International Journal of Methods in Psychiatric Research *Int. J. Methods Psychiatr. Res.* 16(S1): S16–S23 (2007) Published online in Wiley InterScience (www.interscience.wiley.com) **DOI**: 10.1002/mpr.217



A dimensional approach to developmental psychopathology

JAMES J. HUDZIAK, 1,2 THOMAS M. ACHENBACH, 1 ROBERT R. ALTHOFF, 1 DANIEL S. PINE³

- 1 University of Vermont, Burlington, VT, USA
- 2 Vrije University, Amsterdam, The Netherlands
- 3 National Institute of Mental Health, Bethesda, MD, USA

Abstract

The expression psychopathology in general and child psychopathology in particular, is affected by multiple sources of variance. Some of these sources include gender differences, informant differences, and age-related differences. In this paper, we discuss how these sources of variance complicate both research and clinical management. We argue that the current diagnostic system would be aided by the inclusion of a quantitative axis that can take these sources of variance into account. We reason that the fields of genomics and neuroscience are prepared to move the field of developmental psychopathology forward, but need a diagnostic system that allows for these sources of variance to be controlled. We demonstrate how in Conduct Disorder, inclusion of dimensional information would allow the clinician or researcher to demonstrate not only the presence or absence of pathology, but also the degree to which the disorder is manifested in a particular individual. Because dimensional approaches are already used widely as an alternative measure of psychopathology, we argue that there is reason to consider dimensionalizing some aspects of the DSM. Copyright © 2007 John Wiley & Sons, Ltd.

Key words: Dimensional approaches, Conduct disorder, DSM

Multiple sources of variance affect the expression of psychopathology. In this paper, we discuss how these sources of variance complicate both research and clinical management. We argue that these sources of variance must be considered in order to make valid, sensitive, and specific diagnoses appropriate for persons of all ages and both genders. We further argue that a quantitative axis in future Diagnostic and Statistical Manuals (DSMs) will allow adding dimensional features to the DSM that can help clinicians and scientists alike evaluate not only the presence or absence of pathology, but also the degree to which disorders are manifested. Equally important, dimensionalization can facilitate estimation of effect sizes in evidence-based practice and research. We point out that child psychiatrists and developmental psychologists have long used a wide variety of standardized dimensional measures in both research and clinical settings and that a significant amount of research has already been carried out relating these measures to DSM diagnoses. This work provides a foundation for dimensionalizing some aspects of the DSM.

The DSM as a categorical taxonomy

Particularly since the major changes introduced by Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM-III), the DSM has been a categorical taxonomy that has worked reasonably well for adult psychopathology. Its utility for adults may result from the fact that most research on psychopathology prior to DSM-III was done on adults. In fact, the Feighner Criteria, often cited as a key source of the radical changes embodied in DSM-III, essentially listed 14 categories for adult disorders. These disorders were selected because they had been sufficiently researched to engender the Robins–Guze criteria for valid psychi-

atric diagnosis, including clinical description, laboratory studies, delimitation from other disorders, follow-up studies, and family studies (Robins and Guze, 1970). The 14 Feighner diagnoses did not include a single child disorder (Feighner et al., 1972). Since the publication of DSM-III, research on child psychopathology has accelerated dramatically, which has highlighted strengths and weaknesses of the DSM for the developmental study of psychopathology.

Child psychopathology differs from adult psychopathology in many ways. One particularly salient difference is that the expression of psychopathology in children often changes in both magnitude and character as development progresses. Moreover, the developmental study of psychopathology must take account of age-related changes in what is considered normal and adaptive, such that behaviors considered pathological at one age may be considered normal at another age and vice versa. Another salient difference is that assessment of psychopathology in children and adolescents requires multiple sources of information, such as parents, teachers, and children themselves. The modest agreement typically found among sources makes it hard to categorize children as sick versus well. Questions arise, for example, as to whether decisions should be based on averages across reports by multiple informants or on the most severe problems reported by any informant.

Because of these multiple sources of variance in childhood diagnosis, quantitative differences may be more crucial for child than adult diagnoses. The DSM's categorical approach has proven difficult to apply to children because it fails to identify these crucial differences. To take account of developmental differences in the expression of psychopathology, a nosological system needs to take account of: (1) variations in both typical and atypical behaviors across age; (2) gender differences in the expression of psychopathology; (3) differences among sources of information; (4) tendencies for children to manifest multiple kinds of problems. Research stimulated by DSM-III, DSM-III-R, and DSM-IV has contributed to developmental understanding of psychopathology and to its dimensional assessment in recent decades. It is thus a propitious time to consider adding dimensional features to the DSM.

Why add dimensional features to the DSM?

We propose adding dimensional features to complement the categorical aspects of the DSM. The dimensional and categorical approaches each have advantages and disadvantages. The advantages of the categorical approach are detailed elsewhere in this issue (Kraemer et al., article in this issue). Disadvantages of a dimensional-only approach have also been described. These include its inconsistency with the prevailing diagnostic approach that is used by clinicians to make yes-or-no decisions about treatment. However, cutpoints can certainly be applied to dimensional measures as a basis for yes-or-no decisions. It has also been argued that collecting dimensional information might be more expensive than categorical information, although this is not necessarily so, because many dimensional measures can be self-administered by informants. We argue that a purely categorical approach fails to account for important sources of variance. For example, neural systems that underlie behavior differ by gender and age. Consequently, a diagnostic system must take account of gender and age variance, as well as informant variance.

Using dimensional approaches to account for multiple sources of variance

Over the past three decades, thousands of studies of child and adolescent psychopathology have used dimensional approaches in epidemiologic and clinical samples. Some dimensional measures, such as the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001) comprise descriptions of children's problems that were not based directly on DSM criteria, although they have been found to agree well with some DSM diagnostic categories. Other measures, such as the Conners Rating Scales (CRS; Conners, 2001) and the Behavior Assessment System for Children (BASC; Reynolds and Kamphaus, 1998) include paraphrases of DSM criteria. In addition to instruments for broad clinical and epidemiologic applications, other instruments focus on narrower ranges of psychopathology, such as the strengths, weaknesses, and Attention-Deficit/ Hyperactivity Disorder (ADHD) and Normal Behavior Questionnaire (Hay et al., 2007), the Autism Diagnostic Interview (Lord et al., 1994), the Social Responsiveness Scale (Constantino et al., 2000), the Yale-Brown Obsessive-Compulsive Scale (Goodman et al., 1989), and the Young Mania Rating Scale (Young et al., 1978). These instruments (some interviews, some questionnaires) quantify the degree to which individuals manifest particular kinds of problems.

Dimensional measures of child psychopathology have become so common that teachers, pediatricians, and other non-psychiatric personnel are quite accustomed to using them. These instruments address weaknesses inherent in a one-size-fits-all system such as the DSM. They provide quantitative indices of variance in symptoms and normative behavior by age and gender. Although it is beyond the scope of this paper to compare each of the dimensional measures, suffice it to say that each has strengths and weaknesses and proponents and critics. Despite their widespread use, dimensional measures are currently orphaned from the DSM nosology. We argue that they should be more central to the assessment and care of children in order to advance evidence-based psychiatry.

Neuroscientific and genomic explanations of psychopathology may require quantification

In this era of neuroscience and genomics, taxonomic approaches are needed that can encompass diverse neural circuits and genes relevant to psychopathology. Developmental neurobiology research shows that the connections, anatomy, and physiology of the human brain change dramatically across development (Thompson et al., 2000), with important variations by gender (Castellanos et al., 2002) and by genetic makeup (Meyer-Lindenberg et al., 2006). Applying the current categorical taxonomy, in the absence of other approaches, has weaknesses. For example, if genetic or neural aspects of psychopathology show continuous associations with psychopathologic behaviors, the categorical approach will have less statistical power than the current taxonomic approach (Bobb et al., 2005). Moreover, genetic findings and brain imaging document overlaps among DSM categories whereby some genes and neural factors may confer susceptibility to disorders that belong to different DSM categories, such as anxiety and depression, as opposed to narrow DSM-defined conditions. For example, in the case of neural development, a great deal is known about the amygdala's size and function, both of which vary with the age, gender, and genetic makeup of individuals (Durston et al., 2001; Walhovd et al., 2005). Consequently, disorders that may be related to the amygdala, such as conduct disorder (CD), major depressive disorder (MDD), and anxiety disorders (Sterzer et al., 2005) need to be understood in relation to age, gender, and genetic differences. A taxonomy that employs the same diagnostic rules and cutpoints for a 17-year-old male and a 5-yearold female may not be sensitive to underlying neural correlates of psychopathology. Brain regions, such as the prefrontal cortex, implicated in developmental psychopathology exhibit robust age-related changes in structure, function, and in the nature of associations with measures of information processing, specifically the measures of information processing that exhibit parallel changes with age. This raises questions about the degree to which changes in prefrontal cortical structure and function relate to changes in psychiatric symptoms over similar time periods. Symptom scales sensitive to developmental changes in behavior might be more sensitive to changes in the relationship between neural processes and symptoms. These considerations apply to adult and geriatric age groups as well. Our diagnostic system must allow for neural and genetic variations in order to benefit from neuroscientific and genomic advances. It must therefore be sensitive to variance related to age, gender, genes, and comorbidity.

Sources of variance not considered or controlled for in the DSM

We consider here several sources of variance that are largely ignored by the current edition of the DSM but that could be incorporated into future editions by dimensionalizing at least some aspects of diagnostic criteria.

Gender

It has long been known that three to seven times more boys than girls meet DSM diagnostic criteria for ADHD. However, in adulthood, nearly as many women as men meet DSM criteria for ADHD (3.2% versus 5.4%; Kessler et al., 2006). The reasons for the gender disparity in childhood and its disappearance in adulthood are unknown. However, a categorical approach that fails to specify gender may impede understanding of these differences. The CRS employ DSM ADHD items coupled with quantitative norms by gender, age, and informant. The CRS identify just as many girls as boys as meeting criteria for ADHD in early childhood, at least in part because gender-specific norms are used to determine which children are statistically deviant on ADHD scales (Hudziak et al., 2005). Using DSM criteria, by contrast, girls who are significantly impaired often fail to meet the diagnostic threshold, which is the same for both genders at all ages. By slightly decreasing the number of criteria needed to meet diagnostic thresholds for girls, one would find nearly equal percentages of boys and girls with impairment in the attentional

domains. Dimensional approaches provide systematic methods for selecting gender sensitive cutoffs.

Age

Age is another source of variance that DSM criteria do not take into account. Those of us who treat ADHD are often reminded of the weakness of the categorical approach when we are asked to evaluate 2, 12, 22, 32, 42, 52, and even 62-year-old patients according to the same criteria for all ages. The neurodevelopmental level of many 2-year-olds renders them more inattentive, hyperactive, and impulsive than older children. Just 3 years later, the same children are usually more attentive, less active, and less impulsive. Some argue that developmental considerations make the DSM ADHD criteria inappropriate for preschoolers. However, the same can be said about applying the ADHD criteria to 62-year-olds. Many of us have been consulted by seniors who worry that they may have new onset ADHD because they meet many of the DSM criteria. Although it may be possible for new ADHD symptoms to occur in older people, these people often are experiencing normative cognitive decline. When relying only on categorical approaches to taxonomy, it is difficult to incorporate multiple aspects of development into the diagnostic process. The categorical approach renders diagnoses suspect by failing to consider the remarkable changes the human brain undergoes over the course of development.

Dimensional criteria reduce the need for arbitrary decisions about transitions from one developmental period to another. Dimensional criteria also enable us to track psychopathology from childhood into adolescence and adulthood. For example, voluminous research supports a distinction between two dimensions of conduct problems in both children and adults, i.e. overt (or aggressive) versus covert (or rule-breaking) dimensions. CD symptom criteria can be easily quantified by computing symptom scores. However, these scores should be separated into at least the aggressive versus rule-breaking dimensions. Research in several countries indicates that individuals' rankings on the aggressive dimension are more stable across developmental periods and are influenced more by genetic factors than are their rankings on the rule-breaking dimension (Elev et al., 1999; Stanger et al., 1997). Child/adolescent scores for the aggressive and rule-breaking dimensions foretell differences in adult outcomes. Moreover, dividing CD symptoms into aggressive and rule-breaking dimensions avoids the arbitrary cutpoint of age 18 for moving from CD to antisocial personality disorder, for which 40% to 50% of adolescents with CD eventually meet criteria (Steiner and Dunne, 1997). A dimensional approach clearly reveals developmental continuities in aggressive and rule-breaking dimensions into adulthood rather than implying that adolescents suddenly acquire an adult disorder on their 18th birthday.

Informants

In addition to differences by age and gender, informants are also sources of variance in diagnostic data. Although diagnostic data in child psychiatric clinics come primarily from mothers, mothers are only one of several relevant sources of data. Child psychiatrists and psychologists typically collect data from multiple informants to get more complete pictures of children. The current DSM does not provide standardized methods for incorporating data from multiple informants, despite practice parameter recommendations that data from multiple informants be routinely obtained (Dulcan, 1997; American Academy of Child and Adolescent Psychiatry, 2007). We know that mothers and fathers often fail to agree, that parents and teachers rarely agree, and that parent and teacher reports almost never agree with child reports (Verhulst and van der Ende, 1992).

Categorical criteria greatly complicate incorporation of disparate data into the diagnostic process. For example, when a mother reports six criterial symptoms of ADHD, inattentive type with impairment, but the teacher reports only five, it is hard for the conscientious clinician to determine whether the child should be diagnosed as having ADHD. The six-symptom threshold required for a diagnosis of ADHD means that the child has the disorder according to the mother's report but not according to the teacher's report.

A dimensional approach, by contrast, would indicate 83% agreement between the mother's and teacher's reports, while also retaining the context-specific descriptors of the child. From a neuroscience and genetic research perspective, the availability of data from multiple informants enables clinicians and researchers to quantify similarities and differences in the neural and genetic correlates of behaviors recognized by parents, teachers, children, and any other informants. This raises the following question: How can we reconcile the 83% agreement between the

mother and teacher in symptoms but 0% agreement in the DSM diagnosis?

An example of a dimensional answer to this question is provided by the CBCL family of instruments. Data obtained from mothers and fathers with the CBCL, from teachers with the Teacher's Report Form (TRF), and from children with the Youth Self-Report (YSR) are scored using separate norms based on national samples of each type of informant. Each informant is viewed as providing potentially valuable information about the child, as reported by that informant. Correlations between the informants' reports are displayed and are designated as above average, average, or below average on the basis of comparisons with correlations found for large reference samples of similar informants. In this way, evidence can be presented regarding the child's emotional and behavioral strengths and weaknesses in a variety of settings and from a variety of perspectives. It is not uncommon to find that mothers, fathers, teachers, and children report different problems. The clinician and researcher alike can use these data to consider variations in children's functioning and to design interventions accordingly. Additional data from repeated assessments provide evidence-based frameworks for evaluating the progress and outcomes of treatment. The DSM's categorical structure and lack of normative data make it hard to deal with informant variance.

Comorbidity

Some children who meet DSM criteria for ADHD also meet criteria for oppositional defiant disorder (ODD) and MDD. Such children are said to suffer from comorbidity, or the co-occurrence of multiple disorders. Many studies have shown that most children with ADHD also meet diagnostic criteria for other disorders (Faraone et al., 2001). Children who suffer from the constellation of ADHD, ODD, and MDD are often diagnosed as having a broad phenotype of juvenile bipolar disorder (JBD), meaning that criteria are not met for the narrow DSM-IV definition of bipolar affective disorder (Althoff et al., 2006; Faraone et al., 2005). Dimensional approaches show that these children have a condition that is genetically distinct from ADHD, ODD, or MDD. In other words, they may suffer from a single disorder (Hudziak et al., 2005), rather than three comorbid disorders. Just what the disorder is, no one knows for sure. Leibenluft and colleagues (Brotman et al., 2006) have suggested that the condition be called severe mood dysregulation. There is no clear agreement on how best to characterize these children in terms of DSM categories.

Using a CBCL-JBD profile, our group has shown that children with this phenotype have some of the highest endorsement rates for suicidal behavior of any clinical group (Althoff et al., 2006). Despite the lack of agreement about how to fit these children into DSM categories, there are recommendations, at least in the US, to treat them with therapies tested only for narrow spectrum bipolar disorder (American Academy of Child and Adolescent Psychiatry, 2007). Specifically, these children are treated with medications that have been tested only on children with narrow spectrum bipolar disorders, if they are tested on children at all. Although it is not known what the best treatment would be, the lack of a clear phenotypic definition makes it unlikely that appropriate clinical trials of this highly morbid and potentially lethal disorder will be done soon. This is an example of how a categorical system that represents higher order patterns in terms of comorbidity among separate disorders may impede treatment decisions (American Academy of Child and Adolescent Psychiatry, 2007; Kowatch et al., 2005). A dimensional approach can advance our knowledge of complex conditions by reframing comorbidity in terms of higher order patterns.

Putting it all together: the example of CD

To summarize, we use CD to demonstrate the need for a dimensional characterization of developmental psychopathology. CD provides a classic example of differences between the current DSM approach and dimensional approaches. As shown in Table 1, DSM-IV specifies 15 symptoms for CD. The diagnostic rules state that children who have at least three CD symptoms, plus impairment, meet criteria for CD. An 11year-old girl who skips school, stays out after curfew, and has shoplifted thus has CD. So does a 17-year-old boy who has all 15 symptoms, including using a weapon, cruelty to animals and people, stealing while confronting a victim, and forced sex. An 11-year-old girl who has only skipped school and shoplifted would not meet criteria for CD. Thus, the two 11-year-old girls are categorically different from each other, but one is categorically like the 17-year-old boy. This categorical confound illustrates the difficulties in applying DSM criteria to children and adolescents.

The categorical criteria do not take account of differences in the degrees to which children and adoles-

Table 1. DSM criteria for conduct disorder

- A. A repetitive and persistent pattern of behavior in which the basic rights of others or major age-appropriate societal norms or rules are violated, as manifested by the presence of three (or more) of the following criteria in the past 12 months, with at least one criterion present in the past six months:
- B. Aggression to people and/or animals
 - 1. Often bullies, threatens or intimidates others.
 - 2. Often initiates physical fights.
 - Has used a weapon that can cause serious physical harm to others (e.g. a bat, brick, broken bottle, knife, gun).
 - 4. Has been physically cruel to people.
 - 5. Has been physically cruel to animals.
 - Has stolen while confronting a victim (e.g. mugging, purse snatching, extortion, armed robbery).
 - 7. Has forced someone into sexual activity.

Destruction of property

- 8. Has deliberately engaged in fire setting with the intention of causing serious damage.
- Has deliberately destroyed others' property (other than by fire setting).

Deceitfulness or theft

- Has broken into someone else's house, building or car.
- 11. Often lies to obtain goods or favors or to avoid obligations (i.e. 'cons' others).
- Has stolen items of non-trivial value without confronting the victim (e.g. shoplifting, but without breaking and entering; forgery).

Serious violations of rules

- 13. Often stays out at night despite parental prohibitions, beginning before age 13 years.
- 14. Has run away from home overnight at least twice while living in a parental or parental surrogate home (or once without returning for a lengthy period).
- Is often truant from school, beginning before age 13 years.
- C. The disturbance in behavior causes clinically significant impairment in social, academic or occupational functioning.
- D. If the individual is 18 years or older, criteria are not met for antisocial personality disorder.

cents manifest criterial symptoms (e.g. 2/15 symptoms versus 3/15 symptoms versus 15/15 symptoms). They also fail to reflect developmental differences (in this case age 11 versus 17), as well as gender differences. Lastly, they do not take account of informant differences.

ences in reports for each child and also in the differential relevance of different informants' reports for particular kinds of problems, boys versus girls, and different ages. For all these reasons, it is difficult to conceptualize data on CD using the DSM approach in relation to age, gender, informant, and quantitative differences.

When using a dimensional approach to conduct problems, we find that children with ODD or CD can be described in terms of dimensions such as those embodied in the aggressive behavior and rule-breaking behavior syndromes identified and assessed by the CBCL family of instruments. Using this approach, we can evaluate children on dimensions in relation to national norms that include informant, age, and gender variance. The dimensions and norms extend into adulthood, providing continuity in the evaluation of the 17-year-old boy when he reaches age 18 without necessitating a new diagnosis that implies a change of psychopathology on his 18th birthday.

A proposal for how categorical and dimensional approaches can be further developed together

In child and adolescent psychiatry and psychology, there is at least as much research on dimensional approaches as on categorical approaches. Given the abundance of dimensional data, it seems feasible to incorporate provisions for variance related to age, gender, and informant into diagnostic criteria. Clearly, clinicians and researchers need cutpoints in order to make decisions about treatment and about inclusion in clinical trials. In a dimensional system, such cutpoints can be adjusted according to the different sources of variance. Dimensional data can then provide age-, gender-, and informant-specific starting points for treatment studies, longitudinal studies, and outcome studies. The addition of dimensional data could then lead to iterative improvement in categorical rules for treatment decisions.

It has long been held that dimensional approaches are less useful clinically. We envision a synergistic system that allows a categorical descriptor, e.g. ADHD, and a dimensional profile, e.g. the degree to which a child suffers from deviance in attention problems, aggressive behavior, and anxious depressed problems. This dimensional profile can then be used in evidence-based approaches to determine whether the child's categorical state changes (e.g. the child no longer has ADHD), but also to what degree the core symptoms

(attention problems) and associated symptoms (aggression and anxious depression) change (either diminish or, as we have seen in many cases, increase in intensity). Because this 'clinical application' of a combined approach provides gender, developmental, and informant sensitivity, we can determine whether the child's improvement or worsening varies by setting. By combining categorical and quantitative approaches, we can more fully utilize evidence-based approaches in child psychiatry.

Summary

Dimensional approaches are already commonly used in child psychiatry and psychology. We presented examples of ADHD and CD where there is clear support for a dimensional approach. Similar support exists for dimensional approaches to childhood anxiety, depression, and autistic spectrum disorders. The advantages of dimensional approaches include the ability to generate quantitative profiles that cut across common psychopathologies. These profiles present psychopathology in terms that are both sensitive and specific in relation to gender and age variance. Dimensional approaches offer many advantages for neuroscience and genomics. It has been argued that we may identify continua for some kinds of psychopathology and categories for other kinds. For these reasons, we have argued for a complementary system that includes both approaches. We note that dimensional approaches are needed in order to inculcate potentially useful endophenotypic and genetic discoveries into our assessment procedures and that our taxonomy should facilitate rather than impede the advance of knowledge. Dimensional approaches are thus needed to characterize psychopathologies, to search for their underlying genetic and neural mechanisms, and to discover treatments and cures.

References

- Achenbach T, Rescorla L. Manual for the ASEBA Schoolage Forms and Profiles. Burlington, VT: University of Vermont Research Center for Children, Youth, and Families, 2001.
- Althoff RR, Rettew DC, Faraone SV, Boomsma DI, Hudziak JJ. Latent class analysis shows strong heritability of the child behavior checklist-juvenile bipolar phenotype. Biol Psychiatry 2006; 60(9): 903–11.
- American Academy of Child and Adolescent Psychiatry. Practice parameter for the assessment and treatment of children and adolescents with bipolar disorder. J Am Acad Child Adolesc Psychiatry 2007; 46(1): 107–25.

- Bobb AJ, Castellanos FX, Addington AM, Rapoport JL. Molecular genetic studies of ADHD: 1991 to 2004. Am J Med Genet B Neuropsychiatr Genet 2005; 132(1): 109–25.
- Brotman MA, Schmajuk M, Rich BA, et al. Prevalence, clinical correlates, and longitudinal course of severe mood dysregulation in children. Biol Psychiatry 2006; 60(9): 991–7.
- Castellanos FX, Lee PP, Sharp W, et al. Developmental trajectories of brain volume abnormalities in children and adolescents with attention-deficit/hyperactivity disorder. JAMA 2002; 288(14): 1740–8.
- Conners C. Conners' Rating Scales Revised. New York: Multi-Health Systems, 2001.
- Constantino JN, Przybeck T, Friesen D, Todd RD. Reciprocal social behavior in children with and without pervasive developmental disorders. J Dev Behav Pediatr 2000; 21(1): 2–11.
- Dulcan M. Practice parameters for the assessment and treatment of children, adolescents, and adults with attention-deficit/hyperactivity disorder. American Academy of Child and Adolescent Psychiatry. J Am Acad Child Adolesc Psychiatry 1997; 36(10 Suppl): 85S–121S.
- Durston S, Hulshoff Pol HE, Casey BJ, Giedd JN, Buitelaar JK, van Engeland H. Anatomical MRI of the developing human brain: what have we learned? J Am Acad Child Adolesc Psychiatry 2001; 40(9): 1012–20.
- Eley TC, Lichtenstein P, Stevenson J. Sex differences in the etiology of aggressive and nonaggressive antisocial behavior: results from two twin studies. Child Dev 1999; 70(1): 155–68.
- Faraone SV, Althoff RR, Hudziak JJ, Monuteaux M, Biederman J. The CBCL predicts DSM bipolar disorder in children: a receiver operating characteristic curve analysis. Bipolar Disorder 2005; 7(6): 518–24.
- Faraone SV, Biederman J, Mick E, et al. A family study of psychiatric comorbidity in girls and boys with attention-deficit/hyperactivity disorder. Biol Psychiatry 2001; 50(8): 586–92.
- Feighner JP, Robins E, Guze SB, Woodruff RA Jr, Winokur G, Munoz R. Diagnostic criteria for use in psychiatric research. Arch Gen Psychiatry 1972; 26(1): 57–63.
- Goodman WK, Price LH, Rasmussen SA, et al. The Yale–Brown Obsessive Compulsive Scale. I. Development, use, and reliability. Arch Gen Psychiatry 1989; 46(11): 1006–11.
- Hay DA, Bennett KS, Levy F, Sergeant J, Swanson J. A twin study of attention-deficit/hyperactivity disorder dimensions rated by the strengths and weaknesses of ADHD-Symptoms and Normal-Behavior (SWAN) Scale. Biol Psychiatry 2007; 61(5): 700–5.
- Hudziak JJ, Althoff RR, Derks EM, Faraone SV, Boomsma DI. Prevalence and genetic architecture of Child Behavior Checklist-juvenile bipolar disorder. Biol Psychiatry 2005; 58(7): 562–8.

- Hudziak JJ, Derks EM, Althoff RR, Rettew DC, Boomsma DI. The genetic and environmental contributions to attention deficit hyperactivity disorder as measured by the Conners' Rating Scales – Revised. Am J Psychiatry 2005; 162(9): 1614–20.
- Kessler RC, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. Am J Psychiatry 2006; 163(4): 716–23.
- Kowatch RA, Fristad M, Birmaher B, Wagner KD, Findling RL, Hellander M. Treatment guidelines for children and adolescents with bipolar disorder. J Am Acad Child Adolesc Psychiatry 2005; 44(3): 213–35.
- Lord C, Rutter M, Le Couteur A. Autism Diagnostic Interview Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. J Autism Dev Disord 1994; 24(5): 659–85.
- Meyer-Lindenberg A, Nichols T, Callicott JH, et al. Impact of complex genetic variation in COMT on human brain function. Mol Psychiatry 2006; 11(9): 867–77, 797.
- Reynolds C, Kamphaus R. Behaviour Assessment System for Children Manual, Second Edition. Circle Pines, MN: American Guidance Service, 1998.
- Robins E, Guze SB. Establishment of diagnostic validity in psychiatric illness: its application to schizophrenia. Am J Psychiatry 1970; 126(7): 983–7.
- Stanger C, Achenbach T, Verhulst F. Accelerated longitudinal comparisons of aggressive versus delinquent syndromes. Development & Psychopathology 1997; 9(1): 43–58.

- Steiner H, Dunne J. Summary of the practice parameters for the assessment and treatment of children and adolescents with conduct disorder. J Am Acad Child Adolesc Psychiatry 1997; 36(10): 1482–5.
- Sterzer P, Stadler C, Krebs A, Kleinschmidt A, Poustka F. Abnormal neural responses to emotional visual stimuli in adolescents with conduct disorder. Biol Psychiatry 2005; 57(1): 7–15.
- Thompson PM, Giedd JN, Woods RP, MacDonald D, Evans AC, Toga AW. Growth patterns in the developing brain detected by using continuum mechanical tensor maps. Nature 2000; 404(6774): 190–3.
- Verhulst FC, van der Ende J. Agreement between parents' reports and adolescents' self-reports of problem behavior. J Child Psychol Psychiatry 1992; 33(6): 1011–23.
- Walhovd KB, Fjell AM, Reinvang I, et al. Effects of age on volumes of cortex, white matter and subcortical structures. Neurobiol Aging 2005; 26(9): 1261–70, discussion 75–8.
- Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. Br J Psychiatry 1978; 133: 429–35.

Correspondence: James J. Hudziak, M.D., Box 364SJ3, FAHC, 1 South Prospect, University of Vermont, Burlington, VT 05401, USA.

Phone: 802-656-1084 Fax: 802-656-0987

Email: james.hudziak@uvm.edu