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Are Children with ‘Pure’ Generalized Anxiety Disorder Impaired? A Comparison with Comorbid and Healthy Children

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Abstract

Objective—Despite the approach of DSM-5, generalized anxiety disorder (GAD) of childhood continues to face question as to whether it should be considered a distinct clinical disorder. A potentially critical question embedded in this debate involves the role of functional impairment which has yet to be demonstrated in children with ‘pure’ GAD.

Methods—Participants included 41 children between the ages of 6 and 11 years who met diagnostic criteria for primary GAD. Children with pure GAD (n=17) were compared to children with comorbid GAD (n=24) as well as a healthy control group (n=20) in terms of clinician-rated severity and impairment and child-reported adaptive functioning across four domains.

Results—On average, children with pure GAD were more likely to be male and younger than children with comorbid GAD. Based on traditional significance testing, global impairment was greater in the comorbid compared to pure GAD group, although functioning in both groups was in the ‘variable’ range. Both clinical groups reported less adaptive family relationships than controls, while only the comorbid group reported lower levels of home-based functioning. Equivalence testing nonetheless indicated a lack of comparability (i.e., non-equivalence) across the three groups for each of the functional domains examined.

Conclusions—Findings indicate children with pure GAD to be functionally impaired compared to their healthy peers, though not to the same extent as children with secondary psychiatric diagnoses. Child functioning within the family specifically may be among the most vulnerable. Results support consideration of childhood GAD as a distinct clinical disorder.

Keywords

Generalized Anxiety Disorder; Children; Impairment; Adaptive functioning; DSM-5

Generalized anxiety disorder (GAD) is a chronic, often disabling disorder associated with substantial comorbidity, increased service utilization and health care costs, and reduced quality of life in adulthood (Barerra & Norton, 2009; Kessler, DuPont, Berglund & Wittchen, 1999; Roy-Byrne, 1996). Despite early speculation that impairment might be more appropriately attributed to high rates of co-occurring disorders, especially depression (Breier, Charney & Heninger, 1985), research showing impairment to be directly related to

an adult GAD diagnosis now exists (Kessler et al., 1999; Ormel et al., 1994; Schonfeld et al., 1997). For example, primary care patients with ‘pure’ GAD experience a higher number of disability days and reduced social functioning compared to patients without psychiatric disorders (Ormel et al., 1994; Schonfeld et al., 1997). Based on national survey data, Kessler and colleagues (1999) found that the impairment experienced by adults with pure GAD is equivalent in magnitude to the impairment of pure major depressive disorder (MDD).

In contrast, impairment in children with GAD has been scarcely explored. This lack of research seems particularly problematic with the impending publication of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). In fact, questions have continued to beset the diagnosis since its replacement of overanxious disorder (OAD) of childhood in DSM-III-R (APA, 1987). In particular, rates of comorbidity as high as 90% (Masi et al., 1999; 2004) and substantial temporal instability (Bittner et al., 2007; Copeland, Shanahan, Costello & Angold, 2009) have contributed to debate whether early GAD might be better conceptualized as a temperamental disposition for psychopathology, broadly, rather than a distinct clinical condition (Barlow, 1988; Rapee, 1991). It is of course possible that GAD might not reflect the same condition across different periods of development, yet clinical diagnosis at any age requires evidence of impaired functioning. Moreover, longitudinal research suggests that level of childhood functioning, more so than specific symptoms, may serve to predict adult outcomes (e.g., Parker & Asher, 1987).

While the functioning of children with pure GAD remains to be examined, impairment is commonly inferred from research conducted among mixed anxious samples (Benjamin, Costello & Warren, 1990; Essau, Conradt & Petermann, 2000; Ialongo, Edelsohn, Werthamer-Larsson, Crockett & Kellam, 1995; Strauss, Frame & Forehand, 1987) where global and/or specific impairments have been documented among anxiety-disordered youth as a single group [e.g., GAD, social anxiety disorder (SP) and separation anxiety disorder (SAD)]. Arguably, high rates of comorbidity pose considerable challenge in attempting to discern degree and domains of impairment for diagnostic subgroups. Yet for other anxiety disorders the presence and nature of functional deficits have been demonstrated through parallel disorder-focused investigations. Studies comparing children with SP to healthy children, for example, provide clear evidence of impairment across several functional domains (Beidel, Turner & Morris, 1999; Bernstein, Bernat, Davis & Layne, 2008; Essau, Conradt & Petermann, 1999).

Two studies have examined the functioning of youth with GAD specifically. In a clinical sample of 7 to 14 year olds, school functioning was examined by diagnostic subgroups including GAD, SP, and SAD as well as a healthy comparison group (Mychailyszyn, Mendez & Kendall, 2010). Across a number of parent and teacher measures the three anxious subgroups evidenced lower levels of school functioning than healthy children. Although the sample included only seven children with pure GAD, this subgroup did not differ significantly from healthy children on a range of teacher report indices including academic performance, working hard, and learning. Within a clinical sample of youth with primary GAD, 8 to 18 years, those with comorbid MDD evidenced significantly lower levels of global functioning than youth without MDD (Masi, Favilla, Mucci & Millepiedi, 2000). However, in addition to the absence of a healthy control group, a majority of children with

GAD without MDD met criteria for additional diagnoses, obscuring understanding of GAD-specific impairment.

In a community-based sample of children with GAD, symptom predictors of impairment were examined (Layne, Bernat, Victor & Bernstein, 2009). Clinical severity ratings (CSRs) for GAD from the Anxiety Disorders Interview Schedule for DSM-IV-Parent and Child versions (ADIS-C/P; Silverman & Albano, 1996) were used to determine level of impairment. A greater number of symptoms and more intense worry predicted CSRs; however, because symptom and impairment variables were drawn from the same instrument (ADIS-C/P) shared measurement effects are of concern. Distinction between impairment and symptom severity – two related but separate constructs – also deserves comment. In that CSRs are derived from information related to diagnosis severity and interference in daily functioning without specified contribution of each, measurement of either construct is non-distinct.

An additional and more widespread limitation of child psychopathology research includes an overreliance on clinician-based assessments of impairment, even though diagnostic evaluation of children regularly incorporates multiple informants. Clinician ratings have been shown to disproportionately reflect information provided by parents, however (De Los Reyes, Alfano & Beidel, 2010; Hawley & Weisz, 2003). Certainly, children view and prioritize their roles and abilities differently than adults and the extent to which adult observations capture children's self-perceptions is unclear. Thus, greater integration of child report in determining and clarifying domain-specific impairments is needed (Kutash, Lynn, & Burns, 2008).

The current study sought to address several key limitations of previous research by including a pure GAD group as well as a healthy comparison control group, and assessing severity/impairment and adaptive functioning from clinician and child perspectives. Three groups of children, ages 6 to 11 years, were compared: children with pure GAD, children with comorbid GAD, and healthy controls. Further, in order to understand not only whether statistically significant differences were present but also whether the three groups could be considered equivalent (i.e., comparable) in their functioning, both traditional significance testing and equivalence testing (Rogers, Howard & Vessey, 1993) were conducted. Based on available previous research, statistical differences and non-equivalence were hypothesized across all three groups, with the comorbid GAD group exhibiting the lowest levels of functioning followed by the pure GAD group, and controls.

Methods

Participants

The sample consisted of a 61 children ($M=8.8$, $SD=1.5$) from the metropolitan Washington, D.C. area. Forty one had a primary DSM-IV GAD diagnosis based on structured parent/child interviews. Children with GAD were assessed at a child anxiety specialty clinic in a medical setting over a consecutive three year period. Children were referred for clinical services related anxiety or responded to advertisements for a research study on excessive anxiety/worry. All children completed the same diagnostic procedures. Exclusion criteria

included comorbid bipolar illness, autism spectrum disorder, psychosis, suicidal ideation or intent, evidence of less than average IQ, and/or a chronic medical condition requiring regimented care (e.g., diabetes, severe asthma). Expectedly, a majority (n=24; 58%) of children met criteria for at least one other psychiatric disorder (range of 0–3 diagnoses). The most common co-occurring diagnoses were social anxiety disorder (n=9; 22%), attention deficit/hyperactivity disorder (n=9; 22%), separation anxiety disorder (n=4; 10%), depressive disorders (n=4; 10%) and specific phobias (n=3; 7%). Exploratory analyses did not reveal significant differences between children presenting for clinical versus research purposes. See Table 1.

Twenty children recruited from the local community comprised a healthy comparison group. Children were recruited using community flyers and newspaper advertisements and underwent the same assessment procedures as GAD children. Healthy children did not meet criteria for any mental health diagnosis or fulfill any of the exclusion criteria listed above. See Table 1 for demographic characteristics of the three subgroups.

Measures

Anxiety Disorders Interview Schedule for DSM-IV: Children and Parent Versions (ADIS-C/P; Silverman & Albano, 1996)—The ADIS-C/P is a semi-structured interview designed to assess DSM-IV anxiety and other psychiatric disorders in youth. A clinical severity rating (CSR; range of 0–8) of 4 or higher (indicating at least moderate severity/impairment) is required for assigning any diagnosis. The ADIS has excellent inter-rater reliability, retest reliability, and concurrent validity (Lyneham, Abbott, & Rapee, 2007; Silverman, Saavedra & Pina, 2001). Reliability for a GAD diagnosis in the current sample was acceptable ($\kappa=.87$).

Children's Global Assessment Scale (C-GAS; Shaffer et al., 1983)—The C-GAS is a unidimensional (global) measure of social and psychiatric functioning for children ages 4–16 years. The clinician-based rating scale ranges from 1 to 100 (highest functioning) with anchors at 10-point intervals that include descriptors of functioning (e.g., 61–70 = 'Some difficulty in a single area'; 51–60 = 'Variable functioning with sporadic difficulties in several areas'). Scores above 70 are typically considered to be in the normal range (Shaffer et al., 1996). In both research and clinical settings, strong inter-rater and test retest reliability, and concurrent and construct validity have been reported (Bird, Canino, Rubio-Stipec & Ribera, 1987; Bird et al., 1990; Green, Shirk, Hanze & Wanstrath, 1994).

The Child and Adolescent Social and Adaptive Functioning Scale (CASAFS; Price, Spence, Sheffield & Donovan 2002) is a 24-item child report measure of adaptive functioning (i.e., the degree to which an individual is successful at/fulfills various life roles). Four subscales reflecting key domains of functioning include: school performance, peer relationships, family relationships, and home duties/self-care. Responses are given on a four-point Likert scale ranging from 1 (never) to 4 (always). Previous investigation has found CASAFS scores to differentiate between depressed and healthy children, with acceptable levels of internal consistency, test-retest reliability, and construct validity reported (Price et al., 2002). Internal consistency in the current sample was acceptable (Cronbach's $\alpha=.85$).

Procedures

All measures and procedures were approved by an Institutional Review Board and parents and children were required to sign informed consent/assent forms prior to participation. Diagnostic interviews were conducted with parents and children separately by a Ph.D. level psychologist or doctoral student in clinical psychology. Final diagnoses and C-GAS ratings were assigned by interviewers based on information from both sources and after review with a licensed psychologist. CSRs and C-GAS ratings were only made if the child met diagnostic criteria for GAD and/or other psychiatric diagnoses. While all participants were supervised in the completion of self-reports, younger children (ages 6 to 8) were directly assisted with measures by a research assistant.

Analytic Plan

Data were analyzed with SPSS 19.0 software. Descriptive analyses indicated 6% of data values to be missing. In order to maximize power and ensure that assumptions of statistical test were met, diagnostic missing value analysis procedures were conducted in SPSS. For all continuous variables data were found to be missing completely at random (MCAR) or 'ignorably missing' (Little's test: $X^2=50.71, p>.05$). Due to significant skew/kurtosis, all outcome variables were log transformed to meet assumptions of normality.

Traditional null hypothesis significance testing was first conducted to examine whether the groups differed significantly in terms of impairment/functioning. However, because a non-significant result does not establish group comparability (Tryon, 2001) which was of interest in the current study, equivalence testing also was conducted (Rogers et al., 1993). This involves the calculation of Z scores based on deviations of mean group differences from an a priori equivalency point. Specifically, a minimum group difference (δ) is established and considered necessary to demonstrate non-equivalence (i.e., a meaningful difference). For all outcomes, effect sizes (η^2) are reported. Based on criteria provided by Cohen (1988), 0.009 constitutes a small effect, 0.058 a medium effect, and 0.138 a large effect using η^2 .

Results

Preliminary Analyses

Group comparisons for age, sex and race/ethnicity were first conducted. A significant group difference for age was found [$F(2,58)=3.59, p<.05$] and followed with Tukey's post-hoc comparisons, revealing children in the pure GAD group to be significantly younger than children in both other groups. A significant group difference for sex [$X^2(2)=6.76, p<.05$] was followed with comparison of standard residual scores to an alpha of $p<.05$ (critical value ± 1.96). Residual values indicated there were fewer boys in the comorbid GAD group than both other groups. Age and sex were entered as covariates in all analyses.

Differences in Clinician-rated Severity and Impairment in Children with Pure and Comorbid GAD

Clinician-rated severity in the two clinical groups was examined based on GAD CSRs (ADIS-C/P). The ANCOVA result was non-significant [$F(1,37)=2.41, p>.05$]. Global levels of impairment also were examined based on clinician C-GAS scores. A significant result

emerged [$F(1,38)=5.95, p<.05$] where the comorbid group was rated as more impaired than the pure GAD group. Both group had average C-GAS scores in the ‘variable functioning’ range. See Table 2.

Differences in Child-reported Adaptive Functioning in Children with Comorbid and Pure GAD and Healthy Controls

ANCOVAs for each of the four CASAFS subscales (school performance, peer relationships, family relationships, and home duties/self-care) were conducted to examine differences in child-reported adaptive functioning across the three groups. Significant results for family relationships [$F(2, 56)=3.19, p<.05$] and home duties/self-care [$F(2, 56)=3.41, p<.05$] emerged. Post-hoc comparisons indicated both GAD groups reported less adaptive functioning in family relationships than controls but did not differ from each other. For home duties/self-care, the comorbid GAD group reported less adaptive functioning than controls while the pure GAD groups did not differ from the other groups. See Table 2.

Equivalence of Severity, Impairment and Adaptive Functioning in Children with comorbid and pure GAD and Healthy Controls

Consistent with previous research, an equivalence interval (δ) was set at 20% (90% confident interval) of the pure GAD group (Rogers et al., 1993). Based on comparison among the two GAD groups, statistical non-equivalence in global impairment (C-GAS) was found. The clinical groups were comparable however in terms of GAD severity (CSRs). For child-reported adaptive functioning, statistical non-equivalence between the two GAD groups across all four domains was found. Similarly, both GAD groups demonstrated statistical non-equivalence with healthy children across each domain. Results are presented in Table 3.

Discussion

To date, evidence of functional impairment in childhood GAD has mainly been derived from research conducted among heterogeneous samples of anxious youth. Remaining question as to whether GAD constitutes a distinct clinical disorder a full 15 years after the publication of DSM-IV underscores the need to understand whether and how functioning is impaired in this population. In the current study, children with pure versus comorbid GAD were compared based on clinician-rated severity and impairment. Controlling for differences in age and sex, a statistical difference (as well as non-equivalence) were found for clinician-rated of impairment, though both GAD groups fell in the ‘variable functioning’ range. In light of the linear relationship between number of diagnoses and impairment, the direction of this finding is expected. The groups did not differ (and were found to be equivalent) however in terms of overall GAD severity. Collectively, these findings suggest a childhood GAD diagnosis to be independently associated with impairment in global functioning that is not wholly attributable to comorbid psychopathology or severity of GAD symptoms.

In comparison to healthy control children, both GAD groups reported significantly less adaptive family relationships but did not differ from one another. Functioning in home duties/self-care also was significantly lower in the comorbid group compared to controls,

whereas the pure GAD group did not differ from either group. Although differences in school or peer-based functioning were non-significant, non-equivalence was found across all groups for each of the four life domains examined. Whereas null hypothesis testing examines whether differences between groups are large enough such that the groups can be considered different, equivalence testing is interested in “the minimum difference between two groups that would be important enough to make the groups non-equivalent” (Rogers et al., 1993; p. 554). Thus, while detection of significant differences may have been limited by the small sample size, results suggest that the three groups should not be considered comparable in adaptive functioning.

A considerable portion (42%) of children with GAD did not meet criteria for a secondary disorder. Interestingly, these children were significantly more likely to be male and were one year younger on average than children with comorbid GAD. One interpretation of these findings is that pure GAD might reflect an earlier developmental phase of the disorder characterized by similar symptoms but lesser interference. From this view, conceptualizations of GAD as a prodromal versus clinical condition would not necessarily be mutually exclusive since the disorder may be distinguished by features that both cause distress and impairment in the short-term and harbor risk for other psychopathology over time. Prospective studies that follow the functional trajectories of children with GAD are needed in order to adequately evaluate this possibility.

Several methodological issues are noteworthy in considering the current study’s findings. First, in combination with an explicit focus on GAD, a relatively narrow age range of children was examined. Fewer data are available describing the functional impact of pre-adolescent anxiety disorders and deficits are likely to change across development due to changing academic, social, and family expectations. Non-significant group differences in school functioning, for example, may relate to stage of development. On the other hand, specific features of the disorder may be somewhat protective in this domain. School-based worry is among the most prevalent in children with GAD (Layne et al., 2009) and could aid academic performance for many youth. This interpretation merges with other findings wherein children with pure GAD did not differ from controls on a number of school-based measures (Mychailyszyn et al., 2010). In both studies however, the relatively small number of children with pure GAD children preclude any definite conclusions.

The current study is also unique in its investigation of functioning from the child’s perspective. While non-equivalence across all three groups was found for each functional domain, both GAD groups endorsed family relationships that were statistically less adaptive than controls. This finding notably converges with a growing literature highlighting the role of the early family environment in GAD. For example, a negative family environment in childhood has been shown to predict GAD in adulthood (Beesdo, Pine, Lieb & Wittchen, 2010; Moffitt et al., 2007). Manassis and Hood (1998) also found an adverse family environment to predict lower levels of functioning in children with GAD. Further examination of family factors in this population therefore appears merited.

A number of limitations also are noteworthy. Both clinical and research participants were included in this study and results may not therefore generalize to either purely clinical or

community samples. A small sample size limited the power of statistical tests and may in part explain some non-significant results. Based on the preliminary nature of these findings, statistical control for number of comparisons was not used. Additionally, functioning was not examined directly from parental reports. Functioning was examined from the child's perspective using a self-report measure assessing separate domains. Despite a high estimate of reliability in the current sample, the CASAFS was developed among an older age group (12 to 14 years) and its utility in younger children with GAD has not been adequately established. Because validated measures of adaptive functioning in young children are highly limited, this remains a critical direction for future research. Finally, the possibility of biased reports of adaptive functioning among anxious youth (e.g., Weems, Berman, Silverman & Saavedra, 2001) should be considered given evidence of cognitive distortions in this population.

To summarize, findings indicate that children with pure GAD experience global and specific impairments in functioning compared to their healthy peers, though not to the same extent as children with comorbid GAD. Across all impairment/functioning measures, the three groups evidenced non-equivalence. In addition, significant differences emerged for family relationships with all GAD children endorsing less positive relationships than controls. Functioning within the family may therefore represent an important area of clinical focus. Together with age and sex-based differences in the pure GAD group, results provide a basis for future investigation examining how impairment in childhood GAD might change over the course of development and create risk for additional forms of psychopathology.

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Table 1
 Demographic Characteristics of Children with GAD referred for Research versus Clinical Services and Children with Pure and Comorbid GAD and Controls

	GAD Research (n=23)	GAD Clinical (n=18)	Pure GAD ^a (n=17)	Comorbid GAD ^b (n=24)	Control ^c (n=20)
Age in years (M/SD)	8.5(1.5)	8.6(1.6)	8.0(1.5) ^{bc}	9.0(1.5)	9.3(1.3)
Female (n%)	12(52)	12(67)	6(35)	18(75) ^{abc}	10(50)
Race/Ethnicity (n%)					
Caucasian	16(70)	9(50)	10(59)	15(63)	14(70)
African American	2(9)	2(11)	0(0)	4(17)	5(25)
Hispanic	1(4)	1(6)	0(0)	2(8)	0(0)
Asian	1(4)	0	1(6)	0(0)	0(0)
Mixed/Other	3(13)	6(33)	6(35)	3(12)	1(5)
Comorbid Dx (M/SD)	.74(.86)	.89(.83)	0(0)	1.4(.65)	0(0)

Note: Superscripts denote significant group difference at $p < .05$.

Table 2

Means and Standard Deviations for Impairment and Functioning Measures

Measure (M/SD)	PureGAD ^a (n=17)	ComorbidGAD ^b (n=24)	Control ^c (n=20)	F	p	η^2
GAD CSR	5.7(1.0)	6.3(.95)	---	2.41	.13	.06
C-GAS	58.6(4.1)	55.1(3.8)	---	5.95	.02	.15
CASAFS School	17.7(5.1)	18.0(4.2)	19.8(2.8)	1.13	.33	.04
CASAFS Peers	16.3(1.4)	15.7(2.5)	17.5(2.7) ^b	2.75	.07	.10
CASAFS Family	19.1(2.9)	18.9(3.2)	21.2(2.3) ^{a,b}	3.16	.05	.11
CASAFS Home	15.9(3.7)	15.3(3.1)	17.6(3.1) ^b	3.41	.04	.12

Note: Superscripts denote significant group difference at $p < .05$. GAD CSR = GAD Clinical Severity Rating on the Anxiety Disorders Interview Schedule for DSM-IV: Child and Parent version; C-GAS = Children's Global Assessment Scale; CASAFS = Child and Adolescent Social and Adaptive Functioning Scale.

Table 3

Equivalence Testing among Pure and Comorbid GAD Groups and Controls

	EI ($\pm 10\%$)	Pure GAD – Control		Comorbid GAD – Control		Pure GAD – Comorbid GAD		P	η^2
		Lower	Upper	Lower	Upper	Lower	Upper		
GAD CSR	± 0.57	-	-	-	-	-0.49	1.17	.13	.09
C-GAS	± 5.86	-	-	-	-	-1.09	-6.01 ^a	.02	.17
CASAFS School	± 1.77	-0.59	4.53 ^a	-590	3.76 ^a	-2.95	2.18 ^a	.33	.08
CASAFS Peers	± 1.63	-0.18	2.78 ^a	0.44	2.95 ^a	-1.09	1.88 ^a	.07	.11
CASAFS Family	± 1.91	0.37	3.94 ^a	0.45	3.49 ^a	-1.98	1.60 ^a	.05	.17
CASAFS Home	± 1.59	-0.97	3.04 ^a	0.93	4.34 ^a	-0.41	3.61 ^a	.04	.16

Note: Equivalence Intervals (EI) are based on adjusted cell means for the pure GAD group. Superscripts denote non-equivalence. GAD CSR= GAD Clinical Severity Rating on the Anxiety Disorders Interview Schedule for DSM-IV; Child and Parent version; C-GAS=Children’s Global Assessment Scale; CASAFS=Child and Adolescent Social and Adaptive Functioning Scale.