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ORIGINAL ARTICLE

Primary Versus Secondary Diagnosis of Generalized Anxiety Disorder in Youth: Is the Distinction an Important One?

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Abstract Examine whether children with a primary diagnosis of generalized anxiety disorder (GAD) differ from children with a secondary diagnosis of GAD on clinician, parent, teacher, and youth-report measures. Based on consensus diagnoses, 64 youth referred to a general outpatient assessment clinic were categorized as having either a primary or secondary diagnosis of GAD. A semi-structured diagnostic interview was used to guide diagnostic decisions and assign primary versus secondary diagnostic status. We predicted that youth with a primary GAD diagnosis would present with greater anxiety symptomatology and symptom impairment on a variety of anxiety-related measures than youth with a secondary GAD diagnosis. Contrary to our hypotheses, no differences were found between those with primary versus secondary GAD diagnoses on measures of symptom severity and clinical impairment, comorbid diagnoses, or youth and teacher-report measures. Our findings have potential implications for the current practice of requiring primary anxiety diagnostic status as an inclusion criterion in clinical research and treatment outcome studies. Assuming our findings are confirmed in larger samples and with other anxiety disorders, future clinical trials and basic psychopathology research might not exclude youth based on absence of a particular anxiety disorder as the primary disorder but rather include individuals for whom that anxiety disorder is secondary as well.

Keywords Primary · Principal · Diagnosis · Child · Anxiety

Introduction

As noted in the Diagnostic and Statistical Manual [1, 2], when more than one diagnosis for an individual is given in an inpatient or outpatient setting, the principal (hereafter referred to as "primary") diagnosis is generally defined as the "reason for visit." However, the reason for visit may not be totally clear, especially in outpatient assessment clinics and non-specialty clinics where children and adolescents are referred for broadly-defined academic, behavioral, and emotional problems such as not doing well in school, being easily upset, and not getting along well with others [3]. Problems such as these can be due to a variety of reasons. For example, poor school performance might be due to family disruption, bullying, a traumatic event, lower intellectual ability, a learning disability, attention-deficit/hyperactivity disorder, an anxiety disorder, or a mood disorder, among others. Poor school performance as the reason for referral is evident, but what are the diagnoses associated with this problem? In such cases, the child frequently presents with multiple disorders, and sorting out which diagnosis is primary and which is secondary can be difficult. To assist in this process, First [4] suggests that the clinician first rule out whether the presenting symptoms arise from factors such as malingering, substance use/abuse, or general medical conditions. Assuming such factors are not present, First then provides a

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set of decision trees and tables to help one determine the specific diagnoses that are present and which diagnosis is likely the primary one that should be targeted or prioritized for treatment. With this approach, the primary diagnosis is the one that the clinician determines to be most severe or impairing [5].

While guidelines recommended by First [4] are often utilized in clinical settings, there has been variability in how clinical research studies have defined the primary diagnosis. For example, some treatment outcome studies have assigned only one diagnosis as primary and excluded youth from further participation who do not have this primary disorder, whereas other studies have assigned multiple diagnoses as co-primary (all having equal severity/impairment) and included such youth. A recent example of the latter approach is the Child–Adolescent Anxiety Multimodal Study [6] in which 78.7 % of the youth were diagnosed with two or more co-primary anxiety disorders, defined as GAD, social anxiety disorder (SAD), and separation anxiety disorder (SEP). Indeed, of the 488 youth, 175 (35.9 %) received all three anxiety disorders as co-primary and an additional 209 (42.8 %) received at least two of these anxiety disorders as co-primary. Examples of the former approach include several child-focused anxiety treatment studies [7–12], which have included only youth with single disorders such as GAD or SAD. These same decision making rules have been extended to basic psychopathology research where investigators have examined only children with a single primary anxiety diagnosis [13–15] and excluded others from study. The degree to which these two sample ascertainment methods result in samples that differ in severity or other important indicators is presently unknown. We are unaware of research demonstrating that those with primary diagnoses of any one anxiety disorder are different from those with secondary diagnoses of that same disorder in terms of etiology, functional impairment, or response to treatment.

The present study sought to examine this issue by determining whether children with a primary anxiety disorder of GAD differed from children with a secondary anxiety disorder of GAD on clinician, parent, teacher, and youth-report measures. We addressed this issue by identifying groups of children referred for a psychoeducational assessment at an outpatient assessment clinic. We chose to focus on GAD, since Walkup et al. [6] found this disorder to be the most common among treatment-seeking youth, and it was the most common anxiety disorder in our sample of clinically referred youth. The GAD Primary group included only youth with GAD as the primary diagnosis whereas the GAD Secondary group included youth with a variety of other non-anxiety diagnoses as primary but GAD as the secondary diagnosis. Primary diagnoses varied considerably in this latter group (see below). We predicted that youth with a primary GAD diagnosis would present with greater anxiety symptomatology and symptom impairment on a variety of anxiety-related measures than youth with a secondary GAD diagnosis.

Methods

Youth were referred by local schools, pediatricians, and mental health professionals for an Institutional Review Board-approved psychoeducational evaluation. The evaluation was conducted at an outpatient clinic that offers evaluations for a range of presenting problems. Youth and their parent(s) were interviewed and administered self-report measures separately by two clinicians. The Anxiety Disorders Interview Schedule for *DSM-IV*, Child and Parent Versions [14] was administered during the first session to inform diagnoses. Trained-to-criterion graduate students in an APA-approved doctoral program in clinical psychology conducted the ADIS-C/P interviews. Training consisted of a 3-h workshop on the ADIS-C/P, two practice interviews with the trainer, two live observations of administration of the ADIS-C/P with a previously trained clinician, and two interviews conducted with the trainer in the session with the trainee. One clinician met with the child, while the other met with the parents. These clinicians were unaware of information from the other informant prior to the consensus team meeting. At the consensus team meeting, ADIS-C/P results were presented and discrepancies between the parent and child informants were discussed. Since the reason for referral varied considerably at this clinic (see below) and consistent with the approach taken in other clinical research studies, we assigned a primary diagnosis based on consensus team opinion regarding the diagnosis that appeared to be the most severe and/or impairing. We enlisted the differential diagnosis steps recommended by First [4] in this process. The meeting was supervised by a licensed clinical psychologist.

Participants

Participants included 64 youth (mean age = 10.05; *SD* = 2.66; range = 7–17), their primary caregiver(s), and the child's primary teacher. This sample consisted of all consecutively-assessed youth with a diagnosis of GAD as either the primary or secondary diagnosis; the sample was drawn from a larger sample of approximately 400 youth. Youth with primary diagnoses of autism spectrum disorder and schizophrenia were excluded as were youth with IQs below 80. All other referred youth were included, of whom 38 participants were male (59.4 %) and 26 were female (40.6 %). Ethnicity was self-identified as Caucasian

(95.3 %) and African-American (4.7 %). The majority of the living situations involved two-parent households (74.6 %) and biological parents (93.8 % biological mother present; 84.1 % biological father present). Mean family income was $50,781 (SD = $40,121). In terms of parental education, the vast majority (71.9 % fathers; 85 % mothers) completed high school or higher.

All youth in the GAD Primary group ($n = 33$) met criteria for GAD as their primary diagnosis. Youth in the GAD Secondary group ($n = 31$) met criteria for GAD as their secondary diagnosis but met criteria for a number of other primary disorders. Among the most common primary disorders in this group were ADHD (41.94 %), learning disorders (16.13 %), depressive disorders (9.7 %), and oppositional defiant disorder (6.5 %). Among the most common secondary disorders in the GAD Primary group were ADHD (42.42 %), SAD (18.20 %), learning disorders (15.15 %), depressive disorders (12.10 %), and oppositional defiant disorder (12.10 %). Eleven of the 64 participants (17.2 %) were taking medications for anxiety symptomatology (e.g., SSRIs) and 9 other youth (14.1 %) were taking medications for ADHD (e.g., stimulants). All youth receiving medications were reported to be on stable doses for at least 6 weeks prior to the assessment. Finally, the most common referral questions were "academic problems" (29.7 %), "behavioral problems" (10.9 %), "ADHD" (10.9 %), "unspecified emotional problem" (6.5 %), and "anxiety" (4.7 %). This reason for referral was indicated by parents at the time of referral. Interestingly, only 4.7 % of our sample diagnosed with GAD (as either primary or secondary) had "anxiety" reported as the reason for referral, although anxiety-related problems may have been reflected in broader domains such as "academic problems" given the linkage between anxiety and school-related impairment [15–18].

Measures

Anxiety Disorders Interview Schedule for DSM-IV, Child and Parent Versions [14]

The ADIS-C/P versions are semi-structured diagnostic interviews administered separately to the parent(s) and child. These interviews assess anxiety, mood, and other psychiatric disorders seen in childhood and adolescence. During the interview, the clinician assesses symptoms and obtains frequency, intensity, duration and interference ratings (i.e., how much the disorder in question has interfered in the child's daily life) on a nine-point scale (0 = not at all to 8 = very, very much) and assigns a clinician severity rating (CSR) via clinical judgment. In order to meet diagnostic criteria, a CSR of 4 or higher (0–8) is required. For our analyses, we utilized the composite CSR for comparing groups on clinical severity, a measure that uses an algorithm to combine parent and child reports of anxiety [14].

The ADIS-C/P has shown excellent reliability in symptom scale scores and good to excellent test–retest and inter-rater reliability for assigning combined diagnoses [14, 19, 20]. For the current study, all interviews were videotaped and 33 % were coded for reliability. Acceptable levels of inter-rater agreement for video review were found for child ($\kappa = .71$) and parent ($\kappa = .77$) interviews.

Global Assessment of Functioning [1]

GAF was determined based on consensus opinion among the assessment team members. This measure of impairment was chosen due to its established reliability and validity [21] and applicability to overall impairment rather than just anxiety-related symptom impairment. The GAF score ranges from 0 to 100 with scores of 41–50 indicating serious symptoms or impairment, 51–60 reflecting moderate symptoms or impairment, and 61–70 reflecting mild symptoms or impairment.

Child Behavior Checklist [22]

The CBCL is a 113-item checklist completed by parents. Parents are asked to indicate how often the behavior described in each item is true of their child using a three-point scale (often/always true, sometimes true, and not true). The reliability and validity of the CBCL/4–18 has been well established [22]. Internal consistency was adequate for the scales evaluated in this study: Externalizing Problems ($\alpha = .90$), Anxious/Depressed ($\alpha = .76$), and Somatic Complaints ($\alpha = .79$). Competency scales were also examined, but internal consistency could not be calculated in the current data set (i.e., item-level data for these scales were not available). These scales have shown adequate internal consistency in past research (αs = .63–.69) [22].

Multidimensional Anxiety Scale for Children [23]

The MASC is a 39-item self-report questionnaire designed to assess a variety of anxiety dimensions. For each item, the participant is asked to circle one of four choices (i.e., 0 = never true, 1 = rarely true, 2 = sometimes true, 3 = often true). All 39 items are distributed across four scales (1) Physical Symptoms, (2) Harm Avoidance, (3) Social Anxiety, and (4) Separation Anxiety. This instrument provides reliable and valid assessments of anxiety symptoms, discriminates between important anxiety symptoms, and is sensitive to treatment-induced changes in symptoms [23]. Acceptable reliability and validity have

been shown in epidemiological, school, and clinical samples [23–25]. Internal consistency was adequate in this study: MASC Total ($\alpha = .93$), Physical Symptoms ($\alpha = .93$), Harm Avoidance ($\alpha = .85$), Social Anxiety ($\alpha = .87$), and Separation Anxiety ($\alpha = .71$).

Teacher Report Form [26]

The TRF is a questionnaire that includes 113 items to which the teacher is asked to indicate if each behavior/characteristic is often/always true, not true, or sometimes true of the student being assessed. Test–retest reliability over a 15-day period is .90 for the adaptive behavior scales and .95 for the problem behavior scales [26]. Internal consistency has been shown to be adequate for the scales evaluated in this study: Externalizing Problems ($\alpha = .95$), Anxious/Depressed ($\alpha = .86$), and Somatic Complaints ($\alpha = .72$) [26]. Additional scales examined that do not allow for calculation of internal consistency (i.e., based on single items) included the following: Academic Performance, Working Hard, Behaving Appropriately, Learning, and Happy.

Results

Data were analyzed for all participants who met inclusion criteria. Missing data were generally limited for most measures (i.e., <10 %), so listwise deletion was utilized for most analyses as suggested by Little [27] and Allison [28]. However, missing data for the TRF were more substantial, given that some teachers were away during the summer holidays when several assessments were conducted. Since listwise deletion assumes that data are missing completely at random (MCAR), those with and without TRF data were compared on study variables, and no differences were found ($ps > .05$). For study analyses, our sample was divided into a GAD Primary group ($n = 33$) and a GAD Secondary Group ($n = 31$). Analyses included independent t tests and Chi square (χ^2) tests to compare group frequencies. Levene's test was also used for t tests. In cases where Levene's test was significant, we used adjusted t tests. A power analysis revealed that we were powered to detect large effects ($d \sim .7$–$.9$) for our analyses.

Table 1 presents group differences on our study measures. Prior to examining group differences on anxiety-related symptomatology and impairment, we examined differences on demographic variables and comorbid diagnoses. Our GAD Primary and GAD Secondary groups did not differ on age, $t(62) = .71$, $p = .48$, gender, $\chi^2(1) = .09$, $p = .76$, family income, $t(46) = .75$, $p = .46$, or anxiety-related medication status $\chi^2(1) = .78$, $p = .38$. In relation to comorbidity, no differences were found ($ps > .05$) between GAD Primary and GAD Secondary groups for the following disorders: ADHD (42.4 % vs. 50.0 %), SAD (18.2 % vs. 33.3 %), learning disorders (12.1 % vs. 29.0 %), major depressive disorder/dysthymia (12.1 % vs. 19.4 %), or oppositional defiant disorder (12.10 % vs. 6.5 %).

For GAD Primary versus GAD Secondary, a series of Holm–Bonferroni-corrected t tests were utilized for the GAD ADIS CSR, clinician-rated GAF, CBCL Anxious/Depressed, CBCL Somatic Problems, TRF Anxious/Depressed, TRF Somatic Problems, and MASC anxiety factors (see Table 1). Unexpectedly, no differences were found between groups on any of the hypothesized measures (all $ps > .05$) and effect sizes were generally small (ds ranged from 0 to .35).

Discussion

The current study examined differences between youth with a primary versus secondary diagnosis of GAD using a range of clinician, parent, teacher, and child report measures. Contrary to our hypotheses, differences were not found between groups on measures of GAD-relevant symptomatology, GAD symptom impairment, co-morbid disorders, and degree of impairment. Although we were only powered to detect large effects with the current sample size, exploration of post hoc effect sizes revealed that effects were in the small range, suggesting few meaningful differences between the GAD Primary and GAD Secondary groups on our study measures. At the same time, our relatively small sample size yielded somewhat large confidence intervals, suggesting the importance of future research in this area.

Overall, our findings suggest that the primary versus secondary diagnosis distinction, at least with respect to GAD, may have limited utility in clinical outpatient or research settings. Why might this be so? We speculate as follows. First, regardless of whether the diagnosis is primary or secondary, it still meets *DSM* criteria, as specified by diagnostic instruments like the ADIS-C/P [14]. Furthermore, while one disorder may be considered to be primary (and hence more severe for any one child), it does not necessarily follow that the secondary diagnosis is not a significant problem for that child, even though it may be less severe or impairing. We liken this situation to a child who has irritable bowel syndrome and juvenile diabetes. Both disorders are present and problematic and which disorder is designated as primary or secondary is dependent upon a host of factors; furthermore, it might not even be necessary to assign one or the other as primary. They both are simply present and, as such, need to be included in case conceptualization and treatment planning [3, 4].

Table 1 Means, standard deviations, and between group tests for overall sample (n = 64)

Impairment	GAD Primary	GAD Secondary	*t*	*df*	*p*	*d*	95 % CI (*d*)
GAF	63.68 (9.84)	60.68 (8.53)	1.28	60	.21	.33	−.18 to .83
GAD CSR	4.78 (2.14)	4.43 (2.18)	.64	60	.53	.16	−.34 to .66
CBCL							
Activities	44.44 (7.14)	47.26 (8.79)	1.40	61	.17	.35	−.15 to .85
Social	38.88 (8.73)	39.32 (8.90)	.20	62	.84	.05	−.44 to .54
School	35.43 (9.08)	37.52 (9.13)	.10	55	.39	.23	−.49 to .55
Anx/Dep	65.61 (8.85)	67.19 (10.91)	.63	62	.53	.16	−.33 to .65
Somatic	63.70 (10.49)	65.39 (9.94)	.66	62	.51	.17	−.33 to .66
Externalizing	60.15 (11.36)	59.61 (11.29)	.19	62	.85	.05	−.44 to .54
TRF							
Academics	42.57 (7.79)	45.38 (8.73)	1.10	40	.28	.34	−.27 to .95
Work hard	41.23 (6.85)	41.67 (6.64)	.21	41	.83	.07	−.53 to .66
Behaving	43.64 (7.87)	42.14 (7.11)	.65	41	.52	.20	−.40 to .80
Learning	41.00 (6.22)	43.05 (7.06)	1.00	40	.33	.31	−.30 to .92
Happy	41.50 (6.03)	42.24 (6.68)	.38	41	.71	.12	−.48 to .71
Anx/Dep	62.12 (12.74)	58.67 (9.59)	.93	44.51	.29	.27	−.30 to .83
Somatic	55.76 (7.84)	55.78 (10.22)	.01	46	.99	.00	−.12 to .12
Externalizing	57.92 (8.13)	58.38 (9.69)	.18	47	.86	.05	−.50 to .61
MASC							
Total	56.18 (15.41)	57.67 (10.79)	.42	48.44	.68	.11	−.42 to .64
Physical	54.75 (15.20)	55.07 (12.06)	.41	53	.68	.02	−.42 to .64
Harm avoid	51.32 (14.35)	54.85 (12.13)	.98	53	.33	.27	−.27 to .79
Social	55.86 (14.71)	57.56 (13.09)	.45	53	.65	.12	−.41 to .65
Sep/panic	58.14 (15.60)	56.81 (13.27)	.34	53	.74	.09	−.44 to .62

Cohen (1988) recommends the following interpretation of *d*: small = .2, medium = .5, large = .8

Anx/Dep Anxiety/depression, *CBCL* Child behavior checklist, *CI* Confidence interval, *CSR* Composite clinician severity rating, *GAF* Global assessment of functioning, *Harm Avoid* Harm avoidance, *MASC* Multidimensional anxiety scale for children, *Sep/Panic* Separation/panic, *Social* Social anxiety, *TRF* Teacher report form

These findings may have implications for use of primary anxiety diagnosis status as an inclusion criterion in clinical research. Assuming our findings can be replicated in larger samples and with other anxiety disorders, future clinical trials and basic psychopathology studies might choose not to exclude youth based on absence of a specific primary anxiety diagnosis, if that diagnosis is present as a secondary diagnosis. Researchers could integrate the evaluation of differences between youth with a primary versus a secondary diagnosis into their research analytic plans. Such a change in strategy could serve to improve subject recruitment, increase sample sizes, and encourage the systematic exploration of differences between youth with a primary versus secondary diagnosis.

Although our study advances the literature on the primary versus secondary distinction, we recognize limitations in our study. First, as noted, our sample was relatively small in size and powered only to detect "large" effects in our study analyses. Future studies with larger samples are needed to further explore this distinction and to sort out the implications for treatment outcomes. Furthermore, studies should examine etiological and comorbidity differences to determine if such differences are related to the longitudinal course of GAD and its treatment outcomes. Second, our sample was relatively homogeneous in terms of age, race, ethnicity, and socio-economic status, so future studies should seek to examine this distinction in more diverse samples. Third, youth presented at a "generalist" clinic, not a "specialty" research clinic. Our findings thus might not generalize to child anxiety specialty clinics.

Summary

Overall, the current study suggests that we may need to broaden our perspective when considering the inclusion criteria for child anxiety research studies and consider further whether the primary versus secondary distinction is an important one. Based on these preliminary findings, we suggest these distinctions may not be meaningful ones, at

least for GAD. Furthermore, we may need to turn our attention to underlying domains that characterize this disorder and other anxiety disorders as recently recommended in the National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC; http://www.nimh.nih.gov/research-priorities/rdoc/index.shtml).

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