Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 113; No. 3; P37

Assessing the Utility of Electroencephalography for Staring Episodes in Children with Autism

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Abstract

Aim
We aim to assess whether electroencephalography (EEG) has a justified role in assessing staring episodes in children with Autism Spectrum Disorder (ASD); investigating for possible diagnosis of epilepsy.

Methods
This is a retrospective study on an Irish paediatric cohort. We reviewed EEG studies performed on children with ASD referred specifically for staring episodes to Children's Health Ireland at Temple Street between 2010 and 2017.

Results
There are 120 EEG tests; labelled as follows: 59.1%: normal, 22.5%: abnormal, 16.6%: borderline and 1.6%: 'limited study'. Background abnormalities are seen in 22.5% and interictal epileptiform abnormalities are seen in 16.6%. Absence seizures are captured in none.

Conclusions
Interictal EEG in ASD patients often yields false positive findings. EEG for investigating staring episodes in children with ASD are probably not useful.

Introduction

Autism is a term used to describe a developmental disorder which is characterised by impaired social interaction and communication as well as restricted interests and repetitive behaviours.[1] Autism Spectrum Disorder (ASD) is now one term used to describe both the lower and higher functioning forms of autism.[2] Professionals used terms including autism, Asperger's Syndrome, Pervasive Developmental Disorder, PDD Not Specified, high-functioning and low-functioning when discussing ASDs; which is now an umbrella term for syndromes sharing the same symptoms.[3]

Diagnosis of epilepsy in children with ASD is difficult, as children can have non-epileptic episodes which mimic epileptic seizures.[4] These can include focal impaired awareness seizures (FIAS) formerly known as complex partial seizures and absence seizures involving staring and unresponsiveness. [5, 6] Patients with ASD can have increased prevalence of interictal epileptiform activity/abnormalities without the presence of clinical epilepsy, with reports of up to 59%;[4] more than normal children who have rates of 3.5% of interictal epileptiform patterns.[7] They are generally non-specific and include spikes, sharp waves or spike wave discharges.[8] The presence of interictal abnormalities is often unrelated to epileptic seizures.[9] Children with ASD can have behaviours similar to epileptic

seizures such as staring.[5] The staring may reflect the decreased attention span which is common in children with varying degrees of developmental delay.[10] Thus, diagnosis of epilepsy in these patients can be diagnostically difficult.[5]

EEG is an important tool for diagnosis of epilepsy.[11] Appropriate use of EEG is important as it is a relatively scarce resource.[12] Children's Health Ireland at Temple Street (CHI-TS) is a tertiary/quaternary centre, receiving patients from all counties in the Republic of Ireland. It is one of two major EEG referral centres for paediatric EEGs in the Republic. The Clinical Neurophysiology Department in CHI-TS receives a yearly average of 1214 EEG referrals. Often the indication for EEG is clear; for example, history of definite or likely epileptic seizure (whether convulsions, focal or likely absence seizures), developmental regression, encephalopathy and so forth but not always. One of the settings for which rather frequently requested EEG is a child with ASD having "staring" or "blank" episodes. The lack of awareness of imitators of epileptic seizures is a common cause of misdiagnosis and can lead to mismanagement with unjustified use of anti-epileptic drugs (AEDs).[13] Another major cause of misdiagnosis is the over-interpretation of normal EEG patterns as epileptiform activity; the most common misinterpreted are non-specific background fluctuations in the temporal regions, being read as temporal sharp waves.[14]

Inappropriate EEG referrals compete with more appropriate referrals leading to strain on EEG services directly increasing waiting times and costs.[12] We are aware of an earlier study performed in Melbourne, Australia assessing the role of EEG in patients with ASD and staring.[6] No such studies have been performed in Ireland. Indeed, the practice of requesting and performing EEGs on children with ASD and staring is still taking place rather frequently here. Thus, we aim to perform a similar study on an Irish paediatric cohort to assess whether EEG has a justified role in assessing staring episodes in ASD children.

Methods

This is a retrospective study approved by the Ethics Research Committee at CHI-TS. We retrospectively reviewed EEG studies in ASD children referred specifically for staring episodes. EEGs were performed in CHI-TS from 1st January 2010 to 31st December 2017.

Inclusion criteria: children with confirmed ASD; aged ≤16 years; EEG request/referral to solely investigate staring episodes. Exclusion criteria: children with previously confirmed diagnosis of epilepsy; children still under investigation for ASD; significant neurological illness known to be strongly associated with epilepsy (e.g. tuberous sclerosis (TS)) and EEGs abandoned due to lack of patient co-operation resulting in no eligible EEG data.

Patients are identified using Natus Database version 8.1.0. EEGs are recorded using Xltek EEG system with electrode placement using the international 10/20 measurement system and disposable electrodes. EEGs are all reported by one consultant clinical neurophysiologist over the seven year period. The reports are verified and double-checked by both the recording technologists and the consultant before the final report is issued.

The following historic patient data are recorded using SPSS statistic software version 24:
patient gender, age, family history of epilepsy, previous medical history/diagnoses, description of presenting episodes, specified type of ASD when available, current AED use if any and referring consultant. We also recorded if patients had previous EEGs. The following EEG data are recorded: test date, type and duration of EEG; result of EEG including: background EEG general rhythm (normal, slow or otherwise), background non-epileptiform abnormalities (focal slowing, asymmetry etc.), interictal EEG paroxysmal abnormalities (epileptiform and non-epileptiform) and ictal EEG with video detail of episodes recorded during test.

Results

Over the study period 120 EEGs were performed on children with confirmed ASD. Figure 1 outlines the patient characteristics and figure 2 outlines EEG testing details.

The EEG results (summarised figure 3) are labelled: normal, abnormal, borderline and "limited study". The latter are limited because of uncooperative patients whose behaviour during tests elicited significant artefacts. Abnormal EEGs are labelled because of either non-epileptiform background abnormalities or epileptiform abnormalities or both.

Background abnormalities are seen in 27 (22.5%) of the 120 studies and interictal epileptiform abnormalities are found in 20 (16.6%) of the 120 studies. Figure 4 identifies the location of the interictal epileptiform abnormalities.

Typical episodes were recorded in 7 (5.8%) EEGs, all were non-epileptic. Clinically the episodes include staring/unresponsiveness; some also include head deviation, eye blinking or body jerks. Of these 7 EEGs, 5 (71.4%) were normal EEGs and 2 (28.5%) were abnormal EEGs. One abnormal EEG had an asymmetric background and the other EEG had focal spikes and sharp waves in the right parietal region.

Figure 1: Patient Characteristics

Patient Characteristics*
120 Patients

Age:	Range 2 -16 years	Mean age 6.4 years	
		N	**%**
Gender:	Male	95	79.1
	Female	25	20.8
Type of ASD:	Not specified	102	85
	Specified (Aspergers Syndrome)	18	15
Previous Medical Diagnoses:		38	31.6
	developmental delay or learning difficulties	*19*	
	speech delay	*9*	
	developmental & speech delay	*5*	
	febrile convulsions and macrocephaly	*2*	
	ataxia	*1*	
	anxiety	*1*	
	asthma	1	
Presenting Clinical Episodes*:			
Solely staring/unresponsiveness/blankness/dazed look		91	75.8
Additional clinical movements		29	24.1
Including:			
	eye rolling/movement	*16*	
	head turning/nodding	*7*	
	limb tremor/stiffening/jerkiness	*4*	
	hand flapping	*1*	
	unspecified facial movements	*1*	
Positive Family History of Epilepsy:			
Yes~		37	30.8
No		83	69.1

*Information obtained from EEG report details; N= number; % percentage
~ (n=8 (21.6%) of these had an abnormal EEG)

Figure 2: EEG Testing Details

EEG Testing Details

Type of EEG test:	**N**	**%**
Routine	96	80
Sleep deprived	8	6.6
Sedated EEG*	16	13.3
EEG Referral Source:		
Consultant Paediatricians	77	64.1
Consultant Neurologists	36	30
Consultant Psychiatrists	4	3.3
Psychologists	3	2.5
EEG Duration~:		
<30 minutes	92	76.6
30-60 minutes	22	18.3
>60 minutes	6	5
Previous EEGs*:	12	10
Hyperventilation:		
Performed by	73	60.8
Unable/unwilling to perform	47	39.1
Sleep Recording:		
Sleep obtained in EEG	24	20

* Sedated EEG performed when EEG is not possible due to behavioural difficulty.
~ EEG duration varied depending on whether sleep was planned/recorded
*None of the previous EEGs confirmed a diagnosis of epilepsy; N=number

Figure 3: EEG Results/Analysis

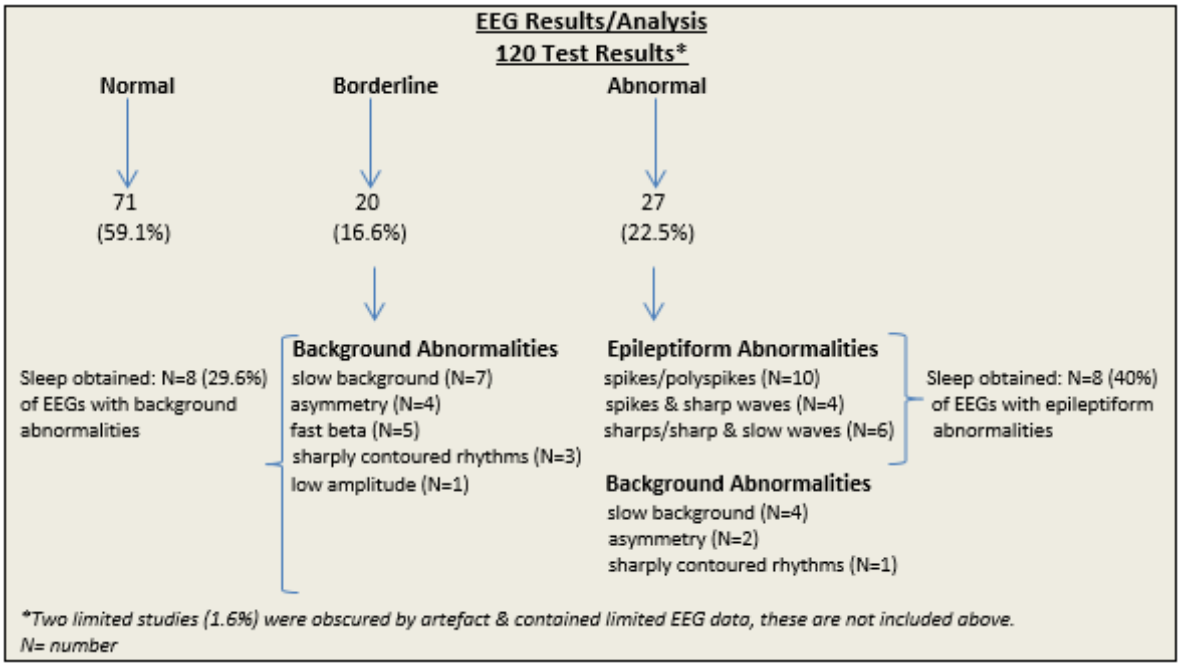
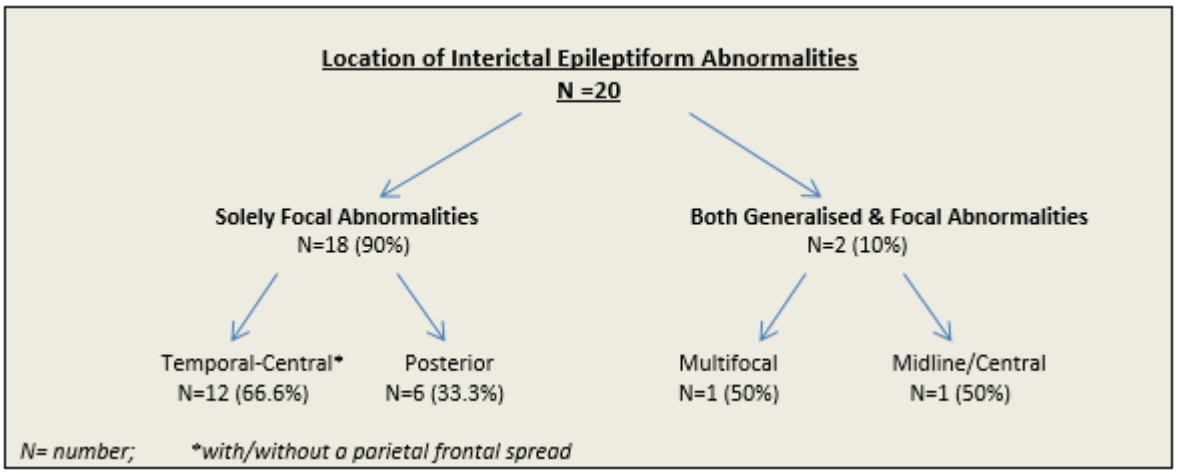


Figure 4: Location of Interictal Epileptiform Abnormalities



Discussion

Rates of reported seizure frequency in ASD vary; possibly due to differences in: age, levels of cognition and type and degree of language dysfunction.[15] In one study the rate of clinical seizures is reported as 46% [16] (in our study, there are no confirmed epilepsy or absence seizures).

On average, 15 EEGs are performed yearly in our institution to assess staring in ASD children. Behavioural issues and lack of cooperation prove challenging for the EEG staff with some EEGs abandoned or limited information recorded with excessive artefact. There is also significant stress placed on patients and their families to try contain children for the test. If there is successful electrode placement; co-operation during activation procedures is not always possible. Hyperventilation can provoke absence seizures in up to 90% of patients with childhood absence epilepsy.[17] Hyperventilation was performed by 60.8% in our study with no absence seizures provoked.

Family history of epilepsy is a known risk factor for epilepsy.[18] Positive family history of epilepsy and an abnormal EEG is seen in a very small minority (6.6%) in our study. Hughes and colleagues report that EEGs of children in their study with significant findings do not have family history of epilepsy.[6] Our exclusion criteria included significant neurological illnesses known to be associated with epilepsy; for example, we excluded a patient with TS as there is a significantly high rate of epilepsy in TS with reports of up to 89.6%[19], thus patients with TS are not viewed as a typical ASD-alone situation.

ASD patients may have several types of epilepsy as in normal population.[9] Reported seizure types include FIAS, generalised and secondary generalised seizures.[20, 21, 22] However, absence epilepsy is not seen or reported significantly in patients with ASD in any of the studies reviewed in the literature.

Interictal EEG aids in diagnosing epilepsy.[11] Prevalence of interictal epileptiform abnormalities in ASD is reported to be up to 59%.[4] We found 16.6% interictal epileptiform abnormalities which is close to the reported 13% by Hughes and colleagues.[6] However, in their study they included patients with history of epilepsy, whereas we excluded patients who had prior diagnosis of epilepsy in order to assess "pure" ASD (only with staring) to assess the potential for first time epilepsy diagnosis.

Both interictal epileptiform and non-epileptiform abnormalities are found in ASD patients with reported higher rates of epileptiform abnormalities compared to non-epileptiform abnormalities. [23, 6] However, not all studies report higher epileptiform abnormalities; Tuchman and colleagues reported 20% of autistic children without epilepsy having an abnormal EEG of which 10% were non-epileptiform abnormalities and 8% were epileptiform.[21] We found a slightly higher rate of non-epileptiform background abnormalities (22.5%) compared to the rate of epileptiform abnormalities (16.6%).

Epileptiform abnormalities in ASD patients can be focal/multifocal and generalised.[4] A study found EEG paroxysmal activities localised in the frontal area in about 50% of cases.[22] Another study found epileptiform abnormalities focal and multifocal and in 45% of the patients, centrotemporal spikes.[9] We found 66.6% of epileptiform interictal activity

in the temprocentral regions, sometimes with parietal and frontal spread and two patients with both generalised and focal epileptiform abnormalities.

In our study 20% of all EEGs include sleep. Only 34% of all EEGs with abnormalities (epileptiform/non-epileptiform) include sleep. Interictal epileptiform discharges occur more often in sleep than wakefulness.[11] Our rate of interictal abnormalities may have been higher if more studies contained sleep. However, obtaining more sleep would not assist with answering our question; assessing staring episodes which are, of course, seen only during wakefulness.

As a bonus finding, we found all (100%) episodes captured to be non-epileptic. This is consistent with the original study from Melbourne.[6] Also Kim and team documented that 93% of ASD patients who had telemetry monitoring had non-epileptic episodes which resembled FIAS.[4]

The main reasons for misdiagnosis of epilepsy professionally are incomplete history taking and misinterpretation of EEGs; misdiagnosis can lead to mismanagement using AEDs.[24] It is therefore of concern we found consultant paediatricians (64.1%) and consultant neurologists (30%) accounted for the vast majority of EEG referrals to investigate staring in ASD children; a finding not reported elsewhere in the literature.

Behavioural non-epileptic staring episodes are a known and frequent feature of ASD. Children with ASD often have abnormal EEGs (epileptiform and/or non-epileptiform abnormalities) without the presence of clinical epilepsy. Performing EEGs on ASD children in context of investigating staring episodes, therefore, is not justified. Clinicians are encouraged to avoid requesting any type of EEG (routine/prolonged/sleep deprived) in this specific context. A useful yield is almost non-existent and very importantly, there is risk of misdiagnosis of epilepsy based on erroneously interpreted abnormalities and high incidence of false positives. There is the unjustified use of limited resources (EEG). However, another aspect not to be ignored is the unjustified significant stress experienced by ASD children and their families to co-operate with a relatively long test involving the difficulty of having to stay still, be restrained or alternatively the unjustified use of sedation. Pointers to when a routine EEG could be useful: associated motor activity (rhythmic limb jerking, tonic stiffening and forceful deviation of the eyes/head), clear convulsions and incontinence with the episodes. We make an extremely important concluding point: patients with ASD can often have stereotypies including manual mannerisms, eye rolling, nodding, tremor, hand flapping, unspecified facial movements and tic-like episodes (see Figure 1). These are best investigated with a home video. No EEG will diagnose these but the clinical expert eye certainly will. This is the mainstay of our clinical skill/ability to diagnose these episodes (including what is described as staring).

Acknowledgements
The authors thank the neurophysiology staff members Odette O Flaherty, Louise Scott, Aoife Lavin and Karen Collins.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare.

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