

Psychosocial And Behavioral Functioning of Cognitively Normal Children with History of Neonatal Seizure: Case Control Study

Yenidoğan Döneminde Nöbet Geçiren Mental Düzeyleri Normal Çocukların Psikososyal ve Davranışsal İşlevleri: Olgu-Kontrol Çalışması

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ABSTRACT

Introduction: Neurological sequelae associated with the neonatal seizures (NS) are known as long-term epilepsy, intellectual disability, and cerebral movement disorders. This study reports the psychosocial and behavioral problems among children whose neurodevelopmental status was not affected in the long-term.

Method: Patients who were diagnosed with and treated for NS between January 2006 and December 2008 were included in this case-control study. Children with physical disabilities, epilepsy, continuous medication use, concomitant chronic diseases and mentally retardation (intelligence quantity <70) were excluded. Typically developing children matched for age, sex, and socioeconomic status were recruited as the control group. All participants were screened for their intelligence and psychosocial and behavioral functioning using a standardized tests and questionnaire. The Wechsler Intelligence Scale for Children IV (WISC-IV) were used to evaluate intelligence quantity. Psychosocial and behavioral functioning were assessed using a set of standardized questionnaires including Strengths and Difficulties Questionnaire (SDQ).

Results: 17 patients (9 female) with NS and 18 healthy controls (10 female), aged 9-12 years, were participated. There was no statistically significant difference observed between children with neonatal seizures and controls in intelligence quantity ($p>0.05$). The total scores and subscale SDQ scores were not statistically different between children with neonatal seizures and controls ($p>0.05$).

Conclusion: Childrens who were diagnosed with NS were exposed to seizures during active stages of brain development, it may be reasonable to monitor them with respect to psychosocial and behavioral problems, when they reach school-age and ensure that problematic high-risk children are referred to psychiatric evaluation.

Keywords: neonatal seizure, behavioral problems, epilepsy, psychiatric evaluation

ÖZ

Amaç: Yenidoğan nöbetleri (YN) ile ilişkili nörolojik sekeller uzun dönemde epilepsi, nörogelişimsel gerilik ve serebral palsi olarak bilinir. Bu çalışma, YN geçirmiş, nörobilişsel açıdan uzun dönemde etkilenmeyen çocukların psikososyal ve davranışsal sorunları araştırmayı amaçlamaktadır.

Yöntem: Ocak 2006 ile Aralık 2008 tarihleri arasında YN tanısı alan ve tedavi edilen hastalar olgu-kontrol çalışmasına dahil edildi. Epilepsi, eşlik eden kronik hastalık, düzenli ilaç kullanımı öyküsü olan ve nöromotor gelişim basamaklarında gecikme olan hastalar çalışmaya dahil edilmedi. Yaş, cinsiyet ve sosyoekonomik düzeyi hasta grubuna benzer olan çocuklar kontrol grubu olarak seçilmiştir. Davranış ve psikososyal değerlendirme için tüm katılımcılara standardize edilmiş sorular ve testler uygulandı. Çocuklar için Wechsler Zeka Ölçeği (WISC-IV) zihinsel performansı değerlendirmek için kullanıldı. Psikososyal ve davranışsal işlevsellik, Güçler ve Güçlükler Anketi (GGA) kullanılarak değerlendirilmiştir.

Bulgular: YN olan 17 hasta (9 kız) ve yaşları 9-12 olan 18 sağlıklı kontrol (10 kız) çalışmaya dahil edildi. YN olan çocuklar ile kontrol grubu arasında zeka düzeylerinde istatistiksel olarak anlamlı bir fark bulunmadı ($p>0.05$). YN ve kontrol grubu arasında toplam puanlar ve alt ölçek SDQ puanları istatistiksel olarak farklı değildi ($p>0.05$).

Sonuç: Beynin gelişim aşamasında nöbetlere maruz kalan riskli çocukların okul çağına geldiklerinde psikososyal açıdan izlenmesi, psikiyatrik değerlendirmeye yönlendirilmesi doğru bir yaklaşım olacaktır.

Anahtar kelimeler: yenidoğan, nöbet, epilepsi, davranış

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INTRODUCTION

Epilepsy, a group of central nervous system disorder, is characterized by seizures generated by abnormal, excessive or hypersynchronous neuronal activity in the brain ⁽¹⁾. Neonatal period has a high risk for seizures, linked to higher seizure susceptibility and lower seizure threshold compared to other ages. The short-term prognosis of neonatal seizures (NS) is considered to be improved by perinatal and neonatal care. However, the long-term neurologic prognosis did not improved especially in terms of intellectual disability and learning disabilities ⁽²⁻⁵⁾.

Psychosocial and behavioral problems including mood, anxiety, attention deficit/ hyperactivity disorders and autism are suggested to be arising from the delayed brain maturation ⁽³⁾. NS could contribute on delay in brain maturation and may increase the likelihood of psychosocial and behavioral problems.

It may be noteworthy to investigate the psychosocial and behavioral problems that may potentially develop in cognitively normal children with neonatal seizures to clarify direct relationship between neonatal seizures and psychosocial and behavioral problems. In this study, we evaluated the influence of neonatal seizures on psychosocial and behavioral functioning.

MATERIALS and METHODS

Participants

The participants were consisted of children presented with NS between January 2006 and December 2008. Review of the medical records revealed a total of 80 patients. The seizures of the neonates were diagnosed by a neonatologist based on clinical observations, and then the patients were referred to our center for consultations. The final diagnoses of the neonatal seizures were confirmed by the child neurologists, which were based either on the direct observation of the clinical and/or electroencephalography (EEG) events.

Children aged 6-16 years who regularly attended school and had an intelligence quantity >70 were included. Children with epilepsy, continuous medication use, concomitant chronic disease and delay in

neurodevelopmental milestones were excluded. All of the children with neonatal seizures were contacted by phone and invited to participate into the study. Typically developing children matched for age, sex, and socioeconomic status were recruited as the control group.

The study was reviewed and approved by the Institutional Ethics Committee at Istanbul Faculty of Medicine. All participants and/or their legal representatives provided written informed consent and assent.

Clinical Data

Data on demographics, prenatal and perinatal history consisted of gestational age; type of delivery, birth weight, APGAR score, requirement for neonatal resuscitation, timing and type of seizures, etiology of neonatal seizure, the presence of status epilepticus, response to antiepileptic medication, treatment duration were abstracted from medical records. Electroencephalography and brain imaging findings were also recorded.

Psychosocial and Behavioral Evaluation

All participants were screened for their intelligence and psychosocial and behavioral functioning using a standardized tests and questionnaire. The Wechsler Intelligence Scale for Children IV (WISC-IV) were used to evaluate verbal, performance and general intelligence quantity and administered by an experienced and certified psychologist. Psychosocial and behavioral functioning including emotional symptoms, conduct problems, hyperactivity and concentration difficulties, peer relationship problems and prosocial properties were assessed using the Turkish version of Parent Form of Strengths and Difficulties Questionnaire (SDQ-Tur) which filled out by parents. The SDQ consist of 5 subscales, each with 5 items, is defined as a reliable and valid screening tool for assessing psychosocial and behavioral problems ⁽⁶⁻⁸⁾. SDQ survey is done and evaluated by child and adolescent psychiatrist (UT).

Statistical analysis

Statistical analysis was performed using the SPSS for Windows version 21.0 software (IBM Corp., Armonk, NY, USA). Demographic variables were expressed in mean and standard deviation (SD), median and per-

centage. The Shapiro-Wilk test was used to assess the normality for demographic variables and questionnaire scores. Intergroup differences in terms of the scores and sub scores of questionnaires were assessed using the Mann-Whitney U test. A p value of <0.05 was considered statistically significant.

RESULTS

Demographics and clinical data

A total of 35 children, 17 patients (9 female) with neonatal seizures and 18 healthy controls (10 female), were participated. Demographic and clinical characteristics of participants are listed in Table 1.

Table 1. Demographic and clinical characteristics of participants.

	Neonatal Seizure	Healthy Group
n	17	18
Mean age at participation (years) (SD)	9.8 (0.8)	9.6 (1.2)
Gender (% female)	9 (53%)	10 (55%)
Etiology		
Structural	7	-
Metabolic	6	-
Genetics	1	-
Unknown	3	-
Status Epilepticus (%)	2 (11.7)	-
Full-scale IQ (SD)	106.2 (17.9)	110.5 (11.14)
SDQ total scores (SD)	10.53 (7.5)	10 (6.2)

Abbreviations: IQ = intelligence quantity; SD = standard deviation.

There were no significant difference observed in demographic characteristics, gestational age, type of delivery, birth weight, Apgar score, requirement for neonatal resuscitation between 2 groups (p>0.05). Seizure timing was within the first 24 hours in 6 (35.2%) patients, within 24 to 72 hours in 7 (41%) patients and after 72 hours in 4 (23.6%) patients. Status epilepticus developed in 2 (11.7%) patients. Based on the data obtained from patient files, the seizure type was tonic in 6 (35.2%), clonic in 6 (35.2%), subtle in 4 (23.5 %) and myoclonic in 1 (5%) patient. The etiology of neonatal seizures was structural in 7 (41%), metabolic in 6 (35%), genetic in 1 (5%) and unknown in 3 (17.6%) patients. The mean time for the last observed clinical seizure was 10.2 months (range: 8 days to 46 months). The mean duration for antiepileptic treatment was 24.7 months (range: 1 month- 6 years). Four patients received no antiepileptic medication.

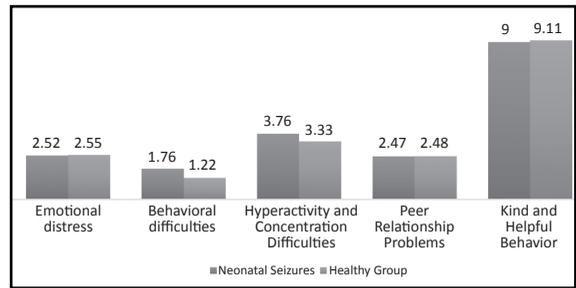


Figure 1. The means of SDQ subscale scores.

Psychosocial and Behavioral Evaluation

There were no statistically significant difference observed in general, verbal and performance intelligence quantity (p>0.05) between children with neonatal seizures and control group. The SDQ total scores and subscale scores relevant to emotional symptoms, conduct problems, hyperactivity and concentration difficulties, peer relationship problems and prosocial properties were not statistically different between children with neonatal seizures and controls (p>0.05).

DISCUSSION

Although the negative influence of NS on a developing brain is still a matter of debate, to the best of our knowledge, this is the first study to report the psychosocial and behavioral problems among children whose neurodevelopmental was not affected in the long-term.

In the present study, school-age children who experienced NS without epilepsy or continuous drug use were compared to the healthy controls in terms of psychosocial and behavioral functioning. Clinical studies investigating the impact of NS on long-term outcome have addressed into the neurological outcomes, although psychosocial and behavioral influences were not previously addressed in any study. Different from previous studies, we investigated whether these children develop potential psychosocial and behavioral problems compared to healthy controls using the SDQ-Tur-parents scale. Based on the parent reports, there was no statistically significant difference between the two groups in terms of the total and sub-scale scores of the SDQ-Tur scale.

The impact of seizures experienced in early stages of

life on social behavior was previously investigated in several animal studies, and these seizures were found to be associated with negative effects in the long-term⁽⁹⁻¹¹⁾. The changes induced by the NS, particularly in the functions of the hippocampus, were considered as the potential causes of such behavioral problems^(12,13). In the literature, we were unable to find any study investigating the impact of NS in the long-term psychosocial and behavioral development of children. On the other hand, previous reports indicated that the frequency of psychosocial and behavioral problems increased in patients diagnosed with childhood epilepsy, and the severity of these psychosocial and behavioral problems considerably increased with increasing frequency of seizures, their intensity as well as the number of anti-epileptics used and their side effects^(14,15). In the present study, we evaluated the permanent negative effects of NS in the clinical practice, which were experienced, when the rate of brain development was still high, on an individual's behaviors in the long-term, irrespective of the effects of still active seizures or anti-epileptics used. Therefore, we excluded patients with conditions such as an intellectual disability, chronic disease, a diagnosis of epilepsy or concomitant medication use, which might affect psychosocial and cognitive functioning. Based on the parent reports, there was no significant difference between the SDQ scores of healthy controls who did not experience a NS and the patients who were neurodevelopmentally healthy and developed intellectual capabilities. In terms of neonatal patient history, our patient population represented a heterogeneous group with low Apgar scores, refractory seizures, history of status epilepticus and neonatal resuscitation. It is evident that further clinical studies including larger patient groups that are more homogeneous in terms of clinical history with data collected from various resources such as the parents, schools, psychiatric examinations and observations, are needed to explore this subject. Epidemiological studies have consistently shown that children with epilepsy have higher rates of behavior problems than children with other chronic physical conditions, but our results are contradictory to those findings.

This study has some limitations. First of all, our patient sample was not classified in terms of the etiologies of their seizures and represented a hetero-

geneous, small population. Secondly, psychosocial and behavioral problems were assessed by a scale based on parents' report, whereas psychiatric examinations were not performed and no data was collected from the schools or teachers. Considering these factors, future studies investigating psychosocial and behavioral problems in NS more objectively by the use of neuropsychiatric testing tools in larger patient populations would be informative and may improve our understanding.

CONCLUSION

In conclusion, the presence of comorbid psychiatric disorders has a significant impact on the quality of life and, thus, recognition of these disorders is of utmost importance to initiate treatment in children with neurological disorders. Our study results showed that the frequency of psychosocial and behavioral problems did not increase among patients who had a history of NS in the absence of epilepsy or an intellectual disability, compared to the healthy controls. Still, as these children were exposed to seizures during active stages of brain development, it may be reasonable to monitor them with respect to psychosocial and behavioral problems, when they reach school-age and ensure that problematic high-risk children are referred to psychiatric evaluation.

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