Psychiatry Research 244 (2016) 223–228

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Impact of psychotic symptoms on cognitive functioning in child and adolescent psychiatric inpatients with severe mood disorders

James B. McCarthy [a,b,*], Shira R. Weiss [c], Kristin T. Segovich [a], Baptiste Barbot [a,d,*]

[a] Pace University, Department of Psychology, New York City, NY, United States
[b] Adelphi University, Garden City, NY, United States
[c] Sagamore Children's Psychiatric Center, Dix Hills, NY, United States
[d] Yale University, Child Study Center, New Haven, CT, United States

ARTICLE INFO

Article history:
Received 9 February 2016
Received in revised form
8 June 2016
Accepted 24 July 2016
Available online 25 July 2016

Keywords:
Psychotic symptoms
Bipolar disorder
Major depression
Cognitive functioning
Mood disorders
Children and adolescents

ABSTRACT

Despite established differences in cognitive functioning of adults with mood disorder-related psychosis and those with non-affective psychotic disorders, there is limited evidence of the impact of psychotic symptoms on the cognitive functioning of children and adolescents with mood disorders. This study investigates IQ, working memory, and processing speed scores in 80 child and adolescent inpatients discharged from an intermediate care state psychiatric hospital, using a retrospective chart review. Associations between diagnosis based on DSM-IV criteria (7 with Major Depression- MDD; 43 with Bipolar Disorders-BD, and 30 with Mood Disorders Not Otherwise Specified-NOS), presence of current psychotic features, and cognitive functioning (WISC-IV IQ, Coding, Symbol Search, and Digit Span) were investigated using Multivariate Analyses of Variance. No differences were found in cognitive functioning between patients with MDD and BD, or between those with severe Mood Disorders (MDD or BD) and those with NOS, when controlling for age, gender, and presence of psychotic features. However, patients with severe mood disorders and psychotic features showed lower IQs and greater working memory deficits than those without psychotic features or NOS. Results are discussed in terms of treatment planning for children and adolescents at risk for developing psychotic symptoms and severe mood disorders.

1. Introduction

Psychotic symptoms are related to the severity of the mood disturbance in children and adolescents with Major Depressive Disorder (MDD) or Bipolar Disorder (BD) (McCarthy and Dobroshi, 2014). Research has shown that the combination of severe mood disturbance (e.g., MDD or BD) and psychotic symptoms in adults is related to deficits in attention (Godard et al., 2012), processing speed, executive functioning, memory (Reichenberg et al., 2009), information processing (Daniel et al., 2013; Sarapas et al., 2012), and poor psychosocial functioning (Godard et al., 2011). In a meta-analysis of studies on the cognitive functioning of adolescents with early-onset BD and schizophrenia, Nieto and Castellanos (2011) reported that both groups of youths had deficits in processing speed, executive control, verbal learning, and memory although the impairments of those with BD were less severe. Although differences in cognitive functioning have been demonstrated between adults with mood disorder-related psychosis and those with non-affective psychotic disorders, those differences have not yet been thoroughly explored in children and adolescents. This study investigated group differences in Full Scale IQ (FSIQ), working memory, and processing speed in child and adolescent psychiatric inpatients with mood disorders (with versus without psychotic features), and child and adolescent psychiatric inpatients with Mood Disorders Not Otherwise Specified (NOS). Given the paucity of research in this area, specific hypotheses regarding cognitive functioning of these groups were partially derived from research on the cognitive functioning on adults with MDD, BD, and their interaction with psychotic features.

1.1. Major depression and cognitive functioning

For adults with MDD, psychotic manifestations of the disorder are associated with executive functioning deficits (Basso and Bornstein, 1999; Hill et al., 2004; Lampe et al., 2003) and attention deficits (DelBello et al., 2003), but not necessarily with mood symptom severity (Caldieraro et al., 2013). For adults with MDD without psychotic features, cognitive deficits seem to be less apparent (Castaneda et al., 2007). Baune et al. (2014) noted that

* Correspondence to: Pace University, Department of Psychology, 41 Park Row, New York, NY 10038, United States.
E-mail addresses: JMcCarthy@Pace.edu (J.B. McCarthy), BBarbot@pace.edu (B. Barbot).

http://dx.doi.org/10.1016/j.psychres.2016.07.049
0165-1781/

symptomatic adolescents and young adults with MDD have worse working memory, executive functioning, processing and psychomotor speed, verbal fluency, and visual memory than controls. A meta-analysis concluded that MDD in youth might negatively impact cognitive maturation, contributing to lower Full Scale IQs (FSIQ) and worse sustained attention, verbal memory, planning ability, verbal fluency, and inhibition capacity (Wagner et al., 2015). However, a recent review did not find evidence of deficits in attention, working memory, and verbal fluency (Vilgis et al., 2015). Hermens et al. (2010) found no significant differences in cognitive functioning between symptomatic depressed 16–32 year olds and those with BD, though both groups had attention and verbal memory deficits. Yet, deficits in attention and concentration have been identified in up to 70% of a community sample of adolescent girls with MDD (Cooper and Goodyer, 1993; Goodyer and Cooper, 1993). MDD has also been associated with processing speed and working memory deficits (Klimkeit et al., 2011; Wilkinson and Goodyer, 2006), which seem to be independent of clinical characteristics (Gu et al., 2016). Investigations of the general intellectual functioning, working memory, and processing speed of children and adolescents with MDD have thus yielded inconsistent results.

1.2. Bipolar disorder and cognitive functioning

There is support for the hypotheses that pediatric BD 1 disrupts cognitive development and that there are associated neuropsychological deficits indicative of prefrontal cortex dysfunction (Bearden et al., 2007) or loss of gray matter in the frontal lobes (Arango et al., 2012). For adults with BD, attention and processing speed deficits appear to be stable over time even when there are significant changes in mood symptoms (Chaves et al., 2011), and cognitive complaints are associated with poor psychosocial functioning (Demant et al., 2015). For children and youth with BD, verbal memory seems to be impaired independent of the severity of the mood symptoms (Glahn et al., 2005), and continuing deficits in executive functioning, working memory, attention, and visual memory have also been detected (Lera-Miguel et al., 2014; Pavuluri et al., 2006). Compared with healthy controls, adolescents with BD have worse working memory (Biederman et al., 2011) and worse processing speed (Udal et al., 2013). For adolescents and adults, visuospatial, verbal memory, and sustained attention deficits appear to be trait features for BD (Cahill et al., 2009). Pavuluri et al. (2006, 2009) similarly suggested that children and adolescents with BD may have cognitive deficits regardless of treatment with medication, and that these vulnerabilities represent characteristic traits of the disorder.

Regardless of whether children or adolescents with BD experience comorbid Attention Deficit Hyperactivity Disorder (ADHD) and Anxiety Disorders (Doyle et al., 2005; Frías et al., 2014), they have more attention, working memory, and processing speed deficits, and lower FSIQs, Vocabulary, Digit Span, Digit Symbol and Coding scores than community controls and might have a greater family history of BD (Kennedy et al., 2005). A meta-analysis of cognitive studies on BD 1 in youth (Joseph et al., 2008) found strong evidence of verbal memory deficits, moderate evidence of attention, visual perceptual ability, memory, and executive functioning deficits with only small differences in FSIQ, motor speed, and reading ability. Horn et al. (2011), similarly noted strong evidence of problems in verbal memory and some evidence of attention and processing speed deficits. McCarthy et al. (2004) reported that youth with BD had significantly lower Performance IQs than those with ADHD, Conduct Disorder, and Oppositional Defiant Disorder. A number of the studies on cognitive functioning of youth with BD have either relied on estimated FSIQs (Singh et al., 2009), or have focused on patients with average or high average FSIQs (Doyle et al., 2005). However, few studies about the FSIQ scores of adolescents with MDD or BD have included patients with very low cognitive functioning (e.g., Han et al., 2011).

1.3. Impact of psychotic features on cognitive functioning in mood disorders

Psychotic symptoms have been clearly associated with severity of cognitive deficits in adults with BD (Martinez-Aran et al., 2008; Nenadic et al., 2015), particularly deficits in attention, verbal learning, memory (Levy and Weiss, 2010), and executive functioning (Levy et al., 2011, 2012)). Although Savitz et al. (2009) found no difference in cognitive functioning in adults with BD, with and without psychosis, other research (Hill et al., 2009; Zanelli et al., 2010) reported cognitive impairments in individuals with BD with psychosis, MDD with psychosis, and schizophrenia, and the least severe deficits in BD only. Children and youth who develop BD generally have less severe cognitive deficits than those who develop schizophrenia (Seidman et al., 2013). However, the presence of psychotic features in children and adolescents with BD has been associated with lower cognitive functioning (Arango et al., 2014; Shiratsuchi et al., 2000), as well as deficits in processing speed (Fitzgerald et al., 2004), verbal memory, and executive functioning (Udal et al., 2012). Importantly, there is often a deterioration in intellectual functioning when adolescents are hospitalized for the first episode of psychosis, regardless of their primary diagnosis and their pre-morbid IQ (Brickman et al., 2004; Müller et al., 2013).

At present, it is unclear how much the association between mood symptoms and cognitive deficits in children and adolescents with MDD or BD might be moderated by accompanying psychotic features and how much the presence of psychotic symptoms has a differential effect on different aspects of cognitive functioning such as working memory and processing speed. In the present study, we explored differences in overall intellectual functioning (measured by the WISC-IV FSIQ), working memory (measured by WISC-IV Digit Span subtest), and processing speed (Coding and Symbol Search subtests) among child and adolescent psychiatric inpatients with MDD or BD with and without psychotic features.

In light of the literature (mainly with adult samples), we had three main hypotheses. First, we hypothesized that patients with BD or MDD and current psychotic symptoms would have lower FSIQs, Digit Span, Coding, and Symbol Search scores than patients with mood disorders without psychosis (Bilginer et al., 2005; Levy and Weiss, 2010; Martinez-Aran et al., 2008; Sarapas et al., 2012). Second, we expected no differences in cognitive functioning in the children and adolescents with BD and those with MDD (Daniel et al., 2013; Nieto and Castellanos, 2011). Third, because studies which have found lower cognitive abilities in MDD and BD than in Mood Disorders NOS have not explored the role of psychotic features (Doyle et al., 2005; Horn et al., 2011; McCarthy et al., 2004; Pavuluri et al., 2009; Wagner et al., 2015; Wilkinson and Goodyer, 2006), we expected that the patients with BD and those with MDD would not have more cognitive deficits than patients with Mood Disorders NOS, if psychotic features were taken into account. Hence, the interaction between psychotic features and severity of mood disturbance would correspond to the greatest deficits in overall intellectual functioning, working memory, and processing speed. This investigation is one of the first of its kind with a sample of chronically disturbed child and adolescent inpatients, including those with very low cognitive functioning.

2. Method

2.1. Study design and participants

Based on *a priori* power analysis specified for planned analyses of variance to detect an effect of small size ($d=0.2$) with 95% power (risk $\alpha=0.05$), we determined that a sample size of 63 subjects was sufficient to investigate our research question. To maximize power, eighty discharged inpatients' records were randomly selected (i.e., by alphabetical order) from the record of patients with MDD and BD (with and without psychotic features), Mood Disorders NOS, Psychosis NOS, schizophrenia or PTSD, at an intermediate care state children's psychiatric hospital. The patients (43 Females, 37 Males) were between 7 and 18 years old at the time of their admission (mean age=14.21 years old, SD=2.47) and were from African American (n=41), Hispanic ($n=36$), Caucasian ($n=6$), or Mixed ($n=1$) descent. Patients were discharged between 2009 and 2012, were referred from acute care inpatient facilities for additional treatment, and had histories of chronic symptomatology and multiple hospitalizations (all had at least two psychiatric hospitalizations for acute symptoms prior to their current admission). Besides gender, age, and demographic information, the following data were recorded for planned analysis: the WISC-IV FSIQ scores, the Coding, Symbol Search, and Digit Span subtest scores, and psychiatric diagnoses. Cognitive testing was routinely done for all patients within 30 days after admission. Consistent with common practice in cognitive assessment in state children's psychiatric hospital settings, no data on non-intellective factors such as current mood states were collected. The diagnoses (Axis I) were made on admission by the treating psychiatrists based on DSM-IV criteria following diagnostic conferences and review of the referring hospitals' discharge diagnoses. The data included 43 patients with BD, 7 with MDD, and 30 with Mood Disorders NOS, along with a dichotomous variable including the presence or absence of current psychotic features ($n=8$ present). None of these diagnosis categories were related to gender ($\chi^2[2]=0.41$, $p=0.82$) or race/ethnicity ($\chi^2[6]=3.04$, $p=0.81$), while the Mood Disorders, NOS group was on average slightly younger than the other groups (F [2,77]=16.04, $p<0.001$). State measures of mood symptom severity were unavailable. Exclusion criteria included patients being diagnosed with a neurological disorder or with other diagnostic categories not in the scope of this study (e.g., Psychosis NOS, or schizophrenia or PTSD). Medication was not considered in relation to cognitive functioning since the patients had been treated with two to five medications concurrently, and there is evidence that cognitive deficits associated with severe mood disorders tend to be stable over time (e.g., Rund, 1998).

2.2. Measures

The Wechsler Intelligence Scale for Children, 4th edition, (WISC-IV; Wechsler, 2003) has been widely used to assess cognitive functioning on the basis of age-appropriate norms, and the FSIQs were included in all cases rather than abbreviated measures. The Digit Span subtest was used as a screening measure for short-term-working memory, and the Coding and Symbol Search subtests as screening measures for visual processing speed. The WISC-IV psychometric properties are well established and comprise evidences for the high reproducibility of test scores (test-retest reliability coefficient ranging from 0.80 for Symbol Search to 0.93 for the FSIQ; Wechsler, 2003), which suggests a limited sensitivity to "time sampling error," including transient state such as fluctuation in mood.

2.3. Data processing and statistical analysis

After preliminary statistical assumption checks, a series of Multivariate Analyses of Variance (MANOVA) were conducted. First, a MANOVA with covariate (MANCOVA) was conducted using the four cognitive functioning variables as dependent variables, and Axis I diagnosis as between-subject factor (age, gender, and presence of psychotic features were used as covariate, to isolate the unique contribution of the Axis I diagnosis). Second, we reiterated the previous analysis by combining the MDD and BD groups, in comparison to the Mood Disorders NOS group. Finally, a MANCOVA was conducted to decompose the effect of (1) Severity of Mood Disorders and (2) Presence of Psychotic Features on the four cognitive functioning variables. The α risk threshold for all analyses was set at $p=0.05$ (two-sided).

3. Results

3.1. Preliminary analyses

Descriptive statistics are presented in Table 1. Cognitive functioning indicators showed low performance across participants with average performance ranging from 0.8 (Digit Span) to 1.7 (Coding) SDs below the norm. Distributional features were within the normal range (Skewness statistics ranging from 0.12 to 0.69, and Kurtosis statistics ranging from −0.53 to 0.40), and multicollinearity diagnosis indicators (min Tolerance =0.38; max variance inflation factors <2.7) suggested that data was proper for planned analyses. Missing values analysis of dependent variables (10.4% missing value on average) confirmed a pattern of Missingness Completely at Random (Little's MCAR test, $\chi^2=8.06$, DF =5, $p=0.15$). Missing data was mostly due to incomplete WISC

Table 1
Descriptive and Univariate Statistics of Group Differences for the Three Clinical Groups and the Complete Sample across the Four Cognitive Functioning Indicators.

Indicator	SMD without Psychosis Mean (SD)	SMD with Psychosis Mean (SD)	Mood NOS Mean (SD)	All Mean (SD)	F (2, 68)[a]	η^{2}[b]	Group differences[c]
Digit Span[d]	8.05 (2.83)	4.63 (2.72)	7.92 (2.90)	7.62 (3.00)	5.02**	0.13	SMDP < SMD = NOS
Coding[d]	5.05 (2.92)	3.25 (2.32)	4.81 (3.11)	4.76 (2.95)	1.24	0.04	SMD = SMDP = NOS
Symbol Search[d]	5.97 (2.72)	4.38 (3.11)	6.00 (3.53)	5.80 (3.08)	0.97	0.03	SMD = SMDP = NOS
Full Scale IQ[e]	77.54 (14.99)	64.13 (10.84)	75.46 (9.58)	75.27 (13.31)	3.60*	0.10	SMDP < SMD = NOS

Note.

[a] = Univariate ANOVA comparing the three clinical groups for each cognitive functioning indicator.

[b] = Partial Eta squared.

[c] = group differences between the Severe Mood Disorder without psychosis (SMD group), the Severe Mood Disorder with psychosis (SMDP group) and the Mood Disorders NOS (NOS) .

[d] = Normative sample (mean=10, SD=3).

[e] = Normative sample (mean=100, SD=15).

* $p<0.05$

** $p<0.01$.

protocols, subtests skipped, or cognitive functioning data not entirely reported in the patient's chart. On this ground, case-wise deletion was used on an analysis to analysis basis.

3.2. Cognitive functioning differences as a function of Axis I diagnosis

Because the first MANCOVA focused on isolating the unique effect of Axis I diagnosis (BD, MD, and Mood Disorders NOS) on cognitive functioning, we controlled for a set of covariates that could act as confounds when examining the effect of the between-subject factors (age, gender, and presence of psychotic features). The omnibus MANCOVA test showed non-significant results on the Wilk's Lambda criterion (F [8,124]=0.46, p=0.88, η^2=0.03), suggesting that the combined dependent variables (Digit Span, Coding, Symbol Search, FSIQ) were not related to Axis I diagnosis and to the combined covariates used in this analysis. The effects of Axis I diagnosis on cognitive functioning was not significant, even after controlling for the effects of Gender (F [4,62]=2.28, p=0 0.07, η^2=0.13), Age (F [4,62]=0.045, p=0.99, η^2=0.00), and Current Psychotic features (F [4,62]=0.045, p=0.99, η^2=0.15). Hence, this analysis revealed a significant effect of moderate size (Current Psychotic Features) on the cognitive functioning variables (with lower mean score on the Digit Span and FSIQ scores for participants with current psychotic features) that was further investigated throughout the subsequent analyses. Because there were no mean differences in the cognitive functioning of the MDD and BD groups, we combined them to represent a group with greater symptom severity, frequency, and chronicity, into a “Severe Mood Disorder” (SMD) group (n=50), that was further compared with the Mood Disorders NOS group (n=30), representing less severe mood disturbance.

3.3. Severity of mood disorder and cognitive functioning

A MANCOVA was conducted using the four cognitive functioning variables as dependent variables, and the recombined diagnosis groups as between-subject factor (SMD vs. Mood Disorders NOS). Here too, we controlled for a set of covariates (age and gender), but did not control for current psychotic features (to be consistent with previous research in the literature usually disregarding this potential confound), which was accomplished in the final set of analyses. The omnibus MANCOVA test showed non-significant results on the Wilk's Lambda criterion (F [4,64]=0.06, p=0.99, η^2=0.00), suggesting no relation between the recombined Axis I diagnosis categories with the four indicators of cognitive functioning. Similar to the previous analyses, the covariates were not significantly associated with the dependent variables.

3.4. Interaction between severity of mood disorders and presence of psychotic features

In this final analysis, the sample was recombined into three groups in order to distinguish SMD participants with current psychotic features (n=37), SMD participants without psychotic features (n=8), and participants with Mood Disorders NOS (n=26). We were thus able to explore the interaction between Mood Disorder and Psychotic Features on cognitive functioning. A MANCOVA was performed using the four cognitive functioning variables as dependent variables, and the three clinical groups as between-subject factor. As in previous analyses, covariates included age and gender. The omnibus MANCOVA test showed non-significant results on the Wilk's Lambda criterion (F [8,128]=1.27, p=0.27, η^2=0.07). However, differences emerged when looking at each dependent variable separately, namely Digit Span (F [2,66]= 5.19, $p<0.008$, η^2=0.14), Coding (F [2,66]=1.08, p=0.35, η^2=0.03), Symbol Search (F [2,66]=0.77, p=0.47, η^2=0.02) and FSIQ (F [2,66]=3.50, p=0.036, η^2=0.10), even after Bonferroni adjustment (adjusted risk α=0.013). In sum, the SMD groups with current psychotic features showed clearly lower scores on Digit Span and FSIQ (about 1 SD lower) than the Mood Disorders NOS and the SMD without Psychotic Features groups, while the two latter groups did not differ significantly on any cognitive functioning variable. See Table 1.

4. Discussion

This study is among the first to investigate the cognitive functioning of hospitalized youth with MDD and BD, with and without psychotic features. The patients' overall low level of cognitive functioning was noteworthy along with their low scores in Digit Span, Coding, and Symbol Search. The presence of psychotic features in patients with severe mood disorders had a negative effect on their general cognitive functioning and particularly, their working memory. These findings point to the importance of including children and youth with low cognitive abilities in studies of pediatric MDD and BD. Consistent with several studies (Daniel et al., 2013; Nieto and Castellanos, 2011), Axis I diagnoses did not have a significant association with the cognitive functioning variables (FSIQ, Coding, Digit Span, and Symbol Search) after controlling for age, gender, and presence of psychotic features. However, consistent with the finding of lowered cognitive abilities in youth with mood disorders and psychotic features (Arango et al., 2014), the SMD group with current psychotic features had consistently low functioning in all cognitive areas, and the lowest FSIQs and working memory (Digit Span scores) of the three clinical groups. We did not find that the SMD group with psychotic features had lower Coding or Symbol Search scores than the groups without psychotic features.

The significant impact of the interaction between psychotic features and BD or MDD on cognitive abilities in hospitalized youth was anticipated because of findings of the negative impact of SMD on cognitive abilities (Bilginer et al., 2005; Levy and Weiss, 2010; Martinez-Aran et al., 2008; Sarapas et al., 2012). Although the extent to which this association might be contributory is unknown, it has been established that hospitalizations for psychosis are often associated with deteriorations in cognitive abilities that are not necessarily explained on the basis of premorbid IQ scores (Bilginer et al., 2005).

Our study has a number of limitations including those of a retrospective chart review study design, the rather low number of patients with psychotic features and MDD, and the absence of symptom severity and mood episode ratings. Since we studied chronically disturbed hospitalized children and adolescents, the results may not be generalizable to a wide spectrum of youth in the community. Beyond the admission psychiatric assessment and psychiatric diagnoses, no additional measures of psychotic features or mood disturbance were recorded. There is some evidence that mood symptom severity is not related to cognitive deficits within groups of youth with BD. However, it's possible that symptom severity might have accounted for the differences in working memory between the youths with psychotic versus non-psychotic manifestations of mood disorders, and this possibility will require further investigation. The possibility of medication effects in differences in FSIQ and working memory in psychotic mood disorders should also be investigated. Although the WISC-IV has been widely used to assess cognitive functioning abilities and has excellent reliability and validity, more targeted measures of cognitive functioning were not available.

The study has several important clinical implications. The possibility that MDD and BD with psychotic features is associated

with decrements in working memory and in general cognitive functioning is of serious concern to child and adolescent clinicians. If the findings are replicated, they add support to the associations between psychotic symptoms, underlying brain deficits, and chronic mood disturbance while underscoring the need to take deficits in working memory and overall cognitive functioning into account when implementing cognitive behavioral interventions and planning for academic supports and additional services. Further research is needed with more comprehensive cognitive measures and more extensive clinical groups (e.g., BD 1 vs BD 2, BD + ADHD), in order to confirm and extend the findings of this study. Further studies might help guide treatment planning for vulnerable children who are at risk for developing psychotic symptoms along with MDD and BD.

Acknowledgement

We thank Maria Flores and Brianna Heuser for assistance in the preparation of this article.

References

Arango, C., Fraguas, D., Parellada, M., 2014. Differential neurodevelopmental trajectories in patients with early-onset bipolar and schizophrenia disorders. Schizophr. Bull. 40, 138–146. http://dx.doi.org/10.1093/schbul/sbt198.

Arango, C., Rapado-Castro, M., Reig, S., Castro-Fornieles, J., González-Pinto, A., Otero, S., Immaculada, B., Moreno, C., Graell, M., Janssen, J., Parellada, M., Moreno, D., Bargalló, N., Desco, M., 2012. Progressive brain changes in children and adolescents with first-episode psychosis. Arch. Gen. Psychiatry 69, 16–26.

Basso, M.R., Bornstein, R.A., 1999. Neuropsychological deficits in psychotic versus nonpsychotic unipolar depression. Neuropsychology 13, 69–75.

Baune, B.T., Fuhr, M., Air, T., Herring, C., 2014. Neuropsychological functioning in adolescents and young adults with major depressive disorder - a review. Psychiatry Res. 218, 261–267. http://dx.doi.org/10.1016/j.psychres.2014.04.052.

Bearden, C.E., Glahn, D.C., Caetano, S., Olvera, R.L., Fonseca, M., Najt, P., Hunter, K., Pliszka, S.R., Soares, J.C., 2007. Evidence for disruption in prefrontal cortical functions in juvenile bipolar disorder. Bipolar Disord. 9, 145–149. http://dx.doi.org/10.1111/j.1399–5618.2007.00453.x.

Biederman, J., Petty, C.R., Wozniak, J., Wilesn, T.E., Fried, R., Doyle, A., Henin, A., Bateman, C., Evans, M., Farone, S.V., 2011. Impact of executive function deficits in youth with bipolar I disorder: a controlled study. Psychiatry Res. 186, 58–64.

Bilginer, L., DeLuca, V., Pogge, D.L., Stokes, J.S., Harvey, P.D., 2005. Intellectual functioning in adolescents with indicators of psychosis: evidence for decline in functioning related to number of psychotic features? J. Neuropsychiatry Clin. Neurosci. 17, 106–113.

Brickman, A.M., Buchsbaum, M.S., Bloom, R., Bokhoven, P., Paul-Odouard, R., Haznedar, M.M., Dahlman, K.L., Hazlett, E.A., Aronowitz, J., Heath, D., Shihabuddin, L., 2004. Neuropsychological functioning in first-break, never-medicated adolescents with psychosis. J. Nerv. Ment. Dis. 192, 615–622.

Cahill, C.M., Walter, G., Malhi, G.S., 2009. Neurocognition in bipolar disorder and juvenile bipolar disorder. J. Can. Acad. Child Adolesc. Psychiatry 18, 221–230.

Caldieraro, M.A., Baeza, F.L., Pinheiro, D.O., Ribeiro, M.R., Parker, G., Fleck, M.P., 2013. Prevalence of psychotic symptoms in those with melancholic and nonmelancholic depression. J. Nerv. Ment. Dis. 201, 855–859.

Castaneda, A.E., Suvisaari, J., Marttunen, M., Perälä, J., Saarni, S.I., Aalto-Setälä, T., Aro, H., Koskinen, S., Lönnqvist, J., Tuulio-Henriksson, A., 2007. Cognitive functioning in a population-based sample of young adults with a history of non-psychotic unipolar depressive disorders without psychiatric comorbidity. J. Affect. Disord. 110, 36–45. http://dx.doi.org/10.1016/j.jad.2007.12.239.

Chaves, O.C., Lombardo, L.E., Bearden, C.E., Woolsey, M.D., Martinez, D.M., Barrett, J. A., Miller, A.L., Velligan, D.I., Glahn, D.C., 2011. Association of clinical symptoms and neurocognitive performance in bipolar disorder: a longitudinal study: symptoms and cognition in bipolar disorder. Bipolar Disord. 13, 118–123. http://dx.doi.org/10.1111/j.1399–5618.2011.00888.x.

Cooper, P.J., Goodyer, I., 1993. A community study of depression in adolescent girls. I: estimates of symptom and syndrome prevalence. Br. J. Psychiatry 163, 369–374. http://dx.doi.org/10.1192/bjp.163.3.369.

Daniel, B.D., Montali, A., Gerra, M.L., Innamorati, M., Girardi, P., Pompili, M., Amore, M., 2013. Cognitive impairment and its associations with the path of illness in affective disorders: a comparison between patients with bipolar and unipolar depression in remission. J. Psychiatr. Pract. 19, 275–287. http://dx.doi.org/10.1097/01.pra.0000432597.79019.e2.

DelBello, M.P., Carlson, G.A., Tohen, M., Bromet, E.J., Schwiers, M., Strakowski, S.M., 2003. Rates and predictors of developing a manic or hypomanic episode 1 to 2 years following a first hospitalization for major depression with psychotic features. J. Child Adolesc. Psychopharmacol. 13, 173–185.

Demant, K.M., Vinberg, M., Kessing, L.V., Miskowiak, K.W., 2015. Assessment of subjective and objective cognitive function in bipolar disorder: correlations predictors and the relation to psychosocial function. Psychiatry Res. 229, 565–571.

Doyle, A.E., Wilens, T.E., Kwon, A., Seidman, L.J., Faraone, S.V., Fried, R., Swezey, A., Snyder, L., Biederman, J., 2005. Neuropsychological functioning in youth with bipolar disorder. Biol. Psychiatry 58, 540–548. http://dx.doi.org/10.1016/j.biopsych.2005.07.019.

Fitzgerald, D., Fitzgerald, D., Lucas, S., Redoblado, M.A., Winter, V., Brennan, J., Anderson, J., Harris, A., 2004. Cognitive functioning in young people with first episode psychosis: relationship to diagnosis and clinical characteristics. Aust. N. Zeal. J. Psychiatry 38, 501–510. http://dx.doi.org/10.1080/j.1440–1614.2004.01403.x.

Frías, Á., Palma, C., Farriols, N., 2014. Comorbidity in pediatric bipolar disorder: prevalence clinical impact, etiology and treatment. J. Affect. Disord. 174, 378–389. http://dx.doi.org/10.1016/j.jad.2014.12.008.

Glahn, D.C., Bearden, C.E., Caetano, S., Fonesca, M., Najit, P., Hunter, K., Pliszka, S.R., Olvera, R.L., Soares, J.C., 2005. Declarative memory impairment in pediatric bipolar disorder. Bipolar Disord. 7, 546–554. http://dx.doi.org/10.1111/j.1399–5618.2005.00267.x.

Godard, J., Baruch, P., Grondin, S., Lafleur, M.F., 2012. Psychosocial and neurocognitive functioning in unipolar and bipolar depression: a 12-month prospective study. Psychiatry Res. 196, 145–153. http://dx.doi.org/10.1016/j.psychres.2011.09.013.

Godard, J., Grondin, S., Baruch, P., Lafleur, M.F., 2011. Psychosocial and neurocognitive profiles in depressed patients with major depressive disorder and bipolar disorder. Psychiatry Res. 190, 244–252. http://dx.doi.org/10.1016/j.psychres.2011.06.014.

Goodyer, I., Cooper, P.J., 1993. A community study of depression in adolescent girls. II: the clinical features of identified disorder. Br. J. Psychiatry 163, 374–380. http://dx.doi.org/10.1192/bjp.163.3.374.

Gu, C., He, H., Duan, H., Su, Z., Chen, H., Gan, J., 2016. Predictors of neurocognitive impairment at 2years after a first-episode major depressive disorder. Compr. Psychiatry 68, 24–33. http://dx.doi.org/10.1016/j.comppsych.2016.03.009.

Han, G., Klimes-Dougan, B., Jepsen, S., Ballard, K., Nelson, M., Houri, A., Kumra, S., Cullen, K., 2011. Selective neurocognitive impairments in adolescents with major depressive disorder. J. Adolesc. 35, 11–20. http://dx.doi.org/10.1016/j.adolescence.2011.06.009.

Hermens, D.F., Naismith, S.L., Redoblado Hodge, M.A., Scott, E.M., Hickie, I.B., 2010. Impaired verbal memory in young adults with unipolar and bipolar depression: verbal memory in young depressed adults. Early Interv. Psychiatry 4, 227–233. http://dx.doi.org/10.1111/j.1751–7893.2010.00194.x.

Hill, S.K., Keshavan, M.S., Thase, M.E., Sweeney, J.A., 2004. Neuropsychological dysfunction in antipsychotic-naive first-episode unipolar psychotic depression. Am. J. Psychiatry, 996–1003. http://dx.doi.org/10.1176/appi.ajp.161.6.996.

Hill, S.K., Reilly, J.L., Harris, M.S.H., Rosen, C., Marvin, R.W., DeLeon, O., Sweeney, J.A., 2009. A comparison of neuropsychological dysfunction in first-episode psychosis patients with unipolar depression, bipolar disorder, and schizophrenia. Schizophr. Res. 113, 167–175. http://dx.doi.org/10.1016/j.schres.2009.04.020.

Horn, K., Roessner, V., Holtmann, M., 2011. Neurocognitive performance in children and adolescents with bipolar disorder: a review. Eur. Child Adolesc. Psychiatry 20, 433–450. http://dx.doi.org/10.1007/s00787-011-0209-x.

Joseph, M.F., Frazier, T.W., Youngstrom, E.A., Soares, J.C., 2008. A quantitative and qualitative review of neurocognitive performance in pediatric bipolar disorder. J. Child Adolesc. Psychopharmacol. 18, 595–605. http://dx.doi.org/10.1089/cap.2008.064.

Kennedy, N., Everitt, B., Boydell, J., Van Os, J., Jones, P.B., Murray, R.M., 2005. Incidence and distribution of first-episode mania by age: results from a 35-year study. Psychol. Med. 35, 855–863. http://dx.doi.org/10.1017/S0033291704003307.

Klimkeit, E.I., Tonge, B., Bradshaw, J.L., Melvin, G.A., Gould, K., 2011. Neuropsychological deficits in adolescent unipolar depression. Arch. Clin. Neuropsychol. 26, 662–676. http://dx.doi.org/10.1093/arclin/acr051.

Lampe, I.K., Sitskoorn, M.M., Heeren, T.J., 2003. Effects of recurrent major depressive disorder on behavior and cognitive function in female depressed patients. Psychiatry Res. 125, 73–79. http://dx.doi.org/10.1016/j.psychres.2003.12.004.

Lera-Miguel, S., Andrés-Perpiñá, S., Fatjó-Vilas, M., Fañanás, L., Lázaro, L., 2014. Two-year follow-up of treated adolescents with early-onset bipolar disorder: changes in neurocognition. J. Affect. Disord. 172, 48–54. http://dx.doi.org/10.1016/j.jad.2014.09.041.

Levy, B., Medina, A.M., Hintz, K., Weiss, R.D., 2011. Ecologically valid support for the link between cognitive and psychosocial functioning in bipolar disorder. Psychiatry Res. 185, 353–357. http://dx.doi.org/10.1016/j.psychres.2010.06.010.

Levy, B., Medina, A.M., Weiss, R.D., 2012. Cognitive and psychosocial functioning in bipolar disorder with and without psychosis during early remission from an acute mood episode: a comparative longitudinal study. Compr. Psychiatry 54, 618–926. http://dx.doi.org/10.1016/j.comppsych.2012.12.018.

Levy, B., Weiss, R.D., 2010. Neurocognitive impairment and psychosis in bipolar I disorder during early remission from an acute episode of mood disturbance. J. Clin. Psychiatry 71, 201–206. http://dx.doi.org/10.4088/JCP.08m04663yel.

Martinez-Aran, A., Torrent, C., Tabares-Seisdedos, R., Salamero, M., Daban, C., Balanza-Martinez, V., Colom, F., 2008. Neurocognitive impairment in bipolar patients with and without history of psychosis. J. Clin. Psychiatry 69, 233–239.

McCarthy, J., Arrese, D., McGlashan, A., Rappaport, B., Kraseski, K., Conway, F., Mule, C., Tucker, J., 2004. Sustained attention and visual processing speed in children and adolescents with bipolar disorder and other psychiatric disorders. Psychol.

Rep. 95, 39–47. http://dx.doi.org/10.2466/PR0.95.5.39-47.
McCarthy, J.B., Dobroshi, Z., 2014. Major depression, bipolar disorder and psychosis in children. J. Infant, Child, Adolesc. Psychother. 13, 249–261. http://dx.doi.org/10.1080/15289168.2014.937984.
Müller, M., Vetter, S., Weiser, M., Frey, F., Ajdacic-Gross, V., Stieglitz, R., Rössler, W., 2013. Precursors of cognitive impairments in psychotic disorders: a population-based study. Psychiatry Res 210, 329–337. http://dx.doi.org/10.1016/j.psychres.2013.05.035.
Nenadic, I., Langbein, K., Dietzek, M., Forberg, A., Smesny, S., Sauer, H., 2015. Cognitive function in euthymic bipolar disorder (BP I) patients with a history of psychotic symptoms vs. schizophrenia. Psychiatry Res. 230, 65–69. http://dx.doi.org/10.1016/j.psychres.2015.08.012.
Nieto, R.G., Castellanos, F.X., 2011. A meta-analysis of neuropsychological functioning in patients with early onset schizophrenia and pediatric bipolar disorder. J. Clin. Child Adolesc. Psychol. 40, 266–280. http://dx.doi.org/10.1080/15374416.2011.546049.
Pavuluri, M.N., Schenkel, L.S., Aryal, S., Harral, E.M., Hill, S.K., Herbener, E.S., Sweeney, J.A., 2006. Neurocognitive function in unmedicated manic and medicated euthymic pediatric bipolar patients. Am. J. Psychiatry 163, 286–293. http://dx.doi.org/10.1176/appi.ajp.163.2.286.
Pavuluri, M.N., West, A., Hill, S.K., Jindal, K., Sweeney, J.A., 2009. Neurocognitive function in pediatric bipolar disorder: 3-year follow-up shows cognitive development lagging behind healthy youths. J. Am. Acad. Child Adolesc. Psychiatry 48, 299–307. http://dx.doi.org/10.1097/CHI.0b013e318196b907.
Reichenberg, A., Harvey, P.D., Bowie, C.R., Mojtabai, R., Rabinowitz, J., Heaton, R.K., Bromet, E., 2009. Neuropsychological function and dysfunction in schizophrenia and psychotic affective disorders. Schizophr. Bull. 35, 1022–1029. http://dx.doi.org/10.1093/schbul/sbn044.
Rund, B.R., 1998. A review of longitudinal studies of cognitive function in schizophrenia patients. Schizophr. Bull. 24, 425–435.
Sarapas, C., Shankman, S.A., Harrow, M., Goldberg, J.F., 2012. Parsing trait and state effects of depression severity on neurocognition: evidence from a 26-year longitudinal study. J. Abnorm. Psychol. 121, 830–837. http://dx.doi.org/10.1037/a0028141.
Savitz, J., van der Merwe, L., Stein, D.J., Solms, M., Ramesar, R., 2009. Neuropsychological status of bipolar I disorder: impact of psychosis. Br. J. Psychiatry 194, 243–251. http://dx.doi.org/10.1192/bjp.bp.108.052001.
Seidman, L.J., Cherkerzian, S., Goldstein, J.M., Agnew-Blais, J., Tsuang, M.T., Buka, S. L., 2013. Neuropsychological performance and family history in children at age 7 who develop adult schizophrenia or bipolar psychosis in the New England Family studies. Psychol. Med. 43, 119–131. http://dx.doi.org/10.1017/S0033291712000773.
Shiratsuchi, T., Takahashi, N., Suzuki, T., Abe, K., 2000. Depressive episodes of bipolar disorder in early teenage years: changes with increasing age and the significance of IQ. J. Affect. Disord. 58, 161–166. http://dx.doi.org/10.1016/S0165-0327(99)00098-1.
Singh, M.K., DelBello, M.P., Fleck, D.E., Shear, P.K., Strakowski, S.M., 2009. Inhibition and attention in adolescents with nonmanic mood disorders and a high risk for developing mania. J. Clin. Exp. Neuropsychol. 31, 1–7. http://dx.doi.org/10.1080/13803390801945038.
Udal, A.H., Øygarden, B., Egeland, J., Malt, U.F., Groholt, B., 2012. Memory in early onset bipolar disorder and attention deficit/hyperactivity disorder: similarities and differences. J. Abnorm. Child Psychol. 40, 1179–1192. http://dx.doi.org/10.1007/s10802-012-9631-x.
Udal, A.H., Øygarden, B., Egeland, J., Malt, U.F., Løvdahl, H., Pripp, A.H., Groholt, B., 2013. Executive deficits in early onset bipolar disorder versus ADHD: impact of processing speed and lifetime psychosis. Clin. Child Psychol. Psychiatry 18, 284–299. http://dx.doi.org/10.1177/1359104512455181.
Vilgis, V., Silk, T.J., Vance, A., 2015. Executive function and attention in children and adolescents with depressive disorders: a systematic review. Eur. Child Adolesc. Psychiatry 24, 365–384. http://dx.doi.org/10.1007/s00787-015-0675-7.
Wagner, S., Müller, C., Helmreich, I., Huss, M., Tadić, A., 2015. A meta-analysis of cognitive functions in children and adolescents with major depressive disorder. Eur. Child Adolesc. Psychiatry 24, 5–19. http://dx.doi.org/10.1007/s00787-014-0559-2.
Wechsler, D., 2003. Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV). Psychological Corporation,, San Antonio, TX.
Wilkinson, P.O., Goodyer, I.M., 2006. Attention difficulties and mood-related ruminative response style in adolescents with unipolar depression. J. Child Psychol. Psychiatry 47, 1284–1291. http://dx.doi.org/10.1111/j.1469–7610.2006.01660.x.
Zanelli, J., Reichenberg, A., Morgan, K., Fearon, P., Kravariti, E., Dazzan, P., Morgan, C., Zanelli, C., Demjaha, A., Jones, P.B., Doody, G.A., Kapur, S., Murray, R.M., 2010. Specific and generalized neuropsychological deficits: a comparison of patients with various first-episode psychosis presentations. Am. J. Psychiatry 167, 78–85. http://dx.doi.org/10.1176/appi.ajp.2009.09010118.