Impact of ADHD on the neurocognitive functioning of adolescents with Bipolar Disorder

Julia J. Rucklidge

Department of Psychology, University of Canterbury & Youth Specialty Service, Canterbury District Health Board

Address for corresponding author: Dr. Julia Rucklidge, Department of Psychology, University of Canterbury, Private Bag 4800, Christchurch, New Zealand. Phone: 64 3 364 2987 7959. Fax: 64 3 364 2181. Email: Julia.rucklidge@canterbury.ac.nz.

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Abstract

Background: Pediatric Bipolar Disorder (BD) has been associated with a number of neurocognitive deficits not dissimilar to ADHD. This study compared neuropsychological profiles of 4 groups of adolescents (14-17 years): 41 Normal Controls (NC), 30 ADHD, 12 BD and 12 combined (BD+ADHD). **Methods:** Participants were identified according to a standardized protocol (WASHU-KSADS mood section, K-SADS-PL and Conners Scales) and completed tests of processing speed, memory, executive functioning, set shifting, and inhibition. ADHD adolescents on stimulant medication did not take it on the day. **Results:** After controlling for covariates, the ADHD-only and combined groups were most impaired, including processing and naming speed, working memory, and response inhibition. The ADHD-only group showed specific impairment in naming objects, numbers and letters than the NC and showed greater deficits than the BD-only group on tests of naming speed. The combined group showed greatest deficits in verbal memory and inhibitory control. Other than working memory, there were no differences between the BD-only and NC groups. Removal of BD-NOS did not impact on the results. **Conclusions:** This study failed to find broad neurocognitive deficits in BD-only adolescents. Only those with comorbid ADHD showed cognitive deficits, highlighting the impact ADHD may have on neurocognitive functioning of BD.

Impact of ADHD on the neurocognitive functioning of adolescents with Bipolar Disorder

ADHD is one of the most prevalent and widely studied developmental disorders diagnosed in childhood, characterized by excessive activity, short attention span, and impulsivity (APA, 2000). In contrast, Bipolar Disorder (BD) was considered an adult disorder that rarely had an onset in childhood, and only recently has received attention in the pediatric literature. Modifications of the full criteria for BD have been suggested for children, creating some controversy over the validity of the diagnosis in childhood (Klein et al 1998; McClellan 1998). While efforts have been made to create clearer guidelines for differentiating between ADHD and BD (Geller et al 2002), that three DSM-IV symptoms overlap between ADHD and mania including overtalkativeness, distractibility, and psychomotor agitation (hyperactivity), continues to challenge the process of differential diagnoses. Despite the documented diagnostic dilemmas and uncertainties, many studies have shown that ADHD and BD can co-occur (Biederman et al 1996; Geller et al 1995). However, we know little about how the two compare in domains other than behavior, in particular neurocognitive functioning.

Neurocognitive deficits have been widely implicated and documented in ADHD populations across the various ADHD subtypes (Tannock 1998). Deficits include poor motor control and working memory (Barkley 1997a; Barkley 1997b), difficulties with time perception (Toplak et al 2003), difficulties with inhibiting or delaying behavioral responses (Barkley 1997a; Nigg 1999), and on-going processing and naming speed deficits (Rucklidge and Tannock 2002; Semrud-Clikeman et al 2000).

Much less is known about the cognitive and neuropsychological functioning of children and youth with BD as the predominant focus has been on adult profiles. Prefrontal involvement has been documented for bipolar illness in both post-mortem and imaging studies (al-Mousawi et al 1996; Rajkowska et al 2001). In the adult literature, there is some

evidence of neuropsychological impairments in BD patients, such as episodic, verbal and working memory, spatial and sustained attention, and problem solving (Atre-Vaidya et al 1998; Clark et al 2002; Sweeney et al 2000), poor arithmetic skills (Lagace et al 2003), poor visual and spatial orientation (Atre-Vaidya et al 1998) and impaired executive functioning (Ferrier et al 1999; Ferrier and Thompson 2002).

Studies on neurocognitive functioning in child and adolescent bipolar patients are more mixed. For example, Meyer and colleagues' (2004) prospective study found prior executive functioning deficits (as measured by the Wisconsin Card Sorting Task during adolescence) predicted development of BD in young adulthood, impairment that could not be accounted for by premorbid attentional disturbance; however, the small BD sample made conclusions preliminary. Both Dickstein et al. (2004) and Doyle et al. (2005) found impaired neuropsychological functioning in youth with BD as compared with the matched controls, differences that remained after controlling for ADHD. However, sample sizes of BD-only were small for both studies making it difficult to draw conclusions about the neuropsychological performance of BD-only children. In contrast, McClure et al. (2005), while they documented significant impairment in their pediatric BD sample in verbal learning and memory, post-hoc analyses dividing the BD group into those with and without ADHD revealed that only the BD group with comorbid ADHD had significant impairment.

To date, no direct comparison on neuropsychological functioning between ADHD and BD adolescent patients has been made and their relative impact on cognitive abilities. It was hypothesized that ADHD is likely impacting on the neuropsychological functioning of BD patients.

Method

Participants

The final sample consisted of 95 participants: 41 controls (22 female, 19 male), 30 ADHD

(17 female, 13 male), and 24 Bipolar Disorder of which 12 (5 females, 7 males) were identified with comorbid ADHD and 12 (10 females, 2 males) were not. Participants were aged 14 to 17. Thirty-nine (95.1%) of the control group, 25 (83.3%) of the ADHD group, and 20 (83.3%) of the BD groups were European New Zealanders. Two (4.9%) of the control group, 5 (16.7%) of the ADHD group and 3 (12.5%) of the BD groups identified as Maori. The remaining participants were Other European. The clinical groups were referred through a specialised service that assesses and treats youth with moderate to severe psychiatric disorders. The control group was recruited through advertising at local schools and community resources and received the same clinical evaluation as the clinical groups (see below). Sample characteristics are provided in Tables 1 and 2.

Insert Tables 1 and 2 about here

Diagnostic Protocol for ADHD, BD, and other psychiatric disorders

Semi-structured interviews. Systematic information about current and lifetime disorders was obtained from both the adolescent and parent using the *Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version* (K-SADS-PL; Kaufman et al 1997) in combination with the mood disorder supplement of the *Washington University in St. Louis Kiddie Schedule for Affective Disorders and Schizophrenia* (WASH-U-KSADS; Geller et al 2001). While the KSADS-PL is used widely for diagnosing Axis I disorders in children, the WASH-U-KSADS has an extensive section on BD that addresses the limitations of applying the adult criteria to children. Therefore, all participants were administered the mood section of the WASH-U-KSADS and the behavioral section of the K-SADS-PL in addition to the K-SADS screen, benefiting from the strengths of both interviews. Further, due to the high overlap in symptoms between ADHD and BD, a diagnosis of BD included elation and/or grandiosity. As per the WASH-U-KSADS administration guidelines, informant

discrepancies were addressed by taking positive endorsement of a symptom by either informant as presence of that symptom.

Rating scales. Both the *Child Behavior Checklist* (CBCL; Achenbach 1991) and the *Conners' Rating Scales-Revised* (CRS-R; Conners 1997) were used to assess specifically for ADHD as well as other internalizing and externalizing disorders.

Inclusion criteria for ADHD-only group. 1) the adolescent met DSM-IV-TR criteria for ADHD according to the clinician summary based on the K-SADS-PL parent and adolescent interview, 2) met the clinical cut-offs for the externalising symptoms of ADHD on both the parent form and teacher form (in those cases where the child was consistently attending school) of the Conners' Scales and CBCL in order to ensure pervasiveness across settings, and 3) showed evidence of ADHD symptoms prior to the age of seven established either through a past diagnosis of ADHD or in newer cases, according to parental report and past school report cards. Impairment was confirmed using the K-SADS-PL. A longstanding pattern of ADHD symptoms over time was essential to differentiate it from those participants with BD who displayed ADHD-like symptoms during a manic episode. Three participants were excluded from the ADHD-only group as they met DSM-IV criteria for a depressive disorder, in order to reduce the likelihood of including participants who would later develop BD.

Inclusion criteria for BD-only group. The child met DSM-IV criteria for BD (BD I or BD II) or BD-NOS as defined by NIMH (2001) based on the clinician summary of the WASH-U-KSADS' mood section. A diagnosis of BD-NOS was usually assigned in cases where symptoms of mania were present but the duration of the elated mood was less than four days or consisted of rapid cycling mood. All BD cases showed onset of symptoms post-puberty.

Inclusion criteria for combined (ADHD+BD) group. The child met inclusion criteria for both ADHD and BD.

Exclusion criteria for all groups. Children were excluded from analyses if they had an

estimated IQ below 75 or above 130, using the Block Design and Vocabulary subtests of the Wechsler Adult Intelligence Scale-III (WAIS-III; Wechsler 1997) or the Wechsler Intelligence Scale for Children-III (WISC-III; Wechsler 1991), a combination of subtests commonly used to estimate full scale IQ. Six participants were excluded due to low IQ (4 ADHD, 1 NC, 1 combined) and four normal controls were excluded due to high IQ.

Specific exclusion criteria for controls. History or current complaints of problems in attention, hyperactivity, impulsivity or significant mood disturbances and T-scores below 60 on the attention/ADHD subscales of both the parent and teacher forms of the Conners' and CBCL. These criteria resulted in five controls being excluded.

Measure of Demographic Variables

SES. The *New Zealand Socioeconomic Index of Occupational Status* (NZSEI*;* Davis et al 1997) was used to establish SES ranking for each participant based on parents' occupation. The NZSEI scores range between 10 and 90 (with higher scores indicating higher SES) and is based on 1991 New Zealand census data.

Dependent Measures

Naming and Processing Speed. Five tests of *Rapid Automatized Naming* (RAN; Denckla and Rudel 1974) were selected to assess rapid naming: Letters, Numbers, Colors, Objects, and Colors/Numbers/Letters. This test was used because of its hypothesized association with more effortful semantic naming and its established association with ADHD (Carte et al 1996; Semrud-Clikeman et al 2000). RAN-Letters consists of five lowercase letters repeated 10 times in random sequence, yielding 50 stimuli presented in five rows of ten items on a chart. RAN-Numbers consists of five digits, RAN-Colors consists of five colors and RAN-Objects consists of five objects presented in the same way as RAN-Letters. Finally, RAN-Colors/Letters/Numbers consists of 50 alternating colors, letters and numbers. Total times (in seconds) to name all stimulus items on each chart were the dependent variables.

Number stated correctly, number of omissions, additions, deletions, and errors were also assessed as control variables. The Processing Speed Index, consisting of Symbol Search and Coding subtests of the WISC-III/WAIS-III, was used to assess speed of information processing.

Memory. The short form of the *Wide Range Assessment of Memory and Learning* (WRAML) was administered to obtain a Memory Screening Index (Sheslow and Adams 1990) based on four subtests: Picture Memory, Design Memory, Verbal Learning and Story Memory. Finger Windows, a measure of spatial span, was also administered in order to obtain a Visual Memory Index. Verbal working memory was assessed using the WISC-III/WAIS-III *Freedom from Distractibility/Working Memory Index.* This index consists of Arithmetic and Digit Span in the case of the WISC-III and these two subtests as well as Letter-Number Sequencing for the WAIS-III.

Executive Functioning

Response inhibition (protection from interference). The *Stroop Color and Word test* (Golden 1978) was administered. This test yields four dependent measures converted to T-scores: number of color words named, number of colors named, number of color names that are printed in a discordant color word named, and an interference estimate that measures the ability to suppress a habitual response in favor of an unusual one, taking into account overall naming speed.

Planning and Set-shifting. The computerized version of the Wisconsin Card Sorting Test (WCST), a test designed for individuals aged 6.5-89 years, was administered (Heaton et al 1993). The variables of interest were number of categories achieved, percent perseverative errors, and percent conceptual level responses.

Visual scanning and cognitive flexibility. Color Trails Test (CTT; D'Elia 1996), a variant of the Trail Making Test, was administered. Part I is similar to Trails A except that the

odd-numbered circles have a pink background and the even-numbered circles have a yellow background. Part 2 shows all the numbers from 1 to 25 twice, one with a pink background and one with a yellow background. Scoring is expressed in terms of time in seconds. An interference ratio (ratio of Part 2 minus 1 over Part 1 time scores) is also calculated. Although rare, color errors, number errors, near-misses and prompts were also recorded.

Inhibitory control. The *Conners' Continuous Performance Test* (CPT-II, Connors 2000) was used as a measure of complex cognitive functioning, including attention, visual-motor speed, visual-motor integration, hyperactivity and impulsivity. In brief, the child is required to respond to the computer screen by pressing a space bar for every letter except the letter "X". The computer generates an output of standardized scores of omissions (believed to be related to inattention), commissions (believed to be a measure of impulsivity), reaction time, and variability of reaction time. A confidence index is also provided.

Procedures

This study received ethical approval from the Human Ethics Committee of the University of Canterbury and the Canterbury Ethics Committee. Clinical interviews and testing were conducted in laboratories within a psychology department in a midsized university. Consent and assent forms were reviewed with both parents and adolescents. Questionnaire packages were sent to the adolescents' teachers with the consent of the parents. The interviews were conducted with both the parent and adolescent separately by doctorate-level clinical psychologists who had established interrater reliability through training. All cases were reviewed with the primary investigator, who had received on-site training on the WASH-U-KSADS at Washington State University, and consensus achieved. Further, 10% of the clinical interviews were videoed and reviewed by a second rater to maintain and review reliability of the diagnoses. There was 100% agreement on the diagnoses of ADHD and BD. The adolescent self-report measures and cognitive measures were administered by clinical

psychology graduate students blind to diagnostic status.

Parents of 23 children on stimulant medication (53.3% of the ADHD group and 58.3% of the combined group) were asked *not* to give their child this medication on the morning of testing as stimulant medications can improve the behavior as well as the cognitive functioning of children taking the medication (Berman et al 1999), potentially confounding the results. Confirmation was obtained on the day of testing that the medication had not been administered. Three (10%) of the ADHD group, 10 (83.3%) of the BD group, 6 (50%) of the combined group and none of the controls were taking a medication other than a stimulant (e.g., clonidine, fluoxetine, citalopram, quetiapine, lithium). Of those adolescents *not* taking stimulants, two were taking fluoxetine, one was taking paroxetine, and two were taking lithium. These other medications were not discontinued. None of the BD patients were in a manic episode during testing, established via the clinical interview.

Results

Statistical Analyses

Results were analyzed using SPSS version 13. Multivariate and univariate analyses of variance and covariance were used to examine group differences. Wilks' lambda was used as the overall test of significance. Partial eta squared (η^2) was calculated as an estimate of overall effect size. Specific group differences were examined with post-hoc Bonferroni tests using a *p* value of .05. Chi-square analyses were used for comparisons on dichotomous variables. Effect sizes on post-hoc analyses were calculated using cohen's *d*.

Sample characteristics

There were no group differences in age (F (3, 91) = 1.68, p = .18), SES (F (3, 87) = 2.56, p = .06), ethnicity (χ^2 (6, N = 95) = 6.52, p = .37), and sex distribution (χ^2 (3, N = 95) = 6.17, p = .10). Chi-square analyses were also performed on the distribution of subtypes (i.e., BD-NOS, BD-I, BD-II; inattentive, hyperactive-impulsive, combined) within the BD groups

(χ^2 (2, N = 24) = 4.444, p = .11) and ADHD groups (χ^2 (2, N = 42) = 5.12, p = .08), with no significant differences observed. Group differences were found in estimated IQ (F (3, 91) = 7.87, p < .001) with post-hoc tests revealing the ADHD-only group had a lower IQ than the control group. Given that these group differences approached significance, IQ, age, sex and SES were entered as covariates following the main analyses and these results are embedded in the results and Tables below. However, IQ was not used as a covariate for the WISC/WAIS variables given the obvious confounding issues involved. While a few results were no longer significant using covariates, the overall pattern of results remained the same.

As expected, there were group differences on the Conners' scales and the CBCL scales between the controls and the clinical groups (see Table 1). However, these scales did not reliably differentiate between those with ADHD and those with BD-only, indicating that in cases of BD, a formal interview is necessary to assess the source of attentional problems. No group differences were found in numbers per group attending school (χ^2 (3, N = 95) = 6.61, p = .1), with over 80% school attendance.

Processing speed and speed of naming

Table 3 shows that on the Wechsler scales, the ADHD-only and combined groups showed impaired processing speed as compared with the controls, in particular on Coding, a task that requires quick scanning ability, working memory and mental and physical speed. In contrast, the BD-only group, performed similarly to the controls. On the RAN, the ADHD-only group showing slowed rapid automatized naming as compared with the controls. Furthermore, group differences were found between the ADHD-only and BD-only groups on speed of letter naming and color/number/letter naming. Like the ADHD-only group, the combined group was more impaired in speed of naming colors as compared with the controls. The pattern of results indicates that the ADHD groups (ADHD-only and combined), were slower at processing automatized information and that the BD-only group were not showing

such processing speed deficits. Further, there were no group differences in number of omissions, additions, deletions, and errors across all five naming tests, suggesting slower responses were due to slower retrieval rather than mediated by inaccurate retrieval.

Given the small sample size and low power available to detect group differences, effect sizes (cohen's *d*) were also calculated on the post-hoc analyses and supported group differences found. Effect sizes were deemed large (.8-1.2) between the controls and the combined group and the controls and the ADHD-only group, medium to large (.5-.9) between the ADHD-only group and BD-only group, medium (.4-.5) between the BD-only and combined groups, and small to medium (.2-.5) between the controls and the BD-only group.

Insert Table 3 about here

Memory

Table 4 illustrates the memory abilities of the four groups. While the three clinical groups had lower scores on the Working Memory Index (likely driven largely by the relatively stronger performance of the controls on the Arithmetic subtest), the ADHD-only group was most impaired in working memory abilities showing the lower overall scores, specifically on Digit Span. Further, both the ADHD-only and combined groups showed specific memory deficits as measured by the WRAML. The combined group showed specific difficulties with Story Memory and the ADHD-only group specific problems with Verbal Learning and Picture Memory as compared with controls although these latter group differences were no longer significant after covariates were included. Finally, the BD-only group showed no deficits in memory abilities on the WRAML as compared with the controls. Effect sizes between the groups were similar to those reported above for processing and naming speed.

Insert Table 4 about here

Executive functioning

Table 5 shows the tests of executive functioning. The overall pattern indicates that having both ADHD and BD (i.e., the combined group) increases the likelihood of having the most difficulty across these tasks. While both the ADHD-only and combined groups were slower on the Stroop and on Color Trails II, the combined group also showed deficits in omission errors and had greater variability in performance on the CPT-II as compared with the controls. Again, the BD-only group did not show any significant difficulties on any of the tasks as compared with the controls. Of interest, all groups performed equally well on the WCST, with no group showing specific difficulties with this set-shifting task. On Color Trails, the number of errors per group was examined and no differences were found, suggesting that the slower responses were not due to inaccuracies in the task; however, controlling for IQ eliminated these group differences, questioning whether psychopathology had an impact on performance of mental flexibility. Interference problems were not noted for any group on either the Stroop or on Color Trails, an index that first takes into account overall processing speed. While IQ likely explained group differences between the BD group and ADHD group on Stroop Color, even after controlling for covariates, the ADHD group and combined group were slower on Stroop Word than the BD group.

On those tasks where group differences were found, effect sizes were large (.8-1.2) between the control and combined groups, the controls and the ADHD-only group, the BD-only and combined groups, and the BD-only and ADHD-only groups whereas effect sizes were small (.1-.2) between the BD-only group and controls.

Insert Table 5 about here

Medication effects

While those participants taking stimulants were asked to not take their medication on the day of testing to minimize the effect medication could have on performance, given that it is possible that the overall poorer performance of the ADHD participants could have been due to removal of medication, the ADHD participants were pooled and those taking stimulants (n = 23) were compared with those not taking stimulants (n = 19). Only two group differences emerged: those taking stimulants were slower at naming letters (F (1, 40) = 5.31, $p < .05$), and made less commission errors on the CPT-II (F (1, 40) = 5.79, $p < .05$), indicating removal of stimulant medication was not driving the results.

Further analyses on BD subtypes

As the distribution of BD subtypes was uneven across the two BD groups and given the ongoing controversy over the BD-NOS subtype, analyses were rerun taking out those individuals with BD-NOS. Despite extremely small sample sizes (BD-I/II-only: 10, ADHD+BD-I/II: 5), *all* significant group differences remained, suggesting that uneven distributions of BD-NOS was not driving the differences found. Indeed, the results were even more striking in that the new combined group was more impaired than the original combined group, with some scores falling two standard deviations below the mean (e.g. Coding: 4.20 (2.59)); resulting in significant group differences emerging between the BD-only and combined groups. Further comparisons within the original combined group showed that those individuals with ADHD+BD-NOS are less impaired neurocognitively than those with ADHD+BD I/II. However, these results must be interpreted with caution as the removal of those individuals with BD-NOS created a new confounding problem in that all those with ADHD+BD-I/II were male and 80% (n = 8) of those with BD-I/II-only were female. While

research has shown that ADHD males and females are as impaired neurocognitively (Seidman et al 2005), less is known about the impact of gender on BD.

Exploratory regressions

Regressions were performed to assess the relative impact of ADHD and manic symptoms on neurocognitive performance. The overall indices (Freedom from Distractibility, Processing Speed Index, Confidence Index, Memory Screening Index, Visual Memory Index) were entered as the dependent variables and predictors entered stepwise in the regression. Predictors were maximum number of manic symptoms displayed within the last six months (every BD participant had experienced at least one manic episode during this time period that could be rated) and maximum number of ADHD symptoms reported in the last six months, all as assessed by the K-SADS. To control for Type I error, $p < .01$ was used.

Other than the Memory Screening Index where both manic and ADHD symptoms entered into the equation (F (2, 92) = 11.32, $p < .001$, with ADHD symptoms being the stronger predictor ($\beta = -.32$, $p < .001$), accounting for 9% of variance, as compared with manic symptoms ($\beta = -.22$, $p < .05$), accounting for 4% of variance), for all the other regressions, only ADHD symptomatology entered into the regression equations. For example, entering Processing Speed Index as the dependent variable, R for the regression was significantly different from zero, F (1, 93) = 16.54, $p < .001$, and ADHD symptoms was the only significant predictor ($\beta = -.39$, $p < .001$), accounting for 15% of the variance. Similar amounts of variance were predicted by ADHD symptoms by the other variables. Therefore, while the regressions confirm the MANOVAs showing that ADHD symptoms have a greater impact on neurocognitive functioning than manic symptoms, nevertheless, there is a significant amount of variance in neurocognitive performance that is unaccounted for.

Discussion

This is the first study to directly compare four groups of adolescents on

neurocognitive functioning: controls, ADHD only, BD-only and combined (ADHD+BD). While there are some exceptions, the overall pattern of results indicates that the ADHD groups, regardless of presence/absence of BD, are showing the most difficulties in processing speed, automatized naming speed, memory, and executive functioning. With the exception of overall working memory where the BD-only group performed similarly to the other two clinical groups, the performance of the BD-only group was more closely matched with the controls than the other two clinical groups. The combined group was most impaired on the test of inhibitory control. While the lower IQ of the ADHD group explained some group differences, particularly on the memory tasks, it was unable to account for the majority of group differences. Regressions confirmed the relative impact of ADHD on neurocognitive performance was greater than that of BD. Finally, removal of those with BD-NOS showed that variability in the subtypes of BD did not drive the results; indeed, it revealed that individuals with BD-I/II *and* ADHD represent a subgroup of young people with significant neurocognitive impairment. Overall, these results suggest that while BD individuals may have some slight deficits in neurocognitive functioning, this impairment is increased significantly in the presence of comorbid ADHD.

While these findings are discrepant from those previously reported in the literature (e.g., Dickstein et al 2004; Doyle et al 2005; Meyer et al 2004) in that overall, those with BD-only were largely unimpaired neurocognitively, these other studies did not investigate the relative impact of ADHD. In contrast, these results support the findings of McClure and colleagues (2005), in that the combination of ADHD *and* BD appears to place one at higher risk for neurocognitive deficits across a broad range of functioning. This study also replicated the findings of McClure et al. (2005) showing that the combined group had verbal memory impairment. This current study suggests that presence of ADHD may at least partially account for the neurocognitive deficits identified in bipolar patients and should encourage researchers

in the adult field to consider ADHD in light of these results. These results also confirm previous work that have documented neurocognitive deficits in ADHD samples, specifically working memory (Kaplan et al 1998), slowed processing (Rucklidge and Tannock, 2002), and naming speed deficits (Nigg, 2001).

No group differences were found on the Wisconsin Card Sorting Task, contrary to the findings of problems with set-shifting in the sample reported by Meyer et al. in their longitudinal study. These results support previous reports on ADHD children who have not identified deficits on the WCST (Willcutt et al 2001) although contrary to others where deficits have been identified (Lawrence et al 2004). The fact that the computerized version was administered could have influenced the overall performance and accuracy of the results.

There has been a recent interest in the neurocognitive profiles of children and adolescents with BD. This research suggests caution be taken when assessing the impact of BD on neurocognitive profiles given the high rate of comorbid ADHD in BD samples. While it would be ideal to have some tests that could discriminate between ADHD and BD given the overlap in symptoms presentation, such tests probably do not exist. Even a test designed specifically for identifying ADHD, such as the CPT-II, was unable to reliably distinguish between the ADHD groups and controls, and indeed, in terms of the confidence index, the only group that reached a marginally adequate level was the combined group at 70%. Nevertheless, these results are comparable to a number of studies that have identified limited usefulness of the CPT-II in identified individuals with attentional deficits (McGee et al 2000).

The one test that did show clear patterns of performance was the Stroop with both the ADHD-only and combined groups showing impaired performance. While no group differences emerged on the interference measure, this finding replicates other research (van Mourik et al 2005) showing that ADHD participants do not have impaired interference scores after controlling for naming speed. A more reliable finding is that ADHD participants, with

and without other comorbidities, are impaired in rapid verbal naming (Nigg 2001). However, while this study has clarified the impact ADHD may have on neuropsychological performance of BD patients, further research is required to determine other ways of identifying those BD children at highest risk for poor developmental outcomes.

Limitations and future directions

Despite extensive recruitment, the sample size for the bipolar groups was small increasing the likelihood of both Type I and type II errors. However, the fact that many group differences were found between the combined group and the controls highlights that the severe cognitive deficits lie with individuals with both BD *and* ADHD as opposed to BD-only. Furthermore, the sample described was comparable to others on pediatric BD in terms of diagnostic profiles and high rates of comorbidity with other disorders and indeed, was large enough to allow for direct comparisons. Further, as all participants with BD showed an onset of full manic symptoms post-puberty, the results cannot be generalized to those with a prepubescent-onset of BD. Future research could compare those with prepubertal-onset and adolescent-onset BD to determine whether the phenomenology is similar across these two subgroups. In addition, given that the clinical groups were recruited from a specialized service, the results may not generalize to the wider psychiatric population.

The use of psychotropic medications presented as another limitation. While those on stimulants were asked not to take the medication prior to testing, it was not ethical or indeed feasible given the different half-lives, to require those on mood stabilizers to refrain from taking medication. Medications have been documented to affect cognitive performance (Alessi et al 1994; Manji et al 2000) and it is difficult to determine how they may have impacted the results. Some confidence that the group differences were not due to the removal of the stimulants comes from the overall lack of group differences between those ADHD participants off stimulants for testing and those not taking stimulants to treat ADHD.

There is some controversy regarding the diagnosis of Bipolar Disorder in pediatric samples. Similar to other international studies, BD I, BD II and BD-NOS were included in the BD groups. Some confidence is gained from the fact that removal of the BD-NOS did not alter the pattern of results; however, future research needs to examine the issue of subtypes in greater depth. Comparisons were also not made across the three ADHD subtypes. Finally, while the analyses were rerun controlling for sex and comparable findings were found, studies with larger samples could investigate sex differences and specific sex effects.

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Table Legend

Table 1: Sample characteristics of clinical groups - Psychiatric diagnoses

Table 2: Sample characteristics by group: means and standard deviations

Table 3: Processing Speed by group: means and standard deviations

Table 4: Memory abilities by group: means and standard deviations

Table 5: Executive functioning by group: means and standard deviations

Table 1

Sample characteristics of clinical groups – Psychiatric diagnoses

	ADHD (n = 30)		BD (n = 12)		Combined (n = 12)	
	n	%	n	%	n	%
ADHD – inattentive type	21	70		N/A	4	33.3
ADHD – hyperactive/impulsive	2	6.7			1	8.3
ADHD - combined	7	23.3			7	58.4
BD I		N/A	6	50	3	25
BD II			4	33.3	2	16.7
BD NOS			2	16.7	7	58.4
ODD	13	43.3	2	16.7	8	66.7
CD	6	20	1	8.3	5	41.7
Any anxiety disorder	3	10	4	33.3	1	8.2

Note: ADHD = Attention-Deficit/Hyperactivity Disorder, BD = Bipolar Disorder, NOS = Not otherwise specified, ODD = Oppositional Defiant Disorder, CD = Conduct Disorder

Table 2

Sample characteristics by group: means and standard deviations

Variable	*NC (n=41)*		*ADHD (n=30)*		*BD (n=12)*		*COMB (n=12)*		F	Contrasts[a]
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	(3,91)	
Age	15.52	1.03	15.15	.97	16.02	1.46	15.54	1.64	1.68	
SES	58.18	18.16	46.64	19.03	45.82	25.02	50.0	15.99	2.56	
WISC/WAIS-III (SS)										
Estimated IQ	107.80	11.34	94.47	10.66	101.25	15.72	98.75	10.33	7.87***	NC>ADHD
GAF	85.22	10.04	59.60	10.43	55.50	8.22	53.83	10.09	61.56***	NC>ADHD, BD, COMB
Number of hospitalizations	.24	.54	.57	.82	.50	.68	1.08	.90	4.66**	NC<COMB
Age first identified with mental illness	N/A		10.63	4.49	15.08	1.73	9.25	3.41	8.05***	BD >ADHD, COMB
CBCL (T-scores)										
Internalizing	42.76	9.48	58.17	11.65	71.17	12.53	61.82	16.85	21.08***	NC<ADHD, BD, COMB; ADHD<BD
Externalizing	44.67	9.05	68.96	8.44	61.5	14.61	73.55	14.08	34.04***	NC<ADHD, BD, COMB
Thought problems	50.55	2.99	61.46	9.66	67.0	10.26	70.09	14.12	20.98***	NC<ADHD, BD, COMB; ADHD<COMB
Attention difficulties	50.88	5.48	69.58	6.87	66.17	7.59	69.82	12.70	37.25***	NC<ADHD, BD, COMB
YRF (T-scores)										
Internalizing	42.91	10.30	53.21	8.14	61.33	15.14	54.91	15.91	9.40***	NC<ADHD, BD, COMB
Externalizing	48.48	9.25	61.88	10.02	58.42	13.64	69.91	13.03	13.88***	NC<ADHD, BD, COMB
Thought problems	52.15	4.09	55.08	8.06	54.92	12.34	61.0	13.47	3.01*	NC<COMB
Attention difficulties	52.15	4.62	61.83	8.13	58.5	12.78	66.0	9.90	11.12***	NC<ADHD, COMB
TRF (T-scores)†										
Internalizing	42.33	7.13	57.50	11.21	56.60	7.23	59.57	4.504	11.45***	NC<ADHD, BD, COMB
Externalizing	47.27	14.96	66.81	12.19	57.00	6.595	66.57	10.63	7.17***	NC<ADHD, COMB

Thought problems	50.53	2.07	58.06	8.92	58.0	16.11	63.86	9.70	4.80**	NC<COMB
Attention difficulties	53.13	6.03	62.75	8.49	47.60	8.14	70.43	12.15	9.53***	NC<ADHD, COMB; BD<ADHD, COMB
CPRS-R:L (T-scores)										
DSM-IV inattentive	48.39	8.26	73.29	9.76	72.92	10.99	75.92	11.91	44.04***	NC<ADHD, BD, COMB
DSM-IV H/I	50.67	8.33	78.29	12.16	69.33	16.74	84.17	9.15	39.45***	NC<ADHD, BD, COMB; BD<COMB
CASS-R:L (T-scores)										
DSM-IV inattentive	44.15	9.59	60.83	12.81	60.50	9.56	64.75	15.45	14.73***	NC<ADHD, BD, COMB
DSM-IV H/I	42.55	9.56	54.50	11.26	55.58	13.66	61.42	15.57	9.24***	NC<ADHD, BD, COMB
CTRS-R:L (T-scores)†										
DSM-IV inattentive	52.00	12.36	69.50	16.11	61.50	21.83	77.57	11.00	6.12**	NC<ADHD, COMB
DSM-IV H/I	51.93	8.07	71.06	18.14	62.50	20.88	75.29	14.90	5.80**	NC<ADHD, COMB

Note: [a]Bonferroni, *p<0.05, ***p* < .01, ****p* < .001, †based on smaller sample: NC = 15, ADHD=16, BD = 4, COMB = 7, COMB = ADHD+BD, SES = socio-economic status, GAF = Global Assessment of Functioning, WISC = Wechsler Intelligence Scale for Children, WAIS = Wechsler Adult Intelligence Scale, CPRS-R:L = Conners' Parent Rating Scale-Revised: Long version, CTRS-R:L = Conners' Teacher Rating Scale-Revised: Long version CASS:L = Conners-Wells' Self-report Scale: long version, CBCL = Child Behavior Checklist, TRF = Teacher Rating Form, YRF = Youth Rating Form, H/I = hyperactive/impulsive, DSM = Diagnostic and Statistical Manual of Mental Disorders

Table 3

Processing Speed by group: means and standard deviations

Variable	*NC (41)*		*ADHD (30)*		*BD (n=12)*		*COMB (n=12)*		F	Contrasts[a]	η^2
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	(3,91)		
WISC/WAIS-III											
Processing Speed Index	111.32	16.05	94.03	14.63	100.25	19.47	93.25	15.82	8.31***	NC>ADHD, COMB	.215
Coding	11.32	3.50	7.73	3.35	9.42	3.87	6.92	3.15	8.57***	NC>ADHD, COMB	.220
Symbol Search	12.68	3.18	9.60	3.27	10.50	4.21	10.25	3.25	5.43**	NC>ADHD	.152
RAN (sec)											
Numbers	18.59	2.45	22.50	4.32	19.74	3.48	21.32	4.92	7.24***	NC<ADHD	.193
Letters	18.54	2.74	24.45	6.15	19.80	3.79	21.77	4.67	10.63***	BD, NC<ADHD	.259
Colors	30.33	5.57	37.59	8.69	33.92	7.27	37.43	6.89	7.22***	NC<ADHD, COMB	.192
Objects	32.38	5.14	39.39	7.28	34.32	5.87	37.03	5.42	8.23***	NC<ADHD	.213
Color/Number/Letter	27.17	5.34	34.38	6.73	28.63	5.09	31.77	6.94	8.89***	BD, NC<ADHD	.227

Note: [a]Bonferroni, *p<0.05, ***p* < .01, ****p* < .001, WISC = Wechsler Intelligence Scale for Children, WAIS = Wechsler Adult Intelligence Scale, RAN = Rapid Automatized Naming

Table 4

Memory abilities by group: means and standard deviations

Variable	*NC (41)*		*ADHD (30)*		*BD (n=12)*		*COMB (n=12)*		F	Contrasts[a]	η^2
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	(3,91)		
WISC/WAIS-III											
Working Memory Index/Freedom from Distractibility	106.88	12.87	88.00	13.08	92.67	15.19	92.00	10.51	13.75***	NC>ADHD, BD, COMB	.312
Digit Span	10.29	2.79	7.93	2.91	8.50	3.12	8.75	2.30	4.41**	NC>ADHD	.127
Arithmetic	12.07	3.09	7.73	2.87	9.17	3.83	8.17	2.73	13.25***	NC>ADHD, BD, COMB	.304
WRAML (SS)											
Story Memory	11.22	2.15	9.87	3.18	9.50	2.75	7.42	3.75	6.09***	NC>COMB	.167
Design Memory	10.71	3.52	9.67	3.23	10.00	3.05	8.33	3.94	1.62		.051
Picture Memory	11.51	2.88	9.70	2.26	9.33	3.17	10.25	3.33	3.33*	NC>ADHD[b, c, d]	.099
Verbal Learning	11.59	3.42	9.17	3.27	10.25	2.83	9.17	2.92	3.84*	NC>ADHD[c]	.112
Finger Windows	11.29	2.84	9.97	2.71	10.67	3.17	10.00	2.86	1.48		.047
Memory Screening Index	109.02	14.49	97.50	14.12	98.17	16.97	91.67	17.64	5.97***	NC>ADHD, COMB[c]	.164
Visual Memory Index	107.71	15.87	98.30	15.23	100.17	13.24	98.83	12.19	2.78*		.084

Note: [a]Bonferroni, *p<0.05, **$p < .01$, ***$p < .001$, [b]not significant after controlling for age, [c]not significant after controlling for IQ, [d]not significant after controlling for SES, SS = Standard Scores, WISC = Wechsler Intelligence Scale for Children, WAIS = Wechsler Adult Intelligence Scale, WRAML = Wide Range Assessment of Memory and Learning

Table 5

Executive functioning by group: means and standard deviations

Variable	*NC (41)*		*ADHD (30)*		*BD (n=12)*		*COMB (n=12)*		F	Contrasts[a]	η^2
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	(3,91)		
Stroop (T-scores)											
Word	45.07	5.66	36.87	5.21	45.92	10.72	37.92	5.107	13.02***	NC, BD>ADHD, COMB	.300
Color	45.49	8.64	35.33	5.74	43.08	9.28	36.00	7.68	11.71***	NC>ADHD, COMB; BD>ADHD[b, c, e]	.279
Color-Word	54.24	10.65	43.27	6.49	50.17	10.99	40.42	7.27	11.84***	NC>ADHD, COMB	.281
Interference	57.73	7.41	54.83	5.65	51.75	9.24	51.83	10.18	3.17*		.095
WCST (SS)											
# of categories	5.90	.49	5.70	.88	5.67	1.16	5.75	.62	.58		.019
% perseverative errors	110.78	12.39	107.03	12.45	109.58	15.70	107.67	12.02	.51		.017
% conceptual level responses	111.17	10.87	104.60	12.68	108.75	16.11	106.42	8.05	1.86		.058
Color Trails (sec)											
Trails 1	33.23	9.21	45.86	15.49	41.88	18.41	38.74	10.64	5.69***	NC<ADHD[c]	.158
Trails 2	67.46	17.41	90.46	25.17	77.93	19.60	88.84	22.43	7.96***	NC<ADHD, COMB[c]	.208
Interference	1.10	.47	1.10	.69	.99	.40	1.38	.66	1.09		.035
CPT (T-scores)											
Omissions	48.29	8.16	52.19	9.65	52.45	12.47	61.41	13.83	5.37**	NC, ADHD<COMB	.150
Comissions	51.42	10.10	54.78	11.46	47.90	10.26	55.49	7.05	1.78		.056
Reaction Times	45.03	10.38	48.77	10.98	53.22	13.77	54.15	10.90	3.10*		.093
Task response variability	45.61	12.58	54.28	10.54	53.20	11.79	61.04	10.48	6.85***	NC<COMB	.184
Confidence index (%)	46.11	20.77	56.37	17.98	50.95	26.27	70.11	19.23	4.64**	NC<COMB	.133

Note: [a]Bonferroni, [b]not significant after controlling for age, [c]not significant after controlling for IQ, [e]not significant after controlling for sex, *p<0.05, **$p < .01$, ***$p < .001$, SS = Standard Scores, WCST = Wisconsin Card Sorting Task, CPT = Continuous Performance Task