

Electroencephalographic epileptiform alterations in individuals without epilepsy - literature review

Alterações eletroencefalográficas epileptiformes em indivíduos não epiléticos: revisão de literatura

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RESUMO

O eletroencefalograma é um exame de fácil realização que vem sendo amplamente indicado para condições não relacionadas à epilepsia. A identificação de atividade epileptiforme nestas circunstâncias deve ser interpretada de forma cautelosa, pois descargas focais ou generalizadas podem ser encontradas em indivíduos normais e sem quaisquer queixas. O objetivo deste estudo é realizar uma revisão de literatura quanto à presença de alterações epileptiformes no EEG de indivíduos sem epilepsia. O diagnóstico equivocado de epilepsia nestas situações é comum, porém a taxa de ocorrência de crises é muito baixa, o que não deve motivar o uso desnecessário de fármacos antiepiléticos.

Unitermos. Achados Incidentais, Eletroencefalografia, Testes Obrigatórios

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ABSTRACT

The electroencephalogram (EEG) is a non invasive and accessible tool most that has been vastly used in conditions other than epilepsy. The finding of epileptiform activity in individuals without epilepsy should be interpreted cautiously because focal or generalized discharges can be found in normal individuals. The goal of this article is to review the finding of epileptiform discharges on EEGs of patients without epilepsy. In summary, the misdiagnosis of epilepsy is common and the rate of seizure occurrence in this context is very low and should not motivate the use of antiepileptic drugs.

Keywords. Incidental Findings, Electroencephalography, Mandatory Testing

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INTRODUCTION

The electroencephalogram (EEG) is a non invasive and accessible tool most often used to diagnose epilepsy. Moreover, it has also been used to support the diagnosis of many conditions other than epilepsy including headache, sleep disorders, syncope, dementia, behavioral and learning disorders¹⁻³.

The EEG has been widely used as a pre-admission test for many professionals such as aircrew, military personnel, heavy machine operators, divers, professional drivers and high rise workers. It has also been used in children and adolescents as a pre-admission testing in military school. Most publications about EEG and pre-admission testing refers to airline crew^{1,4}.

The finding of epileptiform discharges on the EEGs does not necessarily mean that a person has epilepsy. Focal or generalized epileptiform discharges can be found on routine EEGs of healthy individuals⁵.

The prevalence of epileptiform activity on EEGs varies according to the population studied. Epileptiform discharges can be seen in 0.5% to 2.4% of candidates for aircrew training¹, 12.3% of non epileptic individuals with a acute or progressive brain lesion², 2.6% to 13% of children with psychiatric disorders^{6,7} and 6.5% of healthy children⁸. The estimate risk of future epileptic seizures in these populations is 2 to 3%^{1-3,7}.

The aim of this study is to do a literature review on epileptiform discharges in individuals without epilepsy.

METHOD

We searched online resources for English, Spanish or Portuguese language publications in the following databases: Scientific Eletronic Library Online (SciELO), Literatura Latino-Americana e do Caribe em Ciências da Saúde (Lilacs) and Pubmed. We used the terms “admissional EEG”, “EEG in psychiatric disorders”, “EEG and parasomnia”, “EEG and headache”, EEG and syncope”, EEG and dementia” and “Epileptiform discharges in individuals without epilepsy”.

We used glossary of the International Federation of Clinical Neurophysiology to select articles that described epileptiform patterns⁹. According to this publication,

epileptiform patterns “describes transients distinguishable from background activity with a characteristic spiky morphology, typically but neither exclusively nor invariably found in interictal EEGs of people with epilepsy”. Therefore, we included typical spikes or acute focal waves, spike and wave complexes or multiple spike and wave complexes.

The patterns of uncertain significance, periodic lateralized epileptiform discharges (PLEDS), generalized or focal slowing and disorganized background activity were not included in our review.

In this review, the findings of interictal epileptiform discharges (IED) will be described in the following categories: epileptiform discharges in aircrew members; prevalence of IED in psychiatric disorders; prevalence of IED in healthy children and adults; prevalence of IED in memory disorders; prevalence of IED in headache disorders; the impact of epilepsy misdiagnosis.

LITERATURE REVIEW

Electroencephalographic epileptiform discharges in aircrew members

Candidates for aircrew training have been studied due to the fact that EEG is generally required as a pre admission screening test. One study reported that candidates that had IED were generally excluded from the selection process⁴. The EEG finding of IED is seen in 0.5% to 5% of aircrew training candidates (on average in 1% of individuals)¹⁰. The isolated finding of IED in 5% of a studied population might be due to administration of a seizure inducing agent¹¹.

In one study, 5893 jet pilot applicants were evaluated with EEG. Of these, 142 (2.4%) were excluded because of an abnormal EEG and 4 developed epileptic seizures during intermittent photic stimulation⁴. Another study reported that after a follow up period of 5 to 29 years, of 43 candidates of aircrew training with epileptiform discharges on EEG, only one individual developed epilepsy¹.

Literature data is scarce because after being excluded from the admission process, there might be a high rate of patient loss to follow up. A review article estima-

ted that the risk of developing epileptic seizures after a finding of IED is approximately 25%¹⁰. This elevated rate of seizures might be attributed to selection bias and small sample sizes due patient loss on follow up¹¹. A registry review of USA pilots demonstrated that seizures are very rare and have not been linked to death or material loss¹².

There is no evidence supporting an association between IED and future development of epileptic seizures. However, there is a great concern about the occurrence of transient cognitive impairment due to asymptomatic epileptiform discharges and airline security. Less than 1% of all aviation accidents are related to acute pilot incapacitation¹⁰. There is no association between aviation crashes and pilot EEG abnormalities¹³.

In the USA, Canada and Australia the use of EEG as a screening tool for aircrew candidates has been abandoned because the rate of seizures is very low and there is no evidence supporting that submitting these individuals to EEG would reduce the risk of accidents. In European countries, EEG is still used as a screening tool for aircrew candidates. There has been an attempt to evaluate these EEGs in a more homogeneous way in this population by creating standardized methods of evaluation¹³.

There is no data in the literature about EEG in other professions. This might be due to the fact that it is difficult to sample individuals to be submitted to EEG testing. In Brazil, there are neither guidelines about the indication of pre admission EEG testing nor the existence of accredited centers by the Brazilian Clinical Neurophysiology Society for this purpose. In Brazil, pre admission testing is the responsibility of the candidates themselves, who can choose where they will be evaluated. The lack of accredited centers could lead to misinterpretation of EEG findings by electroencephalographers with no experience.

In summary, there is no evidence that pre admission EEG testing is indispensable for aircrew individuals. In fact, EEG testing in this population does not predict or alter outcomes for air crashes and it should not be routinely used as a fundamental selecting criteria.

Electroencephalographic epileptiform discharges in individuals with psychiatric disorders

In the past six decades, a substantial number of

studies about the prevalence of abnormal EEG finding in patients with psychiatric disorders have been published¹⁴. Although EEG testing is not recommended to children with psychiatric disorders, many studies have focused this age group of patients, especially children with attention deficit hyperactivity disorder (ADHD), autism and schizophrenia^{7,14-16}.

Abnormal EEG findings have been documented in hospitalized psychiatric patients. The EEG findings were clinically correlated to depression, mania, anorexia nervosa, personality disorders, suicide without depression and schizophrenia. Epileptiform abnormalities were found in 2.6% of the patients and were characterized by photoparoxysmal response, spike-wave or polyspikes discharges - generalized waves, spike complex - temporal/frontal or central focal wave¹⁷.

The rate of epileptiform activity in patients with schizophrenia varies from 20 to 60%¹⁴. A study has shown that patients with schizophrenia had two times more left temporal abnormalities on EEG when compared to individuals with mood disorders, who had more EEG abnormalities on the right side¹⁸. EEG abnormalities were more frequently found in patients with schizophrenia who had a positive family history, which suggests that genetic factors could be involved in EEG abnormalities. These abnormalities could be due to alterations in cortical neuronal architecture, cellular neuropathology and alterations in neurochemical transmission. All these alterations go in accordance with the theory of schizophrenia pathophysiology in addition to the possible effects of neuroleptics¹⁴.

The rate of psychogenic nonepileptic seizures (PNES) is approximately 30% in patients referred to epilepsy evaluation¹⁹. A study of the incidence and predictive factors of PNES found that out of 350 patients, 22.3% had PNES of organic cause and 18% of non organic cause²⁰. Another study evaluated 187 PNES patients, diagnosed either by EEG video monitoring or by seizure event witnessed by an epilepsy expert. Of 130 patients who had only PNES and not epilepsy, nonspecific EEG abnormalities were found in 53.8% and epileptiform abnormalities in 12.3%. These findings were significantly higher when compared to the general population²¹.

Although IED are common in individual with

PNES, they cannot be interpreted as epilepsy. EEG abnormalities can be attributed to the complex interactions between psychiatric disorders and multiple psychopathologic variables, underlying cerebral disorders, brain trauma, physical and sexual abuse. All of these factors might have a central role in the clinical expression of PNES²¹.

Autism spectrum disorders (ASD) encompasses autism, pervasive developmental disorder not otherwise specified (PDD-NOS), Asperger's syndrome, Rett's syndrome and childhood disintegrative disorder. In this population, studies have shown that EEG abnormalities varies from 5.7% to 60%^{14,16}. Furthermore, epilepsy is more common in individuals with ASD when compared to the general population and ASD is more common in people with epilepsy than in individuals without it²².

Although children with attention deficit hyperactivity disorder (ADHD) are not routinely evaluated by EEG, abnormalities are found in 5.6% to 30.1% of patients when compared to health controls (3.5%)²³. Another study found EEG abnormalities in 21 children (6.1%) with ADHD out of 347. Only 3 of 21 children with epileptiform abnormalities developed a seizure disorder. This study concluded that the prevalence of epileptiform abnormalities is greater in children with ADHD than in controls when hyperventilation and photic stimulation are used. None of the epileptic seizures could be attributed to the use of methylphenidate¹⁵.

The association between stimulant use and the occurrence of epileptic seizures in children with ADHD is a controversial issue. Some centers routinely request EEG to all patients with ADHD, with or without learning difficulties, before starting the use of a stimulant. If there is an irritative focus on the EEG, patients are then prescribed an antiepileptic drug before methylphenidate²⁴.

One study has shown that of 234 children with ADHD without epilepsy, 30 had epileptiform abnormalities on EEG. Seizures occurred in three children (10%) who were prescribed stimulant therapy and had epileptiform abnormalities on EEG. The seizures occurred late in the course of stimulant use and could not be attributed to it. Other studies have also suggested that stimulants are not seizure induced drugs and antiepileptic drugs should not be prescribed because of stimulant use²⁵. Therefore, antiepileptic drugs should not be prescribed to children

with ADHD with EEG abnormalities without the evidence clinical seizures.

Electroencephalographic epileptiform abnormalities in healthy children and adults

Epileptiform abnormalities can be found in approximately 0.8% to 18.6% of healthy children and 0.3% to 12.3% of healthy adults¹⁴. One study with 3726 neurologically normal children found epileptiform abnormalities in 3.54%. After a follow up of 8 to 9 years, seven children developed generalized seizures²⁶.

Another study evaluated 100 healthy male subjects for epileptiform abnormalities on resting or activated EEG. None of the subjects showed EEG abnormalities. The same study identified 14 other studies on EEG abnormalities in healthy individuals and found that the rate of epileptiform activity varied between 0.07% to 2.6%²⁷.

The finding of interictal epileptiform discharges (IED) in individuals with no clinical history of epilepsy should be carefully assessed and should always consider the health status of these individuals as well as their age. Another point to consider is the occurrence of spontaneous IED or IED triggered by photostimulation or hyperventilation. One review article has pointed out that the rates of spontaneous IED in children vary from 0% to 5.6% and in adults from 0% to 6.6%¹¹.

In summary, studies have shown that epileptiform activity can be found on EEGs of healthy individuals without any clinical significance. Patients should be informed that the rate of future epileptic seizures is very low.

Electroencephalographic epileptiform abnormalities in individuals with memory disorders

EEG abnormalities can be found in patients with dementia, including Alzheimer's disease. Although there is no clear indication of EEG screening of all patients with dementia, they have six times more chance of having an unprovoked epileptic seizure than the general population²⁸.

There are only a few studies in the literature about EEG abnormalities in patients with dementia syndrome. There is no clear evidence or precise indication of EEG screening in these patients, except for evaluation of paroxysmal behavior alterations¹¹.

Electroencephalographic epileptiform abnormalities in individuals with headache disorders

The diagnosis criteria of migraine or other types of headaches do not include EEG testing, according to the international headache society. There are only a few reports of unequivocal epileptic activity in individuals with headache. The finding of spikes on EEG of patients with headaches varies from 0.2% to 9%, which does not differ from the control groups²⁹.

There is a clear indication of EEG testing in patients with acute headaches when clinical suspicion points to epilepsy, basilar migraine, migraine with prolonged aura and hemiplegic migraine. The finding of unequivocal epileptiform abnormalities usually points to the diagnosis of epilepsy. Moreover, the finding of occipital spike-wave children points to the diagnosis of benign epilepsy of childhood with occipital paroxysms²⁹.

We would like to point out that the clinical applicability of EEG in the evaluation of headache disorders is low, except when patients have symptoms that might suggest seizures, such as atypical aura or episodes of loss of consciousness.

The impact of EEG misinterpretation

The misdiagnosis of epilepsy is common and there is a tendency to overread normal EEGs as abnormal. The patterns that are most commonly overread include benign, nonspecific, sharply contoured temporal transients³⁰.

According to one author "Routine interictal EEG recording is one of the most abused investigations in clinical medicine and in unquestionably responsible for great human suffering"³¹. Overdiagnosis epilepsy can do more damage to patients than underdiagnosis³². In fact, if aircrew candidates or individuals applying for jobs (that require EEG as a screening test) have an EEG read as abnormal they might be excluded from selection.

Furthermore, if a healthy individual receives a diagnosis of epilepsy based solely on EEG findings, this patient will probably be submitted to a vast array of exams including sequential EEG, Magnetic Resonance Imaging of the brain and other unnecessary testing. This can bring a major economic impact to healthcare systems. It is important to emphasize that neurologists should not

treat EEGs. Epilepsy is a clinical diagnosis and EEG is an aiding tool.

CONCLUSION

Epileptiform discharges can be found on EEG of healthy individuals. However, these findings should be interpreted very carefully. The rate of seizure occurrence in this context is very low and should not motivate the use of antiepileptic drugs.

Some countries have abandoned EEG as a screening tool for aircrew candidates. This fact should bring up the discussion about the applicability of this test for this purpose in Brazil, considering the economic burden for the candidates and society.

The prevalence of electroencephalographic epileptiform alterations in patients with ASD and schizophrenia can be high and might be related to alterations in cortical neuronal architecture, cellular neuropathology and alterations in neurochemical transmission.

The presence of epileptiform activity in children with ADHD should not preclude the use of stimulant drugs. In addition, there is no supporting evidence or indication to prescribe antiepileptic drugs to children with ADHD using stimulant drugs who has epileptiform activity on EEG without clinical features of an epilepsy disorder.

In summary, the indication of EEG testing should not be trivial. It is important that there is a clear indication for ordering this test and it should be interpreted by interpreted very cautiously.

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