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Neuropsychological functioning in childhood-onset psychosis and attention-deficit/hyperactivity disorder

Kimberly Brodsky¹, Erik G. Willcutt¹, Deana B. Davalos², and Randal G. Ross³

¹University of Colorado, Boulder, Colorado, USA

²Colorado State University, Colorado, USA

³University of Colorado School of Medicine, Aurora, Colorado, USA

Abstract

Background—Attention-deficit/hyperactivity disorder (ADHD) and childhood-onset psychosis (COP) are chronic, heterogeneous disorders with symptoms that frequently co-occur, but the etiology of their comorbidity is unknown. Studies of each disorder indicate that both ADHD and COP are associated with a range of neuropsychological weaknesses, but few neuropsychological studies have directly compared groups with ADHD and COP.

Methods—Groups with ADHD only (32 F, 48M), COP only (5 F, 5 M), ADHD + COP (9 F, 21 M), and a control group with neither disorder (25 F, 44 M) completed a neuropsychological battery that included measures of verbal working memory, response inhibition, response speed and variability, and selective attention.

Results—All three clinical groups exhibited significantly lower performance versus the control group on all neuropsychological measures, whereas the only significant difference between the clinical groups was a significantly larger weakness in verbal working memory in the groups with COP.

Conclusions—The frequent co-occurrence between COP and ADHD may reflect shared neuropsychological weaknesses that are most pronounced on measures of working memory and response variability.

Keywords

psychosis; schizophrenia; ADHD; neuropsychology; cognition; comorbidity

Correspondence: Erik Willcutt, Department of Psychology and Neuroscience, University of Colorado, Boulder, CO 80309, USA; erik.willcutt@colorado.edu.

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Supporting Information

Additional Supporting Information is provided along with the online version of this article.

Introduction

Attention-deficit/hyperactivity disorder (ADHD) and childhood-onset schizophrenia (COP) are chronic, heterogeneous disorders with symptoms that frequently co-occur. Rates of ADHD are elevated in groups with COP (30 – 80%; Karatekin, White, & Bingham, 2009b; Ross, Heinlein, & Tregellas, 2006) and in the children of adults with schizophrenia (e.g., Keshavan et al., 2008; Ross & Compagnon, 2001), and early attentional dysfunction is associated with increased risk for the later development of psychosis (Cornblatt, Obuchowski, Roberts, Pollack, & Erlenmeyer-Kimling, 1999; Seidman et al., 2010).

Several alternative explanations have been proposed for the association between ADHD and COP (Karatekin, White, et al., 2009b). DSM-IV criteria exclude a diagnosis of ADHD if the symptoms occur exclusively during psychosis (American Psychiatric Association, 1994), tacitly suggesting that any attentional difficulties exhibited by a child with COP are part of the overall pathophysiology of childhood psychosis rather than symptoms of a distinct comorbid condition that may lead to additional impairment. In contrast, alternative models have suggested that individuals who meet criteria for both ADHD and COP either have a more severe subtype of COP (Elman et al., 1998) or represent the extreme end of the continuum of ADHD symptoms (Bellak, 1987). Both of these hypotheses suggest that the subgroup that meets criteria for both disorders is qualitatively distinct from individuals with COP in the absence of ADHD. Finally, a fourth model suggests that COP and ADHD have complex, multifactorial etiologies, with some shared risk factors leading to the co-occurrence of COP and ADHD, whereas other unique risk factors distinguish the disorders (Willcutt, Sonuga-Barke, Nigg, & Sergeant, 2008). To clarify the nature of the relation between ADHD and COP the current study administered a battery of neuropsychological measures to groups with ADHD, COP, ADHD + COP, and a comparison group without ADHD or COP.

Neuropsychological studies of COP and ADHD

Until recently, most neuropsychological theories proposed that mental disorders were attributable to a single core neuropsychological deficit that was necessary and sufficient to account for most or all cases of the disorder. However, a growing literature has challenged these single-deficit models and precipitated a significant reconceptualization of neuropsychological models of COP, ADHD, and other complex disorders (for reviews see Pennington, 2006; Willcutt et al., 2008). Rather than attempting to identify a single primary neuropsychological weakness that is specific to each disorder, more recent neuropsychological models explicitly hypothesize that the neuropsychological correlates of mental disorders include weaknesses in multiple cognitive domains (e.g., McGrath et al., 2011; Sonuga-Barke, Sergeant, Nigg, & Willcutt, 2008). Consistent with this multiple-deficit approach, an extensive literature suggests that COP and ADHD are associated with weaknesses in a wide range of neuropsychological domains, including processing speed and response variability, stimulus detection and vigilance, working memory and other executive functions, and different aspects of motor control (e.g., Karatekin & Asarnow, 1998; Karatekin, Bingham, & White, 2009; Karatekin, White, & Bingham, 2008, 2009a;

Karatekin, White, et al., 2009b; Rhinewine et al., 2005; Willcutt et al., 2012; Willcutt, Pennington, Olson, Chhabildas, & Hulslander, 2005; Willcutt et al., 2008).

Despite hundreds of studies of the neuropsychological correlates of ADHD and COP, to our knowledge groups with ADHD and early-onset psychosis have only been compared directly on neuropsychological measures in two samples of children (Karatekin & Asarnow, 1998; Karatekin, Bingham, et al., 2009; Karatekin et al., 2008; Karatekin, White, et al., 2009a, 2009b) and two samples of adolescents (e.g., Groom, Bates, et al., 2008; Groom, Jackson, et al., 2008; Oie, Rund, & Sundet, 1998; Oie, Sunde, & Rund, 1999; Oie, Sundet, & Rund, 2010; Rund, Zeiner, Sundet, Oie, & Bryhn, 1998). Results of these individual studies and overall meta-analyses of ADHD and COP (Willcutt et al., 2008) tentatively suggest that both disorders may be associated with slower and more variable response speed and some aspects of executive functions. In addition to these shared weaknesses, individuals with ADHD may have a more pronounced weakness in response inhibition than individuals with COP, whereas early-onset psychosis may be more strongly associated with deficits in verbal working memory and selective attention to relevant stimuli in the environment.

The current study

To clarify the relation between ADHD and COP, groups with and without ADHD and COP completed measures of verbal working memory, response inhibition, selective attention, and response speed and variability. Each of these neuropsychological constructs has been consistently shown to be associated with at least one of the disorders, and no studies to date have reported analyses of all of these constructs in the same sample.

All three clinical groups were expected to exhibit significant weaknesses on all neuropsychological measures. Based on previous meta-analyses (e.g., Willcutt et al., 2008), we hypothesized that slower and more variable response speed would emerge as a significant shared weakness in groups with ADHD and COP after the effects of other neuropsychological variables were controlled. In contrast, we hypothesized that multivariate analyses would show that weak response inhibition was uniquely associated with ADHD but not COP, whereas deficits in verbal working memory and selective attention would be associated with COP but not ADHD. Finally, we predicted that the group with ADHD + COP would exhibit the additive combination of the weaknesses observed in the groups with ADHD only and COP only, arguing against models that suggest that the comorbid group is a distinct diagnostic subtype.

Methods and Materials

Participants and procedures

All study procedures were approved by the Institutional Review Boards of the University of Colorado at Boulder and the University of Colorado Medical School. The total sample included 80 children with ADHD only (40% female), 30 children with COP who also met DSM-IV symptom criteria for ADHD (30% female), 10 children with COP without ADHD (50% female), and 69 comparison children without psychosis or ADHD (36% female).

Subjects ranged in age from 7 to 13 years old, and there were no significant group differences in age, gender ratio, or race (Table 1).

Groups with COP with and without ADHD—Subjects were recruited through the Colorado Childhood-onset Schizophrenia Research Program at the University of Colorado School of Medicine (e.g., Ross, Heinlein, Zerbe, & Radant, 2005; Ross et al., 1999). This program is the primary clinic specializing in the assessment and treatment of COP in the Rocky Mountain region, and regularly receives referrals from throughout Colorado and adjacent states. Best estimate diagnosis of COP was made after the *Schedule for Affective Disorders and Schizophrenia for School-age Children - Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997)* was administered to one parent and the child. Criteria for diagnosis were identical to those utilized in adult populations, and previous work has demonstrated that these children are similar to adult-onset cases in symptom presentation, endophenotype presentation, and genetic associations (e.g., Ross et al., 2006; Ross et al., 2005; Ross et al., 1999). Only children who met full criteria for childhood-onset schizophrenia or psychosis, not otherwise specified were included (Table 1).

Best estimate diagnoses of other mental disorders were made in a non-hierarchical fashion after completion of the K-SADS-PL. Therefore, children with COP received diagnoses of ADHD or other mental disorders if they met DSM-IV criteria, including age of onset prior than seven years of age in the case of ADHD. Results indicated that 75% of the children with COP also met criteria for ADHD, a rate of comorbidity is consistent with results in a subset of this sample (Ross et al., 2006) and other recent studies of COP (Karatekin, White, et al., 2009b).

Group with ADHD without COP—The ADHD group was recruited as part of a larger study of DSM-IV ADHD (e.g., Willcutt, 2012). In the first phase of the study the parents and teachers of all children in a randomly selected, representative sample of elementary schools from five school districts in the Denver metropolitan area were invited to complete an initial set of questionnaires (8,250 children were screened). Parent and teacher ratings of DSM-IV ADHD symptoms (Barkley & Murphy, 1998) were combined based on the algorithm from the DSM-IV field trials for the disruptive behavior disorders (Lahey et al., 1994), and a subset of children who met symptom criteria for DSM-IV ADHD were invited to participate in an individual assessment session during which the neuropsychological testing was completed. The primary caregiver then completed the DSM-IV Diagnostic Interview for Children and Adolescents (DICA-IV; Reich, Welner, & Herjanic, 1997) to confirm that the child met full DSM-IV diagnostic criteria for ADHD and did not meet criteria for COP (one participant with two symptoms of COP was excluded from subsequent analyses).

ADHD subtypes—Consistent with the results of a recent meta-analysis of the DSM-IV subtypes of ADHD (Willcutt et al., 2012), the pattern of results on the neuropsychological measures was nearly identical for the predominantly inattentive type (ADHD-I) and the combined type (ADHD-C). Therefore, to simplify interpretation the subtypes were collapsed.

Control group—A comparison group without ADHD or COP was selected from the remainder of the screening sample. The comparison group was matched to the group with ADHD on age, sex, ethnicity, and school. Children in the control group had never received a clinical diagnosis of ADHD or COP and exhibited fewer than three DSM-IV inattention or hyperactivity-impulsivity symptoms.

Exclusion criteria—Potential participants in all groups were excluded from analyses if they had a documented brain injury or neurological disease, a known genetic syndrome, significant uncorrected hearing or visual impairment, or an estimated IQ below 70. A screening interview conducted with parents of participants in the ADHD and control groups assessed whether the participant had received a previous diagnosis of a pervasive developmental disorder (PDD) or had a developmental history of significant PDD symptoms (1 potential participant in the ADHD group). Similarly, participants in the COP group were evaluated using the Autism Diagnostic Instrument and Autism Diagnostic Observation Schedule as part of the full diagnostic assessment. No children in any of the four groups in the current sample met criteria for PDD. Comorbid disorders other than PDD were free to vary in all groups.

Potential confounding variables

Medication—As expected, children with ADHD were more likely than children with COP to have a current prescription for a stimulant medication, whereas children with COP were more likely to be prescribed an atypical antipsychotic medication, anticonvulsant, or mood stabilizer (Table 1). Parents of participants currently taking psychostimulant medication were asked to withhold medication for 24 hours prior to the administration of the neuropsychological measures. In contrast, due to concerns regarding potential disruption to the participant's ongoing treatment, children taking antipsychotic, anticonvulsant, or mood stabilizing medications were not asked to discontinue their medication. Dummy codes for each type of medication were included as covariates, but no results changed when medication status was controlled.

Other comorbidities—To test the potential impact of other comorbid disorders on the results, a range of disorders that frequently co-occur with ADHD or COP were also assessed (Table 2). Dummy codes for each comorbid disorder were initially included as covariates in analyses of the neuropsychological measures, but all were dropped from final models because they did not change the interpretation of any results.

Neuropsychological measures

The neuropsychological measures were completed as part of a more extensive test battery administered by each project. Analyses were restricted to measures of key constructs of interest that were available for participants in all groups. In the ADHD and control samples the study personnel that completed the neuropsychological testing were blind to the child's diagnostic status. Testers for the groups with COP were blind to the child's diagnosis but knew that the child had been referred to the Childhood-onset Schizophrenia Research Program.

Most of the neuropsychological measures are widely-used tasks that have been described in detail previously. Therefore, due to space constraints each measure is described briefly in this section, and all measures are described in detail in online Appendix S1.

Intelligence—Subtests from the *Wechsler Intelligence test for Children, Third Edition* (Wechsler, 1991) were used to estimate Verbal, Performance, and Full Scale IQ.

Working Memory—On the *Sentence Span* task (Siegel & Ryan, 1989) the participant provides the final word for a series of simple sentences read by the examiner (e.g. “I throw the ball up and then it comes...”). After all sentences in a set are completed, the participant is asked to reproduce the words that they provided for each sentence. The primary dependent measure is the number of correct sets.

Response Inhibition—The *Stop-Signal Task* (Logan, Schachar, & Tannock, 1997) is a computerized measure of inhibitory control that provides an estimate of stop-signal reaction time (SSRT), the primary measure of response inhibition in the battery.

Selective Attention—A computerized selective attention task appropriate for children was adapted from tasks that have been shown to be sensitive to schizophrenia in adults (Boucart & Humphreys, 1997; Giersch, Danion, Boucart, Roeser, & Abenheim, 2002; see Appendix S1 for a full description of the task and an example of the task stimuli). Dependent measures were the total proportion of correct responses and mean response time on correct responses.

Response Variability—In addition to the primary dependent variables on the stop-signal and selective attention tasks, the intraindividual standard deviation of reaction times on these tasks were analyzed as measures of response variability.

Data Analysis

Data cleaning and adjustments—The distribution of each variable was assessed for outliers and adjusted if needed following procedures described in previous publications (e.g., Willcutt et al., 2005) and in the Appendix S1. To facilitate comparisons with other studies the summary statistics in Table 3 are based on raw scores, but age-adjusted scores were used for all statistical analyses.

Primary group comparisons—One-way analyses of variance (ANOVA) were conducted to test for differences in neuropsychological performance, and planned post hoc comparisons between groups were completed with Bonferroni correction for multiple testing. If initial analyses revealed significant differences among the groups on a neuropsychological measure, an analysis of covariance was conducted with Full Scale IQ as a covariate to test whether the effect was explained by group differences in Full Scale IQ.

Tests of multiple deficit models—An additional set of analyses was conducted to test whether each disorder was associated with multiple neuropsychological weaknesses. A multiple logistic regression model was fitted in which ADHD diagnostic status was predicted simultaneously by all neuropsychological measures, then a parallel analysis was

run to test which neuropsychological weaknesses independently predicted COP when the effects of the other measures were controlled.

Power—The current sample size provided adequate power to detect medium effect sizes (Cohen, 1988) for comparisons between groups with ADHD only, COP + ADHD, and the control group (Power = .80 if Cohen's $d = .46 - .54$). Power was lower for comparisons between the groups with COP with and without ADHD, but was adequate to detect group differences with large effect sizes (Power = .70 – .79 if $d = .80$).

Results

Group comparisons

Groups with ADHD only, COP only, and ADHD + COP performed worse than the comparison group without ADHD or COP on all neuropsychological measures (Table 3), and these effects remained significant when group differences in Full Scale IQ were covaried. Although the overall profile of neuropsychological weaknesses was similar in the three clinical groups, the groups with COP had significantly more severe weaknesses in working memory than the group with ADHD alone. In contrast, groups with COP with and without ADHD were not significantly different on any measure.

Multiple deficits models of ADHD and COP

Separate multiple logistic regression models were fitted in which all neuropsychological measures were added in a single step as predictors of a diagnosis of ADHD or COP. Both disorders were associated with weaknesses in working memory (COP Wald = 10.9, $P = .001$; ADHD Wald = 6.8, $P = .009$) and response variability (COP Wald = 9.3, $P = .002$; ADHD Wald = 13.8, $P < .0001$) after accounting for the effects of the other neuropsychological measures. In addition, COS was associated with a marginally significant weakness in selective attention (Wald = 4.1, $P = .05$).

Discussion

This is the largest study to compare the neuropsychological correlates of ADHD and COP to date. Groups with ADHD only, COP only, and both ADHD and COP exhibited significant weaknesses in all neuropsychological domains, which included general intelligence, working memory, response inhibition, response speed and variability, and selective attention. These pervasive cognitive weaknesses replicate and extend results of previous studies of ADHD and COP (e.g., Karatekin & Asarnow, 1998; Karatekin et al., 2008; Rhinewine et al., 2005; Willcutt et al., 2012), and provide additional support for multiple-deficit neuropsychological models of each disorder.

Group comparisons revealed surprisingly few differences between groups with ADHD only, COP only, and ADHD + COP. The only significant differences between the three groups were more severe weaknesses in the groups with COP than the group with ADHD alone on the measure of verbal working memory, and even on this task the magnitude of the difference between the ADHD only and control group was also large and significant ($d = 0.95$).

Implications regarding the relation between ADHD and COP

Based on the assumption that ADHD symptoms have a different meaning when they occur as part of COP, DSM-IV criteria preclude the diagnosis of ADHD when symptoms coincide with symptoms of psychosis. However, the finding that the neuropsychological correlates of ADHD are generally similar whether or not the child meets criteria for COP calls into question the validity of this exclusion criterion. Similarly, no significant differences were observed between groups with COP with and without comorbid ADHD, and statistical trends on several measures suggested that the group with COP without ADHD may be slightly more impaired than the group with both COP and ADHD. Although these results must be interpreted with caution due to the small sample with COP alone ($N = 10$), these preliminary findings also do not support the hypothesis that ADHD is a marker for a more severe subgroup within COP.

Instead, the current results most strongly support a multiple-deficit model in which ADHD and COP are complex, heterogeneous disorders that have shared neuropsychological weaknesses that are most pronounced on measures of response variability and working memory. Groups with ADHD and COP were primarily distinguished by a quantitative difference in the severity of a shared weakness in working memory, rather than a qualitative difference in the presence or absence of a specific neuropsychological deficit.

Potential explanations for the limited neuropsychological differences between ADHD and COP

Although we expected to find stronger distinctions between ADHD and COP on the neuropsychological measures, a similar pattern of results was also reported by several previous neuropsychological studies of groups with ADHD and early-onset psychosis. Oie et al. (1999) reported significant differences between ADHD and COP in only 2 of 29 comparisons, and a second study found a difference between a group with adolescent-onset schizophrenia and a group with ADHD on a measure of verbal learning, but not on five other neuropsychological composite measures (Groom, Bates, et al., 2008). Similarly, results from a series of papers by Karatekin and colleagues also suggest that many of the significant differences between COP and ADHD reflect quantitative differences in severity rather than qualitative differences in the specific neuropsychological weaknesses associated with each disorder (Karatekin & Asarnow, 1998; Karatekin, Bingham, et al., 2009; Karatekin et al., 2008).

Several potential explanations may account for the relatively small differences between ADHD and COP on neuropsychological measures. ADHD and COP might be more clearly distinct on measures of neuropsychological domains that were not assessed in the current study. For example, some studies suggest that in comparison to ADHD, weaknesses in other specific aspects of learning, memory, or perceptual sensitivity may be uniquely or more strongly associated with early-onset psychosis (Groom, Bates, et al., 2008; Groom, Jackson, et al., 2008; Karatekin, Bingham, et al., 2009; Karatekin, White, et al., 2009a; Oie & Rund, 1999; Oie et al., 1999; Rund et al., 1998). Future studies could provide a useful extension of the current results and previous literature by administering a more extensive battery of neuropsychological measures to groups with ADHD and COP.

Group differences in trajectories of cognitive development provide a second potential explanation for the relative similarity of the neuropsychological correlates of ADHD and COP in the current sample. Longitudinal studies of brain volume suggest that the developmental trajectory of ADHD is characterized by a developmental lag in cortical maturation, such that initial differences in brain volume between individuals with and without ADHD become less pronounced by the end of adolescence (Shaw et al., 2007). In contrast, COP is characterized by systematic developmental degeneration in prefrontal and temporal cortices and the cerebellum that may be most pronounced during adolescence (Keller et al., 2003; Rapoport & Gogtay, 2008). This pattern is consistent with the results of a 13-year follow-up study of individuals with ADHD and COP who were initially assessed during late childhood (Oie et al., 2010). The ADHD and control groups exhibited similar developmental gains on the cognitive tasks, whereas the group with COP either failed to make gains or declined on raw score measures of verbal learning, cognitive flexibility, and processing speed. Because the current participants are also fairly young (mean age = 10 years), it remains possible that neuropsychological differences between groups with ADHD versus COP may become more pronounced later in adolescence.

Limitations and Directions for Future Research

Differences in measures and procedures—Because data from two different studies were combined for the current analyses, results should be interpreted in light of several procedural differences. Testers of participants in the control group and the group with ADHD only were blind to the child's diagnosis. In contrast, testers for the COP groups were blind to the child's specific diagnosis and the presence or absence of comorbid ADHD, but knew that the participant was referred to the Colorado Childhood-onset Schizophrenia Research Program. In addition, different diagnostic interviews were used to assess symptoms of ADHD in the groups with COP versus the group with ADHD only and the control group, although both measures are widely-used interviews that specifically assess DSM-IV criteria for ADHD.

Sample size—The sample with COP is among the largest that has been included in any published study, and power calculations indicated that the current sample size was adequate to test most primary hypotheses. Nonetheless, a larger sample with COP will be required to test definitively whether the neuropsychological correlates of COP vary as a function of comorbidity with ADHD.

ADHD secondary to COP—Best estimate diagnoses of ADHD and other mental disorders were made in a non-hierarchical fashion, and most children in the group with COP + ADHD had an onset of ADHD symptoms in early childhood prior to their referral for an evaluation of COP. Nonetheless, in the absence of longitudinal data beginning prior to the onset of each disorder, it is difficult to be certain that the onset of the ADHD symptoms was earlier than the emergence of the first symptoms of psychosis.

Medication effects—Parents of children taking psychostimulant medication were asked to withhold medication for 24 hours prior to the study. In contrast, participants taking antipsychotic, mood stabilizing, or anticonvulsant medications were not asked to discontinue

their treatment due to ethical concerns regarding the potential negative impact of any disruption to the medication regimen. Although the overall pattern of results did not change when medication status was controlled, this analysis may not have fully controlled for the impact of different histories of pharmacological interventions across groups. Future studies of medication-naïve samples would provide a useful extension of the current study.

Conclusions

ADHD and COP are complex disorders that are each associated with multiple neuropsychological weaknesses. The current results suggest that covariance between ADHD and COP may primarily reflect shared neuropsychological weaknesses that are most pronounced on measures of working memory and response variability.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Key Points

- Literature suggests that, in children, attention deficit/hyperactivity (ADHD) symptomology is closely tied to schizophrenia, occurring at high frequency in both children with schizophrenia and in children who, based on a parental diagnosis of schizophrenia, are at risk for schizophrenia.
- It is unclear the degree to which neuropsychological deficits seen in childhood-onset schizophrenia overlap with neuropsychological deficits seen in ADHD.
- Children with schizophrenia without ADHD symptomology, children with schizophrenia with ADHD symptomology, and children with ADHD without psychosis showed similar neuropsychological deficits in general intelligence, working memory, response inhibition, response speed and variability, and selective attention.
- The finding that the neuropsychological correlates of ADHD are generally similar whether or not the child meets criteria for childhood-onset psychosis calls into question the validity of DSM-IV and DSM-V exclusion criteria which exclude a co-morbid diagnosis of ADHD in children with chronic psychosis.
- The current results instead support a multiple-deficit model in which ADHD and childhood-onset psychoses are complex, heterogeneous disorders that have shared neuropsychological weaknesses that are most pronounced on measures of response variability and working memory.

Table 1

Descriptive Characteristics

	Control N = 69	ADHD only N = 80	COP only N = 10	COP + ADHD N = 30	F
<i>Demographic characteristics</i>					
Mean age (SD)	M (SD) 10.4 (1.5)	M (SD) 10.1 (1.5)	M (SD) 10.2 (1.8)	M (SD) 10.3 (1.9)	1.9
	N (%)	N (%)	N (%)	N (%)	χ^2
Number of females/males	25/44	32/48	5/5	9/21	1.6
<i>Race</i>					
White	54 (78%)	54 (68%)	7 (70%)	28 (93%)	2.9
African American/Black	15 (22%)	24 (30%)	2 (20%)	2 (7%)	3.4
Asian/Pacific Islander	2 (3%)	2 (3%)	1 (3%)	0 (0%)	0.4
American Indian	0 (0%)	4 (5%)	0 (0%)	0 (0%)	5.6
<i>Clinical Diagnoses</i>					
Schizophrenia	0 (0%) _a	0 (0%) _a	8 (80%) _b	27 (90%) _b	160.5***
Psychosis NOS	0 (0%) _a	0 (0%) _a	2 (20%) _b	3 (10%) _b	22.0***
ADHD Combined Type	0 (0%) _a	46 (58%) _b	0 (0%) _a	16 (53%) _b	66.4***
ADHD Inattentive Type	0 (0%) _a	34 (42%) _b	0 (0%) _a	14 (47%) _b	46.4***
<i>Current medication</i>					
Stimulant	1 (1%) _a	26 (33%) _b	0 (0%) _a	4 (13%) _c	46.2***
Atomoxetine	0 (0%) _a	6 (8%) _b	0 (0%) _{ab}	1 (3%) _{ab}	6.2
Atypical antipsychotic	0 (0%) _a	4 (5%) _a	7 (70%) _b	22 (73%) _b	107.4***
Anticonvulsant	0 (0%) _a	6 (8%) _a	2 (20%) _{ab}	7 (23%) _b	17.7***
Mood stabilizer	0 (0%) _a	2 (2%) _a	1 (10%) _{ab}	5 (17%) _b	15.9***
SSRI	0 (0%) _a	4 (5%) _a	0 (0%) _{ab}	5 (17%) _b	17.5***
Clonidine	0 (0%) _a	0 (0%) _a	3 (30%) _b	4 (13%) _b	32.9***

Note: If the overall omnibus test was significant planned pairwise comparisons were conducted. Groups with no shared subscripts are significantly different ($p < .05$).

* $p < .05$;

** $p < .01$;

100 > d

Table 2

Rates of comorbid disorders in groups with and without ADHD and COP

	Control N = 69	ADHD only N = 80	COP only N = 10	COP + ADHD N = 30	χ^2
<i>Anxiety Disorders</i>					
Specific Phobia	0 (0%) _a	3 (4%) _a	4 (40%) _b	6 (20%) _b	31.5***
Separation Anxiety Disorder	2 (3%) _a	6 (8%) _a	3 (30%) _b	7 (23%) _b	15.4**
Generalized Anxiety Disorder	2 (3%) _a	14 (18%) _b	3 (30%) _b	6 (20%) _b	11.3**
Obsessive Compulsive Disorder	0 (0%) _a	3 (4%) _a	1 (10%) _{ab}	13 (43%) _b	52.7***
<i>Mood Disorders</i>					
Major Depressive Disorder	1 (1%) _a	12 (15%) _b	2 (20%) _b	6 (20%) _b	10.9*
Bipolar Disorder	0 (0%) _a	6 (8%) _b	2 (20%) _b	1 (3%) _{ab}	10.0*
<i>Disruptive Behavior Disorders</i>					
Oppositional Defiant Disorder	3 (4%) _a	40 (50%) _b	2 (20%) _{ab}	17 (57%) _b	44.6***
Conduct Disorder	0 (0%) _a	18 (23%) _b	0 (0%) _{ac}	3 (10%) _c	20.4***
<i>Other Disorders</i>					
Tourette's Disorder	0 (0%) _a	2 (3%) _a	1 (10%) _{ab}	10 (33%) _b	40.4***

Note: If the overall omnibus test was significant planned pairwise comparisons were conducted. Groups with no shared subscripts are significantly different ($p < .05$).

p < .001;

**
p < .01;

*
p < .05

Table 3

Performance of groups with and without ADHD and COP on the neuropsychological battery

	Summary statistics for each group				Effect sizes for pairwise comparisons between groups				
	Control M (SD)	ADHD only M (SD)	COP only M (SD)	COP+ADHD M (SD)	ADHD only vs. Control	COP only vs. Control	COP+ADHD vs. Control	COP only vs. ADHD	COP+ADHD vs. ADHD only
<i>Intelligence</i>									
Verbal IQ	112.5 (13.8)	100.1 (15.8)	93.9 (15.2)	94.6 (17.5)	0.84***	1.33***	1.19***	0.39	0.33
Performance IQ	112.7 (16.8)	97.8 (17.0)	100.0 (12.2)	93.7 (19.7)	0.88***	0.78*	1.07***	0.13	0.23
Full Scale IQ	112.6 (13.7)	99.0 (16.1)	96.4 (10.9)	94.2 (13.8)	0.91***	1.21**	1.34***	0.17	0.31
<i>Sentence Span</i>									
Correct Sets	6.0 (1.9)	4.2 (2.0)	2.7 (1.5)	3.5 (1.9)	0.95***	1.78***	1.32***	0.77*	0.39*
<i>Stop-signal Task</i>									
Stop-signal RT	273 (114)	419 (132)	466 (126)	421 (136)	1.19***	1.53***	1.22***	0.36	0.02
Go Trial RT	679 (100)	717 (97)	736 (110)	745 (99)	0.39***	0.56*	0.66**	0.19	0.29
Go Trial RT SD	155 (57)	238 (61)	254 (59)	224 (61)	1.35***	1.73***	1.19***	0.26	-0.23
<i>Selective Attention</i>									
Proportion correct	.87 (.10)	.77 (.14)	.71 (.08)	.78 (.13)	0.79**	1.64***	0.82***	0.44	-0.07
Response time	1104 (356)	1374 (351)	1317 (247)	1442 (452)	0.76**	0.62*	0.87***	-0.17	0.18
RT SD	482 (292)	804 (468)	985 (432)	1012 (596)	0.85***	1.39***	1.19***	0.40	0.39

Note: The means in the table are based on raw scores, but age-corrected scores were used in all statistical analyses and to calculate effect sizes (Cohen's *d*). Positive effect sizes indicates that the group listed first is more impaired.

* $P < .05$,

** $P < .01$,

*** $P < .001$