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

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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.

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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 ascertainment 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].
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 largely 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 [6,23,26]. 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 par-
ents and children. However, at the most recent assessment, when sub-
jects were aged 16.4 ± 1.0, the Kiddie Schedule for Affective Disorders
and Schizophrenia (K-SADS; [30]) was administered separately to par-
ents 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] inter-
views, 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,
intrarater 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 clas-
sified 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 collect-
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 assess-
ment 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 dis
orders 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 de
pression 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 diag
nostic disorders in each of these periods. If a disorder was present ac
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 vali
fied 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 diag
oses were investigated, specifically major depressive disorder
(MDD), conduct disorder (CD), anxiety disorder, attention-deficit/
hyeractivity 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 group
ning also included social anxiety (SA) and panic disorder (PD).

Logistic regression models with EP and LP diagnoses as the depend
ent variables and PS diagnoses as the independent variables were uti
lized 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 indepen
dent 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 inter
cept and slope components with an unstructured covariance structure.
Time was defined as the age the CDI was administered (median cen
tered 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 Pubert
al period (i.e., early pubertal vs. later pubertal) and gender were in
cluded as covariates in the models. Interactions between PS MDD and
age and PS MDD and age squared allowed for differing trajectories de
pending 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 informa
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
Demographic and diagnostic characteristics of the sample.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic characteristics</th>
<th>Early pubertal subjects (N = 275)</th>
<th>Later pubertal subjects (N = 184)</th>
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<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
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<tr>
<td>Age at baseline (years)</td>
<td>4.50</td>
<td>0.79</td>
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<td>Age at last assessment (years)</td>
<td>13.64</td>
<td>3.10</td>
<td>13.62</td>
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<tr>
<td>Baseline income-to-needs ratio</td>
<td>2.07</td>
<td>1.18</td>
<td>2.08</td>
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<td>Gender</td>
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<td></td>
<td>Male</td>
<td>154</td>
<td>55.8</td>
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<td>Race</td>
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<td></td>
<td>African-American</td>
<td>80</td>
<td>29.0</td>
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<td></td>
<td>Other</td>
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<td>12.8</td>
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<tr>
<td></td>
<td>%</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>275</td>
<td>184</td>
</tr>
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</table>

Later pubertal diagnoses (N = 184)

- **Depression**
  - Preschool MDD: 1.12 (0.52, 2.68, 1.31, 4.34) OR: 3.87 (1.96, 7.64) 3.87 0.0051
  - Preschool CD: 0.79 (0.39, 1.60, 1.11, 2.43) OR: 0.42 (0.21, 0.83) 0.00 0.8421

Early pubertal diagnoses (N = 275)

- **Depression**
  - Preschool MDD: 1.12 (0.52, 2.68, 1.31, 4.34) OR: 3.87 (1.96, 7.64) 3.87 0.0051
  - Preschool CD: 0.79 (0.39, 1.60, 1.11, 2.43) OR: 0.42 (0.21, 0.83) 0.00 0.8421

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

<table>
<thead>
<tr>
<th>DV</th>
<th>Estimate</th>
<th>SE</th>
<th>OR</th>
<th>95% CI</th>
<th>χ²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early pubertal MDD</td>
<td>Preschool MDD</td>
<td>1.23</td>
<td>0.30</td>
<td>3.43</td>
<td>(1.91, 6.14)</td>
<td>17.10</td>
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<tr>
<td></td>
<td>Preschool CD</td>
<td>0.89</td>
<td>0.40</td>
<td>2.43</td>
<td>(1.12, 5.28)</td>
<td>5.06</td>
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<td></td>
<td>Preschool anxiety</td>
<td>−0.02</td>
<td>0.32</td>
<td>0.98</td>
<td>(0.52, 1.82)</td>
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<td>Preschool ADHD</td>
<td>0.08</td>
<td>0.40</td>
<td>1.08</td>
<td>(0.49, 2.37)</td>
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<td>Preschool ODD</td>
<td>0.78</td>
<td>0.35</td>
<td>2.19</td>
<td>(1.11, 4.32)</td>
<td>5.07</td>
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Logistic regression models of later pubertal disorders by preschool disorders (N = 184).

<table>
<thead>
<tr>
<th>DV</th>
<th>Estimate</th>
<th>SE</th>
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<th>χ²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Later pubertal MDD</td>
<td>Preschool MDD</td>
<td>0.84</td>
<td>0.37</td>
<td>2.32</td>
<td>(1.14, 4.75)</td>
<td>5.32</td>
</tr>
<tr>
<td></td>
<td>Preschool CD</td>
<td>0.47</td>
<td>0.51</td>
<td>1.69</td>
<td>(0.55, 2.31)</td>
<td>0.85</td>
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<tr>
<td></td>
<td>Preschool anxiety</td>
<td>0.16</td>
<td>0.39</td>
<td>1.18</td>
<td>(0.55, 5.25)</td>
<td>0.18</td>
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<td></td>
<td>Preschool ADHD</td>
<td>0.26</td>
<td>0.48</td>
<td>1.30</td>
<td>(0.50, 3.33)</td>
<td>0.29</td>
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<tr>
<td></td>
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<td>−0.10</td>
<td>0.44</td>
<td>0.99</td>
<td>(0.39, 2.13)</td>
<td>0.05</td>
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</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Age at baseline</th>
<th>Early pubertal MDD (N = 275)</th>
<th>Later pubertal MDD (N = 184)</th>
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<td>Mean</td>
<td>SD</td>
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<td>Baseline</td>
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<td>Follow-up 1</td>
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<td>Follow-up 2</td>
<td>4.50</td>
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<td>Follow-up 3</td>
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<td>Follow-up 4</td>
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<td>Follow-up 5</td>
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<td>Follow-up 6</td>
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<td>Follow-up 7</td>
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<td>Follow-up 9</td>
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Logistic regression models of later pubertal disorders by preschool disorders (N = 184).

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<td></td>
<td>Preschool ODD</td>
<td>−0.10</td>
<td>0.44</td>
<td>0.99</td>
<td>(0.39, 2.13)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Download a copy of this dataset at [this link](#).
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).

<table>
<thead>
<tr>
<th>Step 2</th>
<th>Est.</th>
<th>SE</th>
<th>OR</th>
<th>95% CI</th>
<th>$\chi^2$</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline age</td>
<td>0.40</td>
<td>0.25</td>
<td>1.50</td>
<td>(0.91, 2.47)</td>
<td>2.53</td>
<td>0.114</td>
</tr>
<tr>
<td>Baseline income-to-needs ratio</td>
<td>-0.16</td>
<td>0.16</td>
<td>0.85</td>
<td>(0.62, 1.16)</td>
<td>1.02</td>
<td>0.3115</td>
</tr>
<tr>
<td>Female gender</td>
<td>0.31</td>
<td>0.19</td>
<td>1.86</td>
<td>(0.87, 3.97)</td>
<td>2.55</td>
<td>0.1102</td>
</tr>
<tr>
<td>Maternal history of MDD</td>
<td>0.01</td>
<td>0.04</td>
<td>1.01</td>
<td>(0.94, 1.09)</td>
<td>0.14</td>
<td>0.7103</td>
</tr>
<tr>
<td>Preschool MDD</td>
<td>0.49</td>
<td>0.20</td>
<td>2.67</td>
<td>(1.24, 5.73)</td>
<td>6.32</td>
<td>0.0120</td>
</tr>
<tr>
<td>Preschool anxiety disorder</td>
<td>0.44</td>
<td>0.20</td>
<td>2.42</td>
<td>(1.09, 5.36)</td>
<td>4.73</td>
<td>0.0296</td>
</tr>
<tr>
<td>Preschool externalizing disorder</td>
<td>0.13</td>
<td>0.20</td>
<td>1.31</td>
<td>(0.59, 2.91)</td>
<td>0.43</td>
<td>0.5141</td>
</tr>
</tbody>
</table>

Table 7
Preschool depression as a predictor of early pubertal depression (N = 265).

<table>
<thead>
<tr>
<th>Est.</th>
<th>SE</th>
<th>OR</th>
<th>95% CI</th>
<th>$\chi^2$</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline age</td>
<td>0.57</td>
<td>0.18</td>
<td>1.78</td>
<td>(1.24, 2.55)</td>
<td>9.77</td>
</tr>
<tr>
<td>Baseline income-to-needs ratio</td>
<td>-0.28</td>
<td>0.12</td>
<td>0.76</td>
<td>(0.60, 0.96)</td>
<td>5.37</td>
</tr>
<tr>
<td>Female gender</td>
<td>-0.26</td>
<td>0.14</td>
<td>0.59</td>
<td>(0.34, 1.02)</td>
<td>3.52</td>
</tr>
<tr>
<td>Traumatic life events frequency</td>
<td>0.05</td>
<td>0.04</td>
<td>1.06</td>
<td>(0.99, 1.13)</td>
<td>2.44</td>
</tr>
<tr>
<td>Maternal history of MDD</td>
<td>0.48</td>
<td>0.15</td>
<td>2.61</td>
<td>(1.44, 4.73)</td>
<td>10.04</td>
</tr>
</tbody>
</table>

Table 6 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].
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 both the prepubertal and 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.

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.

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

<table>
<thead>
<tr>
<th>Estimate</th>
<th>SE</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>39.7827</td>
<td>0.8868</td>
<td>44.87</td>
</tr>
<tr>
<td>Age</td>
<td>0.2219</td>
<td>0.2837</td>
<td>0.78</td>
</tr>
<tr>
<td>Age squared</td>
<td>0.2927</td>
<td>0.0616</td>
<td>4.75</td>
</tr>
<tr>
<td>Early pubertal period</td>
<td>1.1938</td>
<td>0.8616</td>
<td>1.39</td>
</tr>
<tr>
<td>Female gender</td>
<td>1.7066</td>
<td>0.9508</td>
<td>1.89</td>
</tr>
<tr>
<td>Preschool MDD</td>
<td>3.1738</td>
<td>0.9791</td>
<td>3.24</td>
</tr>
<tr>
<td>Preschool MDD × age</td>
<td>-0.3441</td>
<td>0.3607</td>
<td>-0.95</td>
</tr>
<tr>
<td>Preschool MDD × age squared</td>
<td>-0.0221</td>
<td>0.0881</td>
<td>-0.25</td>
</tr>
<tr>
<td>Intercept</td>
<td>44.1837</td>
<td>1.1527</td>
<td>38.33</td>
</tr>
<tr>
<td>Age</td>
<td>0.1168</td>
<td>0.3354</td>
<td>0.35</td>
</tr>
<tr>
<td>Age squared</td>
<td>0.1433</td>
<td>0.0714</td>
<td>2.01</td>
</tr>
<tr>
<td>Early pubertal period</td>
<td>0.1747</td>
<td>0.0525</td>
<td>1.70</td>
</tr>
<tr>
<td>Female gender</td>
<td>1.3078</td>
<td>1.2315</td>
<td>1.06</td>
</tr>
<tr>
<td>Preschool MDD</td>
<td>5.8027</td>
<td>1.2957</td>
<td>4.48</td>
</tr>
<tr>
<td>Preschool MDD × age</td>
<td>0.0677</td>
<td>0.4359</td>
<td>0.16</td>
</tr>
<tr>
<td>Preschool MDD × age squared</td>
<td>-0.0158</td>
<td>0.1033</td>
<td>-0.15</td>
</tr>
</tbody>
</table>

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

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 emotional 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
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.

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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


