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Brief Report / Kısa Araştırma

When do We Recommend an EEG and Cranial MRI Evaluation for Autistic Children?

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ABSTRACT

When do we recommend an EEG and cranial MRI evaluation for autistic children?

Objective: This study has planned to investigate the role of electroencephalography (EEG) and cranial magnetic resonance imaging (cMRI) in the evaluation and diagnosis of neurological disorders combined with autism in children.

Method: A total number of 121 autistic children ranging from 3 to 18 years of age and who had applied to our hospital's clinics between January 2010 and January 2011 were included. The sociodemographic properties, time of birth, birth history, weight at birth, age at onset of walking and language development were investigated. By means of a reevaluation of cMRI, sleep EEG and other examination findings, additional neurological diagnoses, if any were recorded. Children for whom, a cMRI/ EEG evaluation was carried out and for whom such an evaluation was not carried out was compared statistically as to certain risk factors separately for additional diagnoses and neurological disorders. In addition, the relationship between cMRI and EEG findings and additional neurological disorder was examined.

Results: Autistic children (Male/Female: 92/76) aged 9.30±4.2 years have been diagnosed neurological disorder additionally with a percentage of 40%. The most common of these was the epileptic seizure as 33%. No data was obtained about an additional neurological disorder in 22% of cases who performed cMRI and in 34% of cases who performed EEG. Ratio of presence of a pathological finding in cMRI was high in patients with cerebral palsy, whereas it was not found to be meaningful in patients with epileptic seizures. Analyzing risk factors for neurological disease, birth history of perinatal problems and gait disorders were seen more frequently in patients who required cMRI as compared to those in patients who did not require cMRI. Gait age was older in patients who required cMRI (18±8 months) as compared to patients without cMRI (14±4 months).

Conclusion: In our autistic children, cMRI and EEG examinations had been extensively used for the investigation of additional neurological disorders. Both cMRI and EEG examinations had been requested more frequent in the presence of perinatal problems. The other risk factors for additional neurological disorders were history of premature birth to request EEG and older age at onset of walking, walking problems to request cMRI. However with detailed clinic evaluation of autistic children and clarification for investigations criteria unnecessary EEG and cMRI should be avoided.

Key words: Autism, childhood, cranial magnetic resonance imaging, EEG

ÖZET

Otistik çocuklarda ne zaman EEG ve kraniyal MRG istiyoruz?

Amaç: Bu çalışma otistik çocuklarda görülebilecek nörolojik bozuklukları değerlendirme ve tanılamada elektroensefalografi (EEG), kraniyal manyetik rezonans görüntülemenin (kMRG) yeri ve tetkik amacıyla nasıl kullanıldığını araştırmak amacıyla planlandı.

Yöntem: Hastanemiz kliniklerine Ocak 2010-Ocak 2011 yılları arasında, başvuran 3-18 yaşları arasında toplam 121 otistik çocuk çalışmaya alındı. Hastalara ait sosyodemografik özellikler, doğum zamanı, doğum öyküsü, doğum kilosu, yürüme zamanı, dil gelişim basamakları sorgulandı. kMRG, uyku EEG ve diğer tetkikleri yeniden değerlendirilerek varsa ilave nörolojik tanıları not edildi. kMRG/EEG çekilen ve çekilmeyen çocuklar ayrı ayrı ilave nörolojik tanılar ve nörolojik hastalık için bazı risk faktörleri açısından istatiksel olarak karşılaştırıldı. Ayrıca kMRG ve EEG bulgularının ilave nörolojik bozukluk varlığı ile ilişkisi araştırıldı.

Bulgular: Çalışmaya alınan 9.3±4.2 yaşındaki otistik olguların (Erkek/Kadın: 92/76) %40'ına ek nörolojik tanı kondu. Epileptik nöbet varlığı %33 ile otizme eşlik eden en sık nörolojik bozukluktu. Olguların %34'ünde EEG, %22'sinde kMRG tetkikinin yapılmış olması ek nörolojik bozukluk araştırılmasında bir bilgi vermemiştir. kMRG'de patoloji görülmesi serebral palsi hastalarında yüksek oranda iken, epileptik nöbet geçiren hastalarda anlamlı bulunmadı. Nörolojik hastalık için risk faktörleri incelendiğinde, kMRG istenen olgularda doğumunda sorun tanımlanması ve yürüme bozukluğu, kMRG istenmemiş çocuklardan istatiksel olarak anlamlı oranda daha fazla tespit edildi. Yürümeye başlama yaşı kMRG tetkiki istenen olgularda (18±8 ay) istenmeyen olgulara (14±4 ay) göre daha geç bulundu.

Sonuç: Otistik çocuk grubumuzda kMRG ve EEG tetkiki ek nörolojik bozuklukların araştırılmasında yaygın olarak kullanılmaktadır. Ancak doğumda sorun tanımlanması durumunda her iki tetkikin daha sık istendiği görülmüştür. Ayrıca preterm doğumun EEG istenmesi; yürümenin geç ve sorunlu olmasının kMRG istenmesi için risk faktörü olarak görüldüğü tespit edilmiştir. Otistik çocuklarda klinik olarak daha ayrıntılı değerlendirmenin yapılması ve istem ölçütlerinin netleşmesi ile gereksiz EEG ve kMRG tetkiklerinin yapılmasının önlenebileceği düşünülmektedir.

Anahtar kelimeler: Otizm, çocukluk çağı, kraniyal manyetik rezonans görüntüleme, EEG

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INTRODUCTION

Autism is a neuropsychiatric disorder starting in early childhood and is characterized by repetitive and stereotyped movements together with social interaction disorder, and retardation in language, speech and non-verbal communication (1-4). Complete recovery is rare in this chronic disorder (5,6). The etiology is unclear but studies have reported that psychosocial factors, prenatal-postnatal factors, neurobiological factors and the presence of genetic predisposition may play a role (2,7).

There are many neurological and genetic disorders associated with autism. Both epileptic disorders and electroencephalography (EEG) abnormalities by themselves are often associated with autism (8-12). The association rate changes between 5% and 40% in different studies (11,12).

Imaging studies are important to explain the neuroanatomy as well as the pathophysiology of autism. Structural brain imaging studies have revealed an increase in the total brain volume and the volume of both gray and white matter, particularly in the frontal, temporal and parietal lobes. Functional brain imaging studies have shown differences in activity in the temporal lobes and amygdala, which play a role in the areas of language and social cognition, and an activity increase in the rear cortical areas (13). A recent study reported cranial magnetic resonance imaging (cMRI) to help understand the etiology and pathophysiology of autism and therefore to be useful for determining treatment models (14). Another study has shown the atypical activation observed in cMRI to be a possible indicator to determine the familial risk (15).

A study of 40 children with autism evaluated by EEG and neuroimaging revealed EEG abnormalities in 53%, pathology on computed tomography in 22%, and pathology on cMRI in 24% (16). However, routine cMRI and EEG examinations are not recommended for these children (17-19). It is also not clear to what extent the cranial MRI and EEG examinations are used in the evaluation of children with autism. We aimed to investigate the role of EEG and cranial MRI in the neurological evaluation and diagnosis of children with autism in this study.

METHOD

A total of 121 autistic children between 3 and 18 years old who admitted to a research and training hospital's pediatric neurology and pediatric psychiatry outpatient clinics or health board in Istanbul between January 2010 and January 2011 were included in the study. Autism was diagnosed according to the DSM-IV-TR (Diagnostic and Statistical Manual of Mental Disorders, 4th edition, revised) criteria (20). Patients included in the study were cases diagnosed in the pediatric psychiatry outpatient clinic of our hospital or at another external center and whose autism diagnoses were confirmed by reevaluation by a child psychiatry specialist at our hospital. Cases of not otherwise specified autism, Rett syndrome, disintegrative disorder and Asperger syndrome were excluded.

Consent was obtained from the parents of all cases. The socio-demographic information form was completed by the investigators by interviewing the parents. The time of birth, birth history, birth weight, time of first steps, and language development stages were queried in the form. Language development in children over 5 years old was evaluated in 3 groups as no verbal expression, verbal expression with words, and verbal expression with sentences. If known, a birth history of a low Apgar value, difficult birth with the child turning blue, meconium birth, and intervention to the baby immediately after birth, or monitoring in intensive care unit was noted as a problem during delivery. Delay in walking was defined as independent walking starting after 18 months. All the patients and their previous cMRIs, sleep EEGs and other investigations were evaluated by the same child neurologist. If the child had at least two seizures (febrile or afebrile) after the newborn period (other than those due to acute symptomatic causes such as central nervous system infection, hypocalcemia, hypoglycemia or trauma), these were accepted as epileptic seizures. All EEGs included in the study were 18-channel EEGs and 1-hour sleep EEGs obtained according to the international 10-20 system. EEG findings were divided into two groups as with and without epileptiform activity. After the neurological examination, the additional neurological

diagnoses and the EEG and cMRI results if any were recorded. Children with and without cMRI/EEG were statistically compared in terms of additional neurological diagnoses and some risk factors for neurological disease (time of birth, birth weight, existence of a problem at birth, time of first steps, gait disturbance and language development). cMRI was considered pathological if there was a finding other than normal variation. Cases with a cMRI were divided into 2 groups according to whether the results were normal or pathological; and cases with an EEG were also divided into 2 groups according to whether epileptic activity was present on the EEG or not. These groups were compared in terms of additional neurological disorders.

Statistical Analysis

The unpaired t-test was used for group comparisons and the chi-square test was used for evaluation of qualitative data. Statistical significance was accepted as $p<0.05$.

RESULTS

The 121 cases consisted of 92 (76.0%) males and 29 (24.0%) females with a mean age of 30.0±4.2 years. As a result of the neurological evaluation, 40% of the patients received additional neurological diagnoses. The most common neurological disorder associated with autism was the presence of epileptic seizures (Table 1). Gait disturbance (spastic, fingertip and ataxic) was found in 26 (21.0%) of the cases. Verbal expression was not existent or only with words in 65 (64.0%) of 102 cases over 5 years old.

cMRI had been requested in 76 (62.8%) of the 121 patients. The result was normal in 62 (81.5%) while pathology was identified in 14 (18.4%). These pathologies were summarized as sequela lesions (7.8%), congenital malformations (5.2%), and other abnormalities (hydrocephalus, the lateral ventricle enlargement, delay in myelinization) (5.3%). A neurological disorder was detected in 49 cases with cMRI and none of the cases without cMRI. This difference was statistically highly significant ($p<0.001$). Among the cases with an MRI, a pathology was found in 13 (26.5%) of 49 cases with a neurological diagnosis and in 1 (3.7%) of 27 cases with no neurological diagnosis. This difference was found to be statistically highly significant ($p=0.014$). MRI was performed in 27 (37.0%) of the 72 cases without a neurological diagnosis and pathology was found in only one patient. The difference was statistically significant. The relationship between the presence of a neurological diagnosis and MRI request has been shown in Table 2 (Table 2).

Table 1: Distribution of autistic children (n=121) according to the neurological diagnoses

	n	%
Neurological diagnosis/disorder*	49	40.4
Epileptic seizure	40	33.0
Cerebral Stroke	13	10.7
Genetic (neurocutaneous syndromes)	3	2.4
Involuntary movements	1	0.8

*More than one diagnosis in the same patient is possible

Table 2: Comparison of the autistic cases with or without cMRI according to the presence of neurological diagnosis/ disorder

	cMRI (+)		cMRI (-)		
	n=76	%	n=45	%	p
Neurological Diagnosis					
(+) (n=49)	49	100	0	0.0	<0.001
(-) (n=72)	27	37.5	45	62.5	
Epileptic Seizure					
(+) (n=40)	40	100.0	0	0.0	<0.001
(-) (n=81)	36	44.4	45	55.6	
Cerebral Palsy					
(+) (n=13)	13	100	0	0.0	0.003
(-) (n=108)	63	58.3	45	41.7	

cMRI: cranial magnetic resonance imaging

When the cases with a cMRI request were evaluated in terms of the risk factors for neurological disease, there was a statistically significantly higher rate of a problem at birth and gait disturbance in cases with a cMRI request (Table 3). The mean walking age was 18.3±8.9 months in cases with a cMRI and 14.3±4.2 months in those without. This difference was statistically significant (p=0.05).

The relationship of the normal or pathological cMRI results with the neurological disorders present is shown in Table 4. cMRI was performed in all 13 patients diagnosed with cerebral palsy (CP) and 8 (61.5%) had pathological findings. This rate was statistically significantly higher than those without CP (p<0.001). cMRI was requested for all patients in epileptic seizures and pathology was found in 22.5%. No statistical relationship was found between seizure presence and pathology on cMRI (p=0.334).

EEG examination was requested in 89 (73.5%) cases. This rate is a little higher than for cMRI requests. The distribution of patients with an EEG according to the neurological diagnosis is shown in Table 5 (Table 5). EEG was requested for 47 of the 49 patients with a neurological diagnosis. EEG had been requested for 58.0% of the patients with no additional neurological disorders and 60% of the patients with seizures . EEG was requested at a significantly higher rate for patients with an additional neurological disorder than those without an additional neurological disorder or epileptic seizures (p<0.001). Epileptic activity on EEG was found in 27 (57.4%) of those with an additional neurological diagnosis and in 6 (14.3%) of those without.

Table 3: Comparison of patients with or without cMRI in terms of risk factors for neurological diseases

	cMRI (+)		cMRI (-)		
	n=76	**%**	**n=45**	**%**	**p**
Term Birth (n=105)	65	85.5	40	93.0	0.086
Preterm Birth (n=16)	11	14.5	5	7.0	
Birth Weight					
2500- 3500gr (n=70)	43	56.6	27	60.0	0.866
<2500gr (n=13)	9	11.8	4	8.9	
>3500gr (n=38)	24	31.6	14	31.1	
Problem in birth					
No (n=94)	54	71.1	40	88.9	0.023
Yes (n=27)	22	28.9	5	11.1	
Gait Disorder					
No (n=95)	53	69.7	42	93.3	0.002
Yes (n=26)	23	30.3	3	6.7	
Verbal expression;					
No words (n=31)	21	32.3	10	27.0	0.543
With words (n=34)	23	35.4	11	29.7	
With sentences (n=37)	21	32.3	16	43.2	

cMRI: cranial magnetic resonance imaging

Table 4: Distribution of cMRI findings in patients with cMRI according to the neurological diagnoses

	Normal cMRI		Pathological cMRI		
Neurological diagnosis in cases with cMRI	**n=62**	**%**	**n=14**	**%**	**p**
Neurological Diagnosis					
(+) (n=49)	36	73.5	13	26.5	
(-) (n=27)	26	96.3	1	3.7	0.014
Cerebral Palsy					
(+) (n=13)	5	38.5	8	61.5	
(-) (n=63)	57	90.5	6	9.5	<0.001
Epileptic Seizure					
(+) (n=40)	31	77.5	9	22.5	
(-) (n=36)	31	86.1	5	13.9	0.334

cMRI: cranial magnetic resonance imaging

This difference was statistically significant (p<0.001). No statistically significant difference in terms of epileptic activity on EEG was found between patients who were and were not diagnosed with cerebral palsy. An EEG had been requested in all cases with an epileptic seizure. Epileptic activity was present on the EEG in 25 (62.5%) of those with a history of seizure and 8 (16.3%) of those without such a history. This difference was statistically significant (p<0.001) (Table 6).

When the autistic patients with an EEG were evaluated in terms of the risk factors for neurological disease, EEG was requested statistically significantly

Table 5: Comparison of the autistic cases with or without EEG according to the presence of neurological diagnosis/disorder

	EEG Performed		EEG Not Performed		
Neurological Diagnoses of the Sample	**n=89**	**%**	**n=32**	**%**	**p**
Neurological Diagnosis					
(+) (n=49)	47	95.9	2	4.1	
(-) (n=72)	42	58.3	30	41.7	<0.001
Cerebral Palsy					
(+) (n=13)	12	92.3	1	7.7	
(-) (n=108)	77	71.3	31	28.7	0.105
Epileptic Seizure					
(+) (n=40)	40	100	0	0.0	
(-) (n=81)	49	60.5	32	39.5	<0.001

Table 6: Distribution of EEG findings in cases with EEG according to the neurological diagnoses

	Epileptic activity (-)		Epileptic activity (+)		
Neurological diagnosis in cases with EEG	**n=56**	**%**	**n=33**	**%**	**p**
Neurological Diagnosis					
(+) (n=47)	20	42.6	27	57.4	
(-) (n=42)	36	85.7	6	14.3	<0.001
Cerebral Palsy					
(+) (n=12)	7	58.3	5	41.7	
(-) (n=77)	49	63.6	28	36.4	0.724
Epileptic Seizure					
(+) (n=40)	15	37.5	25	62.5	
(-) (n=49)	41	83.7	8	16.3	<0.001

Table 7: Comparison of patients with or without EEG in terms of risk factors for neurological diseases

	EEG (+) n=89		EEG (-) n=32		
	n	**%**	**n**	**%**	**p**
Term Birth (n=105)	77	86.5	28	93.3	
Preterm Birth (n=16)	12	13.5	4	6.6	0.036
Birth Weight					
2500- 3500 gr (n=70)	50	56.2	20	62.5	
<2500gr (n=13)	13	14.6	0	0.0	
>3500gr (n=38)	26	29.2	12	37.5	0.069
Problem in birth					
Yok (n=94)	65	73.0	29	90.6	
Var (n=27)	24	27.0	3	9.4	0.04
Gait Disorder					
Yok (n=95)	68	76.4	27	84.4	
Var (n=26)	21	23.6	5	15.6	0.346
Verbal expression;					
No words (n=31)	24	30.8	7	29.2	
With words (n=34)	27	34.6	7	29.2	
With sentences (n=37)	27	34.6	10	41.7	0.806

more frequently in preterm cases and in cases where a problem had been defined at birth compared to term newborns and those with no problem at birth (p>0.05). EEG was requested more frequently for cases with low birth weight, gait problems, and no verbal expression than cases with normal birth weight, no gait problems, and with verbal expression, but there was no statistically significant difference between the two groups regarding these variables (Table 7).

The mean walking age (17.4±8.5 months) was higher in cases with EEG than in those without (15.4±5.2 months), but this difference was not statistically significant (p=0.216).

DISCUSSION

Autism is a neuropsychiatric disorder of unknown etiology and there is no clear data on which follow-up examinations should be requested (1-4,17,19). A number of genetic and neurological problems associated with autism are often reported at rates that indicate something other than coincidence. Epilepsy, motor development problems, sleep disorders and involuntary movements are the main accompanying neurological problems (9,21). Such concurrent neurological clinical pictures can have a marked influence on the prognosis of these children. Early recognition of any additional neurological disorders in children with autism is therefore important to ensure the appropriate treatment approaches. cMRI and EEG are the most valuable methods for the evaluation of neurological disorders. Our study investigated the place of EEG and cMRI requests in the practical management of children with autism.

The lack of a difference between the mean age and gender distribution of autistic children with or without an additional neurological diagnosis is important when evaluating our results independently from these variables.

cMRI was performed on a large proportion (63.0%) of our patients with autistic disorder. 64% of these patients had an additional neurological disease. In other words, cMRI was performed although there was no neurological problem in 36% of these cases. cMRI had been performed in 100% of patients with an additional neurological diagnosis. However, the cMRI did not provide any information regarding the additional neurological diagnosis in 27 (22.3%) of our 121 patients. Taking into account that sedation would have been applied to children during cMRI, the need for cMRI in these children is debatable. In fact, the American Academy of Pediatrics and the American Academy of Neurology do not recommend routine neuroimaging if there is no macrocephaly or focal neurological symptom in children with an autistic disorder (17-19). We do not know the head circumference results of our patients during cMRI as this was a retrospective study. However, the pathological finding rate was higher on cMRI in children with an additional neurological disorder. This difference was marked in autistic children with cerebral palsy. The cMRI result was normal in as high as 77.0% of the autistic children who had a history of seizure. These data indicate that cMRI imaging is beneficial in autistic children with cerebral palsy but provides less information in autistic children with seizures.

Some risk factors for neurological diseases are known. We found that cMRI was more often requested in the presence of a problem identified at birth, walking late and gait disturbance in children with autistic disorder. No relationship was found between the birth weight and birth date and the cMRI request. Delayed language development was not used as a measure to request cMRI. These data may indicate that the birth date and birth weight are not considered when requesting cMRI in children with autistic disorder if there is no neurological finding; and that language development problems are thought to be part of the autism clinical picture and therefore not seen as an indication.

Epilepsy is one of the most common neurological disorders associated with autism. Although various rates are reported in different series, the incidence in autistic patients is 25.0% (22). Therefore, the presence of seizures in autistic children should be questioned in detail. It should be noted that families may not notice some seizures. Each paroxysmal attack should be recorded on video and analyzed regarding seizures. EEG is requested for a child with autistic disorder

when the patient's clinical picture deteriorates and epilepsy is suspected (19-21). Epileptic activity on EEG has been reported in 10%-72% of autism cases despite the absence of epileptic seizures (23,24). In fact, some investigators suggest routine EEG in the presence of an autism diagnosis (25). The current recommendation is not to request routine EEG in children with an autism spectrum disorder (17-19). All EEGs were obtained during at least 1 hour of sleep in our study. EEG request was a high ratio such as 73.5%. EEG had been requested for all cases with epileptic seizures as expected, but only for 49 (60.5%) of 81 cases without a history of such seizures. Although 8 of these 49 patients had no history of epileptic seizures, epileptic activity was present on the EEG. EEG therefore did not provide any information about the patient's neurological condition in 41 patients (34%). EEG examination is recommended to exclude the Landau-Kleffner syndrome when there is a regression in language development without taking seizures into account (26). The recognition of this syndrome and differentiating it from autism seems important as different treatment options may affect the prognosis in the presence of this syndrome. We did not find a relationship between verbal expression skills and the EEG request in our study. As mentioned before, this may be because retardation of verbal expression development may be considered as one of autism's own findings. Although epileptic seizures were not identified in our autistic children, an EEG examination was frequently requested in the presence of risk factors that may cause neurological problems such as preterm abnormalities and birth difficulty. The presence of a history of seizures, premature birth and identification of problems at birth in children with an autistic disorder were used as criteria for an EEG request but language development was not in our study.

In conclusion, cMRI and EEG were widely used in the investigation of additional neurological disorders in our autistic children group. However, no information was obtained on any additional neurological disorder from the EEG in 34.0% and from the cMRI in 22.0% of the cases. Both examinations were more frequently requested when a problem was defined at birth. In addition, preterm birth was seen as a risk factor for an EEG request and walking late and with problems for a cMRI request. Unnecessary EEG and cMRI examinations in autistic children can be prevented with a more detailed clinical evaluation and clarification of the request criteria.

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