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Review Article

Nocturnal Enuresis as a Specific Compensatory Syndrome

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Abstract: The pathophysiological nature of the monosymptomatic primary nocturnal enuresis (PNE) in children is still the unresolved problem. The most hypotheses of pathogenesis of nocturnal enuresis are limited within anatomical, biochemical and physiological regulation of the urinary control. Based on our own observations as well as the data reported in the literature, we have concluded that in addition to described biological causes of this disorder, we should focus on the common clinical and developmental features observed in the majority of cases of the monosymptomatic primary nocturnal enuresis that could be united as "enuretic syndrome". In attempt to move "outside of the box" of the urinary control we have put forward a hypothesis that enuresis is a specific compensatory syndrome which is self-developed by the child's organism to "offset" the deviated sleep–wake mechanisms. This concept is based on the general "control system theory" and offers the explanations of the majority of symptoms. From the compensatory "offset" concept the treatment of PNE should be focused not on the suppression of the act of enuresis but on the stabilization of circadian sleep-wake mechanisms. Further investigations are needed to evaluate the validity of this concept.

Keywords: Enuresis, Bedwetting, Adaptation Syndrome, Compensatory Model, Etiology of Enuresis

1. Introduction

Enuresis, or "bedwetting" – is a disorder which is as old as the whole history of mankind. To quote a famous Glucklichs's conclusion: "bedwetting was with us since the down of civilization and, probably will be with us for a long time". The word "enuresis" is derived from a Greek word (enourein) that means "to void urine".

It is very difficult to find another disorder, which on the one hand has so clear clinical picture, has so much written about it, but, on the other hand, we do not have yet clear answers to physiological nature of PNE. Besides the forceful awakening or/and suppressing the symptom we do not have keys to the really control the child's afflicted sleep and its deviations including PNE. We attempted to review of the literature and offer a new approach to resolve the theoretically intriguing and practically important puzzle of PNE. Because PNE is happening in sleep we focused on the relationships between PNE and circadian rhythm.

2. Methods

Because of significant heterogeneity of nocturnal voiding problems we concentrated only on the primary monosymptomatic sleep related nocturnal enuresis in children. We have conducted a review of the relevant literature related to the etiology of enuresis and studies of sleep patterns in enuretic children.

3. Definition and Classifications

Until 2006, there was no clear definition of enuresis that would delimit it from other types of urinary incontinence. This led to the fact that practitioners and researchers, using various literature, put different meanings to the concept of enuresis, which created confusion.

The definition of enuresis, accepted by most experts today and used in this article, was standardized by Nevéus et al. [1], on behalf of the International Children's Continence Society (ICCS) in 2006 and updated by Austin et al. in 2014 [2].

Enuresis means intermittent incontinence while sleeping in children ≥ 5 years old. The terms (intermittent) *nocturnal incontinence* and *enuresis* are *now synonymous*. Thus, both, primary and secondary wetting episode that occurs during sleep is called *enuresis in this article*.

There exist *primary* and *secondary* enuresis [2]. We talk about primary enuresis when a child older than 5 years continues to wet bed during the sleep and there are no other diseases of the nervous, urogenital and endocrine systems detected [3]. It is estimated that 80% of children with nocturnal enuresis have this form. Secondary enuresis - is when child's enuretic events are terminated, and after some time renewed again. It was thought that in children with secondary enuresis the conditioned reflex was elaborated, and then for various reasons got lost [4].

Enuresis is divided into *monosymptomatic* and *non-monosymptomatic* forms. Monosymptomatic enuresis is characterized by uncontrollable urination only during sleep (nocturnal sleep or naps). In children with *monosymptomatic enuresis* there should not be any other clinical manifestations, except episodes of incontinence during sleep and psychological problems (as a result of enuresis). *Non-monosymptomatic enuresis* differs from the monosymptomatic one by periodic urinary incontinence when a person is awake as well as multiple symptoms of other diseases, where we usually consider enuresis as a symptom of an underlying disease [1].

In this paper we study the isolated *primary monosymptomatic enuresis*, which is only in children who have never had a "dry period" from the moment of birth, enuretic events happen only while sleeping, without any signs of urinary incontinence when a child is awake and without any symptoms of other diseases. By "dry period" we mean the absence of urination in sleep minimum period of 6 months. (see *Figure 1*). [3]

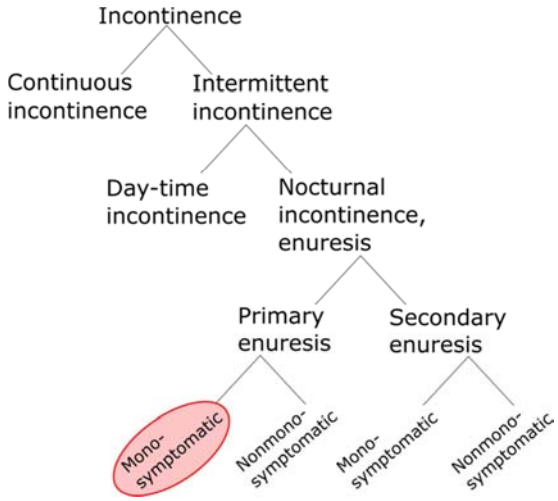

Figure 1. *Classification of Enuresis as subtype of Incontinence (retrieved from [1], expanded and supplemented).*

3.1. Etiology of Primary Monosymptomatic Enuresis

Etiology - is the study of causes [5]. Among many interpretations of the causes of enuresis many experts distinguish two main logical directions. Some authors consider bedwetting to be a result of organic disease of the urogenital and nervous systems. Other researchers believe that enuresis is a functional disorder. There are also intermediate and mixed theories of bedwetting, however etiology of enuresis still remains debated, and therefore it continues to be studied [6].

While conducting the literature review of theories of enuresis we were impressed by the amount of various ideas and explanations. The Table 1 summarized briefly the hypotheses of the occurrence of enuresis, which have been put forward by scientists of different schools of thought. There were many attempts to explain bedwetting and some of the ideas were really eccentric.

Table 1. *Hypotheses of the occurrence of enuresis.*

Year	Author	Hypothesis	Explanation
1905	Freud, S.	Urinary eroticism [7]	"Enuresis as positive act of self comfort with relaxing warm urine". Freud thought that urination was erotic and that wetting the bed was a frustrated sexual act.
1935	Malavazos, A.	Immaturity of the genitourinary organs [8]	Insufficient development of the genitourinary system might be the cause of enuresis in children.
1935	McGuinness, A. C.	Enuresis as an aggressive act in a submissive child [9]	"Sometimes enuresis is as aggressive act in a very submissive child. It may arise from such strong emotions as fear, hatred, jealousy and inferiority."
1938	Mowrer, O. H. and Mowrer, W. M.	Psychogenic factors [10]	Since no physical abnormality or other biomarker has not yet been identified, enuresis was believed to be a psychogenic disease according to this hypothesis.
1938	Michaels, J. J. and Goodman, S. E.	Psychopathic theory [11]	Authors reported that electroencephalographic (EEG) abnormalities were common in children with behavioral disorders (neurotic, personality disorder, delinquency) and enuresis. Thus, enuresis is a biomarker for psychopathic development in children
1940	Gill, S. E.	Toilet training [12]	Poor toilet training. Nowadays in U.S.A., the mean age initiating toilet training ranged from 25 to 27 months in 1980, and it increased to 36.8 ± 6.1 months in 2003.4 The reasons for late toilet training may be due to the introduction of disposable diapers, modern laundry facilities, and busy parents.
1945	Clark, G.	No theory possible [13]	'The experimental evidence on the encephalic control of the bladder is so contradictory that a theoretical explanation is impossible.'
1947	Kugelmass, I. N.	Familial [14]	Approximately 50-75% of enuretic children have a close biological relative with the same problem (in 56% this is father, in 36% - mother, in 40% - brother or sister). If one of the parents suffered from enuresis, the probability of occurrence of this problem in the child is 40-50%, if both parents - 70-80%.
1950	William, S. Walsh, M. D.	Enuresis comes out of "enuretic dreams" [15]	The author suggests that in a dream the child may see running water, a urinal, etc., which suggests voiding, and this suggestion is carried out.

Year	Author	Hypothesis	Explanation
1950	Braithwaite, J. V.	Sleep and Detrusor achalasia [16]	Enuresis is a consequence of a condition in which the muscles fail to relax, limiting the ability of the bladder to stretch for the accumulation of urine.
1950	Breitlander, K.	Sympathetic and Parasympathetic systems Disturbance [17]	He believed that the mobilization body mode and the mode of saving body resources in enuretic children are not completely regulated.
1950	Braithwaite, J. V.	Deep sleep [16]	Parents of enuretic children claimed that their children were deeply asleep at the time of enuretic event. However, critics stated that EEG studies of sleep in enuretic children revealed that they have the same stages of sleep, like children without enuresis, and enuretic events can occur at any stage of sleep.
1957	Hallgren, B.	Genetic theory [18]	The first extensive research was conducted by Hallgren in 1957. Later other researchers also suggested that inheritance occurs in an autosomal dominant manner. In various genetic studies it is informed that the gene responsible for enuresis causation may be located in chromosomes 13, 2, 4, 8, 12 and 22 and, possibly, other. But no major gen is yet identified. (Harari M. D., 2013) [19]
1963	MacDonald, J. M.	Enuretic child is “at risk" for becoming a violent sociopath [20]	The author claimed that these three behaviors (enuresis, animal cruelty and arson), when occurring together, indicate that a child is under substantial stress. The severe childhood stress makes children more likely to become violent criminals.
1968	Broughton, R. J.	Sleep Disorder [21]	Enuresis is classified as a parasomnia - one of a number of sleeping related disorders that cause undesired or unconscious action while asleep due to the “partial arousals” from sleep.
1973	*Mac Keith*, R. C.	Maturational lag [22]	Enuresis is not a disease, but a disorder caused by delays in the maturation of three physiological processes: persistence of spontaneous bladder contractions, bladder volume exceeding the nocturnal functional bladder capacity and persistence of elevated sleep/arousal thresholds.
1973	Zaleski, A., Gerrard, J. W., & Schokier, M. H. K.	Low functional bladder capacity [23]	Functional bladder capacity is the amount of urine that people can hold in the bladder until the unbearable desire to urinate. When functional capacity is small, the bladder does not hold all the urine produced during the night. The reasons for such differences in urodynamics during days and nights are not yet clear.
1980	Puri, V. N.	Hormonal problems: Vasopressin deficiency [24]	Vasopressin is also known as antidiuretic hormone (ADH, a hormone that regulates the density and amount of urine). Normally, vasopressin secretion increases at night. Production of urine decreases, and urine becomes more concentrated. In patients with nocturnal enuresis it is often found a change of vasopressin secretion rhythm. The lack of vasopressin at night leads to secretion of large amounts of urine, bladder overflow, and as a result, enuresis.
1997	Wolfish, N. M. et al.	High awakening threshold [25]	Wolfish et al. conducted an experiment. They taught children to sleep with headphones. Then a sound was played during sleep, and they measured the minimum volume level at which a child woke up. It turned out that children with enuresis woke up at a much louder sound intensity. (High audio threshold).
2017	Nevéus	Three system model [43]	Most current model schematically presented as interconnection or mismatching of three systems involved in the urinary control: 1. Nocturnal urine production, 2. Nocturnal bladder storage ability, 3. Arousal threshold.

Neveus’ article provides the most comprehensive review available. Still, it is not clear, as the author pointed out, how arousal threshold is related to “deep sleep” or to “detrusor overactivity”. Most importantly, it is still astonishing why so many children afflicted with enuresis, why so many boys, how and when to treat it and why does it disappear by itself?

Despite countless points of view, the overall picture of theories of enuresis reminds the story about blind men and an elephant: urologists look into a bladder overactivity, endocrinologists work with the hormonal level of child’s body, physiologists - with the general physical development, genetics are looking for the cause in the genome and so on, - all of them are right in their own way.

Working through a tremendous amount of information that was accumulated over the centuries, it is very easy to drown in the theories and hypotheses. However, there is one certain fact which is accepted by clinicians and researchers working with the mystery of enuresis. This fact is that *enuresis always happens while a child is sleeping*. This fact is a common denominator in all points of view and consolidates all the proposed hypotheses. That is why we shifted our further focus to the literature studying sleep patterns of enuretic children.

3.2. Sleep Patterns in Enuretic Children

In the recent decades, much attention was paid to the study of sleep in children with enuresis [25-42]. Researchers studied sleep architecture, sleep fragmentation, arousal threshold, sleep spindles, delta waves, periodic limb movements etc. In order to understand various aspects of sleep better, different methods and approaches were applied. Some of the most popular techniques used are: EEG (electroencephalography), polysomnographic methods, measurements of arousal thresholds with earphones, electrocardiographic recording of the heart rate variability (24-Hour Holter Recording), detection of night time awakenings by an actigraph, and so on.

While working on this article, we have picked out and examined studies of the sleep patterns in enuretic children, which were conducted by contemporary investigators during the recent 20-year period. The articles were retrieved from the archive database PubMed. We excluded questionnaire studies, considering the fact of subjectivity of this method. We therefore retained only those works, which were published based on the data collected by the specialized methods, where the level of human factor and subjective perception was much

lower (see methods mentioned above, for example). Below, in Table 2, we provide a list of the relevant works, together with a brief summary of the key findings.

Table 2. *Results of studies of sleep patterns in enuretic children, conducted during period from 1997 to 2017 years.*

Year	Author	Subjects	Study	Results of study
1997	Wolfish, N. M. et al.	15	Arousal thresholds	In this investigation 39,7% of controls against 9.3% of enuretics are more likely to awake in the last third of the night (and less likely in the first third). Difficulty in awakening was inversely related to the number of enuretic episodes [25].
1998	Kawauchi, A. et al.	19	Dysfunction of arousal	Arousal of subjects with primary monosymptomatic enuresis is usually similar to those of normal subjects. The measures cystometrogram was stable until the bladder got filled. Then the EEG pattern changed, however, enuresis occurred without patients awakening [26].
1999	Nevéus, T. et al.	25	Relationships between bladder voiding and sleep	The number of voiding acts taking place during the stages 2, 3, and 4 of non-REM (rapid eye movement) sleep were 19 (51%), 7 (19%), and 10 (27%), respectively. Only one enuretic event (3%) occurred during REM sleep [27].
1999	Wolfish, N. M.	35	Arousal threshold	Enuretics were less likely to arouse during the night. Difficulty in awakening was inversely related to the number of enuretic episodes [28].
2000	Hunsballe, J. M.	11	EEG delta power component	Enuretics showed a significant increase in the EEG delta power component during baseline sleep compared with controls, whereas no difference was encountered using a manual sleep score [29].
2001	Dundaröz, M. R. et al.	28	Relationship of autonomic nervous system to enuresis	The differences between the two groups (controls and enuretics) were statistically significant with regard to all parameters except NHR (night time mean heart rate). It was found that sympathetic nervous system hyperactivity was present in enuretic children [30].
2002	Bader, G. et al.	21	Differences between the sleep of enuretic children and controls	Sleep of the enuretic children did not diverge to a large extent from that of the controls. The only significant differences were that the enuretic children had an increased number of sleep cycles. Tachycardia was often seen to precede the enuretic event. In some subjects a short EEG arousal was observed before micturition [31].
2004	Unalacak, M. et al.	32	Cardiac autonomic regulation	SDNN (the standard deviation of all normal sinus R-R intervals over 24 hours), rMSSD (the root mean square of successive differences between normal sinus R-R intervals) and SDANN (standard deviation of all averaged normal sinus intervals for each 5-ninute segment in 24-hour recording) increased in enuretics compared to healthy children. VLF (very low frequency component) and LF (low frequency component) decreased significantly compared to healthy children. The study has shown that parasympathetic nervous system is hyperactive in children with enuresis [32].
2008	Yeung, C. K. et al.	35	sleep patterns and cortical arousal in relation to bladder activity	Light non–REM sleep occurred significantly more frequently, and deep non–REM sleep and REM sleep occurred considerably less frequently in patients with enuresis than in controls. Cortical arousals occurred more frequently in patients with enuresis. It was found that children with enuresis have more light sleep associated with frequent cortical arousals but are unable to awaken completely [33].
2009	Dhondt, K. et al.	29	Sleep characteristics	Preliminary data show evidence of disrupted sleep architecture in children with a high incidence of PLMS (Periodic Limb Movements of Sleep) and increased cortical arousability leading to awakening, instead of classically accepted deep sleep [34].
2011	Cohen-Zrubavel, V. et al.	32	Sleep patterns	Compromised sleep patterns were reflected in a higher number of actigraphic nighttime awakenings, the reduced percentages of motionless sleep, the higher number of reported nighttime awakening, and the increased sleep latency [35].
2014	Dhondt, K. et al.	67	Sleep fragmentation	Children with enuresis had a higher incidence of periodic limb movements associated with cortical arousals in their sleep [36].
2015	Dhondt K. et al.	30	Sleep fragmentation and periodic limb movements	The results of this study confirm both increased PLMS and increased sleep fragmentation. Enuresis was present in different sleep stages. In three children, we observed PLMS 5 min before the alarm signal was registered [37].
2017	Jönson Ring I. et al.	20	Sleep disordered breathing	The mean apnea hypopnea index values were 0.96 ± 0.8 for the patient group and 0.46 ± 0.4 for the control group. The enuretic children reported significantly more subjective sleep disturbances than their healthy peers [42].

Table 2 allowed us to understand the questions which were investigated during the last 20 years, the methods used and techniques applied. These studies gave us the data essential for understanding patterns of sleep in enuretic children, as well as their similarities and differences with normal children.

Knowing the existing literature and based on our long clinical and polysomnographic experience (PSGs with improved registrations of the onset of the enuretic episodes) working with enuretic children, we came up with a list of specific features connected with enuresis. We have distinguished typical sleep disturbances and changes in the level of alertness. The most frequently patterns appeared in children with enuresis were highlighted into the "essential" and "associated" features of enuresis (see *Table 3*) [38-40].

Table 3. *General features and sleep patterns of enuresis.*

Sleep disturbances in enuretic children
Difficulties to fall asleep or "too fast" sleep onset
Variations of the sleep depth from too deep ("dead" sleep) to erratic
Agitated or confused arousals
Changes in body position from immobility to the constant body shifting
Changes in the level of alertness in enuretic children
Significant variation of emotional liability during the day

Frequent self stimulating and /or self soothing habits	
Significant variation of daytime motor activity from passivity to hyperactivity (ADHD)	
Essential features of enuresis	Associated features of enuresis
Spontaneous involuntary urination in sleep	Family patterns of inheritance
Disturbance of sleep	Appearance of other parasomnias
Changes in levels of alertness during the day	Coexisting emotional and behavior problems
Resistance to direct symptom suppression	Mild manifestations of endocrino-,
Spontaneous remission	somatic and soft neurological symptoms

4. Discussion

Enuresis conceals many secrets and paradoxes. The clear and simple symptom (sudden, spasm-like involuntary urination in sleep) contrasts with unclarity of the nature of it and controversial methods of treatment. Enuresis "defied" the traditional rule "each symptom should reflect a broken part in the body". Centuries of intensive search for the organ ultimately responsible for involuntary urination in sleep did not lead anywhere. There is no organ or a system which was not blamed for this affliction, but was acquitted later. No underlying organic pathology was found to clearly explain bedwetting in sleep in the majority of cases. Despite the knowledge of many details of enuresis the main clinical and theoretical questions are still not answered:

1. Primary monosymptomatic enuresis is happening during sleeping but not when a child is awake. Why?
2. Is the process of urination during the sleeping similar to the process of urination when a child is awake or they are different and independent?
3. Both clinicians and parents know well that many treatments are initially helpful but only for a short time (therapeutic resistance). Why?
4. Why does enuresis spontaneously disappear (spontaneous "cure")?
5. Is enuresis associated with other parasomnias epiphenomena or they have a common pathophysiology?

Treatments aiming at suppression of the urination in sleep removed symptoms without treating the enuresis itself, and gave only a short-time result. Awakenings by parents, alarm devices (that work "post factum") cause further sleep disturbance, but not healing. Is enuresis so multifactorial and does it involve so many organs and systems that we could not talk about the nature of enuresis at all? We experienced shame when after a long unsuccessful treatment bedwetting disappeared spontaneously by itself. Therefore it is time to make a paradigm shift and revise general approaches to the paradoxes of enuresis.

We came up with a *hypothesis of enuresis being a specific adaptation (compensatory) syndrome*, actively produced by the body to stabilize the deviated sleep structure (deviations might be caused by any or all developmental, genetic, psychological and parenting factors).

Our hypothesis is based on the results of polysomnographic studies, which we conducted in our laboratory and on medical records of patients. Analyzing the obtained data, and comparing it with the results of other works, we noticed that bedwetting usually has some EEG and behavioral "forerunners" and after the episode "normalization of the followed sleep phase changes occurs" [38-40].

The explanation comes from comparing a normal hypnogram with a hypnogram of enuretic sleep. An example of a hypnogram typical for normal subjects (see Figure 2) has a successive and common algorithm. When a child falls asleep he/she generally reaches the deepest stage of sleep (stage 4) shortly (in about one hour). Afterwards, during the rest of the night the child shifts from the deep sleep stages to REM (seeing dreams) and back every 1.5-2 hours. This pattern is considered to be optimal and illustrates a healthy sleeping behavior, leading to full body recharging during the night and the maximum efficiency during the day-time.

If we look at the hypnogram of the enuretic sleep (see Figure 3), there is one very specific peculiarity. When an enuretic child falls asleep he/she reaches the deepest stages (3 and 4) within the same time-range as normal children. In contrast, the following sleep cycles are not regular. The child remains in sleep stages 3 and/or 4 for a long period of time (about 2 hours) or demonstrates chaotic changes in the hypnogram. The so-called "dead sleep" is often observed during the first 2 sleeping hours with rare breathing and very low heart rate. However, after the enuretic event takes place, the sleep cycle usually normalizes and the sleep pattern for the rest of the night stays similar to that of normal children.

In order to support our hypothesis, we demonstrate an example of the hypnogram measured in an enuretic child before and after treatment (see Figure 4). One can see that the patient with the primary monosymptomatic enuresis before treatment spent more than 3 hours in the deep stages of sleep at the initial stage of observation. Later an enuretic event took place, which however didn't make the child wake up. The subsequent monitoring of sleeping cycle did not show any abnormalities in comparison with the normal behavior (except for a little discomfort caused by sleeping in a wet bed, we suppose). On the other hand, after several months dryness (recovery period) the hypnogram of the same child remained "normal" throughout the whole night.

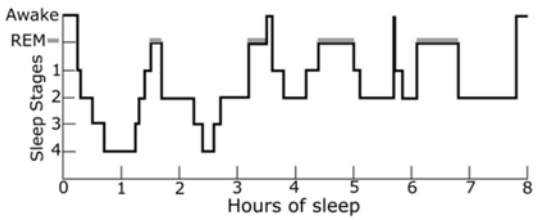

Figure 2. *Sketch of a typical hypnogram of normal sleep.*

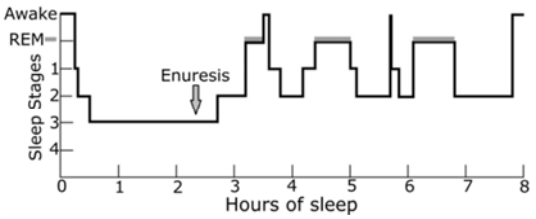

Figure 3. *Sketch of a typical hypnogram of enuretic sleep.*

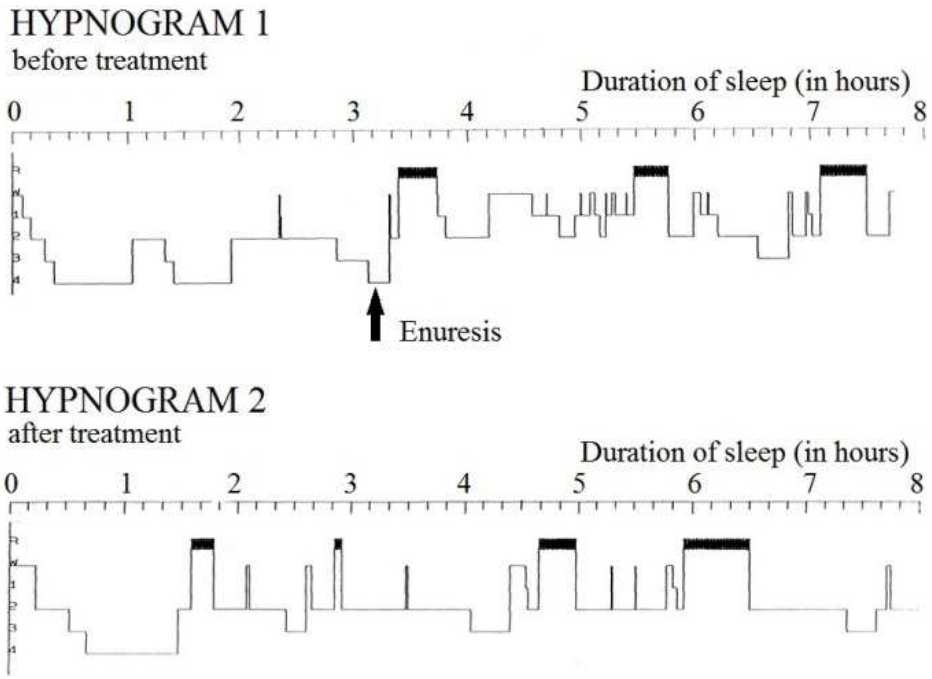

Figure 4. *Hypnograms of enuretic child before and after treatment.*

Based on our hypothesis, we present explanations of generally known and accepted facts about enuresis in Table 4, which fit the logic of compensatory model of enuresis as a specific adaptation syndrome.

Enuresis is a disorder, means "out of order". Conventional wisdom says that having a disorder is a bad thing. The advanced theory of adaptive chaos and the control system theory stated that mild disorders might have an adaptive, corrective and compensational in nature, serve to stabilize the organism as a whole, offset and contain "big disorders" [44]. Enuresis and other parasomnias might be examples of such compensatory, specific adaptive syndromes [38-40].

Table 4. *Explanation of symptoms of enuresis by the compensatory model of enuresis as a specific adaptation syndrome (the "offset" syndrome).*

Facts	Explanations
Involuntary urination in sleep	Enuresis could be a self-organizing adaptive mechanism to maintain or "switch" sleep stages
Normal capacity to hold urine during wakefulness	Because the urinary system "works" normally during the day
Enuretic act in sleep appears suddenly and with large volume	Daytime urination involved voluntary rhythmic contraction of pelvic muscles but in sleep enuresis is a sudden involuntary outburst of urine without contraction of pelvic muscles
The forcefully awakened child could urinate again as he/she falls asleep	Sleep was disturbed and enuretic act "normalizes" sleep architecture
Resistance to direct suppression	Enuresis is "needed" because it serves a specific function as a "switch" of sleep stages
Enuresis disappears spontaneously	When sleep mechanisms restored ("matured") enuresis's compensatory function is no longer "needed" and enuresis spontaneously disappeared ("cured")
PNE gets worse	If the compensatory phase is not helpful, PNE became another "problem" for the organism and the second phase – more maladaptive "offset symptoms" appear.
Enuresis predominantly is seen in boys	Enuresis belongs to parasomnias - the group of circadian rhythm deviations. Almost all parasomnias are gender connected male/female ratio 3:1 as a developmental asymmetry.
Existing therapy do not cure enuresis	Therapeutic methods should be focused not on urinary system but on maturation or restoration of sleep-wake mechanisms.

5. Conclusion

In this study we have performed a thorough literature review of existed multiple theories of etiology of enuresis and results of studies performed during the last 20 years which investigated sleep patterns in enuretic children. Based on the found information and comparison with the results of our own studies, we came up with a hypothesis of enuresis being a specific adaptation syndrome which "offset" deviations of sleep-wake mechanisms and "normalizes" sleep function. When sleep mechanisms mature enuresis disappears ("cured") by itself. If not – the second phase "deterioration"- occurred. If validated in the future large studies, the "offset" (specific compensatory" hypothesis might give a directions for an individual pathophysiological therapy of this socially, emotionally and medically uncomfortable affliction.

To confirm that 'the new is just a forgotten old' let us recall what one of the Fathers of medicine – Avicenna – said in 1012 in his famous "Canon of Medical Science": "Urinating in bed is frequently predisposed by deep sleep. When urine begins to flow, its inner nature and hidden will (resembling the will to

breathe) drives urine out before the child awakes. When children become stronger and more robust, their sleep is lighter and they stop urinating." [45]

References

[1] T. Nevéus, A. von Gontard, P. Hoebeke, K. Hjälmås, S. Bauer, W. Bower, T. M. Jørgensen, S. Rittig, J. V. Walle, C.-K. Yeung, and J. C. Djurhuus, "The Standardization of Terminology of Lower Urinary Tract Function in Children and Adolescents: Report from the Standardisation Committee of the International Children's Continence Society," Int J Urol, vol. 176(1), pp. 314-324, 2006.

[2] P. F. Austin, S. B. Bauer, W. Bower, J. Chase, I. Franco, P. Hoebeke, S. Rittig, J. V. Walle, A. von Gontard, A. Wright, S. S. Yang, and T. Nevéus, "The Standardization of Terminology of Lower Urinary Tract Function in Children and Adolescents: Update Report from the Standardization Committee of the International Childrens Continence Society," Int J Urol, vol. 191(6), pp. 1863-1865, 2014.

[3] G. Lehmkuhl, W. Berner, A. von Gontard, K. Mauer-Mucke, and J. Pluck, "Clinical behavioral problems in day- and night-wetting children," Pediatric Nephrology, vol. 13, pp. 662-667, 1999.

[4] W. L. Robson, and A. K. Leung, "Secondary nocturnal enuresis," Clinical Pediatrics vol. 39(7), pp. 379-85, 2000.

[5] Etiology. Miller-Keane Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, Seventh Edition. (2003).

[6] A. von Gontard, "Klassifikation der Enuresis/ Enkopresis im DSM-5," Zeitschrift für Kinder- und Jugendpsychiatrie und Psychotherapie, vol. 42, pp. 109-113, 2014.

[7] S. Akhtar, A Comprehensive Dictionary of Psychoanalysis. KARNAC BOOKS: 2009.

[8] A. Malavazos, "N/A", The Urologic and cutaneous review, vol. 39, pp. 322, 1935.

[9] A. C. McGuinness, "The treatment of enuresis in childhood", Medical Clinics of North America, vol. 19, pp. 287–294, 1935.

[10] O. H. Mowrer, and W. M Mowrer, "N/A", American Journal of Orthopsychiatry, vol. 8, pp. 436, 1938.

[11] J. J. Michaels, and S. E. Goodman, "N/A," Archives of Neurology & Psychiatry, vol. 40, pp. 699, 1938.

[12] S. E. Gill, "N/A," British Medical Journal, vol. 2, pp. 199, 1940.

[13] G. Clark, "N/A," The Urologic and cutaneous review, vol. 49, pp. 612, 1945.

[14] I. N. Kugelmass, "N/A," New York state journal of medicine, vol. 47, pp. 1369, 1947.

[15] S. William, M. D. Walsh, "Dreams of the feeble-minded," Medical Record, vol. 97, pp. 395-398, 1920.

[16] J. V. Braithwaite, "N/A," Practitioner, vol. 165, pp. 273, 1950.

[17] K. Breitlander, "N/A," Strahlentherapie, vol. 82, pp. 307, 1950.

[18] B. Hallgren, Enuresis a Clinical and Genetic Study, Acta Psychiatrica et Neurologica Scandinavica Sup.: 1957.

[19] M. D. Harari, "Nocturnal enuresis," Journal of Paediatrics and Child Health, vol. 49 (4), pp. 264-271, 2012.

[20] J. M. Macdonald, "The threat to kill," American Journal of Psychiatry, vol. 120 (2), pp. 125-130, 1963.

[21] R. J. Broughton, "Sleep Disorders: Disorders of Arousal?: Enuresis, somnambulism, and nightmares occur in confusional states of arousal, not in "dreaming sleep,"" Science, vol. 159 (3819), pp. 1070-1078, 1968.

[22] I. Kolvin, R. C. MacKeith, and S. R. Meadow, Bladder Control and Enuresis (Ch. 20), Heinemann Medical: 1973.

[23] I. Kolvin, R. C. MacKeith, and S. R. Meadow, Bladder Control and Enuresis (Ch. 12), Heinemann Medical: 1973.

[24] V. N. Puri, "Urinary levels of antidiuretic hormone in nocturnal enuresis," Indian Pediatrics, vol. 17(8), pp. 675-676, 1980.

[25] N. Wolfish, R. Pivik, and K. Busby, "Elevated sleep arousal thresholds in enuretic boys: clinical implications," Acta Paediatrica, vol. 86 (4), pp. 381-384, 1997.

[26] A. Kawauchi, N. Imada, Y. Tanaka, M. Minami, H. Watanabe, and S. Shirakawa, "Changes in the structure of sleep spindles and delta waves on electroencephalography in patients with nocturnal enuresis," BJU International, vol. 81, pp. 72-75, 1998.

[27] T. Nevéus, "Enuretic Sleep: A Polysomnographic Study," Scandinavian Journal of Urology and Nephrology, vol. 33, pp. 27-27, 1999.

[28] N. Wolfish, "Sleep Arousal Function in Enuretic Males," Scand. J. Urol. Nephrol., vol. 33, pp. 24-26, 1999.

[29] J. M. Hunsballe, "Increased Delta Component in Computerized Sleep Electroencephalographic Analysis Suggests Abnormally Deep Sleep in Primary Monosymptomatic Nocturnal Enuresis," Scandinavian Journal of Urology and Nephrology, vol. 34, pp. 294-302, 2000.

[30] M. R. Dundaröz, M. Denli, M. Uzun, H. I. Aydin, S. U. Sarici, M. Yokuşoğlu, and S. Ulgen, "Analysis of heart rate variability in children with primary nocturnal enuresis," International Urology and Nephrology, vol. 32(3), pp. 393-397, 2001.

[31] G. Bader, T. Nevéus, S. Kruse, and U. Sillén, "Sleep of primary enuretic children and controls," Sleep, vol. 25(5), pp. 579-583, 2002.

[32] M. Unalacak, M. Aydin, B. Ermis, A. Ozeren, A. Sogut, F. Demirel, and I. Unluoglu, "Assessment of Cardiac Autonomic Regulation in Children with Monosymptomatic Nocturnal Enuresis by Analysis of Heart Rate Variability," Tohoku University Medical Press, vol. 204, pp. 63-69, 2004.

[33] C. K. Yeung, M. Diao, and B. Sreedhar, "Cortical Arousal in Children with Severe Enuresis," New England Journal of Medicine, vol. 358, pp. 2414-2415, 2008.

[34] K. Dhondt, A. Raes, P. Hoebeke, E. V. Laecke, C. V. Herzeele, and J. V. Walle, "Abnormal Sleep Architecture and Refractory Nocturnal Enuresis," The Journal of Urology, vol. 182, pp. 1961-1966, 2009.

[35] V. Cohen-Zrubavel, B. Kushnir, J. Kushnir, and A. Sadeh, "Sleep and Sleepiness in Children with Nocturnal Enuresis," Sleep, vol. 34(2), pp. 191–194, 2011.

[36] K. Dhondt, E. Baert, C. V. Herzeele, A. Raes, L.-A. Groen, P. Hoebeke, and J. V. Walle, "Sleep fragmentation and increased periodic limb movements are more common in children with nocturnal enuresis," Acta Paediatrica, vol. 103, pp. e268-e272, 2014.

[37] Dhondt, K., Herzeele, C. V., Roels, K. Dhondt, C. V. Herzeele, S. P. Roels, A. Raes, L.-A. Groen, P. Hoebeke, and J. V. Walle, "Sleep fragmentation and periodic limb movements in children with monosymptomatic nocturnal enuresis and polyuria," Pediatr Nephrol, vol. 30, pp. 1157-1162, 2015.

[38] A. Z. Golbin, The World of Children's Sleep, Michaelis Medical Publishing Corp: 1995.

[39] A. Z. Golbin, H. Kravitz, G. Keith Louis, Sleep Psychiatry, Taylor & Francis CRC Press: 2004.

[40] A. Z. Golbin, and D. A Golbin, Parasomnias Could Have Adaptive functions, World Association of Sleep Medicine (Germany), Poster 119, 2005.

[41] J. C. Gilin, J. I. Rapoport, F. J. Mikkelsen, D. Langer, C. Vanskiver, and W. Mendelson, "EEG sleep patterns in enuretics: a further analysis and comparison with normal control," Biol. Psychiatry, vol. 1982 (77), pp. 947-52, 1982.

[42] I. Jönson Ring, A. Markström, F. Bazargani, and T. Nevéus, "Sleep disordered breathing in enuretic children and controls," J Pediatr Urol, 2017.

[43] T. Nevéus, "Pathogenesis of enuresis: Towards a new understanding," International Journal of Urology, vol. 24(3), pp. 174-182, 2017.

[44] A. Z. Golbin, A. Umantsev, "Adaptive chaos: mild disorder may help contain major disease," Medical Hypotheses, vol. 66, pp. 182-187, 2006.

[45] Avicenna (Abu Ali ibn Cina), "Canon of Medical Science", UZSSE: Nauka, Book 3, v. 19: 338, 1986.