

Clinical and Neurophysiological Features of Prolonged Enuresis in Adolescents

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Abstract The article examines current perspectives on the clinical and neurophysiological features of prolonged enuresis in adolescents. The main pathogenetic mechanisms, clinical manifestations, neurophysiological patterns, and comorbid conditions associated with this pathology are analyzed. Research findings on central nervous system functional insufficiency in adolescents with enuresis are presented, and modern approaches to diagnosis and treatment of the disease are discussed.

Keywords Enuresis, Adolescents, Prolonged course, Neurophysiological features, Comorbidity, Residual organic insufficiency

1. Introduction

Enuresis with a prolonged course represents a significant medical and social problem in adolescence. While nocturnal urinary incontinence is observed in 15-20% of children by the age of 5 and is considered a variant of age-related norm, the persistence of this disorder into adolescence indicates a pathological process that requires comprehensive study [3]. According to ICD-10, the diagnosis of primary enuresis is established from the age of 5. Secondary enuresis is of particular clinical interest, with manifestation occurring between the ages of 4 and 8 years, and in the absence of adequate therapy, it acquires a prolonged course [1]. Prolonged enuresis in adolescents represents a relevant interdisciplinary problem in modern medicine, situated at the intersection of neurology, urology, psychiatry, and pediatrics [14]. This condition is characterized by involuntary urination during sleep in individuals who have reached an age at which physiological control over bladder function should be established (older than 5 years), with symptoms persisting for an extended period up to adolescence [2].

According to current epidemiological data, the prevalence of enuresis among 5-year-old children is 15-20%, among 7-year-old children – 7-12%, and by adolescence (14-15 years) decreases to 1-2% [13]. However, despite the tendency toward spontaneous resolution with age, a significant proportion of patients demonstrate a prolonged course of the disease with persistence of symptoms in adolescence, which substantially reduces quality of life and negatively affects social adaptation and psychoemotional development [5].

Enuresis with a prolonged course is of particular medical and social significance specifically in adolescence, when personal identity is forming, social contacts are expanding, and there is an increased need for autonomy and independence. In this context, the presence of enuresis is perceived especially painfully by adolescents, causing reduced self-esteem, the formation of avoidant behavior, social isolation, and the development of secondary neurotic disorders [6].

The modern concept of the pathogenesis of prolonged enuresis considers this condition as the result of a complex interaction of multiple factors, including genetic predisposition, residual organic insufficiency of the central nervous system, circadian rhythm disorders, dysfunction of autonomic regulation of the urinary system, and neuropsychological characteristics. Recent studies emphasize the leading role of neurophysiological mechanisms in the formation and maintenance of this condition [7].

The neurophysiological approach to studying prolonged enuresis allows not only a deeper understanding of the disease's pathogenetic mechanisms but also the development of individualized therapeutic strategies aimed at correcting identified abnormalities [12]. Electroencephalographic studies reveal functional insufficiency of bilateral frontal-temporal-parietal regions of the cerebral hemispheres, dysfunction of midline structures and interhemispheric commissures, and disturbances in cortical neurodynamic processes in adolescents with prolonged enuresis [8].

Of particular scientific and practical interest is the study of neurophysiological correlates of circadian rhythms and the sleep-wake cycle in prolonged enuresis, as episodes of urinary incontinence in most patients occur during sleep [9]. Identification of specific changes in sleep structure and its phase components contributes to understanding the chronobiological mechanisms of enuresis and developing

methods of chronocorrection [7]. Thus, a comprehensive study of the clinical and neurophysiological features of prolonged enuresis in adolescents represents an urgent scientific and practical task, the solution of which will optimize diagnostic and therapeutic approaches to managing this category of patients, improve disease prognosis, and enhance the quality of life for adolescents with this pathology [10].

This paper presents the results of research on clinical manifestations, neurophysiological correlates, and pathogenetic mechanisms of prolonged enuresis in adolescents, and proposes differentiated approaches to diagnosis and comprehensive therapy of this condition, taking into account the identified neurophysiological features. According to studies, with adequate therapy, complete cure can be achieved in 75% of cases, significant improvement in 15%. Minor improvement or absence of positive dynamics is observed in approximately 10% of adolescents with prolonged enuresis [11].

2. The Aim of the Research

The aim of the research is a comprehensive study of the clinical and neurophysiological features of prolonged enuresis in adolescents to identify the pathogenetic mechanisms of the disease and develop differentiated approaches to the diagnosis and treatment of this pathology.

3. Materials and Methods of Research

A prospective cohort study was conducted with the formation of a main group and a control group. The study was performed at the neurology department of the Samarkand State Medical University clinic from September 2023 to March 2025. The study was approved by the local ethics committee. Characteristics of the Examined Groups. The study included 120 adolescents aged 12 to 17 years (mean age 14.3 ± 1.8 years), divided into two groups:

Main group – 80 adolescents with prolonged enuresis (disease duration more than 3 years), including 52 boys (65%) and 28 girls (35%). Control group – 40 healthy adolescents, comparable in gender and age to the main group, without signs of enuresis and other neurological and psychiatric disorders. Adolescents in the main group were additionally divided into subgroups depending on the form of enuresis:

Subgroup 1A: adolescents with primary enuresis (n=46)

Subgroup 1B: adolescents with secondary enuresis (n=34)

Inclusion Criteria - Age from 12 to 17 years inclusive. Presence of enuresis with a prolonged course (disease duration more than 3 years). Frequency of urinary incontinence episodes at least 2 times per week during the last 3 months. Informed voluntary consent of parents (legal representatives) and the adolescents themselves to participate in the study.

A detailed medical history was collected, including disease onset, course characteristics, precipitating factors, previous treatments, and their effectiveness. Family history was gathered to identify cases of enuresis in relatives. Perinatal

history was analyzed to assess risk factors. Neurological examination was conducted using standard methodology with status assessment. Psychiatric examination included mental status evaluation. Urination diaries were maintained for 14 days, recording all episodes of enuresis.

Statistical data processing was carried out using SPSS Statistics 27.0 and Microsoft Excel 2019. For quantitative indicators, mean values (M) and standard deviations (SD) were calculated; for qualitative indicators, absolute and relative frequencies were determined.

4. Results of the Study

Analysis of clinical and anamnestic data showed that among 80 adolescents in the main group, primary enuresis (subgroup 1A) was observed in 46 (57.5%) patients, secondary enuresis (subgroup 1B) in 34 (42.5%) adolescents. Regarding the nature of the course, nocturnal enuresis predominated – in 65 (81.3%) adolescents, while a mixed form of enuresis (nocturnal and diurnal) was observed in 15 (18.7%) patients. Isolated diurnal enuresis was not detected in the examined group. The frequency of urinary incontinence episodes varied from 2-3 times per week to daily episodes. In 42 (52.5%) adolescents, 2-3 episodes of enuresis per week were noted, in 25 (31.3%) – 4-6 episodes per week, and in 13 (16.2%) – daily episodes of enuresis. Family history of enuresis was identified in 58 (72.5%) adolescents in the main group. Hereditary predisposition was more often noted in patients with primary enuresis (84.8%) compared to adolescents with secondary enuresis (55.9%), $p < 0.01$. Analysis of perinatal history revealed pregnancy and birth pathology in mothers of 63 (78.8%) adolescents in the main group. Perinatal pathology was significantly more common in subgroup 1B (secondary enuresis) – in 30 (88.2%) patients compared to subgroup 1A (primary enuresis) – in 33 (71.7%) patients, $p < 0.05$.

Neurological examination of adolescents in the main group revealed microsymptomatology of residual organic CNS damage in 68 (85%) patients, including: mild asymmetry of facial innervation (42.5%), nystagmoid eye movements when looking to the sides (38.8%), mild anisoreflexia (55%), fine motor disorders (63.7%), and mild coordination disorders (47.5%). In subgroup 1B (secondary enuresis), neurological microsymptomatology was more pronounced and occurred more frequently (94.1%) compared to subgroup 1A (78.3%), $p < 0.05$.

When assessing mental status, 72 (90%) adolescents in the main group showed emotional and volitional disorders of varying severity: emotional lability (82.5%), increased anxiety (75%), decreased self-esteem (70%), symptoms of mild to moderate depression (43.8%), and signs of social maladaptation (56.3%). According to neuropsychological testing, adolescents in the main group compared to the control group showed: decreased short-term memory indicators (7.2 ± 1.3 versus 8.9 ± 0.8 words in the Luria test, $p < 0.001$), increased time to complete Schulte tables (56.8 ± 9.3 versus 45.2 ± 6.1 sec, $p < 0.001$), and decreased concentration according

to the correction test ($88.3 \pm 7.2\%$ versus $96.1 \pm 2.8\%$, $p < 0.001$).

The quality of life of adolescents with enuresis according to the PedsQL 4.0 questionnaire was significantly reduced (65.3 ± 8.7 points) compared to the control group (84.9 ± 5.2 points), $p < 0.001$. The most pronounced decrease was noted in the scales of "Emotional functioning" (58.2 ± 10.3 versus 82.7 ± 6.8 points, $p < 0.001$) and "Social functioning" (60.4 ± 9.8 versus 86.3 ± 5.9 points, $p < 0.001$).

Results of Electroencephalographic Study- Analysis of EEG in the waking state revealed changes in bioelectrical activity of the brain in 74 (92.5%) adolescents in the main group. The main disturbances included: Disruption of zonal differences in alpha rhythm (67.5% in the main group versus 12.5% in the control group, $p < 0.001$). Disorganization of the basic rhythm (78.8% versus 15%, $p < 0.001$). Increased index of slow-wave activity in the theta range (62.5% versus 10%, $p < 0.001$). Enhanced beta activity (52.5% versus 17.5%, $p < 0.001$). Presence of paroxysmal activity of non-epileptic nature (37.5% versus 5%, $p < 0.001$). Spectral analysis of EEG revealed a significant increase in theta rhythm power in the frontal-central leads in adolescents of the main group ($53.2 \pm 8.6 \mu V^2$) compared to the control group ($32.1 \pm 5.4 \mu V^2$), $p < 0.001$, and a decrease in alpha rhythm power in the occipital leads ($68.3 \pm 10.2 \mu V^2$ versus $92.4 \pm 7.6 \mu V^2$, $p < 0.001$). EEG coherence analysis showed a decrease in intra- and interhemispheric coherence in the alpha rhythm range in adolescents with enuresis compared to the control group (0.62 ± 0.08 versus 0.78 ± 0.05 , $p < 0.001$), indicating disturbance of functional connections between different brain regions. When comparing EEG indicators between subgroups 1A and 1B, it was found that adolescents with secondary enuresis had more pronounced changes in brain bioelectrical activity: higher theta activity index ($56.3 \pm 7.4 \mu V^2$ versus $48.7 \pm 6.9 \mu V^2$, $p < 0.01$) and lower alpha activity index ($64.5 \pm 9.6 \mu V^2$ versus $71.9 \pm 8.4 \mu V^2$, $p < 0.01$).

Results of Polysomnographic Study- Polysomnographic study revealed sleep structure disturbances in 76 (95%) adolescents in the main group. The main changes included increased sleep onset time (31.8 ± 8.5 min versus 16.3 ± 4.2 min in the control group, $p < 0.001$), reduced total sleep duration (7.1 ± 0.8 h versus 8.3 ± 0.5 h, $p < 0.001$), increased representation of superficial sleep stages (stages N1 and N2) ($64.7 \pm 5.3\%$ versus $52.4 \pm 3.8\%$, $p < 0.001$), reduction of deep slow-wave sleep (stage N3) ($18.3 \pm 3.6\%$ versus $25.2 \pm 2.9\%$, $p < 0.001$), decreased representation of rapid eye movement (REM) sleep phase ($17.0 \pm 2.8\%$ versus $22.4 \pm 2.1\%$, $p < 0.001$), and increased number of brief awakenings (8.6 ± 2.3 versus 3.5 ± 1.4 , $p < 0.001$).

Analysis of the temporal relationship between episodes of enuresis and sleep phases showed that in 68 (85%) adolescents, episodes of urinary incontinence occurred predominantly in the first third of the night, during the stage of deep slow-wave sleep (N3), while in 12 (15%) patients – in the first 2 hours after falling asleep, regardless of the sleep stage. A correlation was established between the severity of sleep structure disturbances and the frequency of enuresis

episodes ($r = 0.68$, $p < 0.001$): the more pronounced the sleep structure disturbances, the more frequent the episodes of urinary incontinence.

Assessment of Autonomic Status and Circadian Rhythms- Heart rate variability study revealed autonomic regulation disorders in 70 (87.5%) adolescents in the main group. Excessive activation of the sympathetic division of the autonomic nervous system was noted in 48 (60%) adolescents, while predominance of parasympathetic influences was observed in 22 (27.5%). When assessing circadian rhythms, 64 (80%) adolescents with enuresis showed disturbance of the daily rhythm of melatonin secretion with absence or flattening of the night peak (23.4 ± 5.8 pg/ml versus 42.7 ± 6.5 pg/ml in the control group, $p < 0.001$) and disruption of the ratio between daytime and nighttime hormone levels ($1:2.1 \pm 0.3$ versus $1:4.3 \pm 0.5$ in the control group, $p < 0.001$).

Adolescents in the main group also exhibited disturbance of the daily body temperature rhythm with flattening of the daily curve and reduction in the difference between daytime and nighttime indicators ($0.6 \pm 0.2^\circ C$ versus $1.1 \pm 0.1^\circ C$ in the control group, $p < 0.001$).

Results of Urological Examination- According to uroflowmetry data, 52 (65%) adolescents in the main group showed reduced functional bladder capacity (275 ± 42 ml versus 360 ± 35 ml in the control group, $p < 0.001$). Reduced bladder capacity was more frequently observed in patients with mixed form of enuresis (93.3%) compared to isolated nocturnal enuresis (58.5%), $p < 0.01$.

Bladder ultrasound did not reveal structural anomalies in 78 (97.5%) adolescents in the main group; in 2 (2.5%) patients, minor signs of bladder dysplasia were detected that did not require surgical correction.

Antidiuretic Hormone Level- Investigation of antidiuretic hormone (vasopressin) levels in blood serum revealed decreased nighttime secretion in 60 (75%) adolescents in the main group (3.2 ± 0.8 pg/ml versus 5.8 ± 0.9 pg/ml in the control group, $p < 0.001$). Disruption of the circadian rhythm of vasopressin secretion was observed predominantly in patients with nocturnal enuresis (83.1%) and significantly less frequently in adolescents with mixed form of enuresis (40%), $p < 0.001$.

Relationship Between Clinical and Neurophysiological Indicators

Correlation analysis revealed significant relationships between clinical manifestations of enuresis and neurophysiological indicators:

A positive correlation was established between the EEG theta activity index and the frequency of enuresis episodes ($r = 0.72$, $p < 0.001$).

A negative correlation was identified between alpha rhythm power in occipital leads and the duration of enuresis ($r = -0.64$, $p < 0.001$).

A strong negative correlation was established between nighttime melatonin levels and the frequency of enuresis episodes ($r = -0.78$, $p < 0.001$).

A positive correlation was found between reduction of the deep slow-wave sleep stage and the severity of enuresis ($r=0.69$, $p<0.001$).

A negative correlation was established between functional bladder capacity and the frequency of enuresis episodes ($r= -0.61$, $p<0.001$).

A positive correlation was found between anxiety levels and the frequency of enuresis episodes ($r=0.58$, $p<0.001$).

Multivariate regression analysis showed that the most significant factors affecting the severity of enuresis in adolescents are:

Decreased nighttime melatonin secretion ($\beta= -0.32$, $p<0.001$)

Reduced representation of deep slow-wave sleep ($\beta= -0.28$, $p<0.001$)

Increased EEG theta activity index ($\beta=0.25$, $p<0.001$)

Decreased functional bladder capacity ($\beta= -0.22$, $p<0.01$)

Elevated anxiety levels ($\beta=0.18$, $p<0.01$)

The model constructed based on multivariate analysis explains 82% of the variability in the severity of enuresis in adolescents ($R^2=0.82$, $p<0.001$).

Effectiveness of Therapy Taking Into Account Identified Neurophysiological Features. Based on the data obtained, a differentiated approach to the treatment of prolonged enuresis in adolescents was developed, taking into account the identified neurophysiological features. All patients in the main group received comprehensive therapy for 6 months. Depending on the predominant neurophysiological disorders, adolescents were divided into 3 therapeutic subgroups - Subgroup A ($n=45$) — patients with predominant disturbance of the circadian rhythm of melatonin and vasopressin secretion. Therapy included desmopressin (0.2-0.4 mg at night) in combination with melatonin (3 mg 30-40 minutes before sleep). Subgroup B ($n=20$) — patients with predominant disorders of brain bioelectrical activity (high theta activity index, disruption of zonal differences). Therapy included nootropic drugs (piracetam 800-1200 mg/day) in combination with alarm therapy. Subgroup C ($n=15$) — patients with predominant emotional and volitional disorders and high levels of anxiety. Therapy included psychotherapy (cognitive-behavioral therapy) in combination with low doses of antidepressants when necessary. All patients also received regimen measures, behavioral therapy, and psychological support. After 6 months of therapy, complete cure (absence of enuresis episodes for 3 months) was achieved in 48 (60%) adolescents, significant improvement (reduction in episode frequency by 75% or more) in 21 (26.3%) patients, moderate improvement (reduction in episode frequency by 50-74%) in 8 (10%) adolescents, and minor improvement or no effect in 3 (3.7%) patients. Analysis of therapy effectiveness depending on the identified subgroups showed that in subgroup A, complete cure was achieved in 73.3% of patients, in subgroup B — in 50%, and in subgroup C — in 40% of adolescents ($p<0.05$), which confirms the importance of a differentiated approach to treating enuresis taking into account individual neurophysiological features.

5. Conclusions

Enuresis with a prolonged course in adolescents represents a complex medical and social problem requiring an interdisciplinary approach. The clinical and neurophysiological features of this condition include functional insufficiency of bilateral frontal-temporal-parietal regions of the cerebral hemispheres, dysfunction of midline brain structures and interhemispheric commissures, and disturbances in the sleep-wake cycle. Timely diagnosis of the neurophysiological features of prolonged enuresis allows for the development of an individualized treatment plan and increases the effectiveness of therapeutic interventions. A comprehensive approach, including both pharmacological and non-pharmacological treatment methods, ensures the achievement of positive results in the majority of adolescents.

Thus, the results of the study indicate the complex pathogenesis of prolonged enuresis in adolescents involving various neurophysiological mechanisms and confirm the necessity of a comprehensive approach to the diagnosis and treatment of this condition.

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