Neuroscience

Functional Impairment Differences among Youth with ADHD: The Role of Comorbid Anxiety and Mood Disorders

Adam M. Reid[1,2,*], Paulo A. Graziano[3], Joseph P. H. McNamara[1,2], Adrian Paneto[4], Gary R. Geffken[1,2]

[1]Division of Medical Psychology, Department of Psychiatry, University of Florida, Gainesville, FL, USA. [2]Department of Clinical and Health Psychology, University of Florida, Gainesville, FL, USA. [3]Center for Children and Families & Department of Psychology, Florida International University, Miami, FL, USA. [4]Psychology and Brain Sciences, Indiana University, Bloomington, IN, USA

The objective of this research was to investigate differences in functional impairment between youth with Attention-Deficit Hyperactivity Disorder (ADHD) and an Anxiety Disorder (ADHD + AD) or a Mood Disorder (ADHD + MD) by comparing average impairment on one clinician-rated (Global Assessment of Functioning) and three parent-rated (Adaptability, Metacognition, and Psychosocial) measures of functional impairment. Participants for this study included 59 youth with 6-17 years of age who were receiving a psychoeducational assessment at a clinic in the Southeastern United States. Results were analyzed using a Multivariate Analysis of Covariance. Overall, youth with ADHD + MD had more functional impairment than youth with ADHD + AD or youth with just solely ADHD. Youth with ADHD + AD did not have significantly worse impairment on three of four archetypes of functional impairment compared to those with solely ADHD. Youth with ADHD + MD represent a unique ADHD cohort that has elevated impairment, highlighting the importance of addressing comorbid mood symptoms in the recommendations given during a psychoeducational assessment for ADHD, as well as adjusting the treatment of youth with ADHD and a comorbid internalizing disorder appropriately. *Journal of Nature and Science, 1(1):e31, 2015.*

Attention | ADHD | Mood | Anxiety | Functional Impairment

Attention-Deficit Hyperactivity Disorder (ADHD) is a prevalent childhood and adolescent psychological disorder, with recent prevalence estimates at 9% in the United States for youth between the ages of eight and 15 years of age (Merkingas et al., 2010), higher than that of Mood Disorders (MD), Conduct Disorder, Anxiety Disorders (AD), and Eating Disorders. ADHD is not only highly prevalent but also globally impairing. ADHD is associated with significant impairment across children's social, cognitive, academic, behavioral, and familial functioning (Mash & Barkley, 2003). Taken together, it is no surprise that ADHD is one of the most economically costly psychological disorders, with annual societal costs of $42.5 billion dollars (Pelham, Foster, & Robb, 2007). However, not all children with ADHD experience similar amounts of impairment. Faraone, Sergeant, Gillberg, & Biederman (2003) reviewed 50 epidemiological studies and found that a substantial number of children (as high as 10% in one national sample) exhibited clinically elevated levels of ADHD symptoms yet were not experiencing severe functional impairment. Hence, identifying which factors contribute to this discrepancy in impairment rates is critical to the clinical care of youth with ADHD in terms of not only contributing to more thorough evidence-based assessments, but also in helping clinicians develop more appropriate targets for treatment.

Investigating the impact of comorbidity status in youth with ADHD has provided some insight into the differences in functional impairment. The most widely studied comorbidity status among youth with ADHD is the presence of another Externalizing Disorder such as Oppositional Defiant Disorder or Conduct Disorder, which co-occurs with ADHD at rates ranging from 30-50% (Biederman, 2005; Spencer, 2006). Not surprisingly, with each addition of a comorbid Externalizing Disorder, youth with ADHD have incrementally worse impairment in terms of school (Larson, Russ, Kahn, & Halfon, 2011) and social functioning (Graziano, Geffken, & McNamara, 2011). For example, children with ADHD and comorbid ODD or CD have more peer problems than children with ADHD alone (Gresham, MacMillan, Bocian, Ward, & Forness, 1998; Hinshaw & Melnick, 1995). The increase in impairment among youth with ADHD and co-occurring ODD or CD is thought to be a result of greater self-regulation difficulties across emotional, behavioral, and cognitive/executive domains (Graziano, et al., 2011; Melnick & Hinshaw, 2000).

Surprisingly, the impact of comorbid internalizing disorders on the functional impairment of youth with ADHD has received much less attention in the literature; despite approximately 25% of children with ADHD exhibiting an Internalizing Disorder (Jarrett & Ollendick, 2008). Emerging research does suggest that the presence of a comorbid MD (ADHD + MD) negatively impacts functional impairment, beyond that of having solely ADHD, across academic (Blackman, Ostrander, & Herman, 2005), social (Greene et al., 1996; Blackman, Ostrander, & Herman, 2005) and daily cognitive functioning (Shear, DelBello, Rosenberg, & Strakowski, 2002; Shear, DelBello, Rosenberg, Jak, & Strakowski, 2004). Youth with ADHD and a comorbid AD (ADHD + AD) also show worse social functioning compared to peers with solely ADHD (Mikami, Ransone, & Calhoun, 2011). However, other research has found that when controlling for ODD symptomology, youth with ADHD + AD do not differ in social functioning compared to peers with solely ADHD (Newcorn et al., 2004). Thus, the impact of a comorbid AD on the functioning of youth with ADHD remains unclear. Most importantly, however, a notable portion of research examining the impact of comorbid Internalizing Disorders in the functioning of youth with ADHD have tended to combine MDs and ADs (e.g., Booster, DuPaul, Eiraldi, & Power, 2010; Carlson & Mann, 2002; Tannock, Schachar, & Logan, 1995).

There are two main reasons for why one may expect differential functional impairment rates among youth with ADHD + MD versus ADHD + AD. First, MD and AD appear to have a differential impact on ADHD treatment. For example, preliminary evidence suggests that comorbid ADs actually improve response to psychological (Buitelaar, Van der Gaag, Swaab-Barneveld & Kuper, 1995) and pharmacological treatment for ADHD (MTA Cooperative Group, 1999b; March et al., 2000), while comorbid MDs hinder response to pharmacological therapy for ADHD (Spencer, Biederman, & Wilens, 1999). Second, the theoretical underpinnings for anxiety and depression differ. For example, Gray's theory (Gray, 1982; Gray, 1987; Depue, Kruass, & Spoont, 1987) postulates that depression is a result of an underactive behavioral activation system (BAS) while anxiety is brought on in part by an overactive behavioral inhibition system (BIS). Along similar lines, the self-regulation profile among MDs and ADs differs such that children with MDs tend to have greater executive functioning deficits and slower processing speed/motoric response compared to children with ADs (Garner, Mrug, Hodgens, & Patternson, 2012). Additionally, symptoms of anxiety in children with ADHD minimize the effects of impulsivity (Schatz & Rostain, 2006). Given the significant differences in the underpinnings of MDs versus ADs, as well as treatment response, it is critical to examine whether youth with ADHD + MD versus ADHD + AD experience differential rates of functional impairment.

Conflict of interest: No conflicts declared.
* Corresponding Author. Email: reidam@phhp.ufl.edu

In fact, to our knowledge, only one study by Karustis and colleagues (2000) has directly compared the functional impairment between youth with ADHD + MD versus ADHD + AD. This study found that parent-reported social functioning was worse in youth with a comorbid MD versus those with an AD. Furthermore, within the academic domain, youth with a comorbid MD were reported by parents as having more difficulty completing homework assignments compared to youth with a comorbid AD. Thus, preliminary evidence suggests that youth with ADHD + MD experience more impairment compared to youth with ADHD + AD. However, the scarcity of research studies highlight the need for more research directly comparing ADHD + MD or ADHD + AD in regards to functioning in domains beyond social and academic functioning.

The first aim of our study is to provide the first comprehensive investigation of the impact of a comorbid AD diagnosis on multiple aspects of functional impairment in youth with ADHD. It is hypothesized that despite the addition of the natural impairment associated with an AD, the general ameliorative effects of anxiety on impulsivity reviewed above will reduce impairment to the point that no significant differences will exists between youth with ADHD and ADHD + AD across domains of impairment. Our findings would echo the theoretical research of Schatz and Rostain (2006), as well as the findings on social impairment reported by Newcorn and colleagues (2004). The second aim to be addressed will investigate differences in functional impairment among youth with ADHD, ADHD + AD, and ADHD + MD. Based on limited past research (Karustis et al., 2000), we expected youth with ADHD + MD to display poor functional impairment across domains compared to youth with only ADHD or those with ADHD + AD. The novelty of our study and value to the literature resides in our diversity of measures utilized to capture functional impairment, the strict diagnostic criteria minimizing the number of additional comorbidities in the clinical groups, and the direct comparison of a comorbid AD and MD versus combining these groups.

Investigation of these two aims will provide valuable information regarding the assessment, diagnosis and clinical treatment of youth with ADHD. In terms of psychoeducational assessment, research has identified that parents are least likely to follow through with recommendations to pursue psychological therapy for comorbid symptoms compared to other common recommendations (Dreyer, O'Laughlin, Moore, & Milam, 2010). Beyond understanding the functional impairment that would remain with these unaddressed internalizing symptoms, research that develops a clear profile for how children with ADHD and various internalizing disorder comorbidities are impaired differently would allow for more effective recommendations to be developed and implemented. Impairment is a key component considered when determining a diagnosis, as well as when arguing for the reclassification of a disorder (Cantwell, 1995), and thus this research has important implications for previous research that has argued for a new ADHD subtype specific to comorbid internalizing disorders (Jensen et al., 2001). Regarding implications on treatment recommendations, a recent movement in the literature has put an emphasis on targeting treatment at the primary diagnosis and continuing until secondary symptoms interfere with treatment or become primary (Modular Therapy; Weisz et al., 2012). Following this orientation, research must continue to understand how comorbidities impact functional impairment so that treatment recommendations can target which presenting disorders are causing the most distress, impairment in functioning, or interference with the treatment of the primary disorder.

Methods

Participants and Procedures

Participants for this study included 59 children (75% male) who were recruited while seeking a psychoeduational assessment, who provided assent along with parental consent, and who met DSM-IV diagnostic criteria for ADHD or ADHD with a comorbid MD or AD (see below for diagnostic procedures). The mean age of the participating children was 12 years, 1 month (range: 6 years to 17 years of age). In terms of ethnic composition, the sample was comprised of 69% Caucasian, 17% Hispanic, and 14% African-American. Average combined family income was $65,000-80,000 annually. The majority of the youth in this sample were referred from a psychiatrist (66%), while other major referral sources were from a pediatrician (14%), self-referral (14%) or from another professional (6%). To aid in diagnosis during the assessment, several standard measures were utilized. ADHD diagnosis was assessed through a combination of parent structured interview (C-DISC; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000) and parent and teacher rating scales, as is the standard and recommended practice in the field (Pelham, Fabiano, & Massetti, 2005). The Revised Children's Manifest Anxiety Scale and the Children's Depression Inventory was provided as an objective measure of anxiety and depression, respectively. A dual clinician review procedure (both of whom were blind to study aims) was used to determine diagnostic status, GAF scores, and study eligibility and, where disagreement occurred; a third clinician was consulted who was also blind to the study aim. Disagreement on diagnostic status occurred in only 3% of all diagnoses given at the conclusion of the assessment. Disagreement on GAF scores (discrepancy > 5) occurred in 5% of the sample.

In terms of the diagnostic rates, 33 children had a sole diagnosis of ADHD, 16 had a diagnosis of ADHD + MD (Major Depressive Disorder or Mood Disorder NOS), and 10 had a diagnosis of ADHD + AD (Generalized Anxiety Disorder, Obsessive-Compulsive Disorder, Separation Anxiety Disorder or Panic Disorder). In terms of ADHD subtypes, over half the sample (53%) had a diagnosis of ADHD-Combined Type and most of the remaining sample had a diagnosis of ADHD-Inattentive Type (42%) with a few having a diagnosis of ADHD-Not Otherwise Specified (5%). The percent of the ADHD, ADHD + MD, and ADHD + AD groups with a diagnosis of ADHD-Combined Type was 51%, 56% and 50%, respectively. The lack of youth with an ADHD-Hyperactive-Impulsive Type is not uncommon in research studies with older children (Greene, Beszterczey, Katzenstein, Park, & Goring, 2002). Exclusionary criteria included a diagnosis of Mental Retardation, Autistic Disorder, Oppositional Defiant Disorder, Conduct Disorder, or a psychotic disorder.

In terms of treatment history, 67.8% of the children in our sample were currently taking medications to address their symptoms at the time of consent. Within the pure ADHD group who were on medication (21), 94% percent were on a stimulant and only 17% had an additional medication beyond that of a stimulant. Of the ADHD + MD group who were on medication (13), only 8% were solely on a stimulant medication but 78% were on a stimulant plus an additional medication. The majority of the ADHD + AD group was on medication (8), most commonly a stimulant plus an additional medication or just another medication beyond a stimulant or non-stimulant for ADHD (60%). It appears, therefore, that a large majority of the sample with a comorbid internalizing disorder was prescribed an additional medication to address these symptoms, and a review of individual responses identified a Selective Serotonin Reuptake Inhibitor as the most common medication outside of a stimulant in these two groups. As described below, functional impairment did not differ based off medication status.

Measures

Conners, 3rd Edition (Conners-3)

The Conners-3 (Conners, 2008) was administered to assess youth's current severity level of ADHD symptoms. The parent-report version used in this study is for youth ages 6-18 years and contains 108 items. Each item on the Conners-3 is rated on a four-point scale with respect to the frequency of occurrence (never, occasionally, often, and very often). The measure yields t-scores on internalizing, hyperactivity/impulsivity, learning problems, executive functioning, defiance/aggression, and peer relations as well as DSM-IV-TR symptom scales. The Conners-3 has

Table 1. Descriptive statistics

	N	Minimum	Maximum	Mean	Std. Deviation	Z Statistic	
						Skewness	Kurtosis
Inattentive[a]	59	52.00	104.00	76.44	12.91	.527	.974
Hyperactive/Impulsive[b]	59	40.00	121.00	72.29	18.18	.961	.507
GAF[c]	59	40.00	80.00	59.92	8.49	.582	.080
Adaptability[d]	59	20.00	65.00	42.09	11.00	1.15	.600
Psychosocial[e]	59	31.67	96.67	64.85	17.56	.524	1.78
Metacognition[f]	59	44.00	89.00	68.85	10.57	.466	1.79

Note: Significant Skewness or Kurtosis is indicated by a Z statisitic greater than 1.96. [a] Conners-3 ADHD-Inattentive Type, [b] Conners-3 ADHD-Hyperactive/Impulsive Type, [c]Global Assessment of Functioning, [d] BASC-2 Adaptability, [e]PEDSQL Psychosocial, [f] BRIEF Metacognition

well-established internal consistency, reliability and validity (Conners, 2008). For the purpose of the present study, the inattention (α = .83 in this sample) and hyperactivity/impulsivity (α = .86 in this sample) t-scores were used to measure severity of ADHD symptoms. For the Conners-3, higher t-scores reflect increased ADHD severity.

Global Assessment of Functioning (GAF)

The GAF score is a clinician-rated item that uses a one to 100 point scale where every ten points represents a range of functioning generally seen in individuals with certain types of symptoms. Higher scores on this rating scale represent better levels of functioning. For example, 61-70 reflects "mild symptoms," 51-60 indicates "moderate symptoms" and 41 to 50 represents "serious symptoms" (American Psychiatric Association, 2000). The GAF score is reliable for analyzing group-level differences in functioning (Söderberg, Tungström & Armelius, 2005). In order to aid in interpretation, GAF scores were converted to *z*-scores for correlational and mean comparison analyses.

Behavior Rating Inventory of Executive Functioning (BRIEF)

The BRIEF (Gioia, Isquith, Guy, & Kenworthy, 2000) was administered to assess youth's executive functioning, specifically their cognitive self-management and problem solving abilities captured by the Metacognition scale of the BRIEF. The Behavioral Regulation scale was not included in this analysis due to its inherent overlap with ADHD symptomology that is already captured with the Conners-3 (McCandless & O'Laughlin, 2007). The parent-report version of the BRIEF is an 86-item survey for youth ages 5-18 years of age that asks parents to rate the frequency that their child displays certain behaviors (e.g., "Cannot stay on the same topic when talking"). The BRIEF has well-established internal consistency, reliability and validity in both community and clinical samples (Gioia et al., 2000; Gioia, Isquith, Retzlaff, & Espy, 2002). The Metacognition scale of the BRIEF collected for this study echoed the findings of these larger community and clinical samples, with a Cronbach's alpha of .74 in this sample. In this study, the BRIEF was reversed scored, which means that lower scores reflect more impairment in Metacognition. This was done so that the BRIEF was consistent with other functional impairment measures.

Behavior Assessment System for Children, 2nd Edition (BASC-2)

The BASC-2 (Reynolds & Kamphaus, 2004) is a widely used multidimensional assessment that was administered to measure youth's behavioral functioning. The parent-report version used for this study is for youth ages 6-21 and contains 148 items; each is rated on a four-point scale with respect to the frequency of occurrence (never, sometimes, often, and almost always). The Adaptability subscale of the BASC-2 was used in this study to assess how youth handle unpredictable changes in their environment, such as adjusting to a new teacher at school. The BASC-2 has well-established psychometric properties, such as internal consistency, convergent validity, etc. (Reynolds & Kamphaus, 2004). Internal consistency for the Adaptability subscale in this study was .79 in this sample. Similar to the BRIEF, the BASC-2 provides a nationally normed T-Score for each child in this study that inherently controls for the increase likelihood of depressive symptoms in adolescents. For the BASC-2, lower scores represent more impairment in adaptability.

Pediatric Quality of Life Inventory, Version 4.0 (PEDSQL)

The PEDSQL (Varni, Seid, & Rode, 1999) was administered to assess youth's quality of life, specifically emotional (five items), social (five items) and school functioning (five items) that is captured by the Psychosocial subscale used in this study. Items are rated on a 5-point scale and lower scores on the PEDSQL indicate more impairment in psychosocial functioning. Developed from focus groups, cognitive interviews, and pilot testing, the 23-item, parent-report PEDSQL has displayed strong reliability and validity in both healthy and patient populations (Varni, Burwinkle, Seid, & Skarr, 2003; Varni, Seid, & Kurtin, 2001). For this study, strong internal consistency was observed for the Psychosocial scale (α =.87 in this sample). In order to aid in interpretation, Psychosocial scores were converted to *z*-scores for correlational and mean comparison analyses.

Data Analytic Strategy

All data analyses were conducted using the Statistical Package for the Social Sciences, version 19.0 and 20.0 (SPSS 19.0/ 20.0). For the measures used, there was no missing data for the clinician-rated GAF scores and no more than 2% missing for any of the parent-report measures per participant. Multiple Imputation with 10 iterations was conducted, which is sufficient to accurately estimate the data for this sample size (Rubin, 1987). First, preliminary analyses were conducted to examine the normative distribution of each variable and to examine whether there were any statistically significant associations between demographic variables (i.e., sex, age, race, family income, drug status) and our functional impairment variables. Second, we conducted intercorrelations to examine the associations between the severity of children's ADHD symptoms and the functional outcome variables. Finally, for our primary analyses, a Multivariate analysis of covariance (MANCOVA) was conducted. Our functional outcome measures (GAF, Metacognition, Adaptability, and Psychosocial scores) were entered as dependent variables and diagnosis status (ADHD, ADHD + AD, or ADHD + MD) was entered as the independent variable. ADHD symptom severity for hyperactivity/impulsivity and inattentiveness, as captured by the two symptom scales of the Conners-3, were entered as covariates to control for differences in ADHD severity. While Hummel and Sligo (1971) suggest that a MANCOVA "protects" additional analyses from family-wise error, this study utilized the more conservative approach (Bray & Maxwell, 1982) and thus each post-hoc analysis was conducted using a Bonferroni correction.

Results

Descriptive statistics for the study variables, including evidence of normality, are presented in Table 1. Test of normality for every study variable in each cohort is reported in Table 2 supports the reliability of these variables in the various sample sizes in each cohort. Preliminary analyses indicated that youth's gender was significantly related to GAF scores (r = -.258, p < .05), indicating

Table 2. Correlations among variables

Variable	1	2	3	4	5	6
Inattentive[a]		-				
Hyperactive/Impulsive[b]	.581**	-				
GAF[c]	-.218	-.264*	-			
Adaptability[d]	-.239^{+}	-.443**	.419**	-		
Psychosocial[e]	-.379**	-.412**	.330*	.648***	-	
Metacognition[f]	-.642***	-.504***	.362**	.523***	.628***	-

Note: All correlations controlled for gender. [a] Conners-3 ADHD-Inattentive Type *T*-score, [b] Conners-3 ADHD-Hyperactive/Impulsive Type *T*-score, [c]Global Assessment of Functioning *Z*-score, [d] BASC-2 Adaptability *T*-score, [e]PEDSQL Psychosocial *Z*-score, [f] BRIEF Metacognition *T*-score. $^{+}p < .08$. *$p < .05$. **$p < .01$. ***$p < .001$.

Table 3. Summary of results comparing comorbidity groups

	Pure ADHD[a]	ADHD+ AD[b]	ADHD+ MD[c]	*p* Value
GAF[a]	.366 (.144)	.264 (.261)	-.920 (.205)	1.000^{ab}, $.000^{ac}$, $.002^{bc}$
Adaptability[b]	48.570 (1.222)	38.168 (2.226)	31.157 (1.745)	$.001^{ab}$, $.000^{ac}$, $.046^{bc}$
Psychosocial[c]	.342 (.142)	.156 (.259)	-.803 (.203)	$.897^{ab}$, $.000^{ac}$, $.015^{bc}$
Metacognition[d]	34.250 (1.430)	32.911 (2.605)	23.665 (2.043)	1.000^{ab}, $.000^{ac}$, $.020^{bc}$

Note. Values enclosed in parentheses represent standard errors. AD = co-occurring Anxiety Disorder, MD = co-occurring Mood Disorder. [a] Global Assessment of Functioning *Z*-score, [b] BASC-2 Adaptability *T*-score, [c] PEDSQL Psychosocial *Z*-score, [d] BRIEF Metacognition *T*-score. *p*-values are reported for contrast tests between comorbidity groups (e.g., [ab] = comparison of Pure ADHD and ADHD + AD groups)

that males had worse clinician rated global functioning than females. Similarly, gender was significantly associated with Adaptability ($r = -.276$, $p < .05$), such that males were rated as having poor adaptability. No other significant associations between demographic characteristics and any of the functional impairment measures were found. Additionally, no significant differences across the functional impairment variables were observed in terms of medication group status ($F(4, 42) = 1.54$, $p = .094$). Therefore, only gender was controlled in all subsequent analyses. Hotelling's Trace Multivariate F-Test for the interaction between comorbidity status and ADHD subtype was non-significant ($p < .067$). While non-significant across impairment measures, an interaction between a MD comorbidity and ADHD-Inattentive Type appeared to be trending.

Associations Among Variables

Partial correlations after controlling for gender are presented in Table 3. Both ADHD symptom clusters (inattention and hyperactivity/impulsivity) were significantly associated with the four domains of functional impairment, with the exception of inattention and GAF scores. Specifically, youth with more severe ADHD symptomology had worse clinician rated global functioning (with the exception of inattention symptoms), adaptability, psychosocial functioning and metacognition. These finds are generally congruent with previous literature and support the need to control for ADHD severity when investigating ADHD comorbidity group differences in functional impairment. It should also be noted that all four domains of functional impairment were significantly positively correlated, supporting the notion that these four scales are reflective of functional impairment.

Categorical Analysis: Functional Impairment

Descriptive statistics for the comorbidity groups status (i.e., ADHD, ADHD + MD, or ADHD + AD) were compared and revealed no significant differences between the groups in terms of children's race, age, gender, or family income. Chi-square analyses also indicated no significant differences in terms of children's medication status and comorbidity group membership ($\chi^2 = 1.95$, $p = .375$).

A MANCOVA was then conducted to investigate whether functional impairment measures differ according to comorbidity status. Functional impairment measures included a global clinician assessment of functioning (GAF) as well as domain specific measures: assessing impairment in ability to adjust in new circumstances (Adaptability), impairment in social, emotional and school functioning (Psychosocial), as well as cognitive functioning (Metacognition). The MANCOVA was significant ($F(8, 100) = 11.68$, $p < .001$, Cohen's $d = .483$), with follow-up ANCOVAs also significant for each domain of functional impairment: GAF ($F(2, 54) = 17.75$, $p < .001$, Cohen's $d = .336$, observed power = .997), Adaptability ($F(2, 54) = 33.68$, $p < .001$, Cohen's $d = .555$, observed power = 1.00), Psychosocial ($F(2, 54) = 6.814$, $p < .001$, Cohen's $d = .284$, observed power = .986), and Metacognition ($F(2, 54) = 9.14$, $p < .001$, Cohen's $d = .253$, observed power = .969).

As seen in Table 3, follow-up contrast tests, using Bonferroni's correction to control for Type I error rate, revealed that across all four measures of functional impairment, only one significant difference occurred between youth with solely ADHD and youth with ADHD + AD. The one exception being on the Adaptability index, where youth with solely ADHD functioned over a standard deviation better then youth with ADHD + AD ($p < .001$). However, youth with solely ADHD *consistently* functioned better than youth with ADHD + MD. Youth with solely ADHD had significantly higher global functioning than their peers with ADHD + MD as measured via the GAF score ($p < .001$). The difference observed in GAF scores was over 10 points, a clinically relevant discrepancy (American Psychiatric Association, 2000). After being converted to a z-score, this discrepancy was over a standard deviation in magnitude. The direction of this finding was echoed across the parent rated Psychosocial ($p < .001$), Adaptability ($p < .001$) and Metacognition scores ($p < .001$), where youth with ADHD + MD functioned one to two standard deviations worse than their ADHD peers.

Lastly, youth with ADHD + MD generally functioned worse than youth with ADHD + AD. On clinician-rated GAF scores, youth with ADHD + MD were rated an average of 10 points lower than youth with ADHD +AD ($p < .01$), indicative of "some difficulty" in functioning compared to "moderate impairment" (American Psychiatric Association, 2000). After being converted to a z-score, this discrepancy was over a standard deviation in magnitude. Similarly, parents reported that youth with an ADHD + AD diagnosis had an average of seven *T*-score points higher than youth with ADHD + MD on Adaptability ($p < .05$). While less than a standard deviation difference, this finding is notable since Adaptability was the one aspect of functioning where youth with ADHD + AD scored significantly lower than youth with solely ADHD. As with Adaptability ratings, parents rated youth with ADHD + MD almost one standard deviation lower on Psychosocial functioning ($p < .05$) and Metacognition ($p < .05$) than youth with ADHD + AD.

Discussion

Overall, our study demonstrates that youth who have ADHD + MD have more functional impairment than youth with ADHD + AD or youth with solely ADHD. Three out of four archetypes of functional impairment displayed this discrepancy, observed as a "V" pattern in Figure 1. The "V" pattern was observed because, with the exception of Adaptability, youth with ADHD + AD had similar levels of impairment to those with just a diagnosis of ADHD, while youth with ADHD + MD consistently had significantly lower functional impairment. In most cases, this discrepancy between youth with a comorbid MD and the other two diagnostic groups reflected at least a one standard deviation difference, suggesting not only statistical but also clinical significance.

The findings of the present study echo previous literature that has found elevated functional impairment in children with ADHD + MD (Biederman et al., 2002; Greene et al., 1996; Shear, DelBello, Rosenberg, & Strakowski, 2002; Shear, DelBello, Rosenberg, Jak, & Strakowski, 2004). To the best of our knowledge, this research stands only with Karustis and colleagues (2000) in its empirical evidence suggesting that children with ADHD + MD have worse functional impairment than children with ADHD + AD. Further, these findings extend the literature by capturing this discrepancy in multiple domains of functioning and separating ADs and MDs, rather than combining into one construct. Specifically, we found that youth with ADHD + MD present with less ability to handle unpredictable changes in their environment (Adaptability), worse social, emotional, and school quality of life (PsychoSocial), and hindered cognitive self-management and problem solving abilities (Metacognition) compared to peers with solely ADHD or ADHD + AD.

One possible explanation for the discrepancy in functioning observed stems from the differences in temperament for ADs and MDs that impacts how youth with these disorders interact with their environment. Gray's (Gray, 1982; Gray, 1987; Depue, Kruass, & Spoont, 1987; Garner, Mrug, Hodgens, & Patternson, 2012) seminal work describing the reward and punishment sensitivities of ADs and MDs may provide a theoretical basis for the results observed in this study. Specifically, the underactive motivation to seek reward (behavioral activation) associated with a MD may contribute to youth with ADHD + MD's lower levels of positive affect and motivation to comply with environmental demands (e.g., classroom rules). Thus, a decreased behavioral activation system may also result in less behavioral regulation and subsequently elevated functional impairment. However, an overactive fear of punishment (behavioral inhibition) associated with an AD may contribute to youth with ADHD + AD being hyper-vigilant and less sensation seeking. Such a behavioral profile likely contributes to a more compliant youth, who is motivated to comply with environmental demands out of fear of punishment. In fact, the attenuating effect of anxiety on ADHD symptoms has been documented in the literature for over twenty years (e.g., Pliszka, 1989). For example, Schatz and Rostain (2006) conducted a review that concluded that comorbid anxiety in ADHD may inhibit impulsivity while making inattention symptoms worse. While not directly collecting data on functional impairment, it could be posited that this decrease in impulsivity and increase in inattentiveness as a result of comorbid anxiety may result in no overall change in functioning from that caused by solely having ADHD. Alternatively, it could be argued that impulsivity is the major factor associated with youth with ADHD's functional impairment, (e.g., social impairment, appropriate behavior) while inattention contributes to more specific domains of impairment, such as academic functioning (Gaub & Carlson, 1997; see Milich, Balentine, & Lynam, 2001).

We believe these findings have important implications in the assessment, diagnosis, and treatment of ADHD. Based off the increased impairment displayed in this study and the known high frequency of ADHD + MD presentation (Jarrett & Ollendick, 2008), clinicians conducting psychoeducation assessments for ADHD should appropriately screen for a comorbid MD, utilizing recommended diagnostic techniques for pediatric populations (e.g., Klein, Dougherty, & Olino, 2005). The recommendations given after the psychoeducational assessment should prioritize recommending psychological or psychopharmacological treatment for comorbid MDs and, given the low adherence to recommendations to seek psychological care (Dreyer et al., 2010), we believe it may also be beneficial for clinicians to directly recommend implementation of techniques shown to improve mood, such as behavioral activation (e.g., joining a sports team or after school activity). Beyond appropriate recommendations, we believe these findings revitalize a classification debate that has been ignored in the literature. Approximately a decade ago, some researchers and clinicians argued for the development of an ADHD with Internalizing Disorder subtype (Jensen et al., 2001). While this issue has received little attention since then, our research suggests that an ADHD + MD subtype may be more fitting as demonstrating an impact on functional impairment is one criteria for developing a new diagnostic subtype (Cantwell, 1995). Future research will need to investigate the impact of a comorbid MD on psychological treatment outcome for ADHD, as this is an additional criterion for validating a subtype.

In the treatment outcome literature, ADHD + AD is associated with improved pharmacological and psychological treatment outcome (Buitelaar, Van der Gaag, Swaab-Barneveld & Kuper, 1995;MTA Cooperative Group, 1999b; March et al., 2000), while ADHD + MD is shown to hinder pharmacological treatment response (Spencer, Biederman, & Wilens, 1999). It is plausible that comorbid depression would relate to worse psychological treatment outcome in pediatric ADHD, similar to what has been found in pediatric treatment literature for ADs (e.g., Dunner, 2001), chronic health conditions (e.g., Hassan, Loar, Anderson & Heptulla, 2006), and other impairing illnesses. Thus, a discrepancy likely exists between ADHD + MD and ADHD + AD, both in functional impairment and treatment response, and therefore clinicians treating ADHD also need to appropriately screen for comorbid MD. As argued by components of Modular Therapy (Weisz et al., 2012), treatment like this study is important in order to help clinicians appropriately prioritize which diagnoses should be targeted first in treatment based off resulting distress, impairment in functioning and/or interference with the treatment of a primary disorder. This study suggests that, at least based off impairment, ADHD + MD may require addressing the comorbid MD first whereas a comorbid AD may truly be secondary to ADHD when they present simultaneously.

In terms of limitations, the reliance on predominantly parent-report measures of impairment and utilizing only one measure per domain of functional impairment suggests that it is possible that these findings may be impacted by source variance. Therefore, including teacher and self-report measures of functioning, as well as multiple measures per domain would have strengthened these findings. The cross-sectional aspect of this study is another limitation in our ability to infer, not only the temporal association between comorbidity status and functional impairment, but also its directionality. Future longitudinal studies will be better able to examine whether having a comorbid diagnosis of a MD is a risk factor for the development of worse functioning in youth with ADHD or if it is a consequence of such problems. Another additional limitation of this study is a small sample size. Researchers disagree regarding the sample size needed to obtain reliable MANCOVA results (VanVoorhis & Morgan, 2007). An appropriate sample size was achieved based off frequently used guidelines for MANCOVA (Tabachnick & Fidell, 1996; Kraemer & Thiemann, 1987). It should also be noted that our categorization of MDs only captured Major Depressive Disorder and Depressive Disorder-Not Otherwise Specified. While that latter can capture aspects of mania, the generalization of these findings to youth with Bipolar Disorder cannot be assumed. In addition, we attempted to cover multiple aspects of functional impairment, but we did not have any objective measures of impairment or a measure of youth's academic functioning. Given that academic functioning is a major developmental milestone of youth in school (Scales et al., 2006)

and it is a strong predictor of future functioning (e.g., Strenze, 2007), it will be crucial to examine any differences in the academic performance among children with ADHD + AD vs. ADHD + MD.

Despite these limitations, our study contributes to literature by showing the detrimental impact of a comorbid MD on the functioning of youth with ADHD and the general lack of impact of a comorbid AD on functioning. These findings have important implications in the assessment, classification and treatment of ADHD. Internalizing disorders are very common in children or adolescents with ADHD and this study builds upon the only other study of this nature by Karustis and colleagues in comparing the functioning of ADHD + AD and ADHD + MD (Karustis et al., 2000).

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, DC: Author.

Biederman, J. (2005). Attention-Deficit/Hyperactivity Disorder: A selective overview. *Biological Psychiatry, 57*, 1215-1220.

Biederman, J., Mick, E., Faraone, S. V., Braaten, E., Doyle, A., Spencer, T., …& Johnson, M. A. (2002). Influence of gender on attention deficit hyperactivity disorder in children referred to a psychiatric clinic. *The American Journal of Psychiatry, 159*, 36-42.

Biederman, J., Santangelo, S. L., Faraone, S. V., Kiely, K., Guite, J., Mick, E., … & Perrin, J. (2006). Clinical correlates of enuresis in ADHD and non-ADHD Children. Journal of Child Psychology and Psychiatry, 36, 865-877.

Blackman, G. L., Ostrander, R., & Herman, K. C. (2005). Children with ADHD and Depression: A Multisource, Multimethod Assessment of Clinical, Social, and Academic Functioning. *Journal of Attention Disorders, 8*, 195-207. Booster, G. D., DuPaul, G. J., Eiraldi, R., & Power, T. J. (2010). Functional impairments in children with ADHD: Unique effects of age and comorbid status. *Journal of Attention Disorders, 16* (3), 179-189.

Bray, J. H., Maxwell, S. E. (1982). Analyzing and Interpreting Significant MANOVAs.

Review of Educational Research, 52, 340-367.

Buitelaar, J., Van der Gaag, R., Swaab-Barneveld, H. S., Kuiper, M. (1995). Prediction of clinical response to methylphenidate in children with attention-deficit hyperactivity disorder, 34, 1025-1032.

Cantwell, D. P. (1995). Child psychiatry: introduction and overview. In H. I. Kaplan & B. J. Sadock (Eds.), *Comprehensive Textbook of Psychiatry/VI* (pp. 2151-2154). Baltimore: Williams & Wilkins.

Carlson, C. L., & Mann, M. (2002). Sluggish cognitive tempo predicts a different pattern of impairment in the attention deficit hyperactivity disorder, predominantly inattentive type. *Journal of Clinical Child and Adolescent Psychology, 31*,123–129.

Conners, K. (2008). *Conners 3rd edition* (3rd ed.). Toronto, Canada: Multi-Health Systems.

Depue, R. A., Krauss, S. P., & Spoont, M. R. (1987). A two-dimensional threshold model of seasonal bipolar affective disorder. In D. Magnuson & A. Ohman (Eds.), *Psychopathology: An interactional perspective* (pp. 95-123). San Diego, CA: Academic Press.

Dreyer, A. S., O'Laughlin, L., Moore, J., & Milam, Z. (2010). Parental adherence to clinical recommendations in an ADHD evaluation clinic. *Journal of clinical psychology, 66* (10), 1101-1120.

Dunner, D. L. (2001). Management of anxiety disorders: The added challenge of comorbidity. *Depression and Anxiety, 13* (2), 57-71.

Farone, S. V., Sergeant, J., Gillberg, C., & Biederman, J. (2003). The worldwide prevalence of adhd: Is it an american condition? *World Psychiatry, 2*, 104-113.

Garner, A. A., Mrug, S., Hodgens, B., & Patterson, C. (2012). Do symptoms of sluggish cognitive tempo in children with ADHD symptoms represent comorbid internalizing difficulties? *Journal of Attention Disorders, 16* (6), 1-6.

Gaub, M., & Carlson, C. L. (1997). Behavioral characteristics of DSM–IV ADHD subtypes in a

school-based population. *Journal of Abnormal Child Psychology, 25*, 103–111.

Gioia, G., Isquith, P., Guy, S., & Kenworthy, L. (2000). *BRIEF: Behavior Rating Inventory of Executive Function*. Odessa, FL: Psychological Assessment Resources.

Gioia, G. A., Isquith, P. K., Retzlaff, P. D., & Espy, K. A. (2002c). Confirmatory factor analysis of the Behavior Rating Inventory of Executive Function (BRIEF) in a clinical sample. *Child Neuropsychology, 8*, 249–1257.

Gray, J. A. (1982). The neuropsychology of anxiety: An inquiry into the functions of the septal–hippocampal system. Oxford, England: Oxford University Press.

Gray, J. A. (1987). *The psychology of fear and stress.* Cambridge, England: Cambridge University Press.

Greene, R. W., Beszterczey, S. K., Katzenstein, T., Park, K., & Goring, J. (2002). Are students with ADHD more stressful to teach? Patterns of teacher stress in an elementary school sample. *Journal of Emotional and Behavioral Disorders, 10*, 79-89.

Greene, R. W., Biederman, J., Faraone, S. V., Ouellette, C., Penn, C., & Griffin, S. (1996). Toward a new psychometric definition of social disability in children with attention deficit–hyperactivity disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 35*, 571–578.

Gresham, F., MacMillan, D., Bocian, K., Ward, S., & Forness, S. (1998). Comorbidity of hyperactivity–impulsivity–inattention and conduct problems: Risk factors in social, affective, and academic domains. *Journal of Abnormal Child Psychology, 26*, 393–406.

Graziano, P. A., Geffken, G. R., & McNamara, J. P. (2011). Atypical Behaviors and Comorbid Externalizing Symptoms Equally Predict Children with Attention-Deficit/Hyperactivity Disorder's Social Functioning. *Child Psychiatry and Human Development, 42*, 377-389.

Hassan, K., Loar, R., Anderson, B. J., & Heptulla, R. A. (2006). The role of socioeconomic status, depression, quality of life, and glycemiccontrol in type 1 diabetes mellitus. *The Journal of Pediatrics, 149* (4), 526-531.

Hinshaw, S. & Melnick, S. (1995). Peer relationships in boys with attention-deficit hyperactivity disorder with and without comorbid aggression. *Developmental Psychopathology, 7,* 627-647.

Hummel, T. & Sligo, J. (1971). Empirical comparison of univariate and multivariate analyses. *Psychological Bulletin, 76,* 49-57.

Jarrett, M. A., & Ollendick, T. H. (2008). A conceptual review of the comorbidity of attention-deficit/hyperactivity disorder and anxiety: Implications for future research and practice. *Clinical Psychology Review*, *28*, 1266-1280.

Jensen, P. S., Hinshaw, S. P., Kraemer, H. C., Lenora, N., Newcorn, J. H., Abikoff, H. B., …& Vitiello, B. (2001). ADHD comorbidity findings from the MTA study: comparing comorbid subgroups. *Journal of the American Academy of Child and Adolescent Psychiatry, 40*, 147–158.

Kraemer, H. C., & Thiemann, S. (1987). How many subjects? Statistical power analysis in research. Newbury Park, CA: Sage.

Karustis, J. L., Power, T. J., Rescorla, L. A., Eiraldi, R. B., & Gallagher, P. R. (2000). Anxiety and depression in children with ADHD: Unique associations with academic and social functioning. *Journal of Attention Disorders, 4*, 133-149.

Klein, D. N., Dougherty, L. R., & Olino, T. M. (2005). Toward guidelines for evidence-based assessment of depression in children and adolescents. *Journal of Clinical Child and Adolescent Psychology, 34*, 412-432.

Larson, K., Russ, S. A., Kahn, R. S., & Halfon, N. (2011). Patterns of comorbidity, functioning, and service use for US children with ADHD 2007. *Pediatrics, 127*, 462-470.

Larson, K., Tamm, L., & Gaub, M. (1997). Gender Differences in Children With ADHD, ODD, and Co-Occurring ADHD/ODD Identified in a School Population. *Journal of the American Academy of Child and Adolescent Psychiatry, 36*, 1706-1714.

March, J. S., Swanson, J. M., Arnold, L. E., Hoza, B., Conners, C. K., Hinshaw, S. P., …Pelham, W. E. (2000). Anxiety as a predictor and outcome variable in the multimodal treatment study of children with ADHD (MTA1). *Journal of Abnormal Child Psychology, 28*, 527-541.

Mash, E.J., & Barkley, R.A. (2003). *Child Psychopathology*. New York, NY: Guilford Press.

McChandless, S. & O'Laughlin, L. (2007). The clinical utility of the Behavior Rating

Inventory of Executive Function (BRIEF) in the diagnosis of ADHD. *Journal of Attention Disorders, 10*, 381-389.

Melnick, S. M. & Hinshaw, S. P. (2000). Emotion regulation and parenting in AD/HD and comparison boys: linkages with social behaviors and peer preference. *Journal of Abnormal Child Psychology, 28*, 73-86.

Merikangas, K. R., Jian-Ping, H., Brody, D., Fisher, P. W., Bourdon, K., Koretz, D. S. (2010). Prevalence and Treatment of Mental Disorders Among US Children in the 2001–2004 NHANES. *Pediatrics, 125*, 75-81.

Mikami, A. Y., Ransone, M. L., Calhoundoi, C. D. (2011). Influence of Anxiety on the Social Functioning of Children With and Without ADHD. *Journal of Attention Disorders, 15*, 473-484.

Milich, R., Balentine, A. C., & Lynam, D. R. (2006). ADHD Combined Type and ADHD Predominantly Inattentive Type are distinct and unrelated disorders. *Clinical Psychology: Science and Practice, 8*, 463-488.

MTA Cooperative Group (1999b). Effects of comorbid anxiety disorder, family poverty, session attendance, and community medication on treatment outcome for attention-deficit hyperactivity disorder. *Archives of General Psychiatry, 56*, 1088-1096.

Newcorn, J. H., Miller, S. R., Ivanova, I., Schulz, K. P., Kalmar, J., Marks, D. J., & Halperin, J. M. (2004). Adolescent outcome of ADHD: impact of childhood conduct and anxiety disorders. *CNS Spectrum, 9*, 668-678.

Pelham, W., Fabiano, G., & Massetti, G. (2005) Evidence-Based Assessment of Attention Deficit Hyperactivity Disorder in Children and Adolescents. *Journal of Clinical Child and Adolescent Psychology, 34*, 449-476.

Pelham, W., & Fabiano, G. (2008). Evidence-based psychosocial treatment for attention deficit/hyperactivity disorder: An update. *Journal of Clinical Child and Adolescent Psychology, 37*, 185–214.

Pelham, W. E., Foster, M. E., & Robb, J. A. (2007). The economic impact of attention-deficit/hyperactivity disorder in children and adolescents. *Ambulatory Pediatrics, 7*, 121-131.

Plizska, S. R. (1989). Effect of anxiety on cognition, behavior and stimulant response in ADHD. *Journal of the American Child and Adolescent Psychiatry, 28*, 882-887.

Reynolds, C. R., & Kamphaus, R. W. (2004). *Behavior Assessment System for Children* (2nd ed.). Circle Pines, MN: American Guidance System Publishing.

Rubin, D. B. (1987). *Multiple Imputation for Nonresponse in surveys*. New York, New York: Wiley & Sons.

Scales, P. C., Benson, P. L., Roehlkepartain, E. C, Sesma, A., Jr., & van Dulmen, M. (2006). The role of developmental assets in predicting academic achievement: A longitudinal study. *Journal of Adolescence, 29*, 691–708.

Schatz, D. B., & Rostain, A. L. (2006). ADHD with comorbid anxiety: A review of the current literature. *Journal of Attention Disorders, 10*, 141−149. doi: 10.1177/1087054706286698

Shaffer, D., Fisher, P., Lucas, C., Dulcan, M., & Schwab-Stone, M. (2000). NIMH Diagnostic Interview Schedule for Children Version IV (NIMH DISC-IV): Description, Differences From Previous Versions, and Reliability of Some Common Diagnoses. *Journal of American Academy of Child and Adolescent Psychiatry,* 39, 28-38.

Shear, P. K., DelBello, M. P., Rosenberg, H. L., Jak, A. J., & Strakowski, S. M. (2004, February). Cognitive functioning in manic adolescents with bipolar disorder: contribution of comorbid ADHD. Paper presented at the International Neuropsychological Society, Baltimore, MD.

Shear, P. K., DelBello, M. P., Rosenberg, H. L., & Strakowski, S. M. (2002). Parental reports of executive dysfunction in manic adolescents. *Child Neuropsychology, 8*, 285-295.

Spencer, T. (2006). ADHD and comorbidity in childhood. *Journal of Clinical Psychiatry, 67*, 27-31.

Söderberg, P., Tungström, S., & Armelius, B. Å. (2005). Reliability of Global Assessment of Functioning Ratings Made by Clinical Psychiatric Staff. *Psychiatric Services, 56*, 434-438.

Spencer, T., Biederman, J., & Wilens, T. (1999). Attention-deficit/hyperactivity disorder and comorbidity. *Pediatric Clinics of North America, 46*, 915-927.

Strenze, T. (2007). Intelligence and socioeconomic success: A meta-analytic review of longitudinal research. *Intelligence, 35*, 401–426.

Tabachnick, B. G., Fidell, L. S. (1996). *Using Multivariate Statistics* (3rd ed.). Boston: Allyn & Bacon.

Tannock, R., Schachar, R., & Logan, G. D. (1995). Methylphenidate and cognitive flexibility: Dissociated dose effects on behavior and cognition in hyperactive children. *Journal of Abnormal Child Psychology, 23*, 235-266.

Van Voorhis, C., & Morgan, B.L. (2007). Understanding power and rules of thumb for determining sample sizes. *Tutorials in Quantitative Methods for Psychology, 3*, 43-50.

Varni, J. W., Burwinkle, T. M., Seid, M., & Skarr, D. (2003). The PEDS-QL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. *Ambulatory Pediatrics, 3*, 329–341.

Varni, J. W., Seid, M., & Kurtin, P. S. (2001). The PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. *Medical Care, 39*, 800–812.

Varni, J. W., Seid, M., & Rode, C. A. (1999). The PedsQL: measurement model for the pediatric quality of life inventory. *Medical Care, 37*, 126–139.

Weisz, J. R., Chorpita, B. F., Palinkas, L. A., Schoenwalk, S. K., Miranda, J., Bearman, S. K.,…& Gibbons, R. D. (2012). Testing standard and modular designs for psychotherapy treating depression, anxiety and conduct problems in youth: A randomized effectiveness trial. *Archives of General Psychiatry, 69*, 274.