On the Misdiagnosis of Non-epileptic Seizures as Tonic-Clonic Seizures: Challenges and Recommendations

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Abstract

Many seizures are a result of epilepsy. In contrast, other episodes, known as non-epileptic seizures(NES), are not caused by abnormal electrical signals in the brain and are, therefore, not a direct cause of epilepsy; however, NES episodes are commonly misdiagnosed as tonic-clonic seizures. The misdiagnosis of NES episodes can result in the inapt use of antiepileptic drugs, which have no beneficial effect for people with NES and are commonly used to prevent further epilepsy-induced seizures, leading to the high risk of side effects and the unnecessary payment for these expensive medications. Other consequences of misdiagnosis include limitations on education and employment prospects, the underlying condition going unrecognized and untreated, and a decline in the quality of life of the subject. Although an electroencephalogram(EEG) can be utilized to detect if a convulsion is a result of epilepsy, the test is not entirely accurate and can all the same result in misdiagnosis and its subsequent consequences. It is vital that the EEG is improved to avoid the negative ramifications of the misdiagnosis of NES as tonic-clonic seizures. In this paper, significant flaws with the EEG and other tests used to diagnose tonic-clonic seizures are addressed and characterized in terms of their specificity and sensitivity, and methods to reduce unnecessary brain waves in brain mapping and neuroimaging such as sedation are proposed. Furthermore, auxiliary solutions such as making alterations in the placements and types of electrodes to the conventional method(10/20 system) when performing an EEG as well as alternate tests are considered with the goal of increasing the true positive rate of the diagnosis of epilepsy.

I. INTRODUCTION

Epilepsy is the predisposition that produces temporary staring spells and loss of voluntary motor movement which are symptoms of seizures. Epileptic seizures are termed tonic-clonic seizures. As a condition affecting approximately 50 million people worldwide, epilepsy is one of the most prevalent neurological conditions in the modern world. Many conditions are commonly misdiagnosed as epilepsy which leads to mistreatment and unnecessary costs. The misdiagnosis of an alternate condition as epilepsy is common with a 20% to 30% chance of occurring in a clinical setting (Smith et. al., 1999). Out of these conditions that are confused with epilepsy, NES episodes are collectively one of the most frequently misdiagnosed as epilepsy. Although partly due to missing medical history and clinical malpractice, this persisting problem is largely due to the occasionally faulty performance of the EEG or the underutilization of methods that can differentiate between NES and tonic-clonic seizures. The EEG is a test that utilizes electrodes to record the brain waves of an individual and is commonly used by clinicians to determine if one has epilepsy. Electrodes are placed in areas around the scalp to detect large groups of neuronal activity or brain waves. An abnormality in these brain waves is a common sign of epilepsy. However, the EEG - in a fairly recent study - has been shown to have a sensitivity value of 17.3% in a sample of adults and a 57.8% sensitivity value in a sample of children (Bouma et. al., 2015). The EEG's low sensitivity value demonstrates a substantial factor in the growing problem of the misdiagnosis of neurological disorders as epilepsy.

While conducting an EEG, signals can be interrupted by other activities in the brain - such as action potentials from motor movement - creating false recordings(termed artifacts) that can affect the accuracy of reading the EEG due to these artifacts having an amplitude that is a higher magnitude than the signal (Gwin et. al., 2010). The ratio between the particular signal of interest(brain waves that can be utilized to diagnose epilepsy) and other noise is termed the signal-to-noise ratio(SNR). Maximizing SNR is an important factor in improving the accuracy of the EEG. Flaws of the EEG - such as its low quality of spatial and temporal resolution - and remedies like the MRI to complement an EEG recording or utilizing different placements of electrodes(known as montages) should be considered to improve the SNR of the EEG. Overall, considering different methods relating to sleep, alternate tests, changing the duration of the EEG and using different montages and electrode types may be significant when understanding methods that can improve SNR and subsequently increase the true positivity rate of the EEG for the detection of signs of epilepsy.

II. EFFECTS OF SEDATION AND SLEEP ON EEG

Sedation could improve the SNR by lowering both internal and external noise. The usage of sedatives prevents motor movement of the patient(especially with small children and infants) including muscle contraction and eyeball movement such as blinking. The limitation of movement would prevent external noise as well as artifacts and would allow for the EEG to focus on the noise of interest, effectively improving the SNR. Sedatives are not only beneficial in reducing unnecessary noise but they have also been used to assist in making the administration of the EEG a congenial process. In clinical settings, chloral hydrate and pentobarbital sodium have been commonly utilized to sedate children and reduce restlessness which shows how sedation can be used to make the procedure of taking an EEG less exacting, especially with those who have trouble staying still in terms of motion, and shows that certain sedatives used on children are safe (Huffman, 2002). Concerns lie in the fact that certain sleep-inducing drugs have been proven to cause a ‘drug effect' on the EEG, causing normal EEGs to appear as abnormal EEGs; however, a bispectral index(BIS) which is FDA-approved may be used to determine the sedative's effects on the results of the EEG and can also provide insightful information on drug concentration (Glass et. al., 1997).

Furthermore, an experimental study has validated the safety of a certain sedative, clonidine, as it has been proven to be safe and innocuous to EEG results as shown by a 99.93% success rate with autistic children who were sedated and tested (Mehta et. al., 2004) and the sedative also assisted in making the process shorter and easier. Therefore, because they prevent movement, sedatives allow for an easier process and improve SNR. Sedation would also be effective during longer assessment periods, providing more substantial data. It should be noted that sedatives would generate surcharges and would most likely cause side effects. Sedatives are not used in the conventional procedure of administering an EEG, but they should be assessed to see if they can be implemented due to the aforementioned benefits they could provide if utilized effectively.

Clinicians have prescribed sleep-deprived EEGs intending to increase interictal epileptiform discharges(IEDs) which occur in bursts(sometimes less than a second) and are similar to spike-and-wave. Sleep-deprived EEGs can be used as a diagnostic tool to clarify the cause of an abnormality of an EEG as epilepsy(EEG Under Sleep-Deprived Conditions) or provide distinct signs of epilepsy that might not be detected by the routine EEG when administered to the same individual (Peters, 2022). This would improve the SNR by providing the EEG with new values that are important to the data of interest. This is significant as the detection of IEDs can occasionally allow clinicians to determine if a convulsion is the result of epilepsy. If not, the case is more likely to be a tonic-clonic seizure which ultimately improves the true positive rate of the detection of epilepsy. A benefit that sleep-deprived EEGs that sedatives do not offer is that they present no additional charges required to employ this method. Furthermore, due to a lack of sleep, patients may be able to achieve deep sleep easier than with a standard amount of sleep which allows for lower movement and an improvement of the SNR. In regard to epilepsy, sleep deprivation is known to cause excess seizures (Malow, 2004). The taking of an EEG during a seizure may allow for more accurate data (which is explored later), but this fact should be considered as the patient may not prefer a sleep-deprived EEG due to the unpleasant experience of an episode. Sleep-deprived EEGs should be utilized more routinely on a case-by-case basis as they can allow for the detection of information that the conventional EEG is likely to miss or produce misinformation due to indistinct data.

III. MONTAGES AND TYPES OF ELECTRODES

The variations of electrode placement are termed montages. The traditional 10-20 system of electrode placement is most orthodox in a clinical setting; however, other montages may be more efficacious in assisting the detection of epilepsy. The American Clinical Neurophysiology Society (ACNS) provides guidelines and restrictions on various montages and should be considered when evaluating the usage of unwonted montages. The location of where the noise of interest originated is vital to understanding which montage to utilize before recording an EEG. The EEG presents flawed spatial and temporal resolution. To compensate, an MRI can be used to understand the location where epileptogenesis originated (Liu et. al., 2007). Furthermore, the use of sphenoidal electrodes during an EEG allows the usage of bipolar montages which can assist in spatial and temporal resolution. Changes in hemispheric positioning, differences pertaining to medial or lateral placement, and alterations in additional factors characterize the unique placements of each montage and each combination of placements in montages allows the EEG to localize activity more effectively in different areas (Acharya et. al., 2016). With information about the origin, certain montages can be prioritized over others before taking an EEG to maximize the test's efficiency.

In the conventional EEG procedure, a gel is applied between the patient's scalp and the electrodes which are termed wet electrodes. Without the gel, the electrodes are termed dry electrodes. Wet electrodes are used most commonly; however, there are varied views on this claim. This recent study, using the typical 10-20 electrode montage, proves that dry electrodes provide a more convenient experience to the individual being tested than wet electrodes in terms of comfort (Hinrichs et. al., 2020). Furthermore, the study claims that the administration process is more rapid without the gel due to a lower amount of time taken on scalp preparation and dry electrodes also present a potential opportunity at decreasing electromagnetic interference - decreasing external noise in the SNR. Wet electrodes, on the other hand, minimize movement artifacts and provide a better quality of noise until the gel dries out. Each type offers benefits and presents flaws; therefore, determining which type of electrodes to use should be done carefully, or else consequences resulting in flawed EEG recordings may occur. This consequence can also affect the diagnosis of epilepsy through an EEG as both types can be considered in any EEG recording. Each method should be tested with montages that are different from the 10-20 montage used in this study to determine the benefits of each type of electrode change.

IV. DURATION AND TIMING OF THE EEG

A significant problem with the EEG is that it may miss abnormalities after a certain period between the taking of the EEG and the time when a patient's convulsion occurred (Sirven & Schachter, 2013). Ictal EEG recordings(EEG recordings done during a seizure episode) may be more effective in determining if an individual has epilepsy than post-ictal EEG recordings. There are not many experimental studies on this subject and further investigation of the difference between a post-ictal and an ictal EEG could be done to provide an alternative to the retrospective observational study that is used to support this claim (Geut et. al., 2017). Patients may also feel uncomfortable in the hospital setting or may not be admitted due to the inconvenience of travel. These factors may result in the false claim that patients do not have epilepsy. The usage of an ambulatory EEG(AEEG) might prove to be substantial in solving this flaw.

The AEEG records data from an individual for one to three days, much longer than a conventional EEG which typically takes less than an hour. AEEGs provide clinicians with more data to examine when making a diagnosis. The AEEG is cost-effective and allows for immediate access to service. Furthermore, a study has demonstrated that the AEEG allows for a high diagnostic yield and can provide considerable data to determine if a seizure was the result of epilepsy or a NES (Dash et. al., 2012). The patient takes an AEEG in their natural setting and may feel more comfortable using this process as opposed to how they would feel during a conventional EEG. The main benefit of interest is that AEEGs have a higher chance of recording data while the patient has a convulsion as they record for a longer period than the conventional EEG (Hernández-Ronquillo et. al., 2020). Downsides to AEEGs include the inability of a clinician to lower medication and that the equipollence of the data gained from an AEEG recording is lower than data taken in a hospital using a conventional EEG. A conventional EEG may be taken, but an individual may be uncomfortable with long recording periods. This would affect diagnosis as the test might be ended before the detection of a seizure and could result in a simple post-ictal recording that provides inaccurate data. The same applies to an AEEG as motor movement can result in artifacts. The usage of sedatives becomes effective in this regard as it can limit motor movement and individuals may be more comfortable in somnolence during an EEG. Higher amounts of accurate data could be gathered over longer periods of recording if a seizure occurs during the EEG, resulting in an ictal recording.

V. CONCLUSION

Considering the persisting problems, related to the misdiagnosis of epilepsy, that arise as a result of a low true positivity rate, clinicians must look to improve the EEG which can be quantitatively measured through the SNR. The factor of sleep associated with the patient, as well as respective sedation, in addition to factors of duration, timing, and various montages that can be used to alter the EEG should be investigated to determine if the supposed benefits could improve the SNR and effectively reduce misdiagnosis.

VI. ACKNOWLEDGEMENT

I would like to thank Mr. Kevin Gonzalez for providing feedback and making the process of writing a narrative review paper an easier challenge to tackle.

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