

Diagnoses and referral pattern at a first seizure clinic in London

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SUMMARY

Background. Epilepsy is among the most frequent neurological conditions and it is estimated that approximately 8% of the population experience a seizure at some time in their lives.

Aim. To examine the characteristics of patients referred to a First Seizure Clinic (FSC) at a University Hospital in South-West London.

Methods. All subjects referred to the FSC at St George's University Hospitals between January and December 2015 were included in this audit.

Results. From a total of 257 patients, males 49.5%, age range 16–90, 30% referred by General Practices (GPs), 59.1% by the Accident & Emergency Department (A&E) and 10.9% by other hospital wards, 24.5% did not attend (DNA) the clinical appointment. Females who did not attend were significantly older than males (49.8 years old vs 39.7; $p=0.007$). Among those who attended the clinical appointment, 17% were diagnosed first unprovoked seizure, 12.4% acute symptomatic seizure and 28.9% epilepsy. These patients were referred mainly by A&E while GPs referred seizure mimics especially non-epileptic attack disorder (NEAD) and syncope. Patients with NEAD were significantly younger than those with seizures (29.4 years old vs 44.2; $p<0.001$) and had a previous psychiatric history (72.7% vs 16.8%; $p<0.001$). The proportion of seizure mimics was similar in the older sample group (>65 years). Regarding acute symptomatic seizures, 33.3% were alcohol-related, 20.8% acute brain insults and 12.5% drug-related (always overdose).

Conclusions. 1 in 4 patients referred to a FSC does not attend the clinical appointment, especially older females. More than 1 in 3 cases represent seizure mimics and are referred mainly by GPs.

Key words: epilepsy • first unprovoked seizure

INTRODUCTION

Epilepsy is amongst the most common serious neurological conditions with incidence rates, in high-income countries, ranging between 40 and 70/100,000 persons per year, and these are generally higher in young children and in elderly people (de Boer et al., 2008; Duncan et al., 2006; MacDonald et al., 2000). It is estimat-

ed that approximately 8% of the population experience a seizure at some time in their lives (Hauser and Kurland, 1975) and a correct diagnosis is crucial for a proper management and prognosis. However, it is well-known that the rate of misdiagnosis of epilepsy is quite high. In fact, a population based study in adults found a misdi-

agnosis rate of 23% (Scheepers et al., 1998) and 26% of patients referred for “refractory epilepsy” were found not to have epilepsy at all (Smith et al., 1999). In children, the problem of misdiagnosis is even more relevant as a prospective study of more than 300 patients referred to a dedicated secondary care clinic showed that only 23% of children were given a final diagnosis of epilepsy (Hindley et al., 2006).

Despite increased awareness of the global burden of epilepsy on individuals, societies and health-care systems, provision of care for people with epilepsy remains inadequate (Mula and Sander, 2016). In May 2015, the World Health Assembly approved the WHO Resolution on the Global Burden of Epilepsy which provides a powerful tool to engage national governments into implementing effective actions to improve medical and social services for people with epilepsy, to promote public awareness about epilepsy and to allocate resources to epilepsy care (Covanis et al., 2015). The establishment of Epilepsy Centres is a recognised strategy to improve the care of patients with epilepsy, especially drug-refractory cases, but data from First Seizure Clinics (FSCs) of Epilepsy Centres is still limited (Firkin et al., 2015; Rizvi et al., 2016). Nevertheless, it seems evident that patients with a suspected seizure should be reviewed by an epileptologist in dedicated services rather than in general neurology clinics. In fact, FSCs have a central role in delivering a correct diagnosis, counselling patients regarding anticipated outcomes and reducing mortality and morbidity with proper prevention strategies. Data regarding referral and attendance pattern as well as diagnoses and outcome are relevant for service development and implementation but information on this regard are scarce and still limited to a few centres in the world (Firkin et al., 2015; Rizvi et al., 2016).

AIM

The aim of the present report is to examine the characteristics of patients referred to the FSCs at a Regional Neuroscience Centre in South-West London.

MATERIAL AND METHODS

All patients aged more than 16 and consecutively referred to the FSCs at St George’s University Hospital, between January and December 2015, are included in this audit. Patients with a suspected epileptic seizure can be referred by General Practices (GPs), hospital Accident and Emergency Department (A&E) or other hospital wards (OHWs) within the trust, using a First Sei-

zure Referral Form (FSRF) that can be faxed or emailed directly to the Neurology Department. The FSRF enquires about demographic and clinical details of the patient and includes a general information sheet about seizures that should be given to the referred patient. Patients are requested to attend the clinic appointment with a family member or friend who can provide witness account of the event.

Following information were acquired from patient’s notes: age, gender, referral source, clinical diagnosis, EEG and MRI results, past medical history, psychiatric history and family history. Acute symptomatic seizures were defined according to ILAE criteria (Beghi et al., 2010). The present study was registered as an audit.

Data storage and management was compliant with the Good Clinical Practice statement in accordance to the Declaration of Helsinki.

Frequencies of categorical demographic and clinical variables were analysed using the χ^2 analysis or Fisher’s exact test while continuous demographic variables using Student’s t-test or ANOVA. The alpha error was set at 0.05. All statistical analyses were 2-tailed and conducted using the Statistical Package for Social Sciences (Version 15 for Windows, SPSS Inc. Chicago, IL).

RESULTS

A total number of 257 patients were referred to the FSC from January to December 2015. Average waiting time to the clinical appointment was at least 6 weeks. Males were 49.5%, mean age (\pm SD) 43.9 (\pm 19.6) (range 16–90). There was no difference in mean age \pm SD between males and females (Males 45.3 years old \pm 20.2; Females 42.45 \pm 18.9 $p=0.243$). In terms of referral source, 30% were referred by GPs, 59.1% by A&E and 10.9% by OHWs. Females were more likely to be referred by GPs (Females = 64.2%) while males by A&E (Males = 55.6%) and OHWs (Males = 65.2%) (Chi Square = 8.092; $df=2$; $p=0.017$).

A total number of 194 patients attended their clinical appointment whereas 63 (24.5%) did not attend (DNA). The DNA group did not differ in terms of referral source (GPs 33.3%, A&E 58.7%, OHW 7.9%), gender (male 44.4%) and age (45.3 \pm 20.2). However, looking at the mean age by gender, females who did not attend the clinical appointment were significantly older than males (Females = 49.8 years old \pm 19.4 vs Males = 39.7 \pm 18.1; $t=2.752$; $p=0.007$).

Among the 194 patients who attended their clinical appointment, females were significantly younger

Table 1. Clinical and demographic data of the study sample

	N = 194 (%)
Age, mean \pm SD	43.4 \pm 19.4
Gender, Male	99 (51.0%)
Referral source	
Referred from General Practices	56 (28.9%)
Referred from Accident & Emergency	115 (59.3%)
Referred from Other Hospital wards	23 (11.9%)
Diagnoses	
Acute symptomatic seizure	24 (12.4%)
First unprovoked seizure	33 (17.0%)
Epilepsy/Remote symptomatic seizure	56 (28.9%)
Syncope	43 (22.2%)
Non-Epileptic Attack Disorder	11 (5.7%)
Transient Ischaemic Attack	3 (1.5%)
Aura/migraine	4 (2.1%)
Arrhythmias	1 (0.5%)
Panic attacks	1 (0.5%)
Hypoglycaemia	1 (0.5%)
Transient Global Amnesia	2 (1.0%)
Uncertain/others	15 (7.7%)

than males (Females 39.7 ± 18.1 vs Males 46.9 ± 20.0 ; $t = -2.60$; $p = 0.010$). In terms of diagnoses, 92.3% received a diagnosis at the clinical appointment and 58.3% were confirmed to have had an epileptic seizure (first unprovoked seizures 17% of the total sample, acute symptomatic seizures 12.4%, epilepsy 28.9%) (Table 1). Among patients older than 65 the proportion of epileptic seizures was 55.8%. Patients with epileptic seizures (ES) that were either acute symptomatic, unprovoked or remote symptomatic were more likely to be referred by A&E while GPs referred mainly seizure mimics including syncope or non-epileptic attack disorder (NEAD) also known as pseudoseizures, dissociative seizures, psychogenic non-epileptic seizures ($\chi^2 = 62.270$; $df = 22$; $p < 0.001$) (Figure 1). There was a significant gender difference in diagnosis pattern, as males were more likely to be diagnosed with acute symptomatic seizures and TIA than females ($\chi^2 = 23.495$; $df = 11$; $P = 0.015$) (Figure 2).

In the group of patients diagnosed with epilepsy, only in 10.7% was it possible to identify previously undiagnosed seizures preceding the index event. In another 10.7% there was a previous history of epilepsy or seizures diagnosed by a physician (e.g. during childhood), while the majority of patients (78.6%) were diagnosed with epilepsy as the index event was either a remote symptomatic seizure at high risk of recur-

Table 2. Causes for acute symptomatic seizures

	N = 24 (%)
Acute brain insults (e.g. stroke, hypoxia, TBI)	5 (20.8%)
Alcohol withdrawal	3 (12.5%)
Alcohol intoxication	5 (20.8%)
Illicit drug use	2 (8.3%)
Drugs	3 (12.5%)
Electrolyte disturbance	2 (8.3%)
Infections	3 (12.5%)
Hypoglycaemia	1 (4.3%)

rence (e.g. stroke, brain tumour, traumatic brain injury) or the patient had a second seizure before the clinic appointment.

Regarding patients with NEAD, although a greater proportion were female compared to those with epilepsy, this difference was not statistically significant (NEAD Females 63.6% vs ES Females 43.4% $p = 0.221$). However, patients with NEAD were significantly younger than those in the ES group (NEAD 29.4 years old ± 9.9 vs ES 44.2 ± 18.9 ; $t = -4.251$; $p < 0.001$). Patients with NEAD were more likely to have a previous history of a psychiatric disorder as compared to those in the ES group (NEAD = 72.7% vs ES = 16.8%; $\chi^2 = 18.399$; $df = 1$; $p < 0.001$).

Regarding acute symptomatic seizures, identified causes are listed in Table 2. In the majority of cases, these seizures happened in the context of alcohol intoxication/withdrawal or an acute brain insult (usually stroke) while 12.5% were drug-related seizures but all of them happened in the context of overdose in major psychiatric disorders.

In terms of investigations, patients with acute symptomatic seizures did not differ in terms of MRI or EEG abnormalities as compared to subjects with a first unprovoked seizure (FUS) (MRI abnormalities acute symptomatic seizure 33.3% vs FUS 18.2%; $p = 0.206$; EEG abnormalities acute symptomatic seizure 20.8% vs FUS 18.2%; $p = 0.802$).

DISCUSSION

The St George's University Hospitals NHS Foundation Trust serves a population of 1.3 million across South-West London. Our findings about pattern and frequency of diagnoses are in keeping with those of other centres (Rizvi et al., 2016), further confirming the average pattern of patients referred to FSCs in terms of age and gender distribution and the range of possible mimics in high-income countries. In our sample, seizure mim-

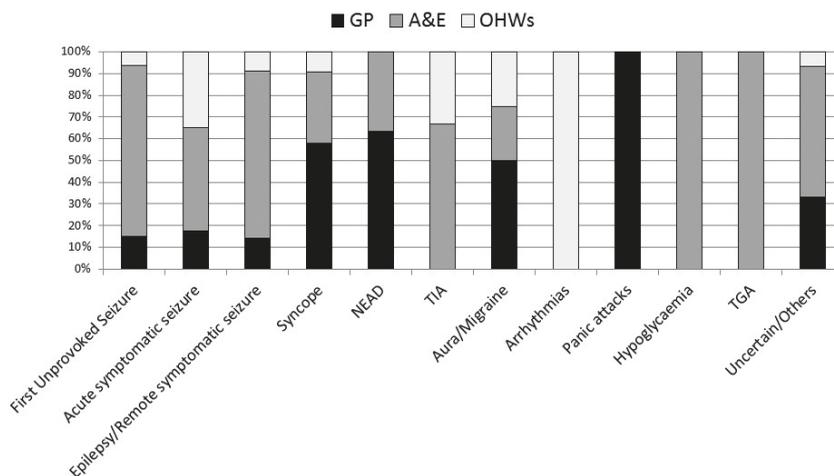


Figure 1. Referral source according to diagnosis.

$\chi^2 = 62.270$; $df = 22$; $p < 0.001$; NEAD – Non-Epileptic attack disorder; TIA – Transient Ischaemic Attack; TGA – Transient Global Amnesia

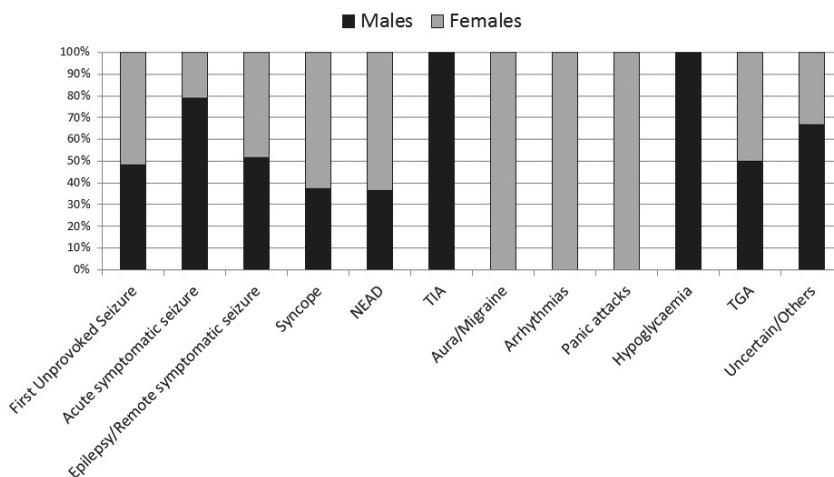


Figure 2. Gender differences according to diagnosis.

Chi Square = 23.495; $df = 11$; $P = 0.015$

NEAD – Non-Epileptic attack disorder; TIA – Transient Ischaemic Attack; TGA – Transient Global Amnesia

ics represent 41.7% of cases and, interestingly, similar figures (i.e. 44.2%), are observed in the older sample group aged more than 65, meaning that cardiac events or cerebrovascular accidents do not impact considerably on the proportion of seizure mimics.

This is the first study investigating in detail the issue of patients not attending the clinical appointment. In fact, our audit shows that 1 in 4 patients do not at-

tend the clinic appointment. According to the National Institute of Clinical Excellence (NICE) guidelines patients with a suspected seizure should be reviewed within 2 weeks (NICE, 2012). In 2015, capacity of FSCs at our Epilepsy Centre was less than demand, resulting in a fairly long waiting time and this may obviously be partially responsible for the high rate of patients not attending the hospital visit. However, it is not possible to

compare our results with those of other centres as data on DNA rates in other FSCs are not available. It is also not possible to exclude the potential role of other variables such as stigma, fear of being discriminated, being in denial or the underestimation of the problem by the individual patient. In our sample, there was no difference in referral source suggesting that, for example, this is not due to a lack of time in busy A&E departments to reinforce the need to attend the clinic appointment. Our data show that females who did not attend the clinic appointment were significantly older than males. Reasons for that are unclear and further studies are needed. In fact, information about ethnic origin, religion and socioeconomic status were not recorded. It is, therefore, not possible to either support or exclude the hypothesis of a specific role of stigma in this regard. In addition, we do not know whether these patients decided to be reviewed elsewhere, including in the private sector. However, other authors have reported that up to 40% of patients with epilepsy do not seek medical advice after the first seizure (Firkin et al., 2015) and our findings, for the first time, document the extent to which this is a specific issue for First Seizure Services. It is evident that further studies in this regard are needed in order to improve and shape FSCs and epilepsy services to efficiently intercept these patients.

Data about referral patterns, especially regarding patients with NEAD, represent another interesting finding. Patients with functional neurological symptoms are diagnosed in neurology clinics and their management is clearly becoming one of the many competencies that neurologists should have (Carson et al., 2016). Diagnosing NEAD can be challenging for non-specialists but a correct diagnosis is important to anticipate outcomes, to recommend a correct treatment as soon as possible and to prevent complications. Our results clearly show that the GP should be the main partner of specialists in the management of patients with NEAD, especially regarding insight reinforcement and education. In fact, these patients are mainly referred by GPs and, as such, go back to the GP practice. Further data on the perception of GPs regarding NEAD and their management will help in implementing specific care pathways. Our results also show that more than 70% of patients with NEAD had a previous psychiatric history. This observation is not obviously new (Mellers, 2005) but further reinforces the need for a comprehensive history taking, including the previous psychiatric history and the family psychiatric history, during epilep-

tological consultations and confirms the need for Epilepsy Centres to develop integrated care pathways with local psychiatric services for the treatment of patients with NEAD. The need for integrated pathways is also supported by the proportion of patients with a first unprovoked seizure that have a previous psychiatric history (15.2%), which is not higher than the general population but definitely higher than that observed, for example, in patients with syncope (4.7%). In this regard, it is important to note that data on psychiatric comorbidities of epilepsy usually comes from drug-refractory patients with limited information about patients with first unprovoked seizures or new onset epilepsies (Pohlmann-Eden et al., 2015). However, it is now becoming evident that psychiatric conditions often precede the onset of epilepsy (Hesdorffer et al., 2006) and our data further support this view.

In our sample, almost one third of patients received a diagnosis of epilepsy. In the majority of cases, patients were offered a prophylactic antiepileptic drug treatment because the index seizure was considered remote symptomatic and the risk of recurrence was considered greater than 60% (Fisher et al., 2014). In 1 out of 5 cases, there was a previous history of seizures but in only 1 out of 10 it was possible to state that the patient had previously undiagnosed seizures, representing 5.3% of the ES group. These figures are definitely lower than those reported by another study done in Australia (Firkin et al., 2015), where the authors concluded that a relative socioeconomic disadvantage was one of the reasons for a delayed diagnosis. However, as already discussed for patients not attending the clinical appointment, data on socioeconomic status was not recorded. It is, therefore, not possible to clarify the nature of this discrepancy.

Our results should be considered bearing in mind the following limitations. First, the retrospective nature of this report, although identified patients were consecutively referred. Second, only subjects referred with the First Seizure Referral Form were included in this audit, thus representing an underestimation of the total volume of subjects referred to the FSCs as some patients were probably referred using general referral letters. Third, our results come from a Regional Neuroscience Centre at a University Hospital with one of the largest Emergency departments in the UK, hosting a Major Trauma Centre and a Hyper Acute Stroke Unit treating patients not only from the local area but also Surrey, Kent & Sussex. It is, therefore, possible that our results are not representative of FSCs in centres without

an emergency department or covering smaller areas.

In conclusion, our results bring further information about the role of FSCs in epilepsy. Further data are urgently needed in order to allocate appropriate resources for the care of people with a first seizure in order to reduce waiting times and offer a prompt and efficient service.

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CONFLICT OF INTERESTS

None of the authors have received payment or services from a third party for any aspect of the submitted work.

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