



HHS Public Access

Author manuscript

J Am Acad Child Adolesc Psychiatry. Author manuscript; available in PMC 2018 January 02.

Published in final edited form as:

J Am Acad Child Adolesc Psychiatry. 2017 March ; 56(3): 250–257. doi:10.1016/j.jaac.2016.12.007.

Predictors and Outcomes of Childhood Primary Enuresis

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Abstract

Objective—Although enuresis is relatively common in early childhood, research exploring its antecedents and implications is surprisingly limited, perhaps because the condition typically remits in middle childhood.

Method—We examined the prevalence, predictors, prognostic factors, and outcomes of primary enuresis in a large ($N = 559$) multi-method, multi-informant prospective study with a community-based sample of children followed from age 3 to age 9.

Results—We found that 12.7% of our sample met criteria for lifetime enuresis, suggesting that it is a commonly occurring childhood disorder. Males were over twice as likely to have a lifetime diagnosis than females. Significant age 3 predictors of developing primary enuresis at age 9 included child anxiety and low positive affectivity, maternal history of anxiety, and low authoritative parenting. In addition, poorer global functioning and more depressive and anxiety symptoms at age 3 predicted a greater likelihood of persistence through age 9. By age 9, 77% of children who had received a diagnosis of primary enuresis were in remission and continent. However, children who had remitted exhibited a higher rate of ADHD and greater ADHD and depressive symptoms at age 9 compared to children with no lifetime history of enuresis.

Conclusions—Results of the present study underscore the clinical significance of primary enuresis and demonstrate that it shows both strong antecedent and prospective associations with psychopathology. The findings also highlight the possible role of parenting in the development of enuresis.

Keywords

primary enuresis; children; internalizing; externalizing; parenting

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Disclosures: None.

Primary enuresis is a commonly occurring¹⁻³, and often distressing childhood condition. According to the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders*⁴, primary enuresis is defined by repeated voiding into bed or clothes at least twice a week for three consecutive months in children who are at least five years of age and who have not yet successfully achieved urinary control. Enuresis is a complex neuropsychiatric disorder and research examining its etiology suggests it is multifactorial. Family and twin studies find that enuresis is highly heritable, suggesting that genetics play an important etiologic factor, but also find that a third of cases arise sporadically, suggesting the etiologic role of environmental influences as well⁴². Physiological factors including maturational deficits⁵, excessive nocturnal urine production due to inadequate production of vasopressin during sleep, abnormalities in the Barrington's nucleus network linking the brain and the bladder and corticotropin-releasing factor (CRP)⁴³, and inability to arouse in response to bladder capacity cues⁶ have also been suggested as possible etiological mechanisms. Less is known, however, about the relationship between enuresis and other psychiatric disorders.

The small body of research that has examined primary enuresis' associations with psychopathology and functioning has yielded mixed findings. Whereas some studies find that enuretic youth are at no greater risk than their dry-counterparts⁷⁻⁹, there is also evidence that externalizing problem behaviors, and most notably, attention deficit hyperactivity disorder (ADHD), occur at strikingly and disproportionately higher rates in enuretic children and adolescents^{1,2,10}. For example, Biederman and colleagues¹¹ found the co-occurrence of ADHD and enuresis is approximately 30% greater than chance. This association may be indicative of shared etiological processes^{2,12}, or causal relations in which one disorder increases risk for the other. However, even when enuresis does not appear to be contemporaneously associated with ADHD, it may predict subsequent ADHD. For example, in a large sample of children from New Zealand, there were no concurrent associations between ADHD and primary enuresis at age 9¹³ however, a history of enuresis was associated with ADHD at age 13¹⁴. Thus, the presence of enuresis may also indicate a liability for ADHD. In contrast to enuresis, it is difficult to diagnose ADHD in young children, particularly those who have not yet entered school¹⁵. Hence, enuresis may be a useful indicator warranting more intensive assessment of ADHD.

ADHD may also affect the course of enuresis. When comorbid ADHD and other externalizing problems are present, enuresis has been shown to be more severe and to have a more persistent course¹⁶. One study found that when compared to children presenting with enuresis only, enuretic children also diagnosed with ADHD were more likely to have enuresis two years later¹⁰. Thus, the presence of comorbid externalizing conditions may also indicate that enuresis is a more clinically concerning condition.

In addition to associations with externalizing psychopathology, other studies have found that enuresis is associated with lower self-esteem and greater levels of internalizing psychopathology^{17,18}. It has been hypothesized that distress, shame, and parental intolerance of enuresis¹⁹ may play a causal role in the onset of internalizing problems. As these studies are cross-sectional, however, it remains unclear whether internalizing symptoms are a consequence or a continuation of pre-existing problems.

To our knowledge, only three studies have examined prospective associations between enuresis during childhood and later psychopathology during adolescence. All of these studies found that children with delayed bladder control and bed-wetting behaviors were at increased risk for later emotional and behavioral problems^{14,16,20}. However, none of these studies examined whether such emotional and behavioral problems were already apparent prior to the development of enuresis. Thus, enuresis may have been associated with later psychopathology and poorer functioning because it was linked to preexisting symptoms and impairment.

In addition, no prospective study has examined psychosocial factors that may be early indicators or contributors to the development of enuresis, though cross-sectional studies have identified a number of factors such as low socioeconomic status and family instability that co-occur with enuresis¹⁹. Examining the temporal ordering of such factors may help elucidate the etiology of enuresis and inform prevention and treatment efforts.

Furthermore, given the possibility that the presence of comorbid conditions may indicate a more severe and chronic course of enuresis¹⁰, identifying factors that predict the persistence of enuresis into later childhood may enable the identification of which enuretic children are most in need of intervention efforts. Finally, more research is necessary to determine whether children who have remitted from enuresis continue to exhibit psychiatric problems and impaired functioning. This will allow us to determine whether primary enuresis is a relatively benign condition, or whether it interferes with future development and increases vulnerability over the longer term.

The present study examined early predictors, prognostic factors, and outcomes of primary enuresis in a community sample of children followed from age 3 to age 9 using a multi-method (interviews, laboratory assessments, and questionnaires) and multi-informant (mother, father, and child) design. Our first aim was to identify age 3 predictors of later enuresis. The following six domains were assessed: demographics; early childhood psychiatric disorders; psychosocial functioning; child temperament; parental psychopathology; and parenting. Next, we examined the early characteristics that distinguished children whose enuresis persisted into the age 9 assessment from those who remitted prior to that assessment. Finally, we explored whether, even after remission, enuresis was associated with maladaptive outcomes later in development¹⁴. These analyses examined whether enuresis predicts psychiatric disorders and symptoms and functional impairment at age 9 among children who no longer had a current diagnosis of enuresis, adjusting for the prior status of these variables. Although there are strong associations among elimination disorders, evidence suggests that co-occurring enuresis and encopresis may be etiologically distinct from other forms of enuresis⁷; therefore, we excluded children with a lifetime history of encopresis.

Method

Participants

Participants were part of a large community sample of families ($N = 559$)²², with 3-year-old children ($M = 3.55$ years, $SD = 0.43$) recruited through a commercial mailing list. Children

with no significant medical conditions or developmental disabilities who were living with at least one biological parent were eligible to participate. In total, 541 parents completed a diagnostic interview and questionnaires regarding their three-year-old child. Of those 541 families, 462 (85.4%) were interviewed again when their child turned six ($M=6.1$, $SD=0.4$ years). At age 9 ($M=9.14$ years, $SD=.32$), 426 families (78.7%) completed questionnaires about the child's current depressive and anxiety symptoms, and mothers and their children completed a diagnostic clinical interview. Fifteen children with a lifetime diagnosis of encopresis and three children with secondary enuresis were excluded from the current study. This report's final sample ($N=408$; 217 females) was 94.1% Caucasian, 2.9% Black or African American, and 2.7% Asian; 9.1% of the final sample was of Hispanic or Latino origin. The Institutional Review Board approved all study procedures. Informed consent was obtained from parents, child assent was obtained at the age 9 assessment, and families were financially compensated for their time.

Measures

Enuresis—All cases of enuresis were identified using the specific criteria listed in the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision*²¹, (DSM-IV-TR). To measure the lifetime rates of enuresis in our sample, we assessed current diagnoses at age 6 and lifetime and current diagnoses at age 9. Children who met DSM-IV-TR criteria for current enuresis at the age 6 assessment or met criteria during their lifetime at the age 9 assessment were included in calculating the sample's lifetime rate of enuresis. At age 6, we assessed enuresis using the Preschool Age Psychiatric Assessment²² (PAPA) with a parent, and at age 9 using the Kiddie-Schedule of Affective Disorders and Schizophrenia—Present and Lifetime²³ (K-SADS-PL) with a parent and the child. At the age 6 assessment, a three-month primary period was used to enhance recall, but symptom onset dates were obtained for all criteria. Although the DSM-IV-TR's definition of enuresis includes secondary as well as primary enuresis, we excluded cases with a lifetime history of only secondary enuresis (i.e. regressive wetting when control has already been acquired) given evidence that it may be an etiologically distinct condition.⁴¹

Children's DSM-IV Psychiatric Disorders—As described in detail elsewhere²⁴, DSM-IV disorders were assessed by master's level psychologists and advanced graduate students in clinical psychology using the PAPA at ages three and six (92.2% mothers); they included any depressive disorder (major depressive disorder, dysthymic disorder, or depression not otherwise specified); any anxiety disorder (specific phobia, separation anxiety disorder, social phobia, generalized anxiety disorder, agoraphobia, selective mutism); ADHD; and oppositional defiant disorder (ODD). We also ran analyses using dimensional symptom scales at ages 3 and 6 for depression, anxiety, ODD, and ADHD.

At the age 3 assessment, due to concerns about administration time, in the first 60% of the sample ($n=324$), the PAPA interviewer used the Early Childhood Inventory-4²⁵ (ECI-4) ADHD and ODD scales as a screen to help determine whether to complete the ADHD and ODD sections of the interview. When parent-reports indicated a low likelihood of ODD or ADHD symptoms (i.e., all items were endorsed as “never” or “sometimes”), interviewers probed the respective broad domains to confirm the absence of symptoms before skipping

out. When parent-reports indicated a potential likelihood of ODD or ADHD symptoms (i.e., items endorsed as “often” or “very often”), the corresponding PAPA sections were administered in their entirety. ECI-4 ADHD and ODD item scores were used to impute missing age 3 PAPA ADHD and ODD item scores using multiple imputation estimation procedures for missing values²⁶.

At the age 9 assessment, one parent (92.2% mothers) and the child were interviewed using the K-SADS-PL. Doctoral students in clinical psychology or a master’s-level clinician administered the K-SADS first to the parent and then to the child. Further information was obtained to reconcile discrepancies. Summary ratings for each symptom were derived based on the combination of parent and child reports. Diagnoses were derived for the following DSM-IV-TR psychiatric disorders: any depressive disorder (MDD, dysthymic disorder, depressive disorder-NOS); any anxiety disorder (specific phobia, social phobia, separation anxiety, GAD, panic, agoraphobia, obsessive compulsive, post-traumatic stress, acute stress, anxiety disorder-NOS); ODD and any ADHD (ADHD-inattentive, hyper-activity or combined type, ADHD-NOS). Symptoms of any depression, anxiety, ODD and ADHD were rated on a 3-point scale (0 = not present; 1 = subthreshold; 2 = threshold) and were summed to create dimensional scores.

Age 9 child depressive and anxiety symptoms—Mothers, fathers and children completed the Child Depression Inventory²⁷ (CDI). The parent and child versions of the CDI have 17 and 27 items, respectively. Additionally, mothers, fathers, and children completed the 41 item Screen for Child Anxiety Related Disorders²⁸ (SCARED) to assess children’s current depressive and anxiety symptoms, respectively.

Functional Impairment—The PAPA interviewer completed the Children’s Global Assessment Scale (CGAS) and functional impairment ratings at age 3 and age 6. The CGAS is a global measure of children’s level of functioning²⁹. Scores range from 0-100, where 0 indicates the worst functioning and 100 indicates superior functioning. Impairment was also rated across several domains (parental relationship quality, household and recreational activities, sibling and peer relationships, school life) on 5-point scales ranging from 0 (no impairment) to 4 (severe impairment). Ratings were summed across domains for a total impairment score.

At age 9, the K-SADS interviewer completed the CGAS and functional impairment ratings following the administration of the K-SADS. Impairment was again rated across several domains (parental relationship quality, household and recreational activities, sibling relationships, peer relationships, school life, overall satisfaction) on a 5-point scale ranging from 0 (very good functioning/no impairment) to 4 (very poor functioning/severe impairment) and averaged across domains for a mean total impairment rating.

Child Temperament—At age 3, each child and a parent visited the laboratory for a 2-hour observational assessment of temperament that included a standardized set of episodes selected to elicit a range of temperament-relevant behaviors. Tasks were selected from the Laboratory Temperament Assessment Battery³⁰ (Lab-TAB). The episodes were selected to elicit a number of affective dimensions, including positive affectivity (PA) and negative

affectivity (NA: fear, anger/frustration and sadness). Coding procedures followed those reported in a previous study³¹.

Parental Psychopathology—At age 3, children’s biological parents were interviewed using the non-patient Structured Clinical Interview for DSM–IV³² (SCID). Interviewers were doctoral students in clinical psychology or a master’s-level clinician. For cases in which completion of the SCID with one parent was not possible, family history information was obtained from the other parent using a semi-structured interview³³. Diagnoses for 24 fathers were derived solely using the family history method.

Parenting—At the age 3 assessment, mothers and fathers completed the Parenting Styles and Dimensions Questionnaire³⁴ (PSDQ) to assess perceived parenting style. Mothers and fathers rated each item on a 5-point scale ranging from 1 (*never*) to 5 (*always*). The questionnaire measures three parenting styles: authoritative (high control, high warmth), authoritarian (high control, low warmth), and permissive (low control, high warmth).

Data Analysis

To examine predictors of enuresis, we conducted binary logistic regression analyses, with lifetime enuresis diagnosis through age 9 as the dependent variable, and each age 3 predictor entered as the independent variable in separate bivariate models. Age 3 predictors included variables from each of the following six domains: demographics, child psychopathology, psychosocial functioning, and temperament, parental psychopathology, and parenting. Age 3 predictors with significant bivariate associations with enuresis were entered into a multivariate logistic regression model to examine which predictors had unique associations.

To determine predictors of persisting enuresis that was still present at age 9, we conducted bivariate logistic regression analyses in the children with a lifetime history of primary enuresis ($n = 52$). In these analyses, the dependent variable was current versus past enuresis diagnosis at age 9, and the independent variable was each age 3 predictor described above.

Finally, in order to examine whether enuresis has implications for future psychopathology and functioning after it has remitted, we conducted binary logistic regression analyses with past history of enuresis as the independent variable and current psychiatric diagnoses at age 9 (depressive disorder, anxiety disorder, ODD, and ADHD) as the dependent variables. These analyses were limited to children who did not have a current diagnosis of enuresis. In addition to reporting unadjusted analyses, models predicting diagnostic outcomes at age 9 were adjusted for the corresponding baseline disorder at age 6. Linear regression analyses were used to examine longitudinal associations between past history of enuresis and current symptoms and functional impairment at age 9. Again, we report unadjusted models and models adjusted for the corresponding measure at age 6.

Results

In the analysis sample ($n = 408$), the combined rate of children meeting criteria for a lifetime diagnosis of enuresis at the age 6 and age 9 assessments was 12.7% ($n=52$); 2.9% ($n=12$) of children were still currently enuretic at age 9. At the age 6 assessment, the rate of enuresis in

our sample was 9.1% ($n=37$). At the age 9 assessment, an additional ($n=15$) children with a lifetime diagnosis of enuresis were identified. This was likely due to recall errors and the fact that a handful ($n=3$) of children with enuresis remitted prior to the three-month period assessed during the age 6 assessment.

Age 3 predictors of lifetime enuresis through age 9

Results from the bivariate logistic regressions are presented in Table 1. Males were more than twice as likely to meet criteria for a lifetime diagnosis of enuresis than females. Age, race/ethnicity, marital status, and parental education were not associated with enuresis. Significant child predictors of enuresis included an anxiety disorder diagnosis, a higher level of anxiety symptoms, lower global functioning (GAF), and lower levels of laboratory observed PA. Significant parent-related predictors included parental lifetime anxiety disorder and lower maternal and paternal authoritative parenting. When the significant bivariate predictors were entered into a multivariate logistic regression model, male gender (OR = 1.99, 95% CI: 1.04-3.80, $p < 0.05$), parental lifetime anxiety disorder (OR = 2.24, 95% CI: 1.19-4.21, $p < 0.05$), and lower parental authoritative parenting (OR = 0.59, 95% CI: 0.42-0.85, $p < 0.01$) remained significant.

Age 3 Predictors of persisting enuresis through age 9

Among children with a lifetime history of enuresis by age 9 ($n = 52$), persisting enuresis by age 9 was predicted by higher levels of age 3 PAPA child depressive (Remitted Enuresis: $M = 3.30$, $SD = 3.58$; Persistent: $M = 6.50$, $SD = 4.98$; OR = 1.19; 95% CI: 1.01-1.40, $p < .05$) and anxiety symptoms (Remitted: $M = 7.39$, $SD = 5.62$; Persistent: $M = 13.52$, $SD = 12.88$; OR = 1.09; 95% CI: 1.01-1.18, $p < 0.05$), and poorer functioning on the GAF (Remitted: $M = 82.70$, $SD = 12.52$; Persistent: $M = 73.08$, $SD = 15.24$; OR = 0.95; 95% CI: 0.90-1.00, $p < .05$). No other age 3 characteristics included in the present study significantly predicted persistence by age 9.

Age 9 correlates of remitted enuresis

Table 2 shows associations between a diagnosis of past enuresis and current disorders at age 9, unadjusted, and adjusted for the corresponding age 6 disorder, among children who were not currently enuretic ($n=396$). In both the unadjusted and adjusted models, a past diagnosis of enuresis was significantly associated with ADHD at age 9. Table 2 also shows associations between a past diagnosis of enuresis and children's current psychiatric symptoms at age 9, unadjusted and adjusted for the corresponding age 6-symptom scale. In unadjusted models, past enuresis was significantly associated with K-SADS current depression and ADHD symptom scale scores, and maternal and paternal-reported CDI at age 9. All associations remained significant in adjusted models, with the exception of K-SADS current depression. Past enuresis was also associated with current lower functioning and higher mean ratings of impairment at age 9, but after controlling for functioning and impairment at age 6, respectively, neither association remained significant (Table 2).

Discussion

Using data from a prospective community study of children from ages 3 to 9, we examined the antecedents, prognostic factors, and psychiatric outcomes of enuresis using a multi-method, multi-informant design. To our knowledge, this is the first study to examine primary enuresis in a community sample while also examining a broad set of predictors and outcomes of enuresis, including demographics, child psychopathology and functioning, child temperament, family history of psychopathology, and parenting. Enuresis was relatively common in our sample. We found that early childhood and parental history of anxiety predicted the development of enuresis, and that greater anxiety and depressive symptoms and lower levels of functioning at age 3 predicted a more persistent course of enuresis. Finally, even after remission, children with a history of enuresis exhibited increased rates of ADHD and elevated levels of ADHD and depressive symptoms.

Consistent with previous studies that have found 3- to 12-month prevalence rates of enuresis in 6-16-year old children and adolescents to range from 1.8%-4.5% and a much greater risk of enuresis among boys than girls¹⁻³, 3.2% of children were currently enuretic at age 9 and males were 2.17 times more likely to have a lifetime diagnosis of enuresis compared to females. With regards to lifetime prevalence, the rate of enuresis in this study was much higher than the rates reported in prior studies¹⁻³—12.7% of children in our sample had a lifetime diagnosis of enuresis. As enuresis declines with age, this discrepancy between rates is likely the result of using multiple assessments with a younger sample of children.

In our sample, primary enuresis exhibited strong links with internalizing psychopathology. Both a prior anxiety disorder at age 3 and parental history of anxiety disorder as well as low positive affectivity predicted later enuresis. Moreover, parental anxiety was a unique predictor of later enuresis in a multivariate model. In addition, at age 9, a remitted lifetime diagnosis of enuresis predicted greater current K-SADs and parent-reported depressive symptoms, even after controlling for depressive symptoms at age 6. These results confirm previous studies finding that internalizing psychopathology and enuresis commonly co-occur³⁵. This is the first study, however, to find that internalizing psychopathology both *preceded* and *succeeded* the development of enuresis and suggests that internalizing problems may both contribute to the development, and be a consequence, of primary enuresis. Indeed, there is evidence to suggest that anxiety interrupts the acquisition of coordinated muscle response that could possibly lead to unstable detrusor activity³⁶. Consistent with previous studies suggesting that internalizing problems may be a consequence of enuresis³⁷, our findings also support the possibility that humiliation and lowered self-esteem associated with enuresis may create risk for the development of later depressive symptoms¹⁹. However, as internalizing psychopathology emerges prior to the development of enuresis, it is likely that preexisting internalizing problems may make an individual more vulnerable to the distress associated with bedwetting and incontinence, which together mutually create risk for later depressive symptoms. Alternatively, it is possible that internalizing problems and enuresis may have a shared vulnerability that is associated with increased risk for both conditions.

With regards to externalizing psychopathology, remitted enuresis was associated with current ADHD and ADHD symptoms at age 9, even after controlling for age 6 ADHD and ADHD symptoms, respectively. In contrast, ADHD at ages 3 and 6 were not associated with a lifetime diagnosis of enuresis. This finding is consistent with the possibility that ADHD is harder to diagnose in early childhood given the limited contexts in which symptoms can be displayed compared to later childhood, and that many enuretic children may have unidentified ADHD symptoms during this period. Furthermore, it highlights the possibility that enuresis may be useful in raising suspicion regarding risk for or presence of undiagnosed ADHD in young children, as enuretic youth had a threefold greater risk of later meeting criteria for a diagnosis of ADHD compared to those children without enuresis. It is unclear whether the association between enuresis and ADHD reflects causal relationships (e.g. enuresis is caused by the undiagnosed ADHD, such that children get distracted from going to the bathroom) or whether both outcomes are influenced by a shared vulnerability that is associated with increased risk for both conditions at different points in development¹⁶. Family studies indicate that ADHD and enuresis are transmitted independently³⁸. However, other studies indicate that the combination of enuresis and ADHD shows different neurophysiological, attentional, and clinical correlates compared to both children with only enuresis or only ADHD, raising the possibility that children who have both enuresis and ADHD may be an etiologically distinct subgroup¹¹. Studies aimed at understanding the relationship between ADHD and enuresis may lead to more effective treatment for both disorders.

While enuresis has a strong genetic basis, we found evidence to suggest that environmental influences, like parenting, also play a role in the emergence of enuresis. In the present study, low levels of maternal and paternal authoritative parenting at ages 3 also predicted later enuresis, and in a multivariate model, low authoritative parenting accounted for unique variance over and above other significant predictors. In the absence of adequate scaffolding, warmth, encouragement, and firm expectations, children may have more difficulty acquiring the skills necessary to master toilet training. There is also emerging evidence that the early caregiving environment can impact brain structure and function. For example, one study found that parental sensitivity in early childhood is positively associated with markers of more optimal brain development at age 8, and suggested that stimulation provided by sensitive caregivers can facilitate increases in brain volume and cortical thickness³⁹. Thus, parenting may contribute to the maturational deficits of the central nervous system that have been postulated to underlie the development of enuresis^{5,40}. This also raises the intriguing possibility that interventions that promote authoritative parenting may reduce children's risk of developing enuresis and possibly even the psychopathology that is subsequently associated with enuresis. It is also possible that the environmental effect of parenting style is a gene-environment correlation. However, future studies are necessary to evaluate that possibility.

Enuresis was predicted by lower global functioning at age 3, and even after remission by age 9, enuresis was associated with lower global functioning and greater impairment at age 9. However, after controlling for baseline functioning and impairment at age 6, this latter association was no longer significant. These findings indicate that enuretic children are a lower functioning and more impaired group compared to those children whose enuresis has

remitted. However, our results also indicate that functional impairment is evident in these youth even before they are eligible for a diagnosis of enuresis, and that later observations of impairment reflect earlier difficulty in functioning. Indeed, evidence suggests that enuretic children are likely to have executive functioning problems⁴⁰, which could impact their daily living. In contrast, after accounting for preexisting impairment, primary enuresis does not appear to have an additional long-term impact on functioning.

Children whose enuresis continued to persist at the age 9 assessment were more likely to have had higher levels of depressive and any anxiety symptoms, and lower levels of functioning at age 3 compared to children whose enuresis had remitted. The presence of early psychopathology may indicate a more severe and persistent course of enuresis and help identify which enuretic children may require more intensive treatment. Additionally, as early-onset psychopathology is associated with increased odds of developing more severe psychopathology later in development, this suggests that persistent enuresis may identify a more severe and high-risk subgroup of individuals. Indeed, in one study, children who continued to wet the bed after the age of 10 years had higher rates later of both externalizing and internalizing psychopathology compared to children who stopped wetting the bed at a younger age¹⁶.

The current study is not without limitations. First, we did not correct for multiple tests, although many more associations were significant than would be expected by chance, and the results were very internally consistent lending confidence in their validity. Second, we assessed child psychopathology at ages three and nine using different measures (PAPA and K-SADS), and the concordance between these measures is unknown. Third, the effect size for low authoritative parenting at age 3 on the emergence of enuresis is relatively small. However, as enuresis is a complex neuropsychological developmental issue, large effect sizes would not be expected. Fourth, we did not collect family history of enuresis, preventing us from disentangling the environmental from the genetic influences on enuresis. Finally, the sample was largely white and middle class. Future research should extend this research to more diverse samples.

In summary, the current study is the first study to examine predictors, prognostic factors, and outcomes of childhood primary enuresis in a longitudinal study of a community sample of children and their parents. Additionally, we identified a potential treatment target in low authoritative parenting. The findings underscore the clinical significance of primary enuresis and demonstrate its strong antecedent and prospective associations with psychopathology; children with a diagnosis of primary enuresis are likely to already have had lower levels of functioning and concomitant internalizing problems as early as preschool age, and even after remission, they are at high risk for ADHD and depressive symptoms. These results underscore the need to assess psychological problems, particularly internalizing disorders and ADHD, in children with enuresis and suggest that these children may benefit from parenting-focused prevention/early intervention.

Acknowledgments

This work was supported by NIMH Grant: RO1MH069942 to DNK

References

1. Park S, Kim B-N, Kim J-W, et al. Nocturnal enuresis is associated with attention deficit hyperactivity disorder and conduct problems. *Psychiatry Investig.* 2013; 10(3):253–258.
2. Shreeram S, He J-P, Kalaydjian A, Brothers S, Merikangas KR. Prevalence of enuresis and its association with attention-deficit/hyperactivity disorder among U.S. children: results from a nationally representative study. *J Am Acad Child Adolesc Psychiatry.* 2009; 48(1):35–41. [PubMed: 19096296]
3. 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(8):837–844. [PubMed: 12912767]
4. Association American Psychiatric Association. *Diagnostic and Statistical Manual of Disorders.* Fifth. American Psychiatric Pub; 2013.
5. von Gontard A, Freitag CM, Seifen S, Pukrop R, Röhling D. Neuromotor development in nocturnal enuresis. *Dev Med Child Neurol.* 2006; 48(9):744–750. [PubMed: 16904021]
6. Butler RJ, Holland P. The three systems: a conceptual way of understanding nocturnal enuresis. *Scand J Urol Nephrol.* 2000; 34(4):270–277. [PubMed: 11095087]
7. Equit M, Klein MEA, von Gontard A. Elimination disorders and anxious-depressed symptoms in preschool children: a population-based study. *Eur Child Adolesc Psy.* 2013; 23(6):417–423.
8. Friman PC, Handwerk ML, Swearer SM, McGinnis JC, Warzak WJ. Do children with primary nocturnal enuresis have clinically significant behavior problems? *Arch Pediatr Adolesc Med.* 1998; 152:537–539. [PubMed: 9641705]
9. Van Hoecke E, Baeyens D, Vande Walle J, Hoebeke P, Roeyers H. Socioeconomic status as a common factor underlying the association between enuresis and psychopathology. *J Dev Behav Pediatr.* 2003; 24(2):109–114. [PubMed: 12692456]
10. Baeyens D, Roeyers H, Demeyere I, Verté S, Hoebeke P, Vande Walle J. Attention-deficit/hyperactivity disorder (ADHD) as a risk factor for persistent nocturnal enuresis in children: a two-year follow-up study. *Acta Paediatr.* 2005; 94(11):1619–1625. [PubMed: 16303700]
11. Biederman J, Santangelo SL, Faraone SV, et al. Clinical correlates of enuresis in ADHD and non-ADHD children. *J Child Psychol Psychiatry.* 1995; 36(5):865–877. [PubMed: 7559850]
12. Van Herzeele C, De Bruyne P, De Bruyne E, Vande Walle J. Challenging factors for enuresis treatment: Psychological problems and non-adherence. *J Pediatr Urol.* 2015; 11(6):308–313. [PubMed: 26182849]
13. McGee ROB, Makinson T, Williams S, Simpson A, Silva PA. A longitudinal study of enuresis from five to nine years. 1973; 954(1):39–42. 984.
14. Feehan M, McGee R, Stanton W, Silva Pa. A 6 year follow-up of childhood enuresis: prevalence in adolescence and consequences for mental health. *J Paediatr Child Health.* 1990; 26(2):75–79. [PubMed: 2361070]
15. Rutter M, Kim-Cohen J, Maughan B. Continuities and discontinuities in psychopathology between childhood and adult life. *J Child Psychol Psychiatry.* 2006; 47(3-4):276–295. [PubMed: 16492260]
16. Fergusson DM, Horwood J. Nocturnal enuresis and behavioral problems in adolescence: a 15-year longitudinal study. *Pediatrics.* 1994; 94(5):662–668. [PubMed: 7936892]
17. Hägglöf B, Andrén O, Bergström E, Marklund L, Wendelius M. Self-esteem before and after treatment in children with nocturnal enuresis and urinary incontinence. *Scand J Urol Nephrol Suppl.* 1997; 183:79–82. [PubMed: 9165615]
18. Collier J, Butler R, Redsell SA, Evans J. An Investigation of the Impact of Nocturnal Enuresis on Children's Self-Concept. *Scand J Urol Nephrol.* 2002; 36(36):204–208. [PubMed: 12201936]
19. Butler RJ. Annotation: night wetting in children: psychological aspects. *J Child Psychol Psychiatry.* 1998; 39(4):453–463. [PubMed: 9599774]
20. Liu X, Sun Z, Uchiyama M, Li Y, Okawa M. Attaining nocturnal urinary control, nocturnal enuresis, and behavioral problems in Chinese children aged 6 through 16 years. *J Am Acad Child Adolesc Psychiatry.* 2000; 39(12):1557–1564. [PubMed: 11128334]

21. Association American Psychiatric Association. Diagnostic and Stastical Manual of Disorders. fourth. American Psychiatric Pub; 2000. text revision
22. Egger HL, Angold A. The Preschool Age Psychiatric Assessment (PAPA): A structured parent interview for diagnosing psychiatric disorders in preschool children. *Handbook of Infant and Toddler Mental Health Assessment*. 2004;223–243.
23. Birmaher B, Ehmann M, Axelson DA, et al. Schedule for affective disorders and schizophrenia for school-age children (K-SADS-PL) for the assessment of preschool children - A preliminary psychometric study. *J Psychiatr Res*. 2009; 43:680–686. [PubMed: 19000625]
24. 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(11):1157–1164. [PubMed: 23128922]
25. Sprafkin J, Volpe RJ, Gadow KD, Nolan EE, Kelly K. A DSM-IV-referenced screening instrument for preschool children: the early childhood inventory-4. *J Am Acad Child Adolesc Psychiatry*. 2002; 41(5):604. [PubMed: 12014793]
26. Acock CA. Working With missing values, 67, November. *J Marriage Fam*. 2005:671012–1028.
27. Kovacs M. The Children's Depression, Inventory (CDI). *Psychopharmacol Bull*. 1985; 21(4):995–998. [PubMed: 4089116]
28. Birmaher B, Khetarpal S, Brent D, et al. The Screen for Child Anxiety Related Emotional Disorders (SCARED): scale construction and psychometric characteristics. *J Am Acad Child Adolesc Psychiatry*. 1997; 36(4):545–553. [PubMed: 9100430]
29. Shaffer D, Gould MS, Brasic J, et al. A children's global assessment scale (CGAS). *Arch Gen Psychiatry*. 1983; 40(11):1228–1231. [PubMed: 6639293]
30. Goldsmith, HH., Reilly, J., Lemery, K., Longley, S., Prescott, A. The Laboratory Temperament Assessment Battery Preschool Version. University of Wisconsin-Madison; 1995.
31. Dyson MW, Olino TM, Durbin CE, et al. The structural and rank-order stability of temperament in young children based on a laboratory-observational measure. *Psychol Assessment*. 2015; 27(4): 1388–1401.
32. First, MB., Spitzer, RL., Gibbon, M., Williams, JBW. Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-CV). American Psychiatric Pub; 1997.
33. Andreasen NC, Endicott J, Spitzer RL, Winokur G. The family history method using diagnostic criteria. Reliability and validity. *Arch Gen Psychiatry*. 1977; 34(10):1229–1235. [PubMed: 911222]
34. Robinson CC, Mandlco B, Olsen SF, Hart CH. Authoritative, Authoritarian, and Permissive Parenting Practices: Development of a New Measure. *Psychol Rep*. 1995; 77(3):819–830.
35. Joinson C, Heron J. Development of nighttime bladder control from 4–9 years: association with dimensions of parent rated child maturational level, child temperament and maternal psychopathology. *Longit Life Course Stud*. 2009; 1(1):73–94.
36. Houts AC. Childhood enuresis as a biobehavioral problem *Behav Ther*. 1991; 22:133–151.
37. Theunis M, Van Hoecke E, Paesbrugge S, Hoebeke P, Vande Walle J. Self-image and performance in children with nocturnal enuresis. *Eur Urol*. 2002; 41(6):660–667. [PubMed: 12074785]
38. Bailey J, Ornitz E, Gehricke J, Gabikian P, Russell A, Smalley S. Transmission of primary nocturnal enuresis and attention deficit hyperactivity disorder. *Acta Paediatr*. 1999; 88(12):1364–1368. [PubMed: 10626523]
39. Kok R, Thijssen S, Bakermans-Kranenburg MJ, et al. Normal variation in early parental sensitivity predicts child structural brain development. *J Am Acad Child Adolesc Psychiatry*. 2015; 54(10): 824–831. [PubMed: 26407492]
40. Equit M, Becker A, El Khatib D, Rubly M, Becker N, von Gontard A. Central nervous system processing of emotions in children with nocturnal enuresis and attention-deficit/hyperactivity disorder. *Acta Paediatr*. 2014; 103(8):868–878. [PubMed: 24799133]
41. von Gontard A, Hollman E. Comorbidity of functional urinary incontinence and encopresis: somatic and behavioral associations. *J Urol*. 2004; 171(6):2644–2647. [PubMed: 15118441]
42. von Gontard A, Heron J, Joinson C. Family history of nocturnal enuresis and urinary incontinence: results from a large epidemiological study. *J Urol*. 2011; 185(6):2303–6. [PubMed: 21511300]

43. Valentino R, Wood S, Wein A, Zderic S. The bladder-brain connection: putative role of corticotropin-releasing factor. *Nature Revs, Urol.* 2011; 185:2303–2307.

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Table 1**Bivariate Analyses: Age 3 Predictors of Lifetime Enuresis Diagnosis at Age 9**

	No Enuresis Diagnosis (n=356)	Enuresis Diagnosis (n=52)	Odds Ratio	95% CI
<i>Demographic Characteristics</i>				
Child mean age: years (SD)	3.50 (0.26)	3.53 (0.25)	1.03	.94-1.13
Child sex: male n (%)	181 (50.8%)	36 (69.2%)	2.17*	1.17-4.02
Child race/ethnicity: White/non-Hispanic n (%)	305 (86.6%)	47 (90.4%)	1.57	.60-4.14
Parental marital status: married n (%)	335 (94.1%)	50 (96.2%)	1.57	.36-6.89
Maternal education: college graduate	204 (58.2%)	30 (53.8%)	.84	.47-1.50
Paternal education: college graduate	158 (48.6%)	20 (41.7%)	.76	.41-1.40
<i>Child Psychopathology and Functioning, n (%)</i>				
Depressive disorder n (%)	5 (1.4%)	1 (1.9%)	1.38	.16-12.02
Anxiety disorder n (%)	61 (17.1%)	16 (30.8%)	2.15*	1.12-4.12
Attention-deficit/hyperactivity disorder n (%)	9 (2.5%)	0 (0%)	0.87	.84-.90
Oppositional defiant disorder n (%)	38 (10.7%)	4 (9.5%)	.70	.24-2.04
Depressive symptoms (SD)	3.65 (4.17)	4.04 (4.13)	1.02	.96-1.09
Anxiety symptoms (SD)	6.40 (5.77)	8.80 (8.15)	1.06**	1.01-1.10
Attention-deficit/hyperactivity symptoms (SD)	2.78 (2.34)	3.62 (2.34)	1.01	.94-1.09
Oppositional defiant symptoms (SD)	2.41 (2.82)	3.12 (2.78)	1.08	.99-1.19
GAF (SD)	85.03 (14.09)	79.67 (14.00)	.98*	.96-1.00
Impairment (SD)	0.78 (1.38)	1.06 (1.48)	1.14	.94-1.37
<i>Child Temperament, mean (SD)</i>				
Lab-TAB Positive Affect	1.64 (0.23)	1.56 (0.22)	.24*	.06-.90
Lab-TAB Negative Affect	0.56 (0.26)	0.54 (0.24)	.75	.24-2.38
<i>Parental Psychopathology, n (%)</i>				
Parental lifetime depressive disorder	151 (42.4%)	23 (44.2%)	1.08	.60-1.94
Parental lifetime anxiety disorder	157 (44.1%)	33 (63.5%)	2.20**	1.21-4.02
Parental lifetime substance use disorder	182 (51.1%)	30 (57.7%)	1.30	.72-2.35
<i>Maternal Parenting, mean (SD)</i>				
Maternal authoritative parenting	61.18 (6.50)	58.80 (7.30)	.95*	.91-.99
Maternal authoritarian parenting	20.06 (4.30)	20.17 (4.23)	1.01	.94-1.08
Maternal permissive parenting	10.72 (3.27)	10.90 (2.77)	1.02	.93-1.11
<i>Paternal Parenting, mean (SD)</i>				
Paternal authoritative parenting	56.65 (8.12)	53.95 (9.53)	.96*	.93-1.00
Paternal authoritarian parenting	20.64 (4.90)	20.91 (4.56)	1.01	.95-1.08
Paternal permissive parenting	11.12 (2.90)	11.91 (2.85)	1.09 [†]	.99-1.19

Note.

*
 $p < .05$;**
 $p < .01$;

 $p < .001$.

OR=Odds Ratio; CI=Confidence Interval; GAF = Global Assessment of Functioning; Lab-TAB = Laboratory Temperament Assessment Battery.
Boldface text indicates a statistically significant predictor of lifetime enuresis.

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Table 2
Associations of Remitted Enuresis (n=40) with DSM-IV Disorders and Symptoms at Age 9

<i>Disorder at Age 9</i>	No Enuresis Diagnosis (n=356)		Enuresis Diagnosis (n=40)		Not Adjusted		Adjusted for Corresponding Age 6 Variable	
		Odds Ratio	Odds Ratio	95%CI	Odds Ratio	95%CI	Odds Ratio	95%CI
Current Anxiety Disorder (%)	62 (17.4%)	.84	8 (15.0 %)	.33-2.08	.72	.28-1.86		
Current ADHD (%)	38 (10.7%)	3.17**	12 (30.0%)	1.47-6.86	3.11**	1.34-7.22		
Current ODD (%)	8 (2.2%)	2.29	2 (5.0%)	.47-11.17	1.99	.33-11.93		
<i>Symptoms at age 9</i>								
Depression symptoms (SD)	.43 (1.54)	.11*	1.05 (2.17)	.59 (.27)	.08	.45 (.26)		
Anxiety symptoms (SD)	3.52 (5.16)	.02	3.07 (4.02)	-.30 (.85)	-.05	-.87 (.80)		
ADHD symptoms (SD)	3.77 (7.62)	.17**	8.40 (11.00)	4.53 (1.33)	.16***	4.20 (1.09)		
ODD symptoms (SD)	.92 (2.37)	.07	1.50 (3.33)	.58 (.41)	.03	.22 (.34)		
<i>CDI</i>								
Mother-reported (SD)	6.87 (4.75)	.14**	8.93 (5.98)	2.21 (.81)	.13*	1.79 (.72)		
Father-reported (SD)	7.03 (4.15)	.16**	9.31 (5.18)	2.25 (.76)	.16**	2.97 (.76)		
Child-reported (SD)	4.57 (4.07)	.04	5.55 (3.73)	.48 (.67)	.04	.48 (.67)		
<i>SCARED</i>								
Mother-reported (SD)	7.45 (7.38)	.09	9.25 (8.21)	2.30 (1.25)	.05	1.11 (1.10)		
Father-reported (SD)	6.37 (6.42)	.04	7.25 (5.47)	.86 (1.13)	.01	.21 (1.08)		
Child-reported (SD)	18.94 (10.57)	-.02	18.28 (11.58)	-.62 (1.78)	-.03	-.83 (1.79)		
<i>Functioning</i>								
CGAS (SD)	79.65 (10.43)	-.10*	76.05 (12.93)	-3.63 (1.79)	-.05	-1.60 (1.63)		
Mean impairment ratings (SD)	19.62 (3.66)	.12*	21.08 (4.46)	1.45 (.63)	.07	1.05 (.61)		

Note.

* $p < .05$;

** $p < .01$;

*** $p < .001$;

ADHD = Attention-deficit/hyperactivity disorder; ODD = Oppositional defiant disorder; CDI = Child Depression Inventory; SCARED = Screen for Child Anxiety Related Disorders; CGAS = Children's Global Assessment Scale. Boldface text indicates statistically significant outcome of remitted enuresis.