Differentiating Major Depressive Disorder in Youths with Attention Deficit Hyperactivity Disorder

Rasim Somer Diler, MD[*], **W. Burleson Daviss, MD**[**], **Adriana Lopez, MScBSc**[***], **David Axelson, MD**[*], **Satish Iyengar, PhD**[***], and **Boris Birmaher, MD**[*]

[*]*Division of Child Psychiatry, Western Psychiatric Institute and Clinic, Pittsburgh, Pennsylvania.*

[**]*Department of Psychiatry, The University of Texas Health Science Center at San Antonio, Texas.*

[***]*Department of Statistics, University of Pittsburgh, Pennsylvania.*

Abstract

Background: Youths with attention deficit hyperactivity disorders (ADHD) frequently have comorbid major depressive disorders (MDD) sharing overlapping symptoms. Our objective was to examine which depressive symptoms best discriminate MDD among youths with ADHD.

Methods: One-hundred-eleven youths with ADHD (5.2−17.8 years old) and their parents completed interviews with the K-SADS-PL and respective versions of the child or the parent Mood and Feelings Questionnaire (MFQ-C, MFQ-P). Controlling for group differences, logistic regression was used to calculate odds ratios reflecting the accuracy with which various depressive symptoms on the MFQ-C or MFQ-P discriminated MDD. Stepwise logistic regression then identified depressive symptoms that best discriminated the groups with and without MDD, using cross-validated misclassification rate as the criterion.

Results: Symptoms that discriminated youths with MDD (n=18) from those without MDD (n=93) were 4 of 6 mood/anhedonia symptoms, all 14 depressed cognition symptoms, and only 3 of 11 physical/vegetative symptoms. Mild irritability, miserable/unhappy moods, and symptoms related to sleep, appetite, energy levels and concentration did not discriminate MDD. A stepwise logistic regression correctly classified 89% of the comorbid MDD subjects, with only age, anhedonia at school, thoughts about killing self, thoughts that bad things would happen, and talking more slowly remaining in the final model.

Limitations: Results of this study may not generalize to community samples because subjects were drawn largely from a university-based outpatient psychiatric clinic.

Conclusions: These findings stress the importance of social withdrawal, anhedonia, depressive cognitions, suicidal thoughts, and psychomotor retardation when trying to identify MDD among ADHD youths.

Keywords

Attention-deficit/hyperactivity disorder; depression; comorbidity

Corresponding author: W. Burleson Daviss Address: Dept. of Psychiatry The University of Texas Health Science Center at San Antonio 7703 Floyd Curl Drive San Antonio, TX 78229−3900 Email: davissw@uthscsa.edu Corresponding Author's Institution: Western Psychiatric Institute and Clinic, Pittsburgh, Pennsylvania

Introduction

Attention deficit hyperactivity disorder (ADHD) occurs in approximately 3% to 7% of all children and adolescents (Cantwell, 1996) and is a major clinical and public health problem because of its associated morbidity and disability (Spencer et al., 2003). Youths with ADHD may develop demoralization related to chronic social and academic difficulties associated with their primary ADHD (Waxmonsky, 2003). Youths with ADHD also have up to a 4 times higher risk of developing depressive disorders than the general adolescent population (Pliszka, 1998), with rates of comorbid major depressive disorder (MDD) ranging from 5% to 47% among children and adolescents with ADHD, especially in clinical samples (Pliszka, 1998;Spencer et al., 1999;Wilens et al., 2002). Such comorbid MDD is distinct from demoralization in youths with ADHD and is associated with higher levels of impairment and rates of hospitalization when compared to ADHD alone (Biederman et al., 1998).

Early identification and prompt treatment of pediatric MDD may reduce its potentially devastating long-term consequences (Birmaher and Brent, 2003). The formal diagnosis of MDD requires the assessment of a broad range of cognitive, vegetative and physical symptoms (Costello and Angold, 1988). However, depression in youths with ADHD may be more challenging to diagnose, given that some symptoms such as restlessness and problems with concentration may overlap between the two disorders (Jensen et al., 1988;Milberger et al., 1995). Moreover, medications used to treat ADHD may cause side effects such as insomnia, appetite changes, sleepiness, tearfulness, and moodiness that resemble symptoms of MDD (Pliszka, 1998). Because of these challenges, total scores on a well-validated depressive measure are significantly less accurate when screening for MDD in children with ADHD compared to those without ADHD (Daviss et al., 2006).

To date there have been no studies to guide the clinician as to which symptoms are most helpful in distinguishing cases of MDD in youths with ADHD. The goal of the current exploratory study was to examine which depressive symptoms best discriminate comorbid MDD in a sample of youths with ADHD.

Methods

Subjects

Subjects selected for this study were youths with ADHD drawn from a larger sample consecutively evaluated as part of two research studies or two specialty psychiatry clinics for mood disorders, all previously detailed in another paper (Daviss et al., 2006), with informed assent/consent obtained as approved by the University of Pittsburgh Institutional Review Board. Subjects had to have a confirmed diagnosis of ADHD based on a semi-structured interview. Youths with bipolar disorder, major depression in partial remission, depressive disorder not otherwise specified, or dysthymia were excluded to increase caseness in regard to the depression, given that other investigators have suggested that demoralization in non-depressed ADHD youths may resemble mild depression (Biederman et al., 1998).

Diagnostic Interview

All subjects and their parents underwent separate, detailed semi-structured interviews to determine mental health diagnoses, using the Schedule for Mood Disorders and Schizophrenia for School-Age Children-- Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997). When youths and parents gave contradictory reports of specific symptoms, interviewers were encouraged to make a best estimate of final diagnoses based on all available information. All interviewers were masters-or doctorate-level research clinicians who had undergone extensive training to assure the reliable and valid administration of this measure. Diagnostic

assessments were supervised by board-certified child and adolescent research psychiatrists, and were completed before the Mood and Feelings Questionnaire (MFQ) and other rating scales were scored by a computer. Kappas for K-SADS-PL interviews were determined by having all interviewers re-rate other interviewers' recorded assessments in 50 subjects randomly drawn from the four sources of this study. Kappas of relevant diagnostic categories were as follows: major depressive disorder (kappa=0.67), any bipolar disorder (kappa=0.71), any mood disorder (kappa=.71), ADHD (kappa=0.80), any anxiety disorder (kappa=0.88) and any externalizing disorder (kappa=0.74). These kappas were all statistically significant (p<.05) and suggested acceptable levels of diagnostic accuracy.

Depressive symptoms

All children or their parents completed their respective versions of the MFQ (MFQ-C and MFQ-P) at the time of the diagnostic interview while the other was completing his or her portion of the K-SADS-PL. These MFQ versions respectively have 33 and 34 items that cover the full range of symptoms of juvenile depressive disorders listed in DSM-IV, as well as related symptoms such as loneliness, tearfulness, worries about the future, and complaints of aches and pains (Costello and Angold, 1988). Both the MFQ-C and MFQ-P have shown high retest reliability and internal consistency (alphas of .94 and .92, respectively) (Wood et al. 1995). The criterion validity of the MFQ-C and MFQ-P for identifying major depressive episodes has been previously documented in juvenile patients (Daviss et al., 2006;Kent et al., 1997;Wood et al., 1995). In the current analysis, one-month retest reliability of MFQ ratings in a subsample of subjects with ADHD was again strong (MFQ-C ICC = .80, n=63; MFQ-P ICC = .80, n=64). In a few younger patients unable to read the MFQ-C on their own, the interviewer read them each item and recorded their answers.

In order to optimize sensitivity for detecting depressive symptoms, the current study combined both child and parent ratings for each symptom, taking the highest rating when there was disagreement. Depressive symptoms were classified as being present if either the parent or child rated them "sometimes" or "true". Three symptoms ("cried a lot", "worried about aches and pains", "felt lonely") were excluded from the current analysis, as they are not strictly DSM-IV criteria for MDD. The remaining symptoms were divided into one of three groups by the lead investigator for subsequent analyses: Mood/anhedonia, Depressed Cognitions, or Physical/vegetative symptoms (Table 2).

Statistical analysis

SPSS Version 11.0 was used for all analyses (SPSS, Inc., Chicago, IL, USA). First, t tests or chi-square tests were used to compare age, race, sex, and comorbidity in the two groups of ADHD youths with and without MDD. Second, a series of logistic regressions was done to show how well each symptom predicted the presence of comorbid MDD, after adjusting for any demographic and comorbid diagnosis differences. Finally, stepwise logistic regression was used to identify the combination of depressive symptoms that best discriminated between the two groups, using significance levels of 0.10 for stepwise selection and cross-validated misclassification rates as the final criterion (Everitt, 1994;Shtatland, et al., 2004). P-values < .05 were considered significant for all analyses.

Results

In the final sample of 111 ADHD youths (age range: 5.2 to 17.8 years old), 18 also had current MDD (MDD/ADHD) and 93 had no mood disorder (Non-MDD/ADHD). As shown in Table 1, the MDD/ADHD and Non-MDD/ADHD groups were equivalent with regard to sex, race and comorbid anxiety disorders. However, subjects in the MDD/ADHD group were significantly older and had higher rates of externalizing disorders (either oppositional defiant

or conduct disorders) than subjects in the Non-MDD/ADHD group. As expected, total scores of MFQ-P, MFQ-C, and a combined-MFQ (taking the highest rating for each symptom as reported by child or parent) were significantly higher in MDD/ADHD group (see Table 1).

Table 2 compares the frequencies (Freq) of various depressive symptoms in each group. Each odds ratio (OR) was calculated by a logistic regression to discriminate MDD/ADHD from Non-MDD/ ADHD subjects, controlling for group differences in age and rates of externalizing disorders. For example, an OR of 11.8 for item #2 (Didn't enjoy anything) indicates that when that item was rated as being present at least "sometimes" by either the child or the parent, the child had a 11.8 times higher likelihood of having MDD. Four out of the six mood/anhedonia symptoms, three out of the eleven physical/vegetative symptoms, and all fourteen of the depressed cognition symptoms significantly discriminated youths with and without comorbid MDD, as shown in Table 2. Note that some symptom items with high ORs, including item #1 as well as items 7, 10, 11, and 21 did not discriminate comorbid MDD because of their high frequencies in non-MDD/ADHD group.

Only four symptom items along with age remained in the final stepwise logistic regression equation to discriminate MDD in ADHD youth: Item# 29 (had no fun at school) (p<.014), item#19 (thought about killing self) (p<.002), item#22 (thought bad things would happen) (p<. 015), and item#13 (talking more slowly) (p<.002). With only these symptoms and age in the model, the logistic regression model correctly classified 92% and 88% of subjects regarding their MDD status using re-substitution and leave-one-out methods, respectively.

Discussion

MDD in youths with ADHD is often recurrent and quite impairing (Biederman et al., 1998). Therefore, accurate diagnosis of such depression in youths with ADHD is critical for early and effective intervention. This is the first study to specifically examine which symptoms of depression discriminate comorbid MDD in youths with ADHD. Our findings stress the importance of anhedonia, social withdrawal, depressive cognitions, suicidal thoughts and psychomotor retardation, in contrast to vegetative symptoms of depression when trying to differentiate MDD in youths with ADHD.

Our results differ somewhat from those of a previous study of the MFQ involving a clinical sample with a similar age range but without ADHD, in which all six mood and anhedonia symptoms discriminated youths with MDD from those without MDD (Kent et al., 1997). Unlike that study, the current study's item analysis controlled for group differences in externalizing disorders and age. Most mood-related symptoms discriminated MDD as expected, including unhappiness when praised, anhedonia at home and school, and social withdrawal. However, there were two exceptions. Item #1 (miserable/unhappy moods) and item #11 (grumpiness with parents) occurred so commonly in Non-MDD/ADHD youths (at 80% and 85%, respectively) that these symptoms did not discriminate youths with MDD/ ADHD, even though they had high odds ratios. Some have suggested that children with ADHD may often experience demoralization, characterized as dysphoric moods that are transient and triggered by negative social or academic events (Pliszka, 2003;Waxmonsky, 2003). On the other hand, "grumpiness" may also suggest externalizing disorders, which are the most common comorbidity in youths with ADHD (Pliszka, 2000). In the current sample externalizing disorders occurred more often in MDD/ADHD youths than in Non-MDD/ADHD youths. Our findings suggest that unhappy and irritable moods rated at least mild in severity are so common in youths with ADHD that only more severe levels of these symptoms may signal which youths have comorbid MDD.

Some have suggested that prominent neurovegetative symptoms may also be important to discriminate MDD/ADHD from Non-MDD/ADHD (Pliszka, 2003;Waxmonsky, 2003). In a clinical sample of youths without ADHD, tiredness discriminated depressed cases (Kent et al., 1997). Tiredness was also significantly more frequent in youths with MDD compared to non-depressed ADHD youths and normal controls (Jensen et al., 1988). However, in our study most neurovegetative symptoms (decreased concentration, indecision, insomnia, fatigue, decreased appetite, increased appetite) *did not* discriminate MDD/ADHD youths from Non-MDD/ADHD youths. The only three exceptions were moving/walking slowly, talking less, and talking more slowly. Most neurovegetative symptoms, as with most mood symptoms, had high overall rates in these ADHD youths, perhaps reflecting the underlying symptomatology of ADHD (e.g. decreased concentration, or restlessness) or side effects related to its pharmacological treatment (e.g. insomnia, reduced appetite).

A final difference between our current study and the previous study by Kent and colleagues (1997) was that depressive cognitive items in the current study were consistently strong predictors of MDD. While all 14 depressive cognition items in the current sample with ADHD discriminated MDD, at least three such symptoms in the previous sample without ADHD did not: felt no good anymore, blamed self, and thought bad things would happen (Kent et al., 1997). Our findings suggest that clinicians should interview children with ADHD carefully along with their parents for reports of hopelessness, suicidal thinking, worthlessness, and other depressive cognitions when considering a comorbid diagnosis of MDD.

Examination of all MFQ items using stepwise selection revealed that only a few depressive symptom items, along with age, remained in the final logistic regression equation to discriminate MDD in ADHD youths. Symptoms in the final model included one mood item (no fun at school), one neurovegetative item (talking more slowly), and two depressed cognition items (thought about killing self, and thought bad things would happen). A regression equation with just these variables in the model correctly classified 89% of the youths in the current sample regarding whether they had comorbid MDD. These symptoms may therefore be particularly helpful to clinicians in trying to distinguish MDD among patients with confirmed diagnoses of ADHD.

This study's findings should be considered cautiously in light of several potential limitations. As with any sample from a university-based outpatient psychiatric clinic, this sample may not reflect the characteristics of youths with ADHD in community settings. We did not have data on the treatment history of the subjects and could not rule out side effects related to the pharmacological treatment. The study's cross-sectional design prevents us from being able to draw conclusions about the temporal course of depressive symptoms in youths with ADHD. Our statistical power was somewhat limited by the relatively small number of youths with MDD. While cases of depression were determined by semi-structured interviews with both child and parent, individual depressive symptoms in the current analysis were categorized based on child and parent reports on depressive questionnaires, which may have been less accurate without a clinician's interpretation.

Nevertheless, this study's findings may be useful to the clinician in judging which youths with ADHD have depressive disorders that warrant alternate or additional treatments. A previous report has highlighted the importance of combining child and parent reports of depressive symptoms in youths with ADHD, because levels of depressive symptomatology are less reliably reported by youths with ADHD relative to their parents, or to youths without ADHD (Daviss et al., 2006). When child and parent reports were combined in the current analysis, we found that many DSM-IV symptoms of MDD discriminated comorbid MDD among youths with confirmed ADHD. On the other hand, irritability, miserable/unhappy moods, and vegetative symptoms related to sleep, appetite, energy levels, and concentration did not,

because they were widely reported in both Non-MDD/ADHD and MDD/ADHD groups. Ultimately, depressive symptoms in youths with ADHD are more likely to represent comorbid MDD and require further clinical attention when they are more severe, persistent, numerous, and associated with a clear decline from previous levels of academic or social function.

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TABLE 1

Sex, race, comorbid diagnoses, age, and MFQ scores in ADHD youths with and without major depressive disorder

Variables	MDD/ADHD		Non-MDD/ADHD		Test
	N	%	N	%	
Sex: Male	11	61.1	58	62.4	$\chi^2_2=.01$
Race: White	14	77.8	68	73.1	$\chi^2_2=.17$
Comorbid Anxiety disorders	3	16.7	13	14.0	$\chi^2_2=.09$
Comorbid Externalizing disorders	12	66.7	35	37.6	$\chi^2_2=5.21*$
	Mean	SD	Mean	SD	
Age	13.3	2.3	11.8	3.2	$t=1.99*$
MFQ-P	33.4	3.06	14.2	12.08	$t=5.90***$
MFQ-C	27.4	12.61	12.7	9.91	$t=5.28***$
Combined-MFQ	40.6	12.06	20.3	12.77	$t=6.20***$

Note: MDD/ADHD= Attention-deficit/hyperactivity disorder (ADHD) subjects with major depressive disorder (MDD); Non-MDD/ADHD= Attention-deficit/hyperactivity disorder subjects without major depressive disorder, SD= Standard deviation; MFQ-P= total parent-MFQ score; MFQ-C= total child-MFQ score; combined-MFQ= total score of combination of the MFQ-C and MFQ-P scores for each symptom, taking the highest rating when there was disagreement; significance levels (P): $* \leq .05$; $** \leq .01$; $*** \leq 0.001$.

TABLE 2

Depressive symptoms in ADHD youths with and without major depressive disorder

Symptoms on MFQ	MDD/ADHD N=18	Non-MDD/ADHD N=93	OR
	Freq (%)	Freq (%)	
A. Mood/anhedonia symptoms			
1. Felt miserable/unhappy	100.0	79.6	17.0
2. Didn't enjoy anything	88.9	39.8	11.8**
11. Grumpy/cross with parent	100.0	84.8	15.0
20. Didn't want to see friends	66.7	32.3	4.3*
29. Had no fun at school	94.4	58.7	10.8*
34. Wasn't happy, even if praised	70.6	31.5	4.0**
B. Depressive cognition symptoms			
8. Felt no good anymore	88.9	41.9	12.6**
9. Blamed self	72.2	44.1	3.3*
15. Felt nothing good in the future	83.3	34.4	7.3**
16. Thought life not worth living	72.2	22.6	8.6***
17. Thought about death/dying	61.1	29.0	5.0**
18. Felt family better off without	72.2	30.1	4.6**
19. Thought about killing self	61.1	15.1	8.1***
22. Thought bad things would happen	83.3	38.7	8.0**
23. Hated self	72.2	34.4	5.4**
24. Felt was a bad person	83.3	38.7	8.4**
25. Thought looked ugly	55.6	30.1	3.1*
28. Felt unloved	94.4	43.0	22.4**
30. Could never be as good as others	88.9	55.9	7.6*
31. Felt did everything wrong	77.8	49.5	4.0*
C. Physical/vegetative symptoms			
3. Was less hungry	61.1	52.7	1.3
4. Ate more	61.1	55.9	1.3
5. Felt so tired that he/she did nothing	72.2	49.5	2.3
6. Was moving/walking slowly	66.7	26.9	4.9**
7. Was very restless	88.9	75.3	2.4
10. Hard to make up her/his mind	94.4	81.7	3.1
12. Felt like talking less	83.3	49.5	3.9*
13. Was talking more slowly	66.7	18.3	12.3***
21. Hard to think/concentrate	94.4	86.0	3.1
32. Didn't sleep as well	72.2	57.0	1.6
33. Slept more	55.6	40.9	1.9

Note: MDD/ADHD = Attention-deficit/hyperactivity disorder (ADHD) subjects with major depressive disorder (MDD); Non-MDD/ADHD = Attention-deficit/hyperactivity disorder subjects without major depressive disorder; OR = odds ratios of logistic regressions; freq = frequencies. Significance levels of ORs are as follows: * ≤ .05; ** ≤ .01; *** ≤ 0.001.