have constrained the ability to distinguish between impulsivity and hyperactivity, and additional research is needed to test whether impulsivity and hyperactivity symptoms may be more clearly separable in adults than in children and adolescents (e.g., Barkley, Murphy, & Fischer, 2008).

Discrimination from other disorders: Because ADHD frequently co-occurs with a range of internalizing and externalizing disorders, it is also essential to test whether the DSM-IV symptom dimensions are separable from symptoms of these correlated disorders. Item pools for several factor analyses included symptoms of DSM-IV ADHD and symptoms of oppositional defiant disorder (ODD), conduct disorder (CD), or internalizing disorders (Supplement Table 2), and one study used CFA to examine the structure of ADHD symptoms in the context of symptoms of all of the most prevalent mental disorders at the same time (Lahey et al., 2008). These studies consistently indicated that symptoms of inattention and hyperactivity-impulsivity load on factors separate from symptoms of these other disorders, with the exception that a subset of hyperactivity-impulsivity symptoms sometimes cross-load with symptoms of ODD (e.g., Lahey, Applegate, et al., 2004). With that caveat, these results provide strong support for the discriminant validity of the DSM-IV inattention and hyperactivity-impulsivity symptom dimensions.

Symptom utility—Although factor analyses provide strong support for the overall internal validity of the DSM-IV symptom dimensions, a closer examination of the psychometric characteristics of the individual items suggests that two inattention symptoms may have important weaknesses. The mean factor loading of inattention symptom c, *does not seem to listen when spoken to directly*, was weaker than the mean loading of any other inattention symptom in analyses of both parent and teacher ratings. In addition, this item cross-loaded on the hyperactivity-impulsivity factor in 73% of studies that reported secondary loadings (Supplement Table 2), had the lowest positive predictive power in the DSM-IV field trials (Frick et al., 1994), and was the least stable symptom over a 5-year period (Todd et al., 2008). Consideration should be given to dropping, replacing, or rewriting this symptom in future diagnostic criteria for ADHD. DSM-IV inattention symptom h, *easily distracted by extraneous stimuli*, also frequently cross-loaded on the hyperactivity-impulsivity factor, but additional research is needed to test whether this item may have greater utility in adults (Barkley et al., 2008).

Inter-rater agreement—Studies of children and adolescents reported moderate correlations between parent and teacher ratings of both symptom dimensions ($r = .43$ for inattention and $.42$ for hyperactivity-impulsivity; Supplement Table 3), and similar results were obtained in studies that examined correlations between self-report ratings by adults and ratings by another adult who knew the individual well ($r = .54$ for inattention and $.47$ for hyperactivity-impulsivity; Supplement Table 4). Rates of inter-rater agreement for the nominal DSM-IV subtypes were low in studies of children and adolescents (19% agreement for ADHD-C, 26% agreement for ADHD-I, 16% agreement for ADHD-H; Supplement Table 5) and the single published study of adults (Dias et al., 2008).

Low to moderate rates of inter-rater agreement are a nearly ubiquitous finding across all measures of psychopathology, indicating that this is a central issue for the field, and not a unique problem for ADHD (e.g., Achenbach & Rescorla, 2001; Gadow & Sprafkin, 1998). In the case of ADHD, differences between parent and teacher ratings are at least partially explained by differences in children's behavior in the home and school settings (e.g., Gomez

et al., 2005; Hart, Lahey, Loeber, & Hanson, 1994). Furthermore, Hart et al. (1994) found that parent and teacher ratings each accounted for unique variance in measures of functional impairment, suggesting that ratings by both reporters are valid and provide unique information that is clinically relevant.

Based on these data, the DSM-IV field trials used an algorithm in which each symptom reported by either the parent or teacher during a structured interview was counted as a positive symptom (Lahey et al., 1994), and the optimal symptoms and diagnostic thresholds for DSM-IV ADHD were determined based on this algorithm. Future research is needed to compare the validity of this procedure to other alternative algorithms for the combination of ratings by multiple informants, but this topic is beyond the scope of the current review.

Conclusions regarding internal validity and reliability—The distinction between inattention and hyperactivity-impulsivity symptoms is strongly supported by factor analytic studies, and both symptom dimensions are internally consistent. Inter-rater agreement is moderate for the symptom dimensions and low for the nominal subtypes, at least partially due to true differences in behavior across settings.

Temporal stability and developmental course

Symptom dimensions

Test-retest reliability was high for both symptom dimensions over periods less than one year ($r = .78 - .82$ in children and adolescents and $.70 - .73$ in adults; Supplement Tables 3 and 4). Importantly, stability correlations were only slightly lower for intervals ranging from one to five years ($r = .64$ for both dimensions), suggesting that the rank ordering of individuals in the population is relatively stable over time for both symptom dimensions.

Although the rank order of individuals in the population remains stable, longitudinal studies suggest that inattention and hyperactivity-impulsivity symptoms follow different developmental trajectories. Over the first nine years of a prospective longitudinal study, children first diagnosed with DSM-IV ADHD in preschool exhibited a significant age-related decline in hyperactive-impulsive behaviors that was not related to pharmacologic or psychosocial treatment, whereas symptoms of inattention did not change significantly (Lahey, Pelham, et al., 2004; Lahey, Pelham, Loney, Lee, & Willcutt, 2005; Lahey et al., 1998; Lahey & Willcutt, 2010). Similar results were reported in a five-year follow-up study of a sample of females with ADHD who were first assessed between 6 and 12 years of age (e.g., Hinshaw et al., 2006), and in a population-based longitudinal study that followed children from 8 - 17 years of age (Larsson, Lichtenstein, & Larsson, 2006).

Subtypes

To our knowledge no studies reported test-retest reliability estimates for the DSM-IV subtypes for periods less than one year, but five studies examined the stability of the subtypes 5 to 9 years after an initial assessment was completed (Table 1 and Supplement Table 6). The majority of children who met DSM-IV criteria for ADHD at the initial assessment continued to meet criteria for one of the DSM-IV ADHD subtypes at the follow-up assessment (59%), but only 35% continued to meet criteria for the same subtype. Further, in the only longitudinal study that assessed the subtypes annually, groups with ADHD-C, ADHD-H, and ADHD-I at an initial preschool assessment each included specific children who met criteria for both of the other subtypes at least once during the next nine years (Lahey & Willcutt, 2010).

In addition to the unpredictable shifts between subtypes exhibited by some individuals with ADHD, longitudinal studies suggest that a subset of individuals shift systematically from

ADHD-C to ADHD-I across development. Individuals with ADHD-C at the initial assessment were equally likely to meet criteria for ADHD-C or ADHD-I at the final follow-up assessment, whereas most individuals with ADHD-I at initial testing either continued to meet criteria for ADHD-I or no longer met criteria for any ADHD subtype (Table 1). These results are consistent with the different developmental trajectories of the two symptom dimensions, as some individuals with ADHD-C may shift to ADHD-I as their hyperactivity-impulsivity symptoms decline below the diagnostic threshold. In contrast, because their hyperactivity-impulsivity symptoms were already below the diagnostic threshold at the time of the initial assessment, individuals with ADHD-I at initial testing typically continued to meet criteria for ADHD-I or no longer met criteria for any ADHD subtype.

Existing data suggest that ADHD-H is less stable than ADHD-C or ADHD-I, although samples are small in all studies (Table 1 and Supplement Table 6). In comparison to individuals with an initial diagnosis of ADHD-C or ADHD-I, significantly fewer individuals with ADHD-H at the initial assessment continued to meet criteria for ADHD 5 - 9 years later (33%), and ADHD-H was especially unstable in the two samples that were initially tested in late childhood (only 13% continued to meet criteria for ADHD five years later). These results seriously challenge the validity of ADHD-H, particularly after early childhood.

Conclusions regarding developmental course and stability

Both DSM-IV symptom dimensions have adequate stability over intervals up to five years, but hyperactivity-impulsivity symptoms decline more than inattention symptoms across development in both population-based samples and groups with ADHD. The overall diagnosis of DSM-IV ADHD has moderate stability over periods up to nine years, but the nominal subtypes are unstable in both systematic and unsystematic ways.

Functional impairment

Symptom dimensions

Both DSM-IV ADHD symptom dimensions are significantly associated with global, social, academic, and adaptive impairment in children, adolescents, and adults (Table 2 and Supplement Table 7). Importantly, most of these associations remained significant in individual studies that controlled a range of potential confounding variables such as socioeconomic status, sex, ethnicity, intelligence, and concurrent mental disorders (e.g., Lahey et al., 1994; Lahey & Willcutt, 2010; Nigg et al., 2005).

The discriminant validity of the symptom dimensions is supported by significant differences in the relative magnitude of their associations with specific aspects of functional impairment. In comparison to hyperactivity-impulsivity symptoms, inattention symptoms are significantly more strongly associated with shy and passive social behavior and impaired adaptive functioning in children and adolescents, global impairment and lower life satisfaction in adults, and impaired academic functioning across the developmental spectrum (Table 2 and Supplement Table 7). In contrast, results of the meta-analysis indicate that hyperactivity-impulsivity symptoms are more strongly associated with overt rejection by peers, and multiple regression analyses conducted by individual studies indicated that only hyperactivity-impulsivity symptoms were significantly associated with relational aggression and more frequent accidental injuries when both symptom dimensions were included in the model (Diamantopoulou, Rydell, Thorell, & Bohlin, 2007; Lahey et al., 1998).

Subtypes

Groups of children and adolescents with ADHD-C, ADHD-I, and ADHD-H are more impaired than groups without ADHD on measures of nearly all domains of concurrent and

future functional impairment (studies of concurrent impairment are summarized in Table 3 and Supplement Table 8; studies of predictive validity are listed in Online Supplement Section 3.2). Furthermore, several individual studies that controlled a range of potential confounding variables reported that the significant impairment that is associated with the subtypes is not explained by group differences in comorbidity, intelligence, sex, age, or socioeconomic status (e.g., Hinshaw, 2002; Lahey et al., 1994; Lahey et al., 1998; Lahey & Willcutt, 2010). Only a few studies have examined impairment in adults with the DSM-IV ADHD subtypes, but initial results suggest that ADHD-I and ADHD-C are also associated with significant academic and social impairment in adulthood (Supplement Table 8).

Discriminant validity of the DSM-IV ADHD subtypes is supported by significant differences in specific aspects of functional impairment, most of which are consistent with the relative levels of inattention and hyperactivity-impulsivity symptoms that characterize the subtypes. Groups of children and adolescents with ADHD-C are significantly more impaired than groups with ADHD-I or ADHD-H on aspects of functioning that are strongly associated with both symptom dimensions, such as global impairment, overall social functioning and prosocial behavior, and tendency to be disliked by peers (Table 3 and Supplement Table 8). Groups with ADHD-C and ADHD-I are significantly more impaired than groups with ADHD-H on measures of academic functioning and are more likely to be ignored by peers, consistent with the stronger associations between these measures and inattention symptoms. In contrast, one individual study found that preschool children with significant hyperactivity-impulsivity (ADHD-C and ADHD-H) were more likely than children with ADHD-I to sustain an injury requiring care from a physician (Lahey et al., 1998). The only result in the meta-analysis that differs from the pattern expected based on the correlates of the symptom dimensions is the finding that ADHD-I is associated with significantly higher levels of shy and passive social behavior than ADHD-C, despite the similar levels of inattention symptoms in the two subtypes.

Conclusions regarding functional impairment

Symptoms of inattention and hyperactivity-impulsivity are associated with multiple aspects of concurrent and future functional impairment after an extensive list of confounds are controlled. Significant differences in the strength of the relations between the symptom dimensions and specific domains of impairment indicate that the distinction between inattention and hyperactivity-impulsivity has discriminant validity and is clinically important. Similarly, ADHD-C, ADHD-I, and preschool ADHD-H are clearly valid in the fundamental sense of being associated with concurrent and future functional impairment, although few studies have included adolescents with ADHD-H or adults with any of the subtypes. Distinctions among the DSM-IV subtypes convey clinically relevant information about functional impairment that is nearly all consistent with the relative levels of inattention and hyperactivity-impulsivity that define the subtypes.

Comorbid Mental Disorders

Symptom dimensions

Inattention and hyperactivity-impulsivity symptoms are significantly associated with symptoms of all other disorders that were included in previous studies, but several of these associations differ in magnitude (Table 4 and Supplement Table 9). Meta-analyses of studies of children, adolescents, and adults indicated that hyperactivity-impulsivity symptoms are more strongly associated with symptoms of externalizing disorders than inattention symptoms, whereas inattention symptoms are more strongly associated with withdrawn behaviors in children and adolescents and elevations of depression symptoms across the developmental spectrum. Studies of substance-use disorders have yielded inconsistent

results; some studies reported that substance use or abuse was independently associated with both symptom dimensions (e.g., (Upadhyaya & Carpenter, 2008), whereas others found that substance use was only independently associated with hyperactivity-impulsivity (e.g., Elkins, McGue, & Iacono, 2007) or inattention (e.g., Molina & Pelham, 2003; studies are listed in Supplement Section 3.3).

Subtypes

Results of the meta-analysis indicated that in comparison to groups without ADHD, each DSM-IV ADHD subtype is associated with significant elevations of symptoms of all measured mental disorders and higher rates of most categorical diagnoses (Tables 5 and 6 and Supplement Tables 10 and 11). In comparison to groups with ADHD-I or ADHD-H, children and adolescents with ADHD-C are more likely to meet criteria for ODD, CD, and bipolar disorder. Children and adolescents with subtypes characterized by significant inattention (ADHD-I and ADHD-C) are more likely than individuals with ADHD-H to meet criteria for MDD and specific learning disorders, whereas individuals with elevations of hyperactivity-impulsivity (ADHD-C and ADHD-H) are more likely than individuals with ADHD-I to meet criteria for externalizing and tic disorders. Studies that compared the subtypes in adults reported similar results for measures of depression and externalizing disorders (Supplement Tables 10 and 11), but only a handful of studies of adults have reported results for any subtypes, and data are particularly sparse for ADHD-H.

Conclusions regarding concurrent mental disorders

Differential associations between inattention and hyperactivity-impulsivity symptoms and symptoms of other mental disorders provide additional support for the distinction between the DSM-IV symptom dimensions. Similarly, significant differences in rates of comorbid symptoms and disorders indicate that the subtypes convey clinically meaningful information that is consistent with the correlates of the two symptom dimensions.

Neurocognitive Correlates

Neuropsychological studies

Symptom dimensions—Both DSM-IV symptom dimensions are inversely correlated with all neuropsychological constructs that were included in the meta-analysis (Table 7 and Supplement Table 12). However, meta-analyses of studies of children and adolescents and multiple regression analyses in several individual studies of adults all indicated that inattention symptoms are more strongly associated with weaknesses in a range of neuropsychological domains, including general cognitive ability, short-term and working memory, processing speed, vigilance, and response variability. Further, most multiple regression analyses indicated that the association between hyperactivity-impulsivity symptoms and these neuropsychological outcomes was no longer significant when inattention was controlled. In contrast, neuropsychological weaknesses specific to hyperactivity-impulsivity have been more difficult to identify, although recent studies reported promising results for some aspects of reward-related processing (e.g., Scheres, Lee, & Sumiya, 2008).

Subtypes—Comparisons among the subtypes on neuropsychological measures are consistent with the results for the symptom dimensions. Groups of children, adolescents, and adults with high levels of inattention (ADHD-C and ADHD-I) performed more poorly than comparison groups without ADHD on nearly all neuropsychological measures, and the only significant differences between these groups in the meta-analysis were slightly larger weaknesses in groups with ADHD-C than groups with ADHD-I on measures of response inhibition and response variability ($g = 0.17$ and 0.18 ; Table 8 and Supplement Table 13).

In contrast to the robust neuropsychological weaknesses that characterize ADHD-I and ADHD-C, differences between groups with ADHD-H and comparison groups without ADHD were smaller and less consistent in the meta-analysis. Studies of children and adolescents found that groups with ADHD-C and ADHD-I performed worse than groups with ADHD-H on measures of processing speed, vigilance, response variability, and multiple dimensions of executive functions. Only a handful of studies have included small samples of adults with ADHD-H, limiting the conclusions that can be drawn.

Electroencephalography and event-related potentials

Studies using electrophysiological measures such as the electroencephalogram (EEG) and event-related potentials (ERPs) have reported robust differences between ADHD and comparison groups, and some have examined the DSM-IV symptom dimensions or subtypes (Supplement Section 3.4 lists these studies). When reported, EEG spectral power and coherence differences between ADHD subtypes were either not significant (e.g., Loo et al., 2010) or reflected quantitative rather than qualitative differences (e.g., Barry, Clarke, McCarthy, & Selikowitz, 2006), such that ADHD-C demonstrated more pronounced EEG abnormality than ADHD-I. Similarly, most ERP studies found that both ADHD-I and ADHD-C differed from controls but did not differ from one another (e.g., Keage et al., 2008), although one set of studies reported qualitative differences between ADHD-I and ADHD-C in early components of the ERP signal during an inhibitory task (e.g., Johnstone & Clarke, 2009).

Neuroimaging

Symptom dimensions—Three structural magnetic resonance imaging (MRI) studies found that higher levels of hyperactivity-impulsivity symptoms were associated with smaller volumes of the ventral striatum, right amygdala, and lateral thalamus, brain regions that are involved in action selection and response to reward and punishment (Carmona et al., 2009; Frodl et al., 2010; Ivanov et al., 2010). In contrast, inattention symptoms were not significantly correlated with volume of the ventral striatum, and were associated with greater volume in the amygdala and medial thalamic surface. The only study that has used functional MRI (fMRI) to examine associations between DSM-IV ADHD symptoms and brain functioning found that inattention symptoms were associated with disrupted neural activity across a large network of brain regions that span areas involved in executive processes, inhibition, and arousal, whereas hyperactivity-impulsivity symptoms were not (Depue et al., 2010).

Subtypes—Groups with ADHD-C and ADHD-I have been compared in five neuroimaging studies, all with small samples. A structural MRI study found no differences in caudate volume between ADHD-C, ADHD-I, and a control group without ADHD (Pineda et al., 2002), and functional imaging studies reported no differences between ADHD-I and ADHD-C on measures of functional connectivity during resting state (Cao et al., 2006), activation of sites subserving inhibition or motor control (Solanto, Schulz, Fan, Tang, & Newcorn, 2009), or metabolism in fronto-striato-thalamic structures (Ferreira et al., 2009). In contrast, an MRI spectroscopy study reported that ADHD-C had significantly lower metabolism than ADHD-I in the right lenticular nucleus (Sun et al., 2005), and secondary analyses by Solanto et al. (2009) suggested that alerting and orienting processes may be less efficient in children with ADHD-I than children with ADHD-C.

Conclusions from neuropsychological, neurophysiological, and neuroimaging studies

Neuropsychological studies provide strong support for the distinction between the inattention and hyperactivity-impulsivity symptom dimensions, and groups with ADHD-C

and ADHD-I are significantly more impaired than groups with ADHD-H on a range of neuropsychological measures. In contrast, neuropsychological studies found few differences between ADHD-C and ADHD-I, and most EEG and ERP studies reported results consistent with a quantitative difference in severity between ADHD-C and ADHD-I. Initial neuroimaging studies have yielded intriguing results, but all studies were dramatically underpowered for subtype comparisons and all findings await independent replication. At present, a dearth of adequately powered brain imaging studies represents an important gap in the knowledge base regarding DSM-IV ADHD dimensions and subtypes.

Etiology

Family and twin studies

Symptom dimensions—Family and twin studies indicate that individual differences in both inattention and hyperactivity-impulsivity are significantly familial and highly heritable, and common genetic influences explain most of the phenotypic covariance between the symptom dimensions (e.g., Larsson et al., 2006; McLoughlin, Ronald, Kuntsi, Asherson, & Plomin, 2007). Nonetheless, a meta-analysis of twin studies indicated that significant independent genetic and environmental influences also contribute to individual differences in inattention and hyperactivity-impulsivity, further cementing the importance of the distinction between the symptom dimensions (Nikolas & Burt, 2010).

Subtypes—A meta-analysis of family studies showed a small but significant increase in subtype-specific familiarity for ADHD-I and ADHD-C (Stawicki, Nigg, & von Eye, 2006), and twin studies suggest that ADHD-I and ADHD-C are significantly heritable (Supplement Section 3.5 lists these studies). However, cotwins and siblings of probands with ADHD-I also exhibited significantly higher rates of ADHD-C than the biological relatives of control probands, suggesting that ADHD-I and ADHD-C are also due in part to shared familial influences.

Family members of probands with ADHD-H were significantly more likely to meet criteria for ADHD than expected by chance (34%), but more family members met criteria for ADHD-C (17%) or ADHD-I (9%) than ADHD-H (7%). Similarly, most twin studies found that ADHD-H was not significantly heritable, arguing against the validity of ADHD-H as a distinct etiological type.

Molecular genetic studies

Molecular genetic studies suggest that the etiology of ADHD is polygenic, with multiple genes that each account for a relatively small proportion of the total variance in ADHD symptoms in the population (e.g., Gizer, Ficks, & Waldman, 2009; Neale et al., 2008). A total of 82 candidate gene studies reported results separately for the DSM-IV symptom dimensions or subtypes. A formal meta-analysis of these studies was not conducted because not enough studies tested the same genetic polymorphisms for most genes. Instead, a qualitative summary of these results is provided in the remainder of this section, and the results of the individual studies are summarized in more detail in Supplement Table 14.

Symptom dimensions—In studies that tested for associations between polymorphisms in 51 candidate genes and the DSM-IV ADHD symptom dimensions, at least one study reported nominally significant associations between 19 genes and inattention symptoms and between 20 genes and hyperactivity-impulsivity symptoms. For 17 of these genes at least one study reported a significant association with each symptom dimension, consistent with the finding that covariance between inattention and hyperactivity-impulsivity symptoms is due to common genetic influences.

Subtypes—Candidate gene studies reported significant associations for 40 of 73 candidate genes tested for ADHD-C, 24 of 48 genes tested for ADHD-I, and 0 of 19 genes tested for ADHD-H. A subset of studies reported that a specific candidate gene was significantly associated with ADHD-C or ADHD-I, but not with the other subtype. However, no studies reported a significant difference in direct comparisons of ADHD-C and ADHD-I, and in many cases the effect of the candidate gene was in the same direction for both subtypes, but only one subtype crossed the threshold of statistical significance. This pattern is particularly important because most studies were dramatically underpowered, especially for ADHD-I.

Candidate gene studies of ADHD-H must be interpreted even more cautiously due to small sample sizes in virtually all studies. Nonetheless, it is striking that no candidate gene study reported a significant association between ADHD-H and any polymorphism, a pattern that is consistent with the low heritability of ADHD-H in twin studies. Similarly, both a meta-analysis of studies of a polymorphism in the dopamine D5 receptor gene (Lowe et al., 2004) and a genome-wide linkage scan (Smalley et al., 2002) reported that genetic effects were strongest when probands with ADHD-H were excluded from the analysis.

Conclusions regarding familial and genetic influences

Twin studies indicate that inattention and hyperactivity-impulsivity symptoms are highly heritable, and are due to both shared and unique genetic influences. Similarly, ADHD-I and ADHD-C are familial and highly heritable, and family, twin, and candidate gene studies suggest that these subtypes are due in part to shared etiological influences. In contrast, family, twin, and molecular genetic studies all suggest that genetic influences may be less important for ADHD-H than for ADHD-C and ADHD-I. Overall, molecular genetic studies of subtype distinctions remain sparse and underpowered, and additional research should be encouraged.

Treatment Response

Medication

Symptom dimensions—Over 25 treatment studies have reported medication effects separately for the two symptom dimensions for atomoxetine, aripiprazole, guanfacine, methylphenidate, mixed amphetamine salts, modafinil, and reboxetine (studies are listed in Online Supplement Section 3.6). All of these studies reported significant reductions in both inattention and hyperactivity-impulsivity symptoms in response to treatment, with little evidence of differential efficacy for the symptom dimensions.

Subtypes—Population-based studies suggest that individuals with ADHD-C are more likely than those with ADHD-I to be prescribed medication (e.g., Sawyer, Rey, Graetz, Clark, & Baghurst, 2002). Nonetheless, similar efficacy for ADHD-I and ADHD-C has been reported for atomoxetine, aripiprazole, methylphenidate, mixed amphetamine salts, and modafinil, although one study found that individuals with ADHD-I may respond optimally to lower doses of methylphenidate than individuals with ADHD-C (Stein et al., 2003). Few separate analyses of ADHD-H have been reported, but recent studies suggest that stimulant medication may also be effective for this group (e.g., Chou et al., 2009).

Psychosocial interventions

Symptom dimensions—The NIMH Collaborative Multisite Multimodal Treatment Study of Children with ADHD (The MTA Cooperative Group, 1999) randomized 579 children with ADHD-C to conditions with systematic medication management only, multicomponent behavior therapy only, both medication management and behavior therapy, or a community control condition. The group that received behavior therapy only showed

significant improvement in both inattention and hyperactivity-impulsivity symptoms after 14 months, and these gains were sustained at a follow-up assessment completed 96 months after the initiation of treatment (Molina et al., 2009). Similarly, a recent study reported that a working memory intervention led to a significant reduction in both inattention and hyperactivity-impulsivity symptoms (Beck, Hanson, Puffenberger, Benninger, & Benninger, 2010).

Subtypes—Three controlled psychosocial treatment studies compared outcomes in groups of children and adolescents with ADHD-I and ADHD-C, and found that both groups showed significant improvement after social skills training (Antshel & Remer, 2003), meta-cognitive therapy (Solanto et al., 2010), and a working memory training intervention (Beck et al., 2010), with few differences in efficacy between the subtypes. To date, no psychosocial treatment studies have included a group with ADHD-H.

Conclusions regarding treatment

The construct validity of DSM-IV ADHD is supported by the significant response to intervention of the two symptom dimensions and both ADHD-C and ADHD-I. To date, treatment studies have provided little evidence of differential efficacy for the dimensions or subtypes, but additional data are needed before definitive conclusions can be drawn regarding ADHD-H.

Evidence based on alternative definitions of ADHD subtypes

To this point we have limited our remarks to studies of DSM-IV ADHD. Due to the mixed support for the distinction between ADHD-C and ADHD-I, several different approaches have been used in an attempt to identify an hypothesized inattentive group without significant hyperactivity that is more clearly distinct from ADHD-C. To provide a comprehensive summary of existing data regarding heterogeneity in ADHD, we briefly review these studies before summarizing the overall conclusions of the review.

Latent class analysis

As an alternative to the DSM-IV model, a number of studies have tested the validity of subtypes identified by latent class analyses of ADHD symptoms (studies listed in Online Supplement Section 3.7). These studies identified subgroups that are related to but partially distinct from those specified in DSM-IV, and some studies found that the LCA groupings may be somewhat more strongly familial than DSM-IV subtypes (Todd et al., 2001). However, latent class types were also highly unstable over a five-year period (Todd et al., 2008), and studies that compared the results of different methods (e.g., taxometric methods, factor mixture analysis, and latent class analysis) supported versions of a continuum model in which ADHD subtypes were distinguished by quantitative differences in severity, rather than distinct configural subtypes (e.g., Frazier, Youngstrom, & Naugle, 2007). Therefore, while the LCA approach is a useful tool for future research on the heterogeneity of ADHD, subtypes derived from this approach do not have sufficient validity to justify their use for clinical purposes.

Refined inattentive subgroup

In their benchmark review, Milich et al. (2001) suggested that the discriminant validity of ADHD-I and ADHD-C might be compromised due to heterogeneity among individuals with ADHD-I. The authors noted that a subset of individuals with ADHD-I exhibit elevations of hyperactivity-impulsivity symptoms that fall only slightly below the diagnostic threshold (i.e., 4 - 5 hyperactivity-impulsivity symptoms), and argued that this subgroup may be better conceptualized as a less severe form of ADHD-C. In contrast, the authors proposed that

individuals with ADHD-I with few or no hyperactivity-impulsivity symptoms may be qualitatively distinct from ADHD-C.

To test this hypothesis, several studies imposed a more stringent upper bound on the hyperactivity-impulsivity symptom dimension by requiring that individuals in a refined inattentive group exhibit no more than two or three hyperactivity-impulsivity symptoms (studies are listed in Online Supplement Section 3.8). These studies have reported potentially important success differentiating these refined inattentive subgroups from ADHD-C on a subset of measures of neuropsychological functioning. However, all studies had small samples, no specific finding has yet been replicated, and most studies found that the ADHD-C and refined inattentive groups exhibited similar weaknesses on a range of other neuropsychological measures. Overall, these initial data are not sufficient to validate this approach to identify a refined inattentive subgroup, but further research should be encouraged.

Sluggish cognitive tempo

DSM-IV diagnostic criteria use the same list of nine inattention symptoms to define both ADHD-I and ADHD-C, implying that the nature of the attentional difficulties that characterize the two subtypes is the same. In contrast, several authors hypothesized that ADHD-I might be uniquely associated with a specific cluster of inattentive behaviors characterized by sluggish cognitive tempo (SCT; potential items are listed in Supplement Table 15), and proposed that a definition of ADHD-I based on these positive criteria might have stronger internal and external validity than diagnostic criteria based on the absence of hyperactivity and impulsivity (e.g., Carlson & Mann, 2002; McBurnett et al., 1999).

Although SCT items and DSM-IV inattention symptoms are highly correlated (Supplement Table 16), exploratory and confirmatory factor analyses indicated that at least a subset of SCT items load on factors separate from either DSM-IV ADHD symptom dimension (Supplement Table 15). As predicted by theoretical models of SCT, groups with ADHD-I exhibited significantly higher levels of SCT than all other groups (Supplement Table 17), and initial studies found that associations between ADHD-I and some aspects of functional impairment were moderated by levels of SCT (e.g., Carlson & Mann, 2002). However, results of the meta-analysis indicate that groups with ADHD-C also exhibit significant elevations of SCT in comparison to groups without ADHD (Supplement Table 17), and several more recent studies found little evidence that levels of SCT moderated associations between ADHD-I and functional impairment, neuropsychological functioning, or treatment response (studies are listed in Supplement Section 3.9). These results suggest that additional research is needed to clarify the external correlates of SCT and the relation between SCT and DSM-IV ADHD, but available data do not support the hypothesis that SCT symptoms identify a primarily inattentive subgroup that is unrelated to ADHD-C.

Overall Conclusions

Important gaps remain in the literature on DSM-IV ADHD, including limited data on ADHD-H in adolescents and on all subtypes and symptom dimensions in adults, small samples in studies of longitudinal stability, and the paucity of neuroimaging studies of ADHD subtypes. Nonetheless, the results of this review support several clear conclusions regarding the validity of the DSM-IV model of ADHD, along with additional conclusions that are necessarily more nuanced.

Conclusion 1: DSM-IV criteria for ADHD identify individuals with significant functional impairment

DSM-IV criteria for ADHD successfully identify children, adolescents, and adults with significant and persistent impairment in social, academic, occupational, and overall global and adaptive functioning when intelligence, demographic factors, and concurrent psychopathology are controlled, with the important exception that the validity of ADHD-H after preschool remains unclear. With that caveat, existing data indicate that any revised diagnostic criteria for ADHD should continue to capture all individuals who meet criteria for DSM-IV ADHD.

Conclusion 2: The DSM-IV inattention and hyperactivity-impulsivity symptom dimensions are valid

Available data overwhelmingly support the concurrent, predictive, and discriminant validity of the distinction between inattention and hyperactivity-impulsivity symptoms. These results argue for the retention of separate inattention and hyperactivity-impulsivity symptom dimensions in the diagnostic criteria for ADHD, whether or not future diagnostic systems include nominal subtypes.

Conclusion 3: Evidence is mixed regarding the discriminant validity of DSM-IV ADHD subtypes

Subtype comparisons revealed quantitative differences between the three subtypes on measures of concurrent mental disorders and some aspects of functional impairment. The distinction between ADHD-H and the other two subtypes is also supported by results indicating that ADHD-H is less heritable and is associated with significantly less academic and cognitive impairment. On the other hand, ADHD-C and ADHD-I are associated with similar adaptive, academic, and neuropsychological impairment, are due at least in part to shared etiological influences, and appear to respond similarly to pharmacological and psychosocial interventions, calling into question the discriminant validity of these subtypes.

Conclusion 4: Correlates of the nominal subtypes are consistent with the differential elevations of the subtypes on the two symptom dimensions

With the exception of the higher rates of sluggish cognitive processing and shy and passive social behavior in ADHD-I than ADHD-C, the external correlates of the subtypes are almost entirely consistent with the relative levels of inattention and hyperactivity-impulsivity symptoms that characterize each subtype. These results suggest that the nominal subtypes may add relatively little unique information beyond that provided by the symptom dimensions.

Conclusion 5: DSM-IV subtype classifications are unstable over time

Emerging longitudinal data present the strongest challenge to the external validity of the nominal DSM-IV subtypes. Although a subset of children with each DSM-IV subtype continued to meet criteria for the same subtype five to nine years later (18 - 41%), nearly as many met criteria for one of the other subtypes (10 - 32%). Critically, some individuals with each subtype at the initial assessment met criteria for each of the other DSM-IV subtypes at least once during a 9-year follow-up study that included annual assessments (e.g., Lahey & Willcutt, 2010). Furthermore, this instability does not appear to be due only to children near the cut points changing by one symptom, nor is it explained solely by lawful changes in symptoms across development (e.g., reductions in hyperactivity with age causing systematic change from ADHD-C to ADHD-I). Rather, the longitudinal data suggest that the nominal DSM-IV subtype categories are unstable due to both systematic and random changes over time. This picture seriously compromises the validity of the DSM-IV subtype model.

Recommendations for future diagnostic systems

The dilemma that is confronted for DSM-5 and other future diagnostic systems is simply stated. Diagnostic criteria for ADHD need to somehow describe the heterogeneity that clearly exists among individuals diagnosed with ADHD without reifying distinctions between symptom dimensions or subtypes that lack sufficient empirical support. Existing data provide no perfect solution to this dilemma, in part because diagnostic criteria must balance multiple considerations. For example, the optimal diagnostic model may differ depending on the relative importance assigned to the clinical utility and user-friendliness of the diagnostic criteria versus the strength of empirical support for the model. In this final section we briefly summarize the strengths and weaknesses of three potential options for future diagnostic criteria in the context of these considerations.

Option #1: Retain the DSM-IV symptom dimensions and subtypes

Advantages of this option are several. The DSM-IV model reflects the well-validated distinction between the inattention and hyperactivity-impulsivity symptom dimensions. Although most of the differences between the DSM-IV subtypes appear to be explained by the symptom dimensions, the nominal subtypes may be more user-friendly for clinicians and more easily understood by individuals with ADHD than diagnostic criteria based on symptom dimensions alone. The paucity of data comparing subtypes in key domains such as molecular genetics and neuroimaging could be used to argue that the elimination of subtypes is premature, and the retention of the DSM-IV subtype structure would encourage additional research on this specific model of heterogeneity.

Despite these advantages, the DSM-IV subtype model has several important weaknesses. The results of this review suggest that nominal subtypes may not be necessary to describe heterogeneity in ADHD, and the retention of the DSM-IV model could tacitly discourage needed research to test alternative approaches. Studies of etiological influences, academic and cognitive functioning, and treatment response provide minimal support for the distinction between ADHD-I and ADHD-C, and existing data call into question the validity of ADHD-H after early childhood. Finally, the strongest argument against the DSM-IV model is the marked instability of the subtype classifications over time (59% of all cases with ADHD continue to meet criteria for ADHD 5 years later, but only 35% meet criteria for the same subtype). These data provide little justification for the conceptualization of nominal subtypes of ADHD as stable, trait-like entities.

If for practical reasons the decision is made to retain the DSM-IV subtypes in DSM-5 or other future diagnostic systems, it would be advisable to emphasize strongly that the subtypes are a description of the individual's current symptom presentation that is likely to change over time in both systematic and unsystematic ways. In addition, rather than continuing to include ADHD-H as a distinct subtype, a better option may be to eliminate ADHD-H while retaining a category of ADHD, Not Otherwise Specified. This revision would allow ADHD diagnostic criteria to continue to capture the subgroup of individuals that currently meet criteria for ADHD-H and experience significant functional impairment, while avoiding the reification of ADHD-H as a discrete subtype in the absence of sufficient data demonstrating its validity.

Option #2: Create new nominal subtype classifications

Earlier we reviewed several alternative approaches that have been proposed to describe heterogeneity in ADHD. These include subtype schemes generated by latent class analyses, the incorporation of new inattention symptoms characterized by sluggish cognitive processing, and the use of a more stringent definition of low hyperactivity-impulsivity to

define a primarily inattentive group that is less contaminated by subthreshold cases of ADHD-C. Each of these approaches would provide a fresh start on subtypes and stimulate new research that could eventually lead to the discovery of new and potentially more valid subtype designations. However, the disadvantages of creating new nominal subtype definitions at this juncture are overwhelming. Although promising results have been reported in individual studies, systematic validity data do not exist for any specific alternative subtype scheme, and revisions to the current diagnostic criteria to create new subtypes would be premature. Nonetheless, continued research should be encouraged to test the validity of these and other alternative models.

Option #3: Single disorder with dimensional modifiers

Finally, the results of this review and meta-analysis suggest that a dimensional approach to describe heterogeneity in ADHD also warrants consideration for DSM-5 and future diagnostic systems. For example, the model proposed by Lahey and Willcutt (2010) would define ADHD as a single disorder without subtypes, with dimensional modifiers that reflect the number of inattention and hyperactivity-impulsivity symptoms at the time of assessment. This dimensional model retains the important distinction between inattention and hyperactivity-impulsivity symptoms, and reflects the consistent finding that most relevant clinical information regarding differences among the subtypes is contained in the two symptom dimensions. Further, in contrast to the nominal subtypes, counts of inattention and hyperactivity-impulsivity symptoms have sufficient stability over time to serve as useful diagnostic modifiers (5-year test-retest $r = .64$ for the symptom dimensions vs. $.30 - .48$ for the subtypes).

This dimensional model also has important potential drawbacks. Any changes to the current diagnostic criteria will complicate interpretation of previous research studies that were based on DSM-IV criteria, and the elimination of nominal subtypes could potentially lead clinicians and researchers to be less attentive to the heterogeneity that clearly exists among individuals with ADHD. Furthermore, a dimensional model may be more complex to communicate effectively between clinicians, patients with ADHD, and their families.

To address these important concerns, one potential option would be to designate specific ranges on the two modifiers as mild / low (e.g., 0 - 2 current symptoms), moderate / subthreshold (e.g., 3 - 5 current symptoms), and high / severe (e.g., 6 or more current symptoms). As suggested for the DSM-IV model, a statement in the text could emphasize that these modifiers describe the individual's current state, and are likely to change over time. In addition to simplifying communication among professionals and individuals with ADHD, this hybrid model would provide a structured framework to encourage and facilitate additional research on the validity of configural subgroups. For example, the high/severe ranges on the dimensional specifiers identify groups consistent with the current DSM-IV subtypes, and the combination of the specifiers for mild / low hyperactivity-impulsivity and high / severe inattention is consistent with the criteria used to define the refined inattentive groups in the studies reviewed earlier.

Limitations

Due to the extensive published literature of 546 studies relevant to the validity of the DSM-IV ADHD symptom dimensions and subtypes, unpublished studies were not included in the review. Statistical tests for publication and other selection biases suggest that the exclusion of unpublished studies and the unintentional omission of any published studies that were not identified by the search procedures had minimal impact on the overall pattern of results. Nonetheless, the results of the review should be interpreted in the context of this potential limitation.

Despite the immense literature synthesized in this report, perhaps the most important limitation of the current review is the limited number of available studies in several important domains. Meta-analyses were underpowered for several key comparisons involving ADHD-H and nearly all analyses of ADHD subtypes in adults, indicating that these are preliminary results that should be interpreted with caution. Similarly, the existing literature on DSM-IV ADHD includes relatively few studies of preschool children, suggesting that the present results are most clearly generalizable to school-age children and adolescents.

In contrast to comparisons involving ADHD-H, power was high for nearly all comparisons of DSM-IV ADHD-C and ADHD-I. However, few studies have compared ADHD-C and ADHD-I using electrophysiological or neuroimaging approaches that may be especially sensitive to subtype differences. Further, very few studies of any subtype reported results separately as a function of sex, age, ethnicity, rater, or comorbid mental disorders, limiting the power to detect effects of these potential moderator variables. Additional research is needed in each of these domains.

Overall Summary and Conclusions

The distinction between inattention and hyperactivity-impulsivity symptoms is strongly supported across nearly all level of analysis, and subtype differences on some measures of functional impairment and concurrent mental disorders provide support for the discriminant validity of the nominal DSM-IV subtypes. In contrast, the validity of the DSM-IV model is compromised by weak evidence for the validity of ADHD-H after first grade, minimal evidence for discriminant validity of ADHD-I and ADHD-C in studies of etiology, academic and cognitive functioning, and treatment response, and the marked longitudinal instability of all three subtypes.

Overall, it is concluded that the DSM-IV ADHD subtypes may provide a convenient clinical shorthand to describe the functional and behavioral correlates of current levels of inattention and hyperactivity-impulsivity symptoms, but do not identify discrete subgroups with sufficient long-term stability to justify the classification of distinct forms of the disorder. Instead, empirical support is strongest for a model that describes heterogeneity among individuals with ADHD by incorporating dimensional modifiers that reflect the number of inattention and hyperactivity-impulsivity symptoms at the time of assessment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Meta-analysis of longitudinal studies of the DSM-IV ADHD subtypes

ADHD subtype at initial assessment				Difference in the rate of ADHD at the follow-up assessment in groups with and without ADHD subtypes at the initial assessment ^d															
No ADHD (N = 899)		ADHD-C (N = 319)		ADHD-I (N = 218)		ADHD-H (N = 64)		ADHD-C vs. Control		ADHD-I vs. Control		ADHD-H vs. Control		ADHD-C vs. ADHD-I		ADHD-C vs. ADHD-H		ADHD-I vs. ADHD-H	
k ^b	% [95% CI]	k ^b	% [95% CI]	k ^b	% [95% CI]	k ^b	% [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]
ADHD subtype at the follow-up assessment																			
Any ADHD	5	6.1%	5	69.8%	5	50.2%	4	33.2%	24.1 ^{*c}	12.3 [*]	2.5 [*]	2.2 [*]	6.1 [*]	1.7					
		[2.0, 16.9]		[54.6, 81.7]		[27.6, 72.6]		[11.1, 66.2]	[14.5, 40.1]	[4.0, 37.9]	[1.2, 5.5]	[1.1, 4.6]	[3.1, 12.0]	[0.8, 3.7]					
ADHD-C	5	1.6%	5	37.0%	5	8.0%	4	14.4%	31.5 [*]	5.1 [*]	3.7 [*]	6.6 [*]	4.1 [*]	0.7					
		[0.2, 4.5]		[28.2, 46.3]		[4.8, 13.1]		[7.5, 25.8]	[8.5, 117.1]	[1.9, 13.9]	[1.2, 11.0]	[3.7, 11.9]	[1.9, 8.9]	[0.3, 2.0]					
ADHD-I	5	4.4%	5	29.8%	5	39.9%	4	5.2%	7.8 [*]	11.9 [*]	1.3	0.6	5.5 [*]	6.2 [*]					
		[1.5, 12.1]		[22.3, 38.6]		[22.3, 60.6]		[0.5, 14.3]	[4.2, 14.7]	[4.1, 34.6]	[0.5, 3.6]	[0.3, 1.4]	[2.1, 14.0]	[1.6, 23.6]					
ADHD-H	5	0.6%	5	2.7%	5	1.6%	4	14.5%	3.1	1.6	15.6 [*]	2.2	0.1 [*]	0.1 [*]					
		[0.2, 1.4]		[1.3, 5.6]		[0.1, 5.0]		[2.6, 52.4]	[0.6, 16.8]	[0.3, 9.5]	[3.2, 76.0]	[0.4, 10.9]	[0.0, 0.2]	[0.0, 0.3]					

^a Note. Supplement Table 6 provides the complete list of effect sizes and a summary of tests for publication bias and heterogeneity among the effects. Overall percentages and odds ratios are weighted estimates from a random-effects model (DerSimonian & Laird, 1986). Odds ratios greater than 1 indicate that the group listed first was more likely to meet criteria for the listed subtype at the follow-up assessment, and odds ratios less than 1 indicate that the group listed second was more likely to meet criteria for the listed subtype.

^b k = number of effect sizes included in the summary statistic.

^c after correction for publication bias OR = 18.0 (P < .001).

* = P < .05.

Table 2

Meta-analysis of correlations between DSM-IV ADHD symptom dimensions and measures of functional impairment

			DSM-IV Symptom Dimension		Difference between dimensions ^d
	Samples ^a		Inattention	Hyp - Imp	
Construct	k ^b	Total N	r [95% CI] ^c	r [95% CI] ^c	
Overall and adaptive functioning					
Global functioning	7	11,142	.47 [.40, .53] ^{*e}	.46 [.36, .55] ^{*e}	ns
Adaptive functioning	5	2,227	.49 [.43, .55] [*]	.37 [.33, .41] [*]	Inatt > Hyp-imp
Social functioning					
Overall social problems	18	10,790	.39 [.34, .44] ^{*e}	.38 [.33, .43] ^{*e}	ns
Disliked by peers	3	6,747	.30 [.27, .33] [*]	.37 [.34, .39] [*]	Hyp-Imp > Inatt
Passive / isolated	5	7,672	.37 [.33, .41] [*]	.18 [.15, .20] [*]	Inatt > Hyp-imp
Social skills / prosocial	10	8,767	.43 [.39, .47] [*]	.28 [.20, .35] ^{*e}	Inatt > Hyp-Imp
Academic functioning					
Academic rating scales	20	21,986	.54 [.49, .59] ^{*e}	.28 [.25, .31] ^{*e}	Inatt > Hyp-Imp
Achievement tests	11	10,670	.33 [.26, .39] ^{*e}	.16 [.12, .19] [*]	Inatt > Hyp-Imp

^a Note. Supplement Table 7 provides the complete list of effect sizes and a summary of tests for publication bias and heterogeneity among the effects.

^b k = number of effect sizes included in the summary statistic.

^c Overall weighted correlation based on a random-effects model (DerSimonian & Laird, 1986). Correlations from each individual study were reverse-scored if necessary so that positive correlations indicate that elevations on the symptom dimension are associated with greater impairment.

^d Weighted correlations are significantly different ($p < .05$).

^e significant heterogeneity among the effects (see Supplement Table 7)

^{*} = $p < .05$

Table 3
Meta-analysis of studies that compared the DSM-IV ADHD subtypes on measures of functional impairment

Construct / Variable	Estimated effect size of the mean difference between groups ^d									
	ADHD-C vs. Control	ADHD-I vs. Control	ADHD-H vs. Control	ADHD-C vs. ADHD-I	ADHD-C vs. ADHD-H	ADHD-I vs. ADHD-H	ADHD-C vs. ADHD-H	ADHD-I vs. ADHD-H	ADHD-C vs. ADHD-H	ADHD-I vs. ADHD-H
	k ^b	g ^c [95% CI]	k ^b	g ^c [95% CI]	k ^b	g ^c [95% CI]	k ^b	g ^c [95% CI]	k ^b	g ^c [95% CI]
Global impairment										
CGAS	12	1.92 ^{*d} [1.54, 2.30]	12	1.45 ^{*d} [1.10, 1.81]	9	1.21 ^{*d} [0.87, 1.58]	13	0.43 [*] [0.31, 0.56]	9	0.38 ^{*d} [0.02, 0.74]
Academic Impairment										
Parent / teacher ratings	10	1.06 ^{*d} [0.87, 1.26]	10	1.08 ^{*d} [0.87, 1.29]	7	0.19 [*] [0.07, 0.31]	18	0.00 [-0.10, 0.10]	14	0.88 [*] [0.71, 1.07]
Achievement Tests	23	0.91 [*] [0.78, 1.04]	23	0.91 ^{*d} [0.74, 1.07]	11	0.48 [*] [0.28, 0.68]	29	0.02 [-0.06, 0.09]	14	0.43 [*] [0.23, 0.62]
Social impairment										
Overall social problems	13	1.68 ^{*d} [1.44, 1.92]	13	1.06 ^{*d} [0.85, 1.27]	9	0.80 [*] [0.55, 1.04]	25	0.53 ^{*d,e} [0.41, 0.67]	15	0.68 [*] [0.55, 0.81]
Disliked by peers	9	1.15 [*] [0.97, 1.35]	9	0.67 [*] [0.45, 0.89]	5	0.73 [*] [0.42, 1.05]	10	0.53 [*] [0.42, 0.64]	6	0.50 [*] [0.27, 0.73]
Ignored by peers	7	0.79 ^{*d} [0.49, 1.09]	7	0.71 [*] [0.61, 0.81]	4	0.42 [*] [0.22, 0.62]	7	0.12 [-0.11, 0.34]	4	0.48 [*] [0.21, 0.75]
Shy / passive	7	0.32 [*] [0.03, 0.62]	7	0.71 [*] [0.49, 0.93]	1	0.09 [-0.32, 0.49]	7	-0.48 [*] [-0.74, -0.23]	1	0.39 [-0.04, 0.81]
Prosocial behavior / friendships	15	1.38 ^{*d} [1.15, 1.61]	15	1.01 ^{*d} [0.81, 1.21]	5	0.79 [*] [0.41, 1.16]	17	0.34 [*] [0.25, 0.43]	7	0.45 [*] [0.24, 0.66]

Note. CGAS = Child Global Assessment Scale.

^d Overall effect sizes are weighted estimates from a random-effects model (DerSimonian & Laird, 1986). Positive effect sizes indicate that the group listed first is more impaired than the group listed second, and negative effect sizes indicate that the group listed second is more impaired. Supplement Table 8 provides the complete list of effect sizes and a summary of tests for publication bias and heterogeneity among the effects.

^b k = number of effect sizes included in the summary statistic.

^c g = Hedges' g.

^d significant heterogeneity among the effects (see Supplement Table 8).

ϵ^2 significant publication bias. After correction the effect size was smaller but remained significant ($\epsilon^2 = .38$)

* = $p < .05$.

Table 4

Meta-analysis of correlations between DSM-IV ADHD symptom dimensions and symptoms of other psychopathology

Construct	Samples ^a		DSM-IV Symptom Dimension		Difference between dimensions ^d
			Inattention	Hyp - Imp	
	k ^b	Total N	r [95% CI]	r [95% CI]	
Anxiety disorders					
Generalized Anxiety Disorder	13	21,204	.45 [.38, .52] ^{*e}	.44 [.38, .49] ^{*e}	ns
Separation Anxiety Disorder	14	12,490	.20 [.13, .27] ^{*e}	.24 [.16, .32] ^{*e}	ns
Social phobia	4	5,474	.28 [.16, .40] ^{*e}	.20 [.04, .34] ^{*e}	ns
Mood Disorders					
Withdrawn	17	6,793	.28 [.24, .32] [*]	.09 [.03, .15] ^{*e}	Inatt > Hyp-imp
Depression	17	19,601	.40 [.35, .44] ^{*e}	.29 [.23, .34] ^{*e}	Inatt > Hyp-imp
Other Internalizing					
Anxious / Depressed	14	9,063	.27 [.23, .32] ^{*e}	.26 [.22, .29] [*]	ns
Somatic Complaints	14	2,829	.19 [.15, .22] [*]	.13 [.10, .17] [*]	ns
Total Internalizing	13	4,154	.32 [.28, .36] [*]	.23 [.17, .29] [*]	Inatt > Hyp-imp
Disruptive disorders					
Oppositional Defiant Disorder	29	41,363	.54 [.50, .58] ^{*e}	.65 [.61, .69] ^{*e}	Hyp-Imp > Inatt
Conduct Problems	25	31,326	.38 [.33, .43] ^{*e}	.47 [.42, .53] ^{*e}	Hyp-Imp > Inatt
Aggressive Behavior	19	7,189	.37 [.33, .41] ^{*e,f}	.57 [.54, .60] ^{*e}	Hyp-Imp > Inatt
Delinquent Behavior	15	5,175	.28 [.23, .33] ^{*e,f}	.33 [.28, .38] ^{*e}	ns
Total Externalizing	13	5,774	.43 [.36, .50] ^{*e}	.59 [.54, .63] ^{*e}	Hyp-Imp > Inatt
Other symptoms					
Pervasive Developmental Dis.	6	2,449	.35 [.26, .43] ^{*e}	.27 [.13, .40] ^{*e}	ns

^aNote. Supplement Table 9 includes the complete list of effect sizes and a summary of tests for publication bias and heterogeneity among the effects.

^bk = number of effect sizes included in the summary statistic.

^cOverall weighted correlation based on a random-effects model (DerSimonian & Laird, 1986).

^dOverall correlations are significantly different ($P < .05$).

^esignificant heterogeneity among the effects (see Supplement Table 9).

^fafter correction for publication bias correlations were slightly higher between inattention and delinquent behavior ($r = .34$), and aggressive behavior ($r = .42$).

^{*} = $P < .05$.

Table 5

Meta-analysis of studies that compared the DSM-IV ADHD subtypes on dimensional measures of comorbid psychopathology

Disorder	Estimated effect size of the mean difference between groups ^d									
	ADHD-C vs. Control	ADHD-I vs. Control	ADHD-H vs. Control	ADHD-C vs. ADHD-I	ADHD-C vs. ADHD-H	ADHD-I vs. ADHD-H	ADHD-C vs. ADHD-H	ADHD-I vs. ADHD-H	ADHD-C vs. ADHD-H	ADHD-I vs. ADHD-H
	k ^b	g ^c [95% CI]	k ^b	g ^c [95% CI]	k ^b	g ^c [95% CI]	k ^b	g ^c [95% CI]	k ^b	g ^c [95% CI]
Internalizing Disorders										
Anxiety / GAD	9	1.38 [*] [0.74, 2.02]	9	0.97 [*] [0.57, 1.37]	4	1.20 [*] [0.46, 1.94]	17	0.35 [*] [0.18, 0.52]	6	0.56 [*] [0.34, 0.78]
Depression	8	1.50 ^{*d} [0.08, 1.92]	8	1.14 ^{*d} [0.75, 1.53]	4	0.64 [*] [0.30, 0.98]	15	0.33 [*] [0.17, 0.50]	6	0.53 [*] [0.31, 0.74]
Anxious/Depressed	9	1.24 ^{*d} [0.86, 1.63]	9	0.92 ^{*d} [0.62, 1.23]	4	0.57 [*] [0.29, 0.84]	15	0.16 ^{d,e} [-0.03, 0.34]	5	0.36 [*] [0.17, 0.56]
Withdrawn	10	0.83 ^{*d} [0.55, 1.11]	10	0.96 ^{*d} [0.73, 1.18]	4	0.33 [*] [0.01, 0.66]	16	-0.14 [*] [-0.28, 0.00]	5	0.42 [*] [0.17, 0.68]
Externalizing Disorders										
ODD Symptoms	18	2.26 ^{*d} [1.91, 2.60]	18	1.01 ^{*d} [0.79, 1.23]	8	1.99 ^{*d} [1.51, 2.48]	26	1.00 [*] [0.90, 1.10]	14	0.32 [*] [0.15, 0.49]
CD Symptoms	11	1.98 ^{*d} [1.47, 2.49]	11	0.90 ^{*d} [0.59, 1.20]	6	1.89 ^{*d} [1.24, 2.54]	18	0.66 [*] [0.53, 0.79]	9	0.22 [*] [0.04, 0.40]
Aggressive Behavior	12	1.89 ^{*d} [1.45, 2.34]	12	0.72 [*] [0.57, 0.88]	4	1.64 ^{*d} [1.14, 2.13]	19	1.04 ^{*d} [0.84, 1.24]	6	0.32 [*] [-0.09, 0.72]
Delinquent Behavior	8	1.92 ^{*d} [1.46, 2.38]	8	0.80 [*] [0.68, 0.92]	4	1.12 [*] [0.81, 1.42]	14	0.77 ^{*d} [0.57, 0.97]	5	0.44 [*] [0.23, 0.64]
Other Disorders										
Perv. Dev. Disorders	3	1.64 [*] [1.37, 1.90]	3	1.20 ^{*d} [0.33, 2.08]	1	0.63 [*] [0.10, 1.16]	5	0.69 [*] [0.45, 0.93]	1	0.73 [*] [0.11, 1.34]
									1	0.22 [-0.35, 0.79]

Note. GAD = generalized anxiety disorder, ODD = oppositional defiant disorder, CD = conduct disorder.

^a Overall effect sizes are weighted estimates from a random-effects model (DerSimonian & Laird, 1986). Positive effect sizes indicate that the group listed first has more symptoms of the comorbid disorder than the group listed second, and negative effect sizes indicate that the group listed second has more symptoms. Supplement Table 10 provides the complete list of effect sizes and a summary of tests for publication bias and heterogeneity among the effects.

^b k = number of effect sizes included in the summary statistic.

^c g = Hedges' g .

^d significant heterogeneity among the effects (see Supplement Table 10).

^e after correcting for heterogeneity, ADHD-C was significantly different from ADHD-I ($g = 0.25$).

* = $P < .05$.

Table 6
Meta-analysis of studies that reported the frequency of comorbid disorders in groups with the DSM-IV ADHD subtypes

Estimated percentage of cases with the comorbid disorder										Comparisons between groups ^d							
No ADHD Diagnosis		ADHD-C		ADHD-I		ADHD-H		ADHD-C vs. Control		ADHD-I vs. Control		ADHD-H vs. Control		ADHD-C vs. ADHD-I		ADHD-I vs. ADHD-H	
k ^b	% [95% CI]	k ^b	% [95% CI]	k ^b	% [95% CI]	k ^b	% [95% CI]	OR [95% CI]	% [95% CI]	OR [95% CI]	% [95% CI]	OR [95% CI]	% [95% CI]	OR [95% CI]	% [95% CI]	OR [95% CI]	% [95% CI]
ODD	27	4.6% [3.2, 6.4]	47	51.8% [47.5, 56.1]	47.2	4.9% [21.4, 28.8]	22	42.9% [37.6, 48.3]	26.9 ^{*c} [18.2, 39.7]	7.1 [*] [6.1, 8.2]	12.8 ^{*c} [8.2, 19.9]	3.4 ^{*c} [3.1, 4.3]	1.6 [*] [1.3, 1.9]	0.5 ^{*c} [0.4, 0.6]			
CD	18	1.3% [0.7, 2.2]	36	21.6% [18.0, 25.5]	36	7.1% [5.0, 10.0]	19	14.9% [10.6, 20.4]	23.2 ^{*c} [12.1, 44.6]	7.6 [*] [5.3, 10.0]	10.9 ^{*c} [5.6, 21.5]	3.5 [*] [2.6, 4.6]	1.8 [*] [1.3, 2.4]	0.6 [*] [0.4, 0.9]			
GAD	7	2.9% [1.3, 6.3]	15	11.3% [7.7, 16.4]	15	10.4% [7.6, 14.1]	9	14.6% [8.7, 23.4]	6.5 ^{*c} [2.8, 14.6]	3.5 [*] [1.9, 6.5]	4.2 [*] [1.7, 10.3]	1.3 [0.9, 1.8]	1.2 [0.7, 1.8]	0.8 [0.5, 1.2]			
SAD	4	2.0% [1.2, 3.2]	13	13.5% [9.3, 19.3]	13	8.7% [5.2, 14.2]	9	10.6% [6.6, 16.6]	8.7 [*] [3.7, 20.2]	3.4 [*] [1.6, 7.4]	5.5 [*] [2.4, 12.5]	1.4 [*] [1.0, 2.0]	1.5 [0.9, 2.3]	0.8 [0.4, 1.5]			
MDD	13	1.5% [0.8, 2.9]	21	9.8% [6.9, 13.7]	21	9.5% [6.4, 13.9]	10	7.6% [4.5, 12.6]	7.4 [*] [3.5, 15.6]	7.2 [*] [3.8, 13.6]	3.9 [*] [2.0, 7.6]	1.1 [0.8, 1.5]	2.0 [*] [1.2, 3.3]	2.0 [*] [1.0, 3.9]			
Bipolar	2	0.0%	4	6.9% [1.8, 23.7]	4	3.2% [0.1, 13.5]	3	6.4% [1.5, 24.0]	97.7 [*] [6.0, 1601]	27.3 [*] [1.6, 478.5]	49.8 [*] [2.6, 955.2]	4.0 [*] [1.4, 11.8]	2.2 [0.9, 6.0]	0.6 [0.2, 2.1]			
LD	11	8.4% [5.9, 12.0]	23	24.2% [19.5, 29.6]	23	29.1% [23.2, 35.7]	11	17.9% [11.6, 25.9]	5.4 [*] [3.6, 8.5]	5.7 [*] [3.4, 9.4]	1.9 [*] [1.1, 3.5]	0.8 [*] [0.7, 1.0]	1.8 [*] [1.0, 3.2]	2.1 [*] [1.2, 3.6]			
Speech / Language	4	10.7%	10	14.8%	10	17.8%	6	13.9%	3.6 [*]	2.4 [*]	1.6	0.9	1.4	1.3			
Tic Dis.	1	4.7% [1.7, 9.9]	6	15.8% [9.2, 25.9]	6	12.1% [8.7, 16.5]	3	22.6% [14.0, 34.4]	7.1 [*] [3.0, 16.8]	3.4 [*] [1.4, 8.2]	8.9 [*] [2.9, 23.4]	1.7 [*] [1.2, 2.5]	0.9 [0.5, 1.6]	0.5 [*] [0.3, 0.9]			

Note: ODD = oppositional defiant disorder. CD = conduct disorder. GAD = generalized anxiety disorder. SAD = separation anxiety disorder. MDD = major depressive disorder. LD = learning Disability.

^a Overall effect sizes are weighted estimates from a random-effects model (DerSimonian & Laird, 1986). Odds ratios greater than 1 indicate that the group listed first had a higher rate of comorbidity than the group listed second, and odds ratios less than 1 indicate that the group listed second had a higher rate of comorbidity. Supplement Table 11 provides the complete list of effect sizes and a summary of tests for publication bias and heterogeneity among the effects.

^b k = number of effect sizes included in the summary statistic.

^c significant heterogeneity among the effects (see Supplement Table 11).

* = $p < .05$.

Table 7

Meta-analysis of correlations between DSM-IV ADHD symptom dimensions and cognitive measures

Construct	Samples ^a		DSM-IV Symptom Dimension		Difference between dimensions ^d
	k ^b	Total N	Inattention <i>r</i> [95% CI] ^c	Hyp - Imp <i>r</i> [95% CI] ^c	
Intelligence	8	4,203	.31 [.28, .34] [*]	.19 [.11, .26] ^{*e}	Inatt > Hyp-Imp
Response Inhibition	8	1,907	.24 [.17, .31] [*]	.20 [.14, .27] [*]	ns
Working Memory	8	3,254	.30 [.26, .34] [*]	.17 [.11, .23] [*]	Inatt > Hyp-Imp
Short-term Memory	6	4,230	.23 [.18, .29] [*]	.14 [.10, .18] [*]	Inatt > Hyp-Imp
Vigilance	4	1,720	.23 [.19, .27] [*]	.12 [.08, .16] [*]	Inatt > Hyp-Imp
Response Variability	3	1,053	.34 [.28, .39] [*]	.22 [.16, .28] [*]	Inatt > Hyp-Imp
Processing Speed	6	3,086	.32 [.26, .38] [*]	.14 [.09, .19] ^{*f}	Inatt > Hyp-Imp
Delay Aversion / Discounting	3	577	.13 [.06, .20] [*]	.15 [.07, .23]	ns

^aSupplement Table 12 provides the complete list of effect sizes and a summary of tests for publication bias and heterogeneity among the effects.^bk = number of effect sizes included in the summary statistic.^cOverall weighted correlation based on a random-effects model (DerSimonian & Laird, 1986). Correlations from each individual study were reverse-scored if necessary so that positive correlations always indicate that elevations on the symptom dimension are associated with greater impairment.^dOverall correlations are significantly different ($P < .05$).^esignificant heterogeneity among the effects (see Supplement Table 12).^fafter correction for publication bias $r = .17$.^{*} = $P < .05$.

Table 8

Meta-analysis of studies that compared the DSM-IV ADHD subtypes on measures of neuropsychological functioning

Construct / Variable	Estimated effect size of the mean difference between groups ^a											
	ADHD-C vs. Control			ADHD-I vs. Control			ADHD-H vs. Control			ADHD-C vs. ADHD-I		
	k ^b	g ^c [95% CI]	k ^b	g ^c [95% CI]	k ^b	g ^c [95% CI]	k ^b	g ^c [95% CI]	k ^b	g ^c [95% CI]	k ^b	g ^c [95% CI]
Intelligence	40	0.67 ^{*d} [0.54, 0.80]	40	0.65 ^{*d} [0.50, 0.80]	12	0.56 ^{*d} [0.29, 0.83]	53	0.00 [-0.07, 0.07]	18	0.27 ^{*d} [0.05, 0.49]	18	0.27 [*] [0.09, 0.46]
Response Inhibition	25	0.65 [*] [0.53, 0.77]	25	0.53 ^{*d} [0.39, 0.67]	5	0.36 [*] [0.07, 0.65]	29	0.17 [*] [0.08, 0.27]	7	0.36 [*] [0.13, 0.60]	6	0.21 [-0.03, 0.45]
Processing Speed	14	0.61 ^{*d} [0.43, 0.79]	14	0.67 ^{*d} [0.48, 0.87]	5	0.31 [*] [0.06, 0.56]	18	-0.04 [-0.17, 0.08]	5	0.45 [*] [0.03, 0.87]	5	0.57 [*] [0.26, 0.89]
Reaction Time	15	0.28 ^{*d} [0.09, 0.47]	15	0.22 ^{*d} [0.03, 0.41]	4	0.02 [-0.20, 0.24]	18	0.10 [-0.04, 0.24]	4	0.23 [-0.15, 0.61]	4	0.25 [-0.17, 0.67]
Response Variability	15	0.81 [*] [0.62, 1.00]	15	0.55 [*] [0.40, 0.71]	4	0.48 [*] [0.26, 0.70]	17	0.18 [*] [0.05, 0.31]	4	0.33 [*] [0.02, 0.65]	4	0.32 [*] [0.00, 0.65]
Vigilance	15	0.64 [*] [0.50, 0.78]	15	0.51 ^{*d} [0.33, 0.69]	3	0.17 [-0.28, 0.63]	17	0.09 ^e [-0.02, 0.20]	4	0.37 [*] [0.13, 0.62]	4	0.44 [*] [0.21, 0.67]
Motor	8	0.51 [*] [0.20, 0.82]	8	0.55 ^{*e} [0.38, 0.73]	4	0.34 [*] [0.07, 0.60]	8	-0.10 [-0.26, 0.07]	4	0.06 [-0.34, 0.46]	4	0.21 [-0.04, 0.42]
Set shifting	14	0.46 [*] [0.31, 0.61]	14	0.37 [*] [0.26, 0.48]	2	-0.03 [-0.36, 0.31]	18	0.11 [-0.04, 0.25]	2	0.38 [*] [0.01, 0.75]	2	0.17 [-0.46, 0.80]
Short-term memory	13	0.42 [*] [0.28, 0.57]	13	0.41 [*] [0.30, 0.52]	4	0.25 [*] [0.04, 0.47]	17	0.03 [-0.08, 0.15]	5	0.35 [*] [0.06, 0.65]	5	0.35 [*] [0.10, 0.59]
Working Memory	11	0.71 [*] [0.58, 0.84]	11	0.68 [*] [0.51, 0.86]	4	0.61 [*] [0.43, 0.80]	15	0.06 ^f [-0.05, 0.16]	5	0.18 [*] [0.01, 0.35]	5	0.21 [*] [0.04, 0.38]
Interference Control	6	0.34 [*] [0.08, 0.59]	6	0.25 [*] [0.03, 0.48]	1	0.20 [-0.13, 0.53]	8	0.06 [-0.18, 0.29]	1	-0.11 [-0.46, 0.24]	1	-0.12 [-0.46, 0.21]
Planning	13	0.61 [*] [0.43, 0.79]	13	0.51 [*] [0.33, 0.69]	1	0.12 [-0.13, 0.37]	15	0.12 [-0.18, 0.42]	1	0.13 [-0.17, 0.43]	1	0.35 [-0.04, 0.74]