Comprehensive Psychiatry 86 (2018) 39–46

Contents lists available at ScienceDirect

Comprehensive Psychiatry

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

Continuity and stability of preschool depression from childhood through adolescence and following the onset of puberty

Michael S. Gaffrey [a,b,*], Rebecca Tillman [a], Deanna M. Barch [a,c], Joan L. Luby [a]

[a] Washington University, Department of Psychiatry, Saint Louis, MO, United States of America
[b] Duke University, Department of Psychology and Neuroscience, Durham, NC, United States of America
[c] Washington University, Department of Psychological and Brain Sciences, Saint Louis, MO, United States of America

ARTICLE INFO

Article history:
Received 9 April 2018
Received in revised form 16 July 2018
Accepted 21 July 2018

ABSTRACT

Background: A growing body of research now supports the validity, clinical significance, and long-term negative impact of depression occurring during the preschool period. However, the prospective continuity of depressive symptoms and risk for major depressive disorder (MDD) from childhood through adolescence for preschoolers experiencing this highly impairing disorder remains unexplored. Such information is likely to be critical for understanding the developmental continuity of preschool depression and whether it continues to be a salient risk factor for an MDD diagnosis following the transition into adolescence and the onset of biological changes associated with it (i.e., puberty).

Methods: Subjects were participants in the Preschool Depression Study conducted at the Early Emotional Development Program at Washington University School of Medicine in St. Louis. Subjects and their parents completed baseline assessments that included comprehensive measures of psychopathology and development at baseline and up to 9 follow-up assessments between 2003 and 2017. N = 279 subjects had diagnostic and clinical data available for the preschool period and the early pubertal and/or later pubertal periods and were included in the analyses. There were N = 275 subjects assessed during the early pubertal period and N = 184 subjects assessed during the later pubertal period.

Results: Preschool depression was a highly salient predictor of prepubertal and mid-to-post pubertal MDD. Across all modeled time points children with a history of preschool depression continued to demonstrate elevated levels of depressive symptoms from childhood through adolescence, suggesting a heightened trajectory of depressive symptoms relative to their same age peers.

Conclusion: Findings from the current study suggest that children with a history of preschool depression follow a trajectory of depression severity elevated relative to their same age peers from childhood through adolescence but with a similar shape over time. They also support the homotypic continuity of preschool depression into adolescence and the onset of puberty.

© 2018 Elsevier Inc. All rights reserved.

1. Introduction

A growing body of research now supports the validity, clinical significance, and long-term negative impact of depression occurring during the preschool period. Data supporting the validity and significance of preschool depression are highly similar to those reported for older groups, including symptom specificity [1], familial transmission [2], disrupted stress reactivity [3], impairment across multiple contexts [4], gene x environment interactions [5], continuity during the preschool period [6], and altered functional brain activity in regions important for emotion regulation [7,8]. Evidence demonstrating that depression and related emotional behavior during the preschool period are robust risk factors for later DSM-5 mood and anxiety disorders at school age has also been provided [9]. However, the prospective continuity of depressive symptoms and risk for major depressive disorder (MDD) from childhood through adolescence for preschoolers experiencing this highly impairing disorder remains unexplored. Such information is likely to be critical for understanding the developmental continuity of preschool depression and whether it continues to be a salient risk factor for an MDD diagnosis following the transition into adolescence and the onset of biological changes associated with it (i.e., puberty).

To date, samples ascertained via epidemiological, community sampling, or high-risk screening methods have supported the presence of depression during the preschool period (ages 3–5 years) [9–12].

* Corresponding author at: Duke University, Department of Psychology & Neuroscience, 417 Chapel Drive, Campus Box 90086, Durham, NC 27708-0086, United States of America.
E-mail address: michael.gaffrey@duke.edu (M.S. Gaffrey).

https://doi.org/10.1016/j.comppsych.2018.07.010
0010-440X/© 2018 Elsevier Inc. All rights reserved.

Critically, this work has also suggested that the experience of depression during the preschool period is highly impairing and likely alters the course of early emotional development for a given child. More specifically, prospective data from multiple independent samples has supported the continuity of preschool depression and the symptoms associated with it into later school-age [9,13,14]. For example, a recent study of preschoolers with early emerging depression reported that >50% of these children went on to qualify for a DSM-5 diagnosis of MDD within ~6 years of their initial identification [9]. Therefore, prior research supports the homotypic continuity (i.e., early depression predicts later depression) of preschool depression following the important developmental transition into school-age. However, it also underscores the need to further explore the continuity of preschool depression following the entry into adolescence and the onset of puberty, later occurring developmental transitions widely held to be key for understanding MDD risk and prevention [15].

Given a sharp rise in the prevalence of MDD in adolescence [16,17], this developmental period has been considered key to understanding depression risk and etiology. Research on MDD during adolescence has frequently pointed to earlier MDD diagnoses and elevations in depressive symptoms as highly salient risk factors for depression during this period [18]. In addition, this work has also indicated a normative increase in depressive symptoms during adolescence that is likely associated with ongoing social, emotional, and biological changes [19]. One of the most well documented of these associations has been between the onset of puberty and a steep rise in rates of depression, highlighted by a well-replicated relationship between early onset puberty and elevated depressive symptoms and rates of MDD in girls [17]. Research investigating the onset of puberty and its association with depression in boys has reported more mixed results, although higher rates of internalizing problems in boys who enter puberty earlier and/or experience a more accelerated rate of pubertal change have been reported [20]. In light of an increased rate of MDD following puberty, the potential influence of a very early diagnosis of depression on risk for MDD following the onset of puberty has been unlargely explored, leaving open the question as to whether preschool depression continues to place a child at further increased risk for MDD during this key developmental period.

Interestingly, more recent work investigating the longitudinal trajectory of depressive symptoms from childhood to adolescence has suggested that the transition to adolescence may be a critical developmental turning point in the expression of depressive symptoms. More specifically, this work indicates that depressive symptoms decline from early-to-late school age and begin to climb again as a child enters adolescence [21]. Considering theoretical models [22] and empirical data [18] positing that an individual child's future expression (i.e., presence/absence of symptoms and diagnosis) and trajectory (i.e., continuous vs. discontinuous) of a given disorder are intimately linked to their previous experience with it, this discontinuous pattern raises the important question as to whether children experiencing depression during the preschool period exhibit a similar or altered trajectory of depressive symptom expression from school age through adolescence compared to children without preschool depression. It also raises the question of whether the prospective relationship between preschool depression and later MDD persists beyond this key developmental juncture. While previous research has suggested both homotypic and heterotypic relationships between childhood and adolescent depressive symptom levels and other psychopathology (e.g., anxiety) [21,23], and altered risk for later recurrence of childhood diagnoses during adolescence [16,21], the influence of preschool depression on these relationships and the developmental course of depressive symptoms has not been directly addressed. Answering these questions would not only further clarify the public health and clinical significance of preschool depression, it would also critically inform conceptual models seeking to describe the course of depression across the lifespan.

Given the recognized need for understanding the influence of early childhood psychopathology on later development and risk for future psychiatric disorders [24], the current study investigated the developmental trajectory of depressive symptoms from childhood through adolescence for children with and without the experience of depression during the preschool period. It also tested whether depression during the preschool period exhibited homotypic continuity with MDD following the onset of puberty during adolescence. In line with prior work, it was anticipated that one of at least four possible trajectories would characterize preschool depression's relationship with future depressive symptom levels from childhood through adolescence. One potential trajectory would reflect the persistence of depressive symptoms regardless of age and anticipated normative trajectory (i.e., consistently elevated though not increasing). Another potential trajectory would suggest a continually increasing level of depressive symptoms as a child ages (i.e., a linear increase in depressive symptoms). Alternatively, another potential trajectory could indicate decreasing depressive symptoms across age (i.e., linear decrease in depressive symptoms). And a fourth possibility would indicate that children with preschool depression would have a developmental trajectory of depressive symptoms like their same age non-depressed peers in terms of shape (i.e., slope) but not height (i.e., persistently elevated depressive symptoms across ages). We hypothesized that this fourth possibility was most likely to be found based on previous work suggesting that depressive symptoms follow a 'U' shaped trajectory from childhood through adolescence [21] and prior research indicating that a history of depression is associated with elevated levels of depressive symptoms across the lifespan [6,25,26]. It was also hypothesized that preschool depression would be associated with increased odds for a diagnosis of MDD following the onset of puberty and, following our previous work in this sample [9], increased odds for other related disorders including anxiety and oppositional defiant disorder.

2. Methods

2.1. Study population

Subjects were participants in the Preschool Depression Study conducted at the Early Emotional Development Program at Washington University School of Medicine in St. Louis. Details of the study's recruitment and subject flow have been previously reported [9]. In summary, children age 3.0–5.11 years were recruited from primary care and day care sites and screened with the Preschool Feelings Checklist (PFC), a validated measure assessing depressive symptoms in preschool-age children. Children with depressive symptoms were selected for study participation, and children with other psychiatric disorders and healthy children were included in the sample as comparison groups. Subjects and their parents completed baseline assessments that included comprehensive measures of psychopathology and development at baseline and up to 9 follow-up assessments between 2003 and 2017. Parents and children provided written informed consent and assent, respectively. All study procedures were approved by the Washington University School of Medicine institutional review board.

2.2. Measures

2.2.1. Child psychopathology and life events

Child psychopathology was assessed at each study wave using an age-appropriate diagnostic interview. Interviewers were blind to diagnoses from previous study waves. In addition to assessing for DSM axis I disorders, information regarding stressful and traumatic life events was also collected. When subjects were age 3.0–7.11, the Preschool Age Psychiatric Assessment (PAPA; [27]) was administered to parents. The PAPA has established validity and reliability for identifying psychiatric disorders, including mood (e.g., depression) and behavioral (e.g., conduct disorder), in very young children [28]. When subjects were age 8.0–8.11, the Child and Adolescent Psychiatric Assessment (CAPA; [29]) was administered to parents only, and when subjects

were age 9.0 and older, the CAPA was administered separately to parents and children. However, at the most recent assessment, when subjects were aged 16.4 ± 1.0, the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS; [30]) was administered separately to parents and children. The time period assessed for each interview was since the child's last assessment and parent and child report on the CAPA and K-SADS were combined by taking the most severe rating [31]. Traumatic life events were similarly evaluated using each interview.

As recommended by the authors of the PAPA and CAPA [28,29] interviews, raters are trained to reliability on the PAPA and/or CAPA prior to independently administering this interview. Once trained to reliability using practice and ratings of previously recorded interviews, interviews are taped for later quality control and interviewer calibration. For the current PAPA and CAPA interview data, approximately 20% of tapes were reviewed by a master coder and when discrepancies arose they were resolved in consultation with a senior child psychiatrist (J.L.L.). For the K-SADS, following common practices with this interview, interrater reliability was calculated as percent agreement about the presence/absence of a given disorder. Values ranged from a low of 87% agreement for ODD to near (i.e., >95%) or perfect (i.e., 100%) agreement for all other disorders assessed. Importantly, percent agreement was 97% for MDD, 94% for GAD, 100% for Panic, 97% for social phobia, 97% for PTSD, 100% for conduct disorder, and 100% for ADHD.

2.2.2. Pubertal status

The Pubertal Development Scale [32] was administered to children at each wave to subjects age 10 and older. Pubertal status categories were pre-pubertal, early pubertal, mid-pubertal, late pubertal, and post-pubertal. Subjects younger than 10 were assumed to be pre-pubertal. Following previous research suggesting that rates of MDD increase for child groups classified as mid-pubertal or later [17], for the analyses that follow two pubertal groups were created based on pubertal status at time of data collection. One group included children classified as pre-pubertal and early pubertal (EP) and another included children classified as mid-pubertal, late pubertal, and post-pubertal (LP).

2.2.3. Income-to-needs ratio

An income-to-needs ratio was calculated as the total family income at baseline divided by the federal poverty level in the year of data collection based on family size [33].

2.2.4. Depression severity

When children were age 7 years or older, the Children's Depression Inventory (CDI) was administered separately to children and parents at each of four subsequent assessment points (range 1–4 assessments, mean (SD) assessments = 3.32 (0.88), median 4 assessments). The first three assessment points used the CDI [34] and the fourth assessment used the CDI 2 [35]. In order to combine data from the CDI and CDI 2, T-scores from each version of this questionnaire were used as the primary measure of depression severity in the current study.

2.2.5. Maternal history of depression

The Family interview for genetic studies (FIGS; [36]) was completed by each child's parent and used to obtain family history of affective disorders in first- and second-degree relatives. The FIGS was updated at each study wave. Maternal depression was reported as absent, suspected, or present. For these analyses, mothers with suspected depression were considered to have depression.

2.3. Data analysis

Three developmental periods were identified: preschool (PS), early pubertal (EP), and later pubertal (LP). The PS period was from age 3.0–5.11 years, the EP period was from age 6.0 through early puberty, and the LP period was from mid-puberty through post-puberty.

Dichotomous variables were used for the presence/absence of diagnostic disorders in each of these periods. If a disorder was present according to DSM criteria at any assessment wave occurring in a given period, it was considered present. However, for preschool depression, age adjusted and developmentally appropriate criteria previously validated for identifying depression during the preschool period were used for children 7 years old and younger [1,2,37]. Subjects could have more than one diagnosis at an assessment wave. Relevant Axis I diagnoses were investigated, specifically major depressive disorder (MDD), conduct disorder (CD), anxiety disorder, attention-deficit/hyperactivity disorder (ADHD), and oppositional defiant disorder (ODD). Anxiety disorders included generalized anxiety disorder (GAD), separation anxiety disorder (SAD), and post-traumatic stress disorder (PTSD). For the EP and LP groups, the anxiety disorder grouping also included social anxiety (SA) and panic disorder (PD).

Logistic regression models with EP and LP diagnoses as the dependent variables and PS diagnoses as the independent variables were utilized to determine whether diagnostic characteristics in the PS period were associated with later diagnoses. Separate models were run for each EP and LP diagnosis with all 5 PS diagnoses included as independent variables.

Hierarchical logistic regression models were conducted to test for an association between environmental and family predictors of EP MDD and LP MDD. Independent variables, baseline income-to-needs ratio, PS traumatic life events frequency, and maternal history of depression were entered into the models at step 1 and PS MDD, PS anxiety disorder (PS GAD, PS SAD, or PS PTSD), and PS externalizing disorder (PS ADHD, PS ODD, or PS CD) were entered at step 2. Baseline age and gender were covariates in the models.

Multilevel modeling was used to examine the relationship between PS MDD and the trajectory of depression severity as measured by the CDI over time. Separate models using Maximum Likelihood Estimation to adjust for missing data were conducted for CDI-Child (CDI-C) and CDI-Parent (CDI-P) total T-Scores. The models included random intercept and slope components with an unstructured covariance structure. Time was defined as the age the CDI was administered (median centered at 12 based on previous research indicating that depressive symptoms decline from early-to-late school age and begin to climb again as a child enters adolescence [21]), and age squared was included in the models to account for quadratic slopes. Dummy codes for Pubertal period (i.e., early pubertal vs. later pubertal) and gender were included as covariates in the models. Interactions between PS MDD and age and PS MDD and age squared allowed for differing trajectories depending on PS MDD status. All analyses were conducted using SAS v9.4.

3. Results

There were N = 306 subjects completing at least one wave of the study. N = 279 subjects had data available for the preschool period and the early pubertal and/or later pubertal periods and were included in the analyses. There were N = 275 subjects assessed during the early pubertal period and N = 184 subjects assessed during the later pubertal period. Demographic and diagnostic characteristics are shown in Table 1 and mean age and sample size for each assessment wave, as well as CDI average score for each age, are reported in Table 2. The mean (SD) assessment ages for the preschool, early pubertal, and later pubertal periods were 4.97 (0.49), 8.69 (0.96), and 13.75 (1.77) years, respectively. Please see Supplemental Table 1 in supplemental information for a comparison between subjects with mid-late pubertal data and those without this information.

Results of logistic regressions of early pubertal diagnoses and late pubertal diagnoses are shown in Tables 3 and 4, respectively. PS MDD and PS ODD were both significantly associated with all early pubertal disorders except for early pubertal CD. Significant OR's for PS MDD ranged from 2.2 for early pubertal anxiety to 3.43 for early pubertal MDD, and significant OR's for PS ODD ranged from 2.10 for early

Table 1
Demographic and diagnostic characteristics of the sample.

	Full sample (N = 279)		Early pubertal subjects (N = 275)		Later pubertal subjects (N = 184)	
	Mean	SD	Mean	SD	Mean	SD
Demographic characteristics						
Baseline age (years)	4.50	0.79	4.49	0.79	4.58	0.77
Age at last assessment (years)	13.64	3.10	13.62	3.11	15.27	2.20
Baseline income-to-needs ratio	2.07	1.18	2.08	1.17	1.96	1.20
	%	N	%	N	%	N
Male	52.7	147	53.1	146	51.1	94
Race						
Caucasian	54.8	153	55.6	153	50.0	92
African-American	32.3	243	32.0	88	37.0	68
Other	12.9	279	12.4	34	13.0	24
	%	N	%	N	%	N
Diagnoses						
Preschool-Onset Diagnoses (N = 279)						
MDD	33.7	94	33.5	92	38.0	70
Conduct disorder	17.2	48	17.1	47	16.9	31
Anxiety disorder	30.8	86	30.9	85	30.4	56
ADHD	18.3	51	18.2	50	17.9	33
Oppositional defiant disorder	27.6	77	28.0	77	27.7	51
Early pubertal diagnoses (N = 275)						
Depression	35.3	97	35.3	97	38.3	69
Conduct disorder	14.9	41	14.9	41	16.7	30
Anxiety disorder	27.3	75	27.3	75	29.4	53
ADHD	25.5	70	25.5	70	27.2	49
Oppositional defiant disorder	22.9	63	22.9	63	25.6	46
Later pubertal diagnoses (N = 184)						
Depression	25.5	47	25.0	45	25.5	47
Conduct disorder	8.2	15	7.8	14	8.2	15
Anxiety disorder	29.4	54	29.4	53	29.4	54
ADHD	17.4	32	16.7	30	17.4	32
Oppositional defiant disorder	12.0	22	11.1	20	12.0	22
Psychotic disorder	2.7	5	2.2	4	2.7	5

pubertal anxiety to 4.30 for EP ODD. In addition, PS CD was significantly associated with early pubertal MDD and early pubertal CD, with OR's of 2.43 and 6.49, respectively. PS Anxiety was significantly associated with early pubertal Anxiety with an OR of 1.97. PS MDD was significantly associated with all late pubertal disorders except later pubertal anxiety, with significant OR's ranging from 2.32 for later pubertal MDD to 3.64 for later pubertal CD. The only other significant associations for later pubertal diagnoses were between PS CD and later pubertal CD (OR = 9.30) and PS ADHD and later pubertal ADHD (OR = 2.91). Highly similar

Table 2
Age at baseline and follow-up assessments and Average Child Depression Inventory scores by age.

	N	Mean	SD	Min	Max
Baseline	276	4.50	0.79	3.02	6.00
Follow-up 1	263	5.51	0.80	3.98	6.99
Follow-up 2	251	6.48	0.78	4.99	7.99
Follow-up 3	232	9.04	0.82	7.44	10.69
Follow-up 4	257	10.16	0.89	8.32	12.54
Follow-up 5	234	11.15	0.88	9.31	13.51
Follow-up 6	124	12.41	0.94	10.48	14.89
Follow-up 7	65	13.56	0.96	11.50	15.74
Follow-up 8	2	13.81	0.09	13.74	13.87
Follow-up 9	138	16.42	1.00	14.05	19.35

	Child total CDI T-score			Parent total CDI T-score		
Age (years)	N	Mean	SD	N	Mean	SD
7	3	44.67	3.79	3	48.00	4.36
8	14	44.93	6.40	14	46.64	10.12
9	51	45.18	8.74	51	48.24	8.75
10	68	43.18	5.59	69	47.12	9.88
11	108	42.86	8.21	109	47.86	9.33
12	91	42.26	7.37	90	46.59	9.51
13	65	41.28	8.11	65	47.69	10.54
14	29	45.45	6.75	29	46.59	6.74
15	37	49.38	9.94	36	51.14	13.11
16	50	47.64	8.27	50	50.96	11.57
17	38	49.03	5.87	36	49.56	10.26
18	2	50.00	12.73	2	54.50	16.26

Table 3
Logistic regression models of early pubertal disorders by preschool disorders (N = 275).

	Estimate	SE	OR	95% CI	χ^2	p
DV: Early pubertal MDD						
Preschool MDD	1.23	0.30	3.43	(1.91, 6.14)	17.10	<0.0001
Preschool CD	0.89	0.40	2.43	(1.12, 5.28)	5.06	0.0245
Preschool anxiety	−0.02	0.32	0.98	(0.52, 1.82)	0.01	0.9386
Preschool ADHD	0.08	0.40	1.08	(0.49, 2.37)	0.04	0.8443
Preschool ODD	0.78	0.35	2.19	(1.11, 4.32)	5.07	0.0243
DV: Early pubertal CD						
Preschool MDD	0.48	0.40	1.62	(0.74, 3.56)	1.45	0.2278
Preschool CD	1.87	0.44	6.49	(2.76, 15.28)	18.31	<0.0001
Preschool anxiety	0.50	0.41	1.64	(0.74, 3.65)	1.48	0.2243
Preschool ADHD	0.09	0.50	1.10	(0.42, 2.90)	0.04	0.8506
Preschool ODD	0.39	0.46	1.48	(0.60, 3.68)	0.72	0.3961
DV: Early pubertal anxiety						
Preschool MDD	0.79	0.29	2.20	(1.25, 3.88)	7.38	0.0066
Preschool CD	−0.14	0.39	0.87	(0.40, 1.88)	0.13	0.7155
Preschool anxiety	0.68	0.29	1.97	(1.11, 3.49)	5.35	0.0207
Preschool ADHD	−0.00	0.39	1.00	(0.46, 2.14)	0.00	0.9927
Preschool ODD	0.72	0.34	2.05	(1.05, 4.03)	4.36	0.0367
DV: Early pubertal ADHD						
Preschool MDD	0.99	0.32	2.68	(1.42, 5.06)	9.28	0.0023
Preschool CD	0.35	0.41	1.42	(0.63, 3.17)	0.72	0.3970
Preschool anxiety	−0.03	0.35	0.97	(0.49, 1.91)	0.01	0.9219
Preschool ADHD	0.77	0.40	2.15	(0.98, 4.71)	3.68	0.0549
Preschool ODD	1.13	0.36	3.10	(1.52, 6.32)	9.74	0.0018
DV: Early pubertal ODD						
Preschool MDD	0.96	0.34	2.61	(1.33, 5.10)	7.83	0.0051
Preschool CD	0.72	0.41	2.06	(0.92, 4.62)	3.09	0.0787
Preschool anxiety	0.10	0.36	1.10	(0.54, 2.24)	0.07	0.7923
Preschool ADHD	0.31	0.42	1.37	(0.60, 3.14)	0.55	0.4571
Preschool ODD	1.46	0.38	4.30	(2.06, 8.97)	15.08	0.0001

Table 4
Logistic regression models of later pubertal disorders by preschool disorders (N = 184).

	Estimate	SE	OR	95% CI	χ^2	p
DV: Later pubertal MDD						
Preschool MDD	0.84	0.37	2.32	(1.14, 4.75)	5.32	0.0210
Preschool CD	0.47	0.51	1.60	(0.59, 4.32)	0.85	0.3554
Preschool anxiety	0.16	0.39	1.18	(0.55, 2.51)	0.18	0.6691
Preschool ADHD	0.26	0.48	1.30	(0.50, 3.33)	0.29	0.5912
Preschool ODD	−0.10	0.44	0.91	(0.39, 2.13)	0.05	0.8217
DV: Later pubertal CD						
Preschool MDD	1.29	0.66	3.64	(1.01, 13.15)	3.87	0.0490
Preschool CD	2.23	0.71	9.30	(2.32, 37.19)	9.94	0.0016
Preschool anxiety	−0.13	0.66	0.88	(0.24, 3.19)	0.04	0.8486
Preschool ADHD	0.21	0.73	1.23	(0.30, 5.09)	0.08	0.7763
Preschool ODD	0.35	0.70	1.42	(0.36, 5.64)	0.25	0.6204
DV: Later pubertal anxiety						
Preschool MDD	0.54	0.33	1.71	(0.90, 3.25)	2.66	0.1030
Preschool CD	0.22	0.47	1.25	(0.49, 3.16)	0.22	0.6414
Preschool anxiety	−0.02	0.35	0.98	(0.50, 1.94)	0.00	0.9603
Preschool ADHD	−0.29	0.45	0.75	(0.31, 1.81)	0.42	0.5170
Preschool ODD	0.01	0.39	1.01	(0.47, 2.15)	0.00	0.9875
DV: Later pubertal ADHD						
Preschool MDD	0.99	0.43	2.68	(1.16, 6.23)	5.27	0.0217
Preschool CD	0.51	0.56	1.67	(0.56, 4.96)	0.84	0.3601
Preschool anxiety	0.00	0.46	1.00	(0.41, 2.46)	0.00	0.9928
Preschool ADHD	1.07	0.51	2.91	(1.08, 7.86)	4.46	0.0346
Preschool ODD	0.13	0.50	1.13	(0.43, 3.01)	0.06	0.8014
DV: Later pubertal ODD						
Preschool MDD	1.12	0.52	3.05	(1.11, 8.38)	4.69	0.0303
Preschool CD	0.69	0.61	2.00	(0.60, 6.62)	1.29	0.2567
Preschool anxiety	0.07	0.52	1.07	(0.38, 2.98)	0.02	0.8976
Preschool ADHD	0.62	0.59	1.85	(0.58, 5.89)	1.09	0.2957
Preschool ODD	0.62	0.55	1.87	(0.63, 5.53)	1.27	0.2601

Table 5
Preschool depression as a predictor of early pubertal depression (N = 265).

	Est.	SE	OR	95% CI	χ^2	p
Step 1						
Baseline age	0.57	0.18	1.78	(1.24, 2.55)	9.77	0.0018
Baseline income-to-needs ratio	−0.28	0.12	0.76	(0.60, 0.96)	5.37	0.0205
Female gender	−0.26	0.14	0.59	(0.34, 1.02)	3.52	0.0606
Traumatic life events frequency[a]	0.05	0.04	1.06	(0.99, 1.13)	2.44	0.1184
Maternal history of MDD[a]	0.48	0.15	2.61	(1.44, 4.73)	10.04	0.0015
Step 2						
Baseline age	0.68	0.20	1.98	(1.33, 2.94)	11.32	0.0008
Baseline income-to-needs ratio	−0.15	0.13	0.87	(0.67, 1.12)	1.24	0.2652
Female gender	−0.19	0.15	0.68	(0.37, 1.24)	1.58	0.2090
Traumatic life events frequency	0.02	0.03	1.02	(0.95, 1.09)	0.28	0.5946
Maternal history of MDD	0.42	0.17	2.32	(1.21, 4.45)	6.40	0.0114
Preschool MDD	0.49	0.16	2.69	(1.41, 5.12)	9.08	0.0026
Preschool anxiety disorder	0.04	0.17	1.08	(0.56, 2.08)	0.05	0.8204
Preschool externalizing disorder[b]	0.65	0.16	3.67	(1.93, 6.98)	15.75	<0.0001

[a] Traumatic life events frequency and maternal MDD was during the preschool period.
[b] Includes conduct disorder and oppositional defiant disorder.

results from identical analyses that exclude children under 10 years of age without available pubertal data (i.e., those assumed to be prepubertal) are reported in Supplemental Tables 2 and 3 in supplemental information.

Table 5 details results of a hierarchical logistic regression model of early pubertal MDD with environmental and family variables as independent variables. In the first step, baseline income-to-needs ratio and maternal history of MDD were significantly associated with early pubertal MDD. The association between maternal history of MDD and early pubertal MDD remained significant in step 2 when PS MDD, PS anxiety, and PS externalizing disorder were added to the model. Both PS MDD and PS externalizing disorder were significantly associated with early pubertal MDD.

The hierarchical regression model of later pubertal MDD with environmental and family variables as independent variables is shown in Table 6. Similar to the early pubertal MDD model, maternal history of depression was significantly associated with later pubertal MDD. This association remained significant when PS MDD was added at step 2. PS anxiety and externalizing disorders were not significantly associated with later pubertal MDD.

As shown in Table 7, in the multilevel models, the main effects of PS MDD and age squared were significantly associated with both CDI-C and CDI-P total T-scores. Their interaction was not significant. This indicated that subjects with PS MDD had significantly higher CDI-C and CDI-P T-scores than subjects without PS MDD, but the nonlinear trajectories did not differ significantly across the age span (see Fig. 1). The pattern of results reported in Table 7 remained unchanged when age groups including low numbers (i.e., ages 7 and 18 years) were removed.

4. Discussion

The current study investigated how preschool depression influences later development and risk for future MDD during adolescence, a critical next step in understanding the developmental continuity of preschool depression across the lifespan. In line with previous research, we found that preschool depression was a highly salient predictor of prepubertal MDD. Extending previous work, we also found that preschool depression was a significant predictor of MDD in mid-to-post pubertal children, extending the predictive validity and homotypic continuity of preschool depression into this important developmental period of heightened risk for MDD. To our knowledge this is the first available longitudinal data that demonstrates homotypic continuity between preschool depression and mid-to-post pubertal depression, providing some of the strongest evidence yet for developmental continuity of this early onset form of depression. These findings further underscore the importance of early identification of depression and suggest that it is an early marker of the adolescent form.

Previous research has shown that depression can be identified during the preschool period and, once identified, that it is highly likely to persist into school age [9]. In addition, previous research has also clearly demonstrated that MDD rates dramatically increase in prevalence from childhood into adolescence [16] and following the onset of puberty [17].

Table 6
Preschool school depression as a predictor of later pubertal depression (N = 177).

	Est.	SE	OR	95% CI	χ^2	p
Step 1						
Baseline age	0.46	0.24	1.58	(0.98, 2.55)	3.49	0.0617
Baseline income-to-needs ratio	−0.21	0.16	0.81	(0.60, 1.11)	1.74	0.1867
Female gender	0.29	0.19	1.79	(0.86, 3.74)	2.42	0.1195
Traumatic life events frequency[a]	0.03	0.03	1.03	(0.96, 1.11)	0.79	0.3733
Maternal history of MDD[a]	0.52	0.19	2.83	(1.36, 5.90)	7.68	0.0056
Step 2						
Baseline age	0.40	0.25	1.50	(0.91, 2.47)	2.53	0.1114
Baseline income-to-needs ratio	−0.16	0.16	0.85	(0.62, 1.16)	1.02	0.3115
Female gender	0.31	0.19	1.86	(0.87, 3.97)	2.55	0.1102
Traumatic life events frequency	0.01	0.04	1.01	(0.94, 1.09)	0.14	0.7103
Maternal history of MDD	0.49	0.20	2.67	(1.24, 5.73)	6.32	0.0120
Preschool MDD	0.44	0.20	2.42	(1.09, 5.36)	4.73	0.0296
Preschool anxiety disorder	0.13	0.20	1.31	(0.59, 2.91)	0.43	0.5141
Preschool externalizing disorder[b]	0.06	0.21	1.13	(0.50, 2.56)	0.08	0.7780

[a] Traumatic life events frequency and maternal MDD was during the preschool period.
[b] Includes conduct disorder and oppositional defiant disorder.

Table 7
Preschool onset depression predicts an elevated trajectory of depressive symptom level across development (N = 168).

	Estimate	SE	t	p
DV: CDI-Child total T-score				
Intercept	39.7872	0.8868	44.87	<0.0001
Age	0.2219	0.2837	0.78	0.4347
Age squared	0.2927	0.0616	4.75	<0.0001
Early pubertal period[a]	1.1938	0.8616	1.39	0.1667
Female gender	1.7066	0.9038	1.89	0.0607
Preschool MDD	3.1738	0.9791	3.24	0.0014
Preschool MDD × age	−0.3441	0.3607	−0.95	0.3410
Preschool MDD × age squared	−0.0221	0.0881	−0.25	0.8019
DV: CDI-Parent total T-score				
Intercept	44.1837	1.1527	38.33	<0.0001
Age	0.1168	0.3354	0.35	0.7279
Age squared	0.1433	0.0714	2.01	0.0456
Early pubertal period	0.1747	1.0052	0.17	0.8621
Female gender	1.3078	1.2335	1.06	0.2905
Preschool MDD	5.8027	1.2957	4.48	<0.0001
Preschool MDD × age	0.0677	0.4359	0.16	0.8768
Preschool MDD × age squared	−0.0158	0.1033	−0.15	0.8783

[a] Early pubertal period was dummy coded to include early (1) versus later (0) puberty status.

The current study bridges these two relatively independent bodies of data. More specifically, and aligning with and extending our previously published work including the current study sample, preschool depression was highly predictive of MDD prior to- and following the onset of puberty. In addition, relative to other preschool psychopathology, preschool depression was the only preschool disorder predictive of MDD during the later pubertal period. Importantly, this suggests that the impact of preschool depression on risk for later MDD is not constrained to earlier developmental periods (i.e., prepuberty) and persists in its predictive utility for MDD following puberty while other preschool disorders do not (i.e., preschool ODD and CD). As a result, the current data support an important role for preschool depression in understanding individual differences related to risk for MDD following the onset of puberty, a developmental transition point associated with a significant increase in MDD prevalence. Not surprisingly, maternal history of depression was also a significant predictor of depression both prior to- and following puberty. Previous research has suggested that children with prepubertal depression and a maternal history of depression have the highest risk of MDD recurrence later in life [38]. Nevertheless, in the current regression analyses, preschool depression remained a significant predictor of pre- and postpubertal MDD even when maternal depression was included in the model. As such, the reported findings support the homotypic continuity of preschool depression following the onset of puberty and further underscore the importance of providing developmentally appropriate interventions for preschoolers with depression as soon as they are identified. While some progress has been made in developing novel interventions capable of effectively treating preschool depression [39], much more work is needed in this area.

Though not a specific focus of the current study, our findings provide important information regarding the unique predictive power of other forms of preschool psychopathology. In line with previous research, we found support for homotypic continuity between preschool and prepubertal (school age) conduct disorder [40–42]. Importantly, homotypic continuity between conduct disorder during the preschool and later pubertal period was also found, suggesting that many preschoolers with conduct disorder will continue to struggle with this disorder well into adolescence. Homotypic continuity between preschool ADHD and ADHD during puberty, as well as between preschool and early pubertal anxiety, were also found, replicating and extending earlier work indicating homotypic continuity into school age for preschool ADHD and anxiety [43–45]. In line with the reported findings for preschool depression, our results suggest that the manifestation of CD and ADHD during the preschool period are not transient developmental phenomenon or nonspecific precursors of later psychopathology, adding further weight to the public health importance of early identification and treatment of psychiatric disorders during the preschool period.

Joining an earlier longitudinal follow-up including this sample [9], preschool depression was found to be predictive of DSM disorders other than MDD during the prepubertal period, including anxiety disorders, attention deficit hyperactivity disorder (ADHD), and oppositional defiant disorder (ODD). The current results extend this pattern of heterotypic continuity into the pubertal period as well, with children with preschool depression significantly more likely than children without this disorder to have conduct disorder, ADHD, and ODD during this time. Similar findings of heterotypic, in addition to homotypic, continuity of early onset depression have been reported in several other longitudinal studies as well [46, 47]. Importantly, ODD was also found to be a similarly strong predictor of multiple disorders during the early pubertal period, including MDD, anxiety disorders, and ADHD. One factor that has been suggested to underlie heterotypic relationships between emotion and behavioral disorders has been the symptom of irritability, a diagnostic feature of depression, conduct disorder, and ODD and highly predictive of both internalizing and externalizing psychopathology [48]. Similarly, recent research suggests that a general psychopathology factor may underlie most forms of psychopathology and accounts in large part for the comorbidity between them [49–51], potentially explaining the heterotypic relationships between preschool depression and other disorders including anxiety and ADHD. Interestingly, the

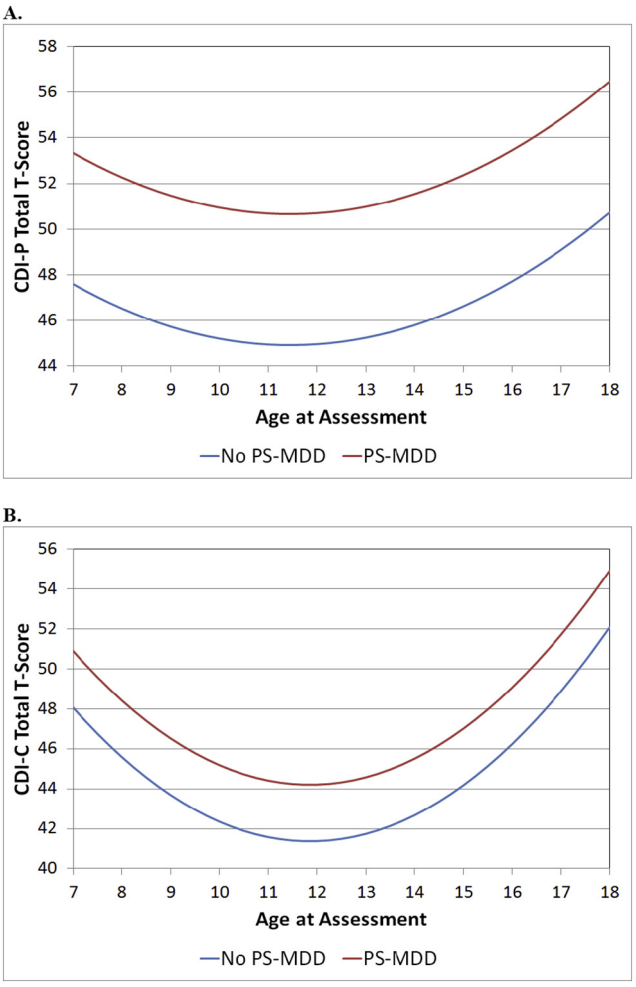

Fig. 1. Estimated trajectories of CDI-P (A) and CDI-C (B) total T-scores across age and by Preschool-onset depression group (N = 168). *Figures represent models with non-significant interaction terms removed.

heterotypic continuity observed between preschool disorders other than MDD and early pubertal psychopathology was less prevalent in our later pubertal group. Recent neuroimaging data raises the possibility that developing relationships between brain regions involved in negative emotion (e.g., amygdala) and those that may regulate them (e.g., medial prefrontal cortex) is prolonged, with the mature form of these connections and the events influencing them potentially determining the relationship between early elevations in negative affect and the presence/absence of later psychopathology [52]. Future research will be needed to further delineate the role of these and other possible explanations for heterotypic continuity among preschool depression and other disorders across development.

The identified trajectory of depressive symptoms did not differ between children with and without a history of preschool depression and followed a 'U' shaped pattern, with symptom levels decreasing from ages 7 to 12 and then increasing into adolescence. A recent study by Cohen and colleagues [21] also reported a similarly discontinuous trajectory of depressive symptom levels from school age through adolescence, with age 12 also marking the point when symptom trajectories began to differ. However, while the trajectory shape did not differ between groups in the current study, the preschool depression group was found to have elevated depression scores relative to their non-depressed peers at each time point. Critically, this suggests that while the trajectory of depressive symptoms from childhood through adolescence for children with a history of preschool depression is similar to their same age peers without this history, they nevertheless continue to experience elevated depressive symptoms even when out of episode across development. Whether the identified pattern of consistently elevated depressive symptoms reflects an ongoing consequence of preschool depression, the emerging stability of genetic influences associated with depression, and/or additional pathways leading to a similar outcome (i.e., consistently elevated depressive symptoms) across children with preschool depression is an important issue for future studies. Nevertheless, emerging research has suggested that preschool depression is associated with altered function in- and connectivity between- brain regions important for emotional response and regulation [7,8,53]. It has also suggested that the relative contributions of genes and environmental experience to the expression of depressive symptoms likely varies with age [13]. As a result, longitudinal studies using genetically informed designs and collecting brain imaging data are likely to play a critical role in understanding the etiological factors influencing depressive symptom trajectories following the very early experience of depression.

Some limitations should be noted. First, the current study used both child and parent report to determine the presence or absence of an MDD diagnosis as well as to model the trajectory of depression severity from childhood through adolescence. While the use of parent and child report is a strength, especially as it relates to both forms of data resulting in identical depression severity trajectory findings, past research does suggest that parent reported symptoms of depression in the child may be inflated by caregiver psychopathology. Also, though this study includes the largest sample of children with preschool depression followed prospectively from childhood through adolescence to date, the relatively small sample size for multilevel modeling (including for ODD and CD in the later pubertal assessment) may have impacted the current study's power to accurately detect gender differences or other more complex interactions including gender, pubertal status, and history of preschool depression. Our use of a sample enriched for preschool depression may prevent the generalization of findings to more representative community samples. Given the use of CDI T-scores, identified trajectories do not reflect absolute changes in level (i.e., raw scores) of CDI scores across time. Rather, they indicate changes across time relative to normative data for each questionnaire (i.e., CDI and CDI 2) and should be interpreted in this way. Lastly, given the age of the children involved in the current study, child report was used to measure pubertal status. Direct measurement (i.e., physical examination) is the gold standard for making these distinctions. Nevertheless, previous research does support the validity of questionnaire based measures of pubertal status for this age range [32].

5. Conclusions

Findings from the current study suggest that children with a history of preschool depression follow a trajectory of depression severity similar, though elevated, to their same age peers from childhood through adolescence. They also support the homotypic continuity of preschool depression into adolescence and the onset of puberty. As a result, from childhood through adolescence, preschool depression is a significant marker of increased risk for depression related difficulties across both continuous as well as categorical outcomes. As such, the current study further strengthens the clinical significance and public health importance of identifying and treating depression during the preschool period.

Acknowledgements

We would like to thank the children and their families who participated in this study.

Funding

The National Institute of Mental Health (NIMH; Grants R01 MH064769 to JL and MH090876 to JL and DB; Grants K23 MH098176 and R01 MH110488 to MSG) supported this work. The NIMH had no further role in the design and conduct of the study; collection, management, analysis, and interpretation of data; or preparation, review, or approval of the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.comppsych.2018.07.010.

References

[1] Luby J, Heffelfinger A, Mrakeotsky C, Hessler M, Brown K, Hildebrand T. Preschool major depressive disorder: preliminary validation for developmentally modified DSM-IV criteria. J Am Acad Child Adolesc Psychiatry 2002;41:928–37.
[2] Luby JL, Belden AC, Spitznagel E. Risk factors for preschool depression: the mediating role of early stressful life events. J Child Psychol Psychiatry 2006;47:1292–8.
[3] Luby JL, Heffelfinger A, Mrakotsky C, Brown K, Hessler M, Spitznagel E. Alterations in stress cortisol reactivity in depressed preschoolers relative to psychiatric and no-disorder comparison groups. Arch Gen Psychiatry 2003;60:1248–55.
[4] Luby JL, Belden AC, Pautsch J, Si X, Spitznagel E. The clinical significance of preschool depression: impairment in functioning and clinical markers of the disorder. J Affect Disord 2009;112:111–9.
[5] Bogdan R, Agrawal A, Gaffrey MS, Tillman R, Luby JL. Serotonin transporter-linked polymorphic region (5-HTTLPR) genotype and stressful life events interact to predict preschool-onset depression: a replication and developmental extension. J Child Psychol Psychiatry 2013;55:448–57.
[6] Luby JL, Si X, Belden AC, Tandon M, Spitznagel E. Preschool depression: homotypic continuity and course over 24 months. Arch Gen Psychiatry 2009;66:897–905.
[7] Gaffrey MS, Barch DM, Singer J, Shenoy R, Luby JL. Disrupted amygdala reactivity in depressed 4- to 6-year-old children. J Am Acad Child Adolesc Psychiatry 2013;52:737–46.
[8] Gaffrey MS, Barch DM, Bogdan R, Farris K, Petersen SE, Luby JL. Amygdala reward reactivity mediates the association between preschool stress response and depression severity. Biol Psychiatry 2018;83:128–36.
[9] Luby JL, Gaffrey MS, Tillman R, April LM, Belden AC. Trajectories of preschool disorders to full DSM depression at school age and early adolescence: continuity of preschool depression. Am J Psychiatry 2014;171:768–76.
[10] Egger HL, Angold A. Common emotional and behavioral disorders in preschool children: presentation, nosology, and epidemiology. J Child Psychol Psychiatry 2006;47:313.
[11] Wichstrom L, Berg-Nielsen TS, Angold A, Egger HL, Solheim E, Sveen TH. Prevalence of psychiatric disorders in preschoolers. J Child Psychol Psychiatry 2012;53:695–705.
[12] Lavigne JV, Gibbons RD, Christoffel KK, Arend R, Rosenbaum D, Binns H, et al. Prevalence rates and correlates of psychiatric disorders among preschool children. J Am Acad Child Adolesc Psychiatry 1996;35:204–14.

[13] Nivard MG, Dolan CV, Kendler KS, Kan KJ, Willemsen G, van Beijsterveldt CE, et al. Stability in symptoms of anxiety and depression as a function of genotype and environment: a longitudinal twin study from ages 3 to 63 years. Psychol Med 2015;45:1039–49.
[14] Wichstrom L, Belsky J, Steinsbekk S. Homotypic and heterotypic continuity of symptoms of psychiatric disorders from age 4 to 10 years: a dynamic panel model. J Child Psychol Psychiatry 2017;58:1239–47.
[15] Petersen AC, Compas BE, Brooks-Gunn J, Stemmler M, Ey S, Grant KE. Depression in adolescence. Am Psychol 1993;48:155–68.
[16] Hankin BL, Abramson LY, Moffitt TE, Silva PA, McGee R, Angell KE. Development of depression from preadolescence to young adulthood: emerging gender differences in a 10-year longitudinal study. J Abnorm Psychol 1998;107:128–40.
[17] Angold A, Costello EJ, Worthman CM. Puberty and depression: the roles of age, pubertal status and pubertal timing. Psychol Med 1998;28:51–61.
[18] Birmaher B, Arbelaez C, Brent D. Course and outcome of child and adolescent major depressive disorder. Child Adolesc Psychiatr Clin N Am 2002;11:619–38.
[19] Thapar A, Collishaw S, Pine DS, Thapar AK. Depression in adolescence. Lancet 2012;379:1056–67.
[20] Mendle J, Harden KP, Brooks-Gunn J, Graber JA. Development's tortoise and hare: pubertal timing, pubertal tempo, and depressive symptoms in boys and girls. Dev Psychol 2010;46:1341–53.
[21] Cohen JR, Andrews AR, Davis MM, Rudolph KD. Anxiety and depression during childhood and adolescence: testing theoretical models of continuity and discontinuity. J Abnorm Child Psychol 2017;46:1295–308.
[22] Cicchetti D, Toth S. The development of depression in children and adolescents. Am Psychol 1998;53:221–41.
[23] Moffitt TE, Harrington H, Caspi A, Kim-Cohen J, Goldberg D, Gregory AM, et al. Depression and generalized anxiety disorder: cumulative and sequential comorbidity in a birth cohort followed prospectively to age 32 years. Arch Gen Psychiatry 2007;64:651–60.
[24] Casey BJ, Oliveri ME, Insel T. A neurodevelopmental perspective on the research domain criteria (RDoC) framework. Biol Psychiatry 2014;76:350–3.
[25] Paykel ES. Partial remission, residual symptoms, and relapse in depression. Dialogues Clin Neurosci 2008;10:431–7.
[26] Israel JA. The impact of residual symptoms in major depression. Pharmaceuticals (Basel) 2010;3:2426–40.
[27] Egger HL, Ascher B, Angold A. The Preschool Age Psychiatric Assessment: Version 1.4. Durham, NC: Duke University Medical Center; 2003; 1999.
[28] Egger HL, Erkanli A, Keeler G, Potts E, Walter B, Angold A. Test-retest reliability of the preschool age psychiatric assessment (PAPA). J Am Acad Child Adolesc Psychiatry 2006;45:538–49.
[29] Angold A, Costello EJ. The child and adolescent psychiatric assessment (CAPA). J Am Acad Child Adolesc Psychiatry 2000;39:39–48.
[30] Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, et al. Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry 1997;36:980–8.
[31] Bird HR, Gould MS, Staghezza B. Aggregating data from multiple informants in child psychiatry epidemiological research. J Am Acad Child Adolesc Psychiatry 1992;31:78–85.
[32] Petersen AC, Crockett L, Richards M, Boxer A. A self-report measure of pubertal status: reliability, validity, and initial norms. J Youth Adolesc 1988;17:117–33.
[33] McLoyd VC. Socioeconomic disadvantage and child development. Am Psychol 1998;53:185–204.
[34] Kovacs M. The Children's depression, inventory (CDI). Psychopharmacol Bull 1985;21:995–8.
[35] Kovacs M. Child's depression inventory 2: CDI 2. Toronto: Multi-Health Systems; 2004.
[36] Maxwell E. The family interview for genetic studies: Manual. Washington, DC: Intramural Research Program, Clinical Neurogentics Branch, National Institute of Mental Health; 1992.
[37] Gaffrey MS, Belden AC, Luby JL. The 2-week duration criterion and severity and course of early childhood depression: implications for nosology. J Affect Disord 2011;133:537–45.
[38] Weissman MM, Wolk S, Wickramaratne P, Goldstein RB, Adams P, Greenwald S, et al. Children with prepubertal-onset major depressive disorder and anxiety grown up. Arch Gen Psychiatry 1999;56:794–801.
[39] Luby J, Lenze S, Tillman R. A novel early intervention for preschool depression: findings from a pilot randomized controlled trial. J Child Psychol Psychiatry 2012;53:313–22.
[40] Kim-Cohen J, Arseneault L, Caspi A, Tomás MP, Taylor A, Moffitt T. Validity of DSM-IV conduct disorder in 4–5-year-old children: a longitudinal epidemiological study. Am J Psychiatry 2005;162:1108–17.
[41] Kim-Cohen J, Arseneault L, Newcombe R, Adams F, Bolton H, Cant L, et al. Five-year predictive validity of DSM-IV conduct disorder research diagnosis in 4(1/2)-5-year-old children. Eur Child Adolesc Psychiatry 2009;18:284–91.
[42] Keenan K, Boeldt D, Chen D, Coyne C, Donald R, Duax J, et al. Predictive validity of DSM-IV oppositional defiant and conduct disorders in clinically referred preschoolers. J Child Psychol Psychiatry 2011;52:47–55.
[43] Bufferd SJ, Dougherty LR, Carlson GA, Rose S, Klein DN. Psychiatric disorders in preschoolers: continuity from ages 3 to 6. Am J Psychiatry 2012;169:1157–64.
[44] Lahey BB, Hartung CM, Loney J, Pelham WE, Chronis AM, Lee SS. Are there sex differences in the predictive validity of DSM-IV ADHD among younger children? J Clin Child Adolesc Psychol 2007;36:113–26.
[45] Finsaas MC, Bufferd SJ, Dougherty LR, Carlson GA, Klein DN. Preschool psychiatric disorders: homotypic and heterotypic continuity through middle childhood and early adolescence. Psychol Med 2018:1–10.
[46] Costello EJ, Mustillo S, Erkanli A, Keeler G, Angold A. Prevalence and development of psychiatric disorders in childhood and adolescence. Arch Gen Psychiatry 2003;60:837–44.
[47] Shevlin M, McElroy E, Murphy J. Homotypic and heterotypic psychopathological continuity: a child cohort study. Soc Psychiatry Psychiatr Epidemiol 2017;52:1135–45.
[48] Vidal-Ribas P, Brotman MA, Valdivieso I, Leibenluft E, Stringaris A. The status of irritability in psychiatry: a conceptual and quantitative review. J Am Acad Child Adolesc Psychiatry 2016;55:556–70.
[49] Caspi A, Houts RM, Belsky DW, Goldman-Mellor SJ, Harrington H, Israel S, et al. The p factor: one general psychopathology factor in the structure of psychiatric disorders? Clin Psychol Sci 2014;2:119–37.
[50] Lahey BB, Applegate B, Hakes JK, Zald DH, Hariri AR, Rathouz PJ. Is there a general factor of prevalent psychopathology during adulthood? J Abnorm Psychol 2012;121:971–7.
[51] Olino TM, Dougherty LR, Bufferd SJ, Carlson GA, Klein DN. Testing models of psychopathology in preschool-aged children using a structured interview-based assessment. J Abnorm Child Psychol 2014;42:1201–11.
[52] Tottenham N, Gabard-Durnam LJ. The developing amygdala: a student of the world and a teacher of the cortex. Curr Opin Psychol 2017;17:55–60.
[53] Luking KR, Repovs G, Belden AC, Gaffrey MS, Botteron KN, Luby JL, et al. Functional connectivity of the amygdala in early-childhood-onset depression. J Am Acad Child Adolesc Psychiatry 2011;50:1027–41 [e3].