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Evaluation of neuropsychological development of children diagnosed with primary monosymptomatic nocturnal enuresis: A pilot study

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ABSTRACT

Objective: Studies on primary monosymptomatic nocturnal enuresis have supported neuromotor development delay. This study aims to examine the neuropsychological development of children with primary monosymptomatic nocturnal enuresis.

Material and methods: This study included 30 children diagnosed with primary monosymptomatic nocturnal enuresis and 30 healthy children. Both groups were analyzed by pediatric psychologists using the Wechsler Intelligence Scale for Children–Revised (WISC-R) and the Bender Gestalt Visual Motor Detection test. The WISC-R test is an intelligence test that includes six verbal subscales (information, similarities, arithmetic, vocabulary, judgment, and digit span) and six performance subscales (picture completion, picture arrangement, block design, object assembly, coding, and labyrinths). The Bender Gestalt test is a psychological assessment instrument used to evaluate visuomotor functioning, visuospatial functions, spatial memory, visuomotor integration skills, and visual perception skills.

Results: There were no differences in age (7.66±0.9 versus 8±1.07 years, p>0.05) or sex (20 females versus 20 males, p>0.05) between the groups. Picture completion (p=0.024), picture arrangement (p=0.001), and object assembly test (p=0.000) performance was found to be worse in subjects with primary monosymptomatic nocturnal enuresis. Similarity (p=0.021) and judgment tests (p=0.048) of the verbal subtests were also found to be delayed in the nocturnal enuresis cases.

Conclusion: Our results suggest that children with nocturnal enuresis have lower performance compared with the control group in terms of abstract thinking, correct expression of thought, cause-result relation, short-term memory, and problem-solving ability. These children should be routinely tested by neurodevelopment tests and receive support in areas in which they are delayed.

Keywords: Neuropsychological tests; primary monosymptomatic nocturnal enuresis; WISC-R.

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Introduction

Urinary incontinence is frequently seen in children. At the age of 5, 15% to 20% of children are incontinent at night.[1,2] Most of these children have primary (nocturnal urinary control never achieved) and monosymptomatic (without additional lower urinary tract symptoms with the exclusion of nocturia or a history of bladder dysfunction) enuresis.[1,3] It has been reported that enuresis is related to genetics, nocturnal polyuria, nocturnal detrusor overactivity, high arousal thresholds, functional immaturity of the central nervous system, and neuromotor development delay.[4,5] Developmental problems are one of the most accepted theories of the etiopathogenesis of primary monosymptomatic nocturnal enuresis (PMNE), which is defined as the biological expression of neurophysiological immaturity. Neuropsychiatric and neurodevelopment problems observed in patients with PMNE also support this theory.[5-9]

Emotional disorders are higher in patients with PMNE than in the general population. A study examining the effects of neuropsychological development of children affected by PMNE in the Turkish population found that depression scale scores were significantly higher in the nocturnal enuresis group compared to the control group.[10] Another study found that 48%

of enuretic children had poor school performance.[11] Okur et al.[12] reported that the prevalence of attention-deficit/hyperactivity disorder is higher in children with PMNE compared with the healthy population. The role of psychological factors in the development of PMNE remains unclear. Therefore, the biological development of children with PMNE has not yet been completed elucidated. Neurophysiological development, whether as a cause or effect, appears to be affected in children with enuresis. We hypothesized that neurodevelopmental delay in children with enuresis is significant and can be evaluated using scoring tests. For this purpose, we compared the neuropsychological development between children with enuresis and healthy children.

Material and methods

The study was conducted between March 2017 and June 2017 and included children between 6 and 10 years of age. We enrolled 30 subjects diagnosed with PMNE (20 boys) and 30 healthy children (20 boys) whose follow-up was performed at our Pediatrics Outpatient Clinic. The study was approved by the Erenköy Mental and Neurological Diseases Training and Research Hospital Clinical Research Ethics Committee (06.03.2017/4-2017). All procedures involving human participants were carried out in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Both children and their parents signed informed consent forms. The PMNE inclusion criteria were as follows: bed-wetting at night but asymptomatic during the daytime, bed-wetting frequency of twice per week or more for 3 consecutive months, never dry for more than 6 months, symptoms not caused by any related disease or medicine use, and no other lower urinary tract diseases. The control group consisted of healthy outpatient children with no known chronic disease, enuresis, or neurological problems. Children with any other neurological diseases (such as attention-deficit/hyperactivity disorder, autism, known neurological disorder, and neuromotor development retardation) were excluded from the study. All children were right-handed. Pediatric psychologists applied the Wechsler Intelligence Scale for Children–Revised (WISC-R) and the Bender Gestalt Visual Motor Detection test.

Main Points:

- Children with PMNE had lower scores on the similarities and judgment tests and these results suggest that they do not have an adequate cause-effect relationship.
- Children with PMNE obtained lower scores on picture completion, picture arrangement, and object assembly, these results suggest that children with PMNE have lower analysis-synthesis skills and visuospatial reasoning ability compared with controls.
- It has been noted that children with enuresis have central nervous system dysfunction that leads to low performance on neurodevelopment tests.
- The evaluation of neuropsychological development in these children is important to improve adherence to behavioral therapy.

Neuropsychological tests

Wechsler tests are the gold standard in intelligence and its measurement worldwide. This assessment also applies to the Wechsler child form. The WISC-R test is an individually administered intelligence test validated for children between 6 and 16 years of age.[13] The average intelligence quotient (IQ) of all children was calculated using the subtests of the WISC-R. While using a neuropsychological test, special care should be taken to avoid possible cultural bias. In 1995, a standardization study was conducted on the child form of the WISC-R and adapted to the Turkish culture. The split-half reliability of the test was found to be 0.97 for the verbal section, performance and 0.97 for the total score.[14]

The full-scale WISC-R IQ score was calculated on the basis of the subtest scores for verbal and performance IQ. The test includes six verbal (general similarities, information, judgment, vocabulary, arithmetic, and digit span) and six performance (picture completion, object assembly, block design, picture arrangement, labyrinths, and digit symbol) subscales. The full-scale WISC-R IQ score was calculated on the basis of the subtest scores for verbal and performance IQ. Visuomotor abilities were assessed using the Bender Visual Motor Gestalt test.[15] The Bender Gestalt test, or the Bender Visual Motor Gestalt test, is a psychological assessment instrument used to evaluate visuomotor functioning, visuospatial functions, spatial memory, visuomotor integration skills, and visual perception skills in children and adults. Scores on the test are used to identify possible organic brain damage and the degree of maturation of the nervous system ("organicity"). Norms valid for children in the 6- to 13-year age range were determined by Yalin.[16,17] The scoring system is based on the number of mistakes. The mistakes are classified into four groups: rotation, merging, shape distortion, and repetition.

Each difference in the shapes as seen and drawn was scored differently, and the visuomotor detection score of the individual was calculated. A score was considered normal if the patient achieved an age-appropriate score and abnormal otherwise. The scale was administered in the morning after a good sleep and when the child was not hungry.

Statistical analysis

For descriptive data, percentage and number were used for categorical variables and mean ± standard deviation values used

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for continuous variables. Data were compared by Fisher's exact test for categorical variables and by Mann-Whitney U test for continuous variables. Statistical Package for the Social Sciences (SPSS Inc.; Chicago, IL, USA) version 15.0 was used for all calculations, and a confidence level of 95% was used to determine statistical significance.

Results

According to the results, no differences were found between the PMNE and control group with respect to age or gender. Performance IQ scores for the WISC-R scale were found to be significantly lower in the PMNE group compared to the control group. When the performance subtests were considered separately, a statistically significant decrease was found in the PMNE group in terms of picture completion, picture arrangement, and object assembly subtests as compared with the control group (p=0.024, p=0.001, p<0.001; Table 1). There were no differences among the groups with respect to other parameters of the WISC-R. The Bender Gestalt test result was found to be normal in both the control and PMNE groups.

Table 1. Clinical and WISC-R parameters of the study groups

	PMNE (n=30)	Control (n=30)	p
Age. year	7.66±0.9	8±1.07	0.120
Sex (F/M)	10/20	10/20	1.00
WISC-R			
Verbal	107.36±11.40	108.13±5.63	0.158
Performance	106.20±8.51	112.63±7.69	0.0012[b]
Full Scale	107.17±9.05	111.17±6.60	0.191
Verbal			
Information	9.93±2.61	10.33±1.12	0.909
Similarities	9.97±2.37	11.07±1.26	0.0211[a]
Arithmetic	11.30±2.10	11.13±1.43	0.326
Vocabulary	12.20±2.40	12.27±2.13	0.719
Judgment	11.10±1.52	12.03±2.44	0.0481[a]
Digit Span	9.63±2.34	10.00±2.85	0.237
Performance			
Picture completion	10.83±1.68	11.87±1.72	0.0241[a]
Picture arrangement	10.70±1.70	12.13±1.97	0.0012[b]
Block design	10.13±1.81	11.07±2.39	0.115
Object assembly	9.67±2.00	11.57±1.52	<0.001[c]
Coding	13.03±2.39	12.40±2.15	0.138
Labyrinths	12.23±2.03	11.60±2.16	0.077

PMNE: Primary monosymptomatic nocturnal enuresis, F: female; M: male; WISC-R: Wechsler Intelligence Scale for Children–Revised

[a]Significant at 95% confidence level

[b]Significant at 99% confidence level

[c]Significant at 99.9% confidence level

Discussion

In this study, we examined the neuropsychological differentiation between children with PMNE and healthy children using the WISC-R and found that children with PMNE had lower scores on performance test parameters and some verbal performance subtests.

Whereas verbal tests assess the linguistic-verbal domain, performance tests assess the visuomotor domain. In general, the verbal field demonstrates the child's ability to use and organize knowledge acquired through learning. There was no significant difference in verbal test scores between the two groups. When we look at the verbal subtests, children with PMNE had lower scores on the similarities and judgment tests. Similarity measures the child's ability to think in an abstract manner and to express his or her opinions accurately and clearly. The judgment subtest demonstrates the child's level of reasoning and emotional maturity. These test results suggest that they do not have an adequate cause-effect relationship. It may be said that the categorization and abstraction skills of the basic and essential connections between facts and ideas are underdeveloped in children with PMNE as compared with the control group. Several clinical observations have suggested an association between bed-wetting and decreased learning ability, minor neurological impairment, delay in walking, and speaking skills.[7,8,18] This result may be secondary to the child's problem, or the mother's problem may have contributed to the emergence of the child's situation. This shows us that various factors have a negative impact on the neuropsychological development of children with primary enuresis.

The prefrontal cortex is believed to be involved in both the planning of our movements and abstract thinking skills. Myelination of the prefrontal cortex is protracted, and developmental changes in the prefrontal cortex continue during adulthood.[19] However, there appears to be another process causing the deviation from the general population in individuals with PMNE. In functional magnetic resonance imaging studies performed on children with PMNE, abnormal activation was found in the prefrontal cortex, pons, cerebellum, frontal lobe, thalamus, cerebello-thalamo-frontal region, right precentral gyrus, right inferior parietal lobe, postcentral gyrus, frontal gyrus, and insular cortex.[17,20-23] Compilation of existing data indicated the involvement of the central nervous system (as a general neuromotor delay) in nocturnal enuresis. However, this trait was not correlated with intelligence. The psychologically negative perspective of both

the child and the family may have affected the child's neuropsychological development. This encourages the idea that neuropsychological problems may be detectable and correctable.

Children with PMNE obtained lower scores on picture completion, picture arrangement, and object assembly compared with the healthy control group. Picture completion is a subtest used for measuring the visual attention of children. Picture arrangement measures the ability of children to establish a cause-and-effect relationship between events along with visual attention. This subtest evaluates short-term memory where the working memory enters the circuit. In a study by Yu et al.[20], 67 children with PMNE and 66 healthy controls were examined using the China–Wechsler Intelligence Scale for children. Those authors revealed that the memory/caution factor was significantly lower in the PMNE group. These results indicate that children with PMNE may have a delay related to short-term memory. It is not yet clear whether this is a factor that may lead to enuresis or is a result of general neuropsychological influence. Object assembly measures the ability of children to grasp the piece/whole relationship as well as level of visuomotor coordination. Results on this measure suggest that children with PMNE have lower analysis-synthesis skills and visuospatial reasoning ability compared with controls.

In a study by Esposito et al.[9], 31 children with PMNE and 61 healthy children underwent neuropsychological tests. The authors emphasized that the PMNE group had a higher prevalence of borderline performance for motor coordination and pathologic performance for fine motor coordination and visuomotor integration. In our study, the results of the Bender Gestalt Visual Motor Detection test, which evaluates the visuomotor development of children, were found to be similar between the groups. This makes us think that there is no visuomotor problem in our patients with PMNE. However, it supports the idea that there may be problems in areas where information is processed and stored.

The severity of enuresis has been discussed by several scholars.[24,25] This discussion has mainly focused on bladder capacity, urinary osmotic pressure, bladder wall thickness, good compliance with behavioral interventions, and appetite. In our study, we did not select children with secondary or polysymptomatic enuresis. However, evaluating the association between the neurodevelopment and severity of enuresis would provide more evidence for etiologic factors.

Unfortunately, we could not evaluate the WISC-R after treatment. In the literature, it was reported that many (neuro) psychological dysfunctions and sleep problems were resolved after 6 months of desmopressin treatment; however, attention did not significantly improve, and differences in spatial planning/working memory and behavior regulation did not meet the threshold for statistical significance.[26] It seems that the evaluation of neuropsychological parameters after treatment is an area that requires further research.

There are no studies on the adequacy of the validity of the WISC-R in healthy Turkish samples. In our country, the updated form WISC-IV was standardized from 2008 to 2011. It was argued that clinical validation of the algorithms should be established in a sample of children with neurological dysfunction.[27] The WISC-IV was found to underestimate intelligence in disadvantaged children.[28] In addition, the profiles generated by the WISC-IV battery in the case of intellectual disability and overall IQ are overestimated.[29] Recently, an electronic version of the WISC-V was developed. Some have advocated that the WISC-V is more developmentally appropriate; however, cultural bias needs to be considered.[30] It seems that, despite some limitations, intelligence tests are being updated over time. Using both more actual and more standardized scales would be more suitable. In academic studies, working with a control group may partially overcome these problems. However, when choosing a control group, consideration of sociocultural status, and not just age and gender, is also important.

The main limitations of our study are the small sample and a low number of applied tests. In addition, we did not consider the sociocultural status of our patients. The differences could be explained by the disparity in the sociocultural and economic status of the neuropsychological test patients and control groups.

In conclusion, no specific problems were identified. It has been noted that children with enuresis have central nervous system dysfunction that leads to low performance on neurodevelopment tests. Whether a cause or effect, neuropsychological development seems to be affected in children with PMNE. We believe that evaluation of neuropsychological development in these children is important to improve adherence to behavioral therapy. Further studies with more current and standardized tests are needed to determine the differences in terms of neuropsychological development. After further studies, these children may routinely undergo neurodevelopment testing and should receive support in the areas in which they are delayed.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Erenköy Mental and Neurological Diseases Training and Research Hospital Clinical Research Ethics Committee (06.03.2017/4-2017).

Informed Consent: Written informed consent was obtained from patients and the parents of the patients who participated in this study.

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