

## Epilepsy and musical perception. A perspective involving 14 patients

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**Introduction.** The relationship between epilepsy and music is poorly understood. Musicogenic epilepsy, which involves seizures triggered by music, and epilepsy that triggers or involves musical experiences are rare. Anti-seizure medications (ASMs) may affect cognition and possibly the musical sphere. The relationship between epilepsy, ASMs and music perception is insufficiently investigated in the literature. This study describes the clinical characteristics of patients with epilepsy with advanced musical knowledge, and aims to understand the disease's involvement in the musical sphere.

**Patients and methods.** A qualitative study was conducted in epileptic patients with musical knowledge, investigating their musical perception before and after a diagnosis of epilepsy and after a change of ASM when this was possible. Questionnaires and recordings of music were used to assess musical perception.

**Results.** Fourteen patients had musical knowledge, and the majority of these (50%) had temporal lobe epilepsy. A total of 92.8% of the patients stated that epilepsy or its medications had affected them in the musical sphere. There was no clear relationship between the lateralisation of the epilepsy and musical involvement. 42.9% were professional musicians, and had to give up their profession. The patients prescribed with more than one ASM had greater musical involvement.

**Conclusions.** Temporal lobe epilepsy appears to have the greatest effect on music perception, and more studies with ASM and music perception are needed to determine its effects.

**Key words.** Anti-seizure medication. ASM. Drug-resistant epilepsy. Epilepsy. Music. Musical perception.

### Introduction

The relationship between epilepsy and music remains one of the least known parts of the current epilepsy landscape. Both musicogenic epilepsy, i.e. epilepsy with reflex seizures triggered by music, and epilepsy in which seizures are triggered by the production or hearing of musical phenomena, are rare and little discussed in the literature. Likewise, the involvement of epilepsy and anti-seizure medications (ASMs) with musical production and understanding has not been extensively studied, although ASMs are known to affect cognition in general, and several studies have also linked this to involvement of the musical domain [1].

It is now accepted that the interpretation of auditory stimuli begins in Heschl's gyrus, but subsequent musical processing requires complex neural activation in the auditory brain area associated with mesolimbic and even cerebellar activation and other sensory areas in the parietal lobe and is preferentially based in the right hemisphere [1-3]. It

has been postulated that musical training, especially at an early age, could lead to changes in brain anatomy [2]. A 1995 study explored the differences between the brains of professional musicians and non-musicians and found that musicians' brains had a larger or bulkier corpus callosum than non-artists [4].

The term musicogenic epilepsy was defined by Critchley in 1937 [5], who described in a series of 11 patients a rare form of epilepsy with focal seizures that were triggered by music. However, there are references to music-induced seizures in the 19<sup>th</sup> century literature.

Musicogenic epilepsy has a prevalence of approximately one case per 10,000,000, although as sound stimulation is not routinely used during electroencephalograms, the prevalence may be higher [5,6]. It is classified by the International League Against Epilepsy as a special type of focal seizures, usually triggered by musical stimuli, such as listening to songs, although there are cases that occur when playing the instrument or even when think-

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ing about music, however, it is not the only phenomenon related to music in patients with epilepsy. We could distinguish others, such as seizures involving 'music production,' like singing and/or humming music or familiar songs [7]. On the other hand, we can also find seizures that include hearing musical phenomena without the external stimulus (musical hallucinations).

The relationship between epilepsy, ASMs and music perception has been much less studied in the literature, with very few articles discussing this association and how epilepsy and the choice of ASMs may affect music understanding and processing [8-10].

## Objectives

To describe the characteristics of epilepsy in people with higher education in music or professional musicians and the repercussion of this pathology on their musical processing.

## Patients and methods

We retrospectively reviewed all epileptic patients in a second-level hospital consultation room, identifying those who had a professional relationship with music or, alternatively, who had studied music at an advanced level (conservatory up to a professional degree or higher). A qualitative study was carried out on these patients' perception of music before and after their diagnosis of epilepsy. The type of epilepsy these patients had was described to try to determine whether it was related to interference with music. To carry out this study, a questionnaire with five questions was administered (Annex).

In addition, where possible, in patients for whom a change of ASM was indicated by routine clinical practice, a prospective qualitative study was conducted on musical perception and understanding in relation to the previous and subsequent ASM. In these patients, the reason for the change of ASM was also recorded, which was subdivided into lack of efficacy, cognitive adverse effects (CAEs) and other adverse effects (AEs), whether there was an improvement in AEs or number of seizures after the change, and whether there was a change in music perception. The choice of ASM was based on the criteria of the neurologist responsible for the patient. To assess musical understanding, a recording made by the principal investigator –who has a musical background– incorporating musical scale changes (major to minor) and modulation (whole

tone, tone and a half and half tone), as well as several world-famous rock and pop songs with noticeable key and/or scale changes were used. Both the recordings and the songs were also played to three people without epilepsy and professional or higher musical knowledge for validation. The patients were asked to recognise such changes in scale or modulation before and after the ASM change.

We waited two months between the start of ASM treatment and the music test to assess possible changes in perception.

## Results

Of all the epileptic patients in the practice, a total of 14 were professional musicians or had a professional music degree or higher.

Most of them were male (71%,  $n = 10$ ) and the mean age was 36.9 years with a standard deviation of 10.8. Of these patients four had idiopathic generalised epilepsy (28.6%), two had epilepsy of undetermined origin (14.3%), one had focal frontal epilepsy (7.1%) and the majority ( $n = 7$ ) had focal epilepsy located in the temporal lobe (50%). The patient with frontal focal epilepsy had semiology compatible with frontal focal epilepsy and a frontal focal cortical dysplasia. The patients with temporal lobe epilepsy had either a temporal lesion or an electroencephalogram and compatible or localising semiology.

In terms of semiology, three of the four patients with idiopathic generalised epilepsy had myoclonus and tonic-clonic seizures and one had only tonic-clonic seizures.

The patient with frontal epilepsy had tonic seizures during sleep. The patients with temporal lobe epilepsy had mostly focal seizures with and without altered level of consciousness, two of them developed bilateral tonic-clonic seizures (Table 1). Two patients also had reflex seizures when playing music, both with temporal lobe epilepsy.

The majority had professional music studies (64.3%;  $n = 9$ ), 14.3% ( $n = 2$ ) were professional musicians and two others had higher education, one patient had a degree equivalent to a professional conservatory.

Only one patient had been diagnosed with epilepsy more than 10 years ago. Three (21.4%) of the patients had been recently diagnosed with epilepsy, 35.7% ( $n = 5$ ) had received a diagnosis of epilepsy between 1 and 5 years ago and another 35.7% ( $n = 5$ ) between 5 and 10 years ago.

The vast majority ( $n = 13$ , 92.8%) felt that epilepsy or its treatments had affected their perception and

**Table I.** Clinical characteristics of patients.

Gender	Age	Hand dominance	Seizure type	Epilepsy type	Lateralization	DRE	Impairment of musical perception
Male	29	Right-handed	Myoclonic and T-C	IGE	N/A	No	Slightly
Female	46	Right-handed	Probable focal onset T-C	Unknown	N/A	No	Slightly
Male	36	Right-handed	T-C	Unknown	N/A	No	A lot
Female	39	Right-handed	Focal, impaired awareness, automatisms, RINCH	TLE	Right and left	Yes	A lot
Male	44	Right-handed	Focal with aphasia, aura	TLE	Left	No	Slightly
Male	31	Right-handed	Myoclonic and T-C	IGE	N/A	No	A lot
Female	47	Right-handed	Focal with automatisms and absences	TLE	Left	Yes	A lot
Male	36	Right-handed	Focal, automatisms	TLE	Right	No	A lot
Male	37	Right-handed	Focal, automatisms, impaired awareness, to bilateral T-C	TLE	Right	Yes	A lot
Male	29	Right-handed	Focal, postictal language impairment, automatisms	TLE	Left	No	A lot
Male	63	Right-handed	Tonic during sleep	FLE	Right	No	Not at all
Female	33	Right-handed	Focal with impaired awareness, occasional automatisms, and slight postictal language impairment	TLE	Left	No	A lot
Male	27	Right-handed	Myoclonic and T-C	IGE	N/A	No	Slightly
Male	19	Right-handed	T-C	IGE	N/A	No	Slightly

DRE: drug-resistant epilepsy; FLE: frontal lobe epilepsy; IGE: idiopathic generalised epilepsy; N/A: not applicable; RINCH: rhythmic ictal non clonic hand; T-C: tonic-clonic; TLE: temporal lobe epilepsy.

development of music, 57.1% ( $n = 8$ ) felt they had affected them 'a lot' and 35.7% ( $n = 5$ ) felt they had affected them 'a little'. Only one patient felt that it had not affected his perception of music.

Eight patients (57.1%) had noticed differences in their perception or understanding of music throughout the course of their illness or with changes in their medication. Two of them (14.3%) had not noticed any differences throughout their illness and the rest could not specify. Six patients (42.9%) were professional musicians prior to the diagnosis of epilepsy and were unable to continue their professional work. Three patients (21.4%) had drug-resistant epilepsy.

Six of the eight patients (75%) who indicated that their epilepsy affected them 'a lot' had a temporal lobe epilepsy. All patients with drug-resistant epilepsy indicated that it affected them 'a lot'. The remaining two patients who were affected 'a lot' had an epilepsy of unknown origin and an idiopathic generalised epilepsy.

Four of the six patients (66.6%) who had to give up their work as professional musicians had temporal lobe epilepsy, the rest had idiopathic generalised epilepsy. All patients who had to stop their professional activity as musicians indicated that it had affected them 'a lot'. All patients with drug-resistant epilepsy who were professional musicians had to

**Table II.** Patients according to number of ASMs, musical involvement, initial ASM and other concomitant medication.

Number of ASMs	Impairment of musical perception	First ASM	Other concomitant ASMs
1	Not at all	LCM	–
1	Slightly	BRV	–
1	Slightly	ESL	–
1	Slightly	BRV	–
1	Slightly	LEV	–
1	Slightly	LEV	–
1	A lot	LTG	–
1	A lot	LEV	–
1	A lot	LTG	–
2	A lot	LEV	–
2	A lot	LEV	LTG
3	A lot	LCM	LTG, TPM
3	A lot	LEV	LCM, PER
4	A lot	LEV	LCM, PER, ESL

ASM: anti-seizure medications; BRV: brivaracetam; ESL: eslicarbazepine; LCM: lacosamide; LEV: levetiracetam; LTG: lamotrigine; PER: perampanel; TPM: topiramate.

stop their work as musicians. When asked why, they reported that they did not feel able to perform their musical work as before.

The only person who indicated that epilepsy did not affect him 'at all' had focal frontal epilepsy.

In terms of medication, 64.3% ( $n = 9$ ) had a single ASM prescribed, 14.3% ( $n = 2$ ) had two drugs, 14.3% ( $n = 2$ ) had three and a single patient (7.1%) had four ASMs prescribed. All patients with more than one ASM prescribed indicated that it affected their musical ability 'a lot' (Table II).

The only patient who was 'not at all' affected by epilepsy had only one ASM and that was lacosamide. The other ASMs used can be seen in table II.

As for the prospective study regarding musical understanding with change of ASM, it was performed in seven of the 14 patients (50%). The rea-

sons for change and the improvement or worsening of music perception can be seen in table III.

The drug change was due to non-cognitive AEs in three patients, due to CAEs in another three patients and only in one patient due to lack of efficacy. Five of them (71%) reported that they felt more capable in the musical domain with the drug change and the remaining two reported a worsening of their musical perception.

In the two patients who worsened, the change was made in one case due to lack of efficacy and in the other due to CAE. In the former, the patient persisted with the same number of seizures after the switch, although his music perception worsened. The patient who switched ASM due to CAE had no improvement in AEs after the change, and, in addition, his music perception worsened.

In the five patients who improved their music perception after the drug change, the reason for the change was CAE in two and non-cognitive AEs in three of them. Among the patients in whom the reason for change was CAE, in one of them their AEs and their music perception improved afterwards, and in the other case, only their music perception improved. Of the three patients with non-cognitive AE, two of them had their AE and music perception improved after the change of medication, and in the other case only their music perception, with no change in AE.

## Discussion

The relationship between epilepsy and musical composition is complex. In the history of classical music, attempts have been made to attribute this illness to composers such as Chopin, who suffered from hallucinations, without a clear basis [11]. It is therefore difficult to go back to examples of other musicians to assess the effect of this pathology on their work. More recent and proven is the case of Hikari Oe, son of Nobel literature prize winner Kenzaburo Oe, who has suffered from epilepsy since adolescence. As a child he was able to identify and memorise the keys and titles of the music he listened to. He could compose his own works in his head but was not skilled enough to play. From the age of 30, his epilepsy worsened, and with it his ability to compose, as evidenced by the simplicity of his scores from that time on [8]. As we have already mentioned, musical interpretation or understanding activates many brain areas, but its most direct relationship is the temporal lobe, so it is logical that temporal lobe epilepsy is the one that most

**Table III.** Reason for change of ASM and improvement/worsening of music perception.

Reason for change	Previous ASM	Posterior ASM	Improvement AEs/seizures	Musical perception
Cognitive AEs	LEV	LTG	No	Worsening
Cognitive AEs	LEV	LCM	Yes	Improvement
Cognitive AEs	LTG	LEV	No	Improvement
Non-cognitive AEs	CBZ	LEV	Yes	Improvement
Non-cognitive AEs	LEV	BRV	Yes	Improvement
Non-cognitive AEs	OXC	LCM	No	Improvement
Ineffectiveness	LEV	TPM	No	Worsening

AE: adverse effects; ASM: anti-seizure medications; BRV: brivaracetam; CBZ: clobazam; LCM: lacosamide; LEV: levetiracetam; LTG: lamotrigine; OXC: oxcarbazepine; TPM: topiramate.

often affects this domain [12]. Our data, although limited in number, seem to provide the same results with the majority of our temporal lobe epilepsy patients indicating that epilepsy greatly affected their musical understanding.

Although, as previously reported in the literature, musical perception and ability is usually established more in the right hemisphere, in our study –despite the limited number of patients– we did not find a clear relationship between right-sided epilepsy and musical impairment. Most of the cases described correspond, as in our study, to patients with musical knowledge. It is therefore likely that these effects are underestimated in the general population, either because they are not used to discerning between key changes or because they are not affected in the same way in their daily lives.

There are several cases described in the literature of reversible alterations in tonal perception in patients treated with sodium channel blockers. A review of the literature reports cases of patients treated mainly with clobazam, although one case has been reported with lacosamide and one with oxcarbazepine [9]. There is also a reported case of impaired auditory perception in a patient after starting levetiracetam treatment, which improved after switching to zonisamide [13]. It has been postulated that this could be due to changes in the organ of Corti [14] or due to a possible involvement of the sarcolemma of the stapedius muscle.

There are few references in the literature describing that lamotrigine can induce changes in

music perception, although possibly part of this effect is because it shares the same mechanism of action as the drugs mentioned, but lamotrigine also has other mechanisms of action and not only on sodium channels, which could explain its apparent worse profile in this aspect.

Our case series is too limited in the number of patients to draw conclusions in this respect. In our series, although the number is small, all the patients who had more than one ASM prescribed were markedly affected in the musical sphere, although it is true that patients who have more than one ASM prescribed have a more resistant epilepsy, it is plausible to hypothesise the possible influence of ASM on the musical sphere.

On the other hand, most of the published cases correspond to Japanese patients, mainly women, compared to our study in which the majority are Caucasian men.

Among the limitations of this study are those derived from its retrospective nature, as it can be difficult to distinguish from the clinical history whether the musical performance disorder derives from the medication or from the disease itself. This was compensated for by the prospective collection of information when the patient required a change of medication. Other limitations are the small sample size and the qualitative nature of the data collected. It would be ideal to carry out studies with a larger number of patients and with different drugs in order to draw hypotheses on the impact, if any, of different ASM on the musical sphere.

## Conclusions

The relationship between epilepsy and music is very complex. Among the different forms of epilepsy, temporal lobe epilepsy seems to have the strongest relationship with music. Further studies in this subgroup of patients are needed to discern the best course of treatment.

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**Annex.** Musical perception qualitative questionnaire.

1. What musical studies do you have?

Higher education (conservatory)	Professional studies (professional conservatory)	Other professional or higher equivalent qualification	I am a professional musician, although without a degree
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2. How many years have you been suffering from epilepsy?

Less than a year	More than a year but less than five	More than five years but less than ten	More than 10 years
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3. Do you think epilepsy has affected your perception of music?

Not at all	Slightly	A lot
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4. Have there been any changes in your perception of music in the last few years or in relation to a change of treatment?

Yes	No	I don't know
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5. Are you still able to work as a professional musician?

Yes	No	I was never a professional musician
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## Epilepsia y percepción musical. Una visión a través de 14 pacientes

**Introducción.** La relación entre la epilepsia y la música es poco comprendida. La epilepsia musicógena, que involucra crisis desencadenadas por la música, y la epilepsia que produce o involucra experiencias musicales son poco comunes. Se sabe que los medicamentos anticrisis (MAC) pueden afectar a la cognición y posiblemente a la esfera musical. La relación entre la epilepsia, los MAC y la percepción musical está insuficientemente investigada en la bibliografía. El objetivo de este estudio es describir las características clínicas de pacientes con epilepsia con conocimientos musicales avanzados e intentar comprender la afectación de la enfermedad a la esfera musical.

**Pacientes y métodos.** Se llevó a cabo un estudio cualitativo en pacientes epilépticos con conocimientos musicales, investigando su percepción musical antes y después del diagnóstico de epilepsia y, cuando fue posible, tras el cambio de MAC. Se utilizaron cuestionarios y grabaciones musicales para evaluar la percepción musical.

**Resultados.** Catorce pacientes tenían conocimientos musicales, la mayoría (50%) con epilepsia del lóbulo temporal. Un 92,8% de los pacientes indicó que la epilepsia o sus medicamentos le habían afectado en la esfera musical. No había una clara relación entre lateralización de la epilepsia y afectación musical. Un 42,9% eran músicos profesionales y tuvieron que dejar la profesión. Los pacientes con más de un MAC pautado tenían mayor afectación musical.

**Conclusiones.** La epilepsia del lóbulo temporal parece ser la que más afecta a la percepción musical, y hacen falta más estudios con MAC y percepción musical para dilucidar sus efectos.

**Palabras clave.** Epilepsia. Epilepsia farmacorresistente. MAC. Medicamentos anticrisis. Música. Percepción musical.