EPILEPSY

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Dear Doctor,

Greetings from Micro Labs. We are happy to bring you "EPILEPSY Newsletter'' which contains latest and interesting news in the field of Neuropsychiatry.

This issue contains:

- **Feasibility of combining smart shirt-based nocturnal sleep features and machine learning for seizure-day forecasting**
- **Efficacy of Neuromodulation for Drug-Resistant Epilepsy Following Failed Surgical Intervention**
- **Diagnostic performance of Montreal cognitive assessment in detecting cognitive impairment in epilepsy**
- **Case report on Neurocysticercosis as a Hidden Contributor to Acquired Epilepsy**

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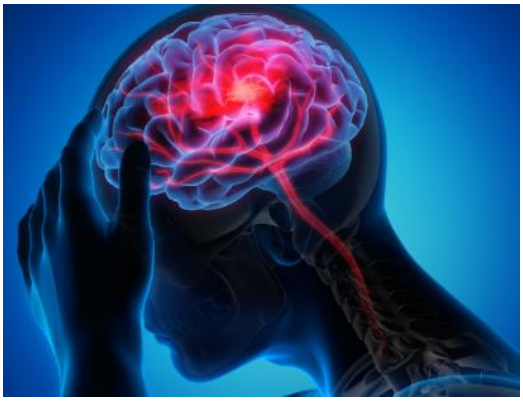
Feasibility of combining smart shirt-based nocturnal sleep features and machine learning for seizure-day forecasting

INTRODUCTION



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In certain epileptic patients, smart shirt-based nocturnal sleep study shows potential as a non-invasive method for seizure-day prediction.

Epilepsy, which impacts around 60 million people globally, is marked by the spontaneous and repeated occurrence of seizures. Although numerous antiseizure medications are available, about one-third of individuals with epilepsy (PWE) are unable to attain sufficient control over their seizures.[1] Earlier research has provided encouraging evidence for the creation of automated seizure prediction algorithms, which could be integrated into closed-loop intervention systems or advisory devices.[2] Significant progress has been made with intracranial EEG recordings, including the identification of cyclical patterns in epileptic activity and the role of networks in seizures. However, the international seizure forecasting community has recently shifted focus to investigate whether noninvasive multimodal wearable devices can be utilized for seizure prediction. Wearable devices offer the potential to serve a broader and more representative group of individuals with epilepsy and are generally more practical and preferred by these patients compared to implantable devices based on intracranial EEG.[1] Interestingly, beyond their ability to record physiological signals like electrocardiography and respiration, new wearable devices can also provide quantitative assessments of sleep quality. This feature could be used to predict seizures in a non-invasive manner.[3] Sleep duration has been shown to have a correlation with seizure frequency, as sleep deprivation is known to trigger seizures and is frequently used for clinical purposes in the Epilepsy Monitoring Unit (EMU).[1] So, this study evaluated the feasibility of using nocturnal sleep features from a smart shirt combined with machine learning to predict seizure days, with forecasting horizons of 16 and 24 hours. The researchers created a forecasting algorithm using nocturnal sleep data gathered from a large group of individuals with epilepsy in the Epilepsy Monitoring Unit (EMU), who wore a multimodal smart shirt.

METHODS

Seventy-eight individuals with epilepsy, admitted to the Centre hospitalier de l'Université de Montréal's epilepsy monitoring unit, wore the Hexoskin biometric smart shirt throughout their stay. This shirt continuously recorded electrocardiography, respiratory, and accelerometry data. Using the Hexoskin sleep algorithm, ten sleep metrics were automatically calculated:

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sleep efficiency, sleep latency, sleep duration, time in non-rapid eye movement (NREM) and rapid eye movement (REM) sleep, wakefulness after sleep onset, average heart and breathing rates, high-frequency heart rate variability, and the number of position changes. These nightly features were then normalized based on a reference night for each patient. A support vector machine classifier was developed for pseudo-prospective seizure-day forecasting with 16-hour and 24-hour horizons, to account for both daytime and nighttime seizures (24 hours) or daytime seizures alone (16 hours). The performance of the algorithm was evaluated using a nested leave-one-patient-out cross-validation method. The sole inclusion criterion was a confirmed diagnosis of epilepsy.

RESULTS

Improvement over chance (IoC) performance was observed in 48.7% of patients for the 16-hour forecasting horizon and in 40% of patients for the 24-hour horizon. Among those with IoC performance, the proposed algorithm achieved mean IoC scores of 34.3% and 34.2%, sensitivity rates of 86.0% and 64.4%, and average times in warning of 51.7% and 30.2% for the 16-hour and 24-hour horizons,

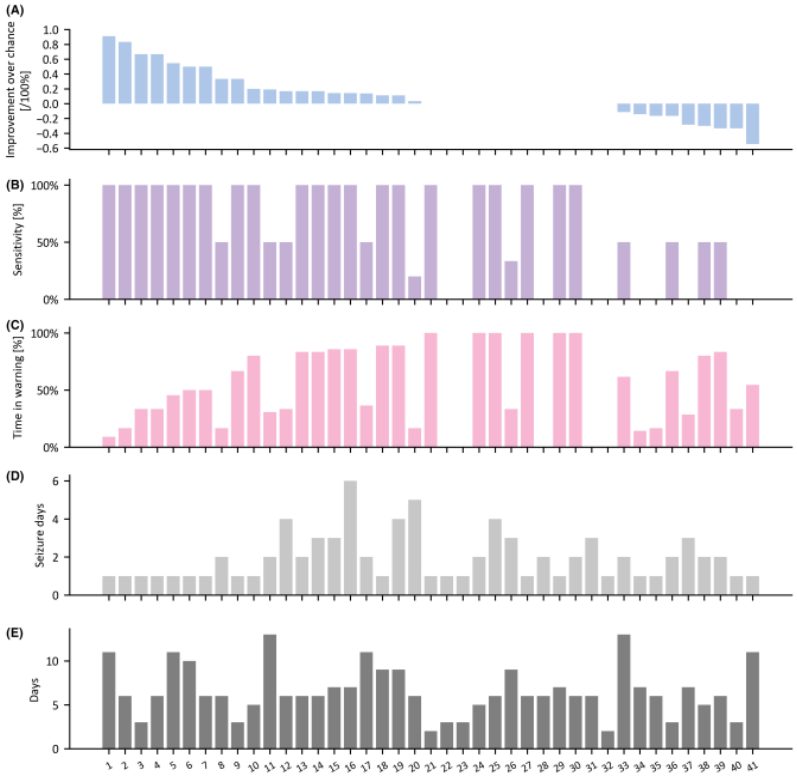

Figure 1. Forecasting results for the test folds of the 16-hour prediction horizon for the 41 epileptic individuals.

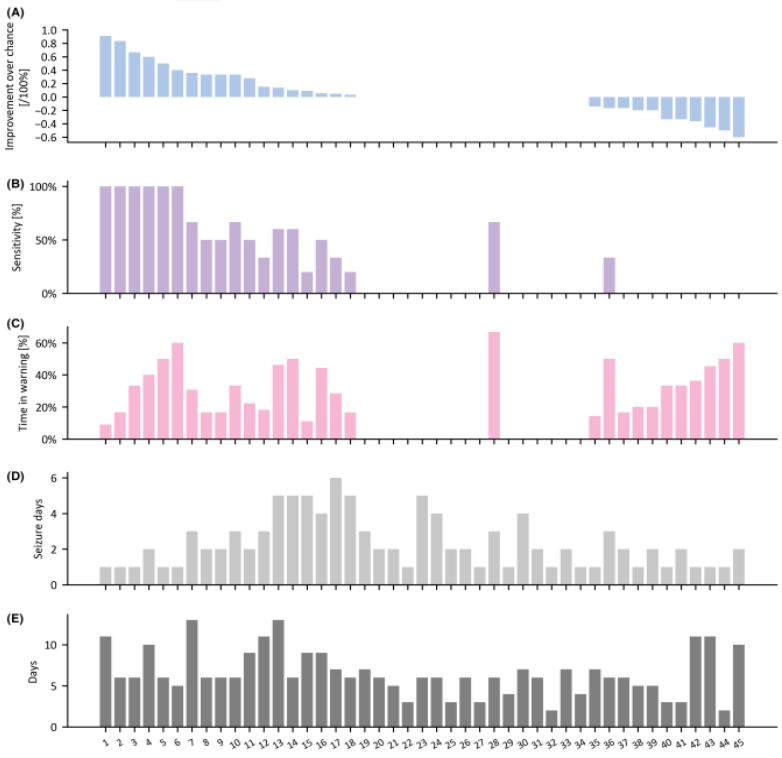

Figure 2. Forecasting results for the test folds of the 24-hour prediction horizon for the 41 epileptic individuals.

respectively (Figure 1 and 2). The algorithm demonstrated IoC performance in 14 out of 27 males and 6 out of 14 females for the 16-hour horizon, and in 11 out of 28 males and 7 out of 17 females for the 24-hour horizon. No significant differences in mean age were found between genders for either forecasting horizon ($p > 0.05$). Additionally, no significant differences in IoC performance were noted between patients with temporal lobe epilepsy and those with other epilepsy types for both forecasting horizons ($p > 0.05$, Chi-squared test). Among patients with nocturnal seizures, 30 out of 45 and 26 out of 41 were included in the 16-hour and 24-hour forecasting horizons, respectively, with no significant differences observed between these groups ($p > 0.05$, Chi-squared test).

DISCUSSION

The results of this study using a smart shirt are consistent with recent forecasting research that has employed smartwatches or bands. However, direct comparisons are challenging due to variations in data acquisition methods and forecasting timeframes. In a study by Meisel et al., seizure prediction exceeding chance levels was achieved for about half of the patients (30 out of 69) in an Epilepsy Monitoring Unit (EMU) setting, with a mean IoC of approximately 28.5% and prediction horizons averaging 31.6 minutes.[4] Similarly, Stirling et al. achieved above-chance performance for seizure prediction in 7 out of 8 individuals with epilepsy (PWE) for hourly forecasts and 4 out of 8 PWE for daily forecasts in real-life settings. Their models yielded mean ROC-AUC values of 0.68 and 0.59, respectively.[5] In this study, the overall forecasting algorithm reached a mean ROC-AUC of 0.813 for individuals with epilepsy (PWE) with improvement over chance for the 24-hour forecasting horizon. The study suggested that patient-specific algorithms could enhance these results further. Wearable devices hold promise for continuous monitoring, diagnosis, prediction, and treatment of various medical conditions. Organizations such as the International League Against Epilepsy (ILAE) and the International Federation of Clinical Neurophysiology (IFCN) have advocated for the use of neurophysiological methods, including wearable technology, for automated seizure detection in outpatients with epilepsy.[6]

CONCLUSION

This study demonstrated that forecasting seizure days is feasible using noninvasive nocturnal sleep data from smart shirts combined with machine learning models, with successful results in half of a sizable cohort of epilepsy patients in the Epilepsy Monitoring Unit (EMU). These results encourage further research in residential settings to develop and test long-term, patient-specific forecasting algorithms. Exploring various wearable monitoring technologies, including options for continuous recording or focusing solely on nocturnal sleep data, as well as varying forecasting horizons, could provide people with epilepsy with tailored solutions that best meet their individual needs.

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Efficacy of Neuromodulation for Drug-Resistant Epilepsy Following failed Surgical Intervention

INTRODUCTION

In DRE patients, neuromodulation may significantly decrease the rate of seizures in over half of cases following unsuccessful surgical intervention.

Epilepsy affects at least 50 million people globally, with up to 40% experiencing drug-resistant epilepsy (DRE). DRE often progresses severely, leading to significant disability and a mortality rate that is 5 to 10 times higher than that of the general population. While resection surgeries for DRE are generally effective and often result in complete seizure freedom, they are not suitable for all patients. Surgical intervention may be inappropriate in cases with bilateral or widespread epileptic activity, when the epileptogenic zone is near critical brain areas, or when the seizure onset zone cannot be precisely located. Furthermore, 20 to 30% of patients may still experience seizures following resective surgery, indicating that the procedure was not fully successful.[1] Currently, in addition to modifying antiepileptic medications and considering repeat surgery, neuromodulation techniques are available for patients with drug-resistant epilepsy.[2] The most prevalent neuromodulation methods for drug-resistant epilepsy today include vagus nerve stimulation (VNS), responsive neurostimulation (RNS), and deep brain stimulation (DBS) targeting the anterior nucleus of the thalamus (ANT) or the hippocampus (HP).[3] This study aimed to evaluate the effectiveness of neuromodulation in patients with drug-resistant epilepsy who had previously undergone unsuccessful resection surgeries.

METHODS

A retrospective analysis was conducted on 23 patients with drug-resistant epilepsy who received vagus nerve stimulation (VNS) or deep brain stimulation (DBS) of the anterior nucleus of the thalamus (ANT) or hippocampus (HP) following unsuccessful resection surgeries. Data were obtained from medical records during follow-up visits or through telephone surveys. All patients had previously undergone resections for drug-resistant epilepsy

and subsequently experienced seizure recurrence. Of the 23 patients, 6 (26.1%) had repeat surgeries due to ongoing seizures. VNS was implanted in 18 patients (78.3%), DBS of the hippocampus was used in 3 patients (13.0%), and DBS of the ANT was used in 2 patients (8.7%). Outcomes were evaluated using the Engel scale for surgical interventions, the McHugh (MH) scale for VNS therapy, and the percentage reduction in seizure rate for DBS therapy. The average follow-up period was 56.5 months. Prior to neuromodulation, the outcomes were classified as Engel 3a in 2 patients, Engel 3b in 2 patients, Engel 4a in 7 patients, and Engel 4b in 12 patients.

RESULTS

Vagus nerve stimulation (VNS) therapy outcomes were classified as MH Ia–IIIb in 13 cases (72.2%), with MH Ia–IIb results in 3 patients (16.7%) and MH IIIa–IIIb results in 10 patients (55.5%). Five patients (27.8%) had MH IV–V outcomes (Figure 1). In the hippocampus deep brain stimulation (HP-DBS) group, 2 patients achieved over a 50% reduction in seizure frequency over a 2-year observation period. One patient showed no decrease in seizure frequency, although the severity of seizures was somewhat reduced without changes in antiepileptic medication. In the anterior nucleus of the thalamus deep brain stimulation (ANT-DBS) group, one patient experienced a 60% reduction in seizure frequency and a reduction in seizure severity, while the other patient showed no change in seizure frequency.

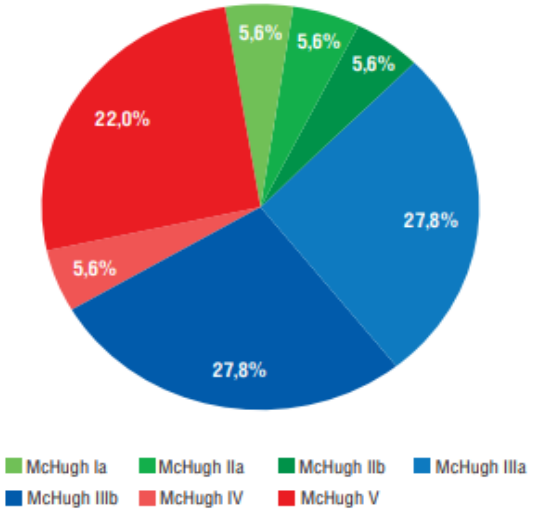

Figure 1. McHugh scale results following the insertion of a vagus nerve stimulator (VNS)

DISCUSSION

This study shown that neuromodulation significantly reduces seizure frequency and enhances quality of life for more than half of patients with drug-resistant epilepsy (DRE). According to F.L. Vale et al., data from 37 patients with refractory epilepsy (RE) who had poor outcomes following resection surgeries (lobectomy or callosotomy) showed that those who received a vagus nerve stimulation (VNS) system experienced varied results: 24 patients (64.9%) had less than a 30% reduction in seizure frequency, 9 patients (24.3%) saw a 30-60% reduction, and 4 patients (10.8%) achieved reductions greater than 60%.[3] Ding P et al. reported on the use of unilateral hippocampal stimulation in 5 patients with bitemporal drug-resistant epilepsy (DRE) who had previously undergone unsuccessful anterior medial temporal lobectomy. In their study, 18 patients with bitemporal epilepsy received anterior medial temporal lobectomy on the side where at least two-thirds of their seizures were recorded. Post-surgery, 55.6% (10/18) of patients were seizure-free at 1 year, 50.0% (9/18) at 2 years, and 44.4% (4/9) at 5 years. These outcomes were significantly better compared to a control group of 12 patients who only received medication therapy. Subsequently, 5 of the patients had deep brain stimulation (DBS)

systems implanted in the hippocampus on the side opposite the surgery. During DBS therapy, seizure frequency decreased by 80–100%, and 80% of these patients were seizure-free after one year of treatment.[4]

CONCLUSION

Neuromodulation has been shown to significantly reduce seizure frequency and enhance quality of life in over half of patients with drug-resistant epilepsy (DRE) following unsuccessful surgical interventions. This study indicated that neurostimulation was effective in more than 50% of cases. Future research involving larger patient groups is needed to compare the effectiveness of different neuromodulation techniques.

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Diagnostic performance of Montreal cognitive assessment in detecting cognitive impairment in epilepsy

INTRODUCTION

For older persons with epilepsy, the MoCA can be a useful tool for screening for cognitive impairment.

Epilepsy is a widespread neurological condition affecting more than 50 million people worldwide, with older adults being the fastest-growing demographic among those with the disorder.[1] In older adults, both the occurrence and management of seizures can accelerate cognitive decline. Additionally, epilepsy may be complicated by pre-existing cognitive dysfunction that predates the initial seizure, diagnosis, and treatment.[2] Considering the risks of cognitive impairment, cognitive decline, and dementia, the International League Against Epilepsy (ILAE) taskforce on epilepsy in the elderly has recommended regular cognitive and behavioral screening for all older adults with epilepsy.[3] The MoCA stands out as a compelling choice due to its extensive translation into nearly 100 languages, along with established training and quality control processes. Its increasing use internationally across various health conditions further supports its suitability. The MoCA has demonstrated greater sensitivity in detecting cognitive impairment in epilepsy compared to other tools, thanks to its assessment of multiple cognitive domains, whereas some other measures, like the MMSE, focus primarily on memory.

Additionally, the MoCA's broad application and familiarity in both the general population and various neurological disorders make it a reasonable choice for formal adoption in epilepsy, particularly in late-onset cases.[1] This study assessed the effectiveness of the widely used Montreal Cognitive Assessment (MoCA) in identifying cognitive impairment in older patients (age ≥ 55) with epilepsy, using the International Classification of Cognitive Disorders in Epilepsy (ICCoDE) as the standard reference.

METHODS

Patients were recruited for the BRain, Aging, and Cognition in Epilepsy (BrACE) study, a prospective longitudinal investigation of cognitive and brain aging in older adults with epilepsy. Inclusion criteria included being 55 years or older, having a diagnosis of focal epilepsy, no history of prior epilepsy-related neurosurgery (such as resection, laser ablation, or neuromodulation device), and proficiency in English for cognitive testing. All participants underwent a uniform, comprehensive neuropsychological assessment, which included the MoCA (version 7.1 in English), the Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog), and standard measures of memory, language, executive function, and processing speed. A total of 50 older adults with focal epilepsy completed the MoCA and neuropsychological tests. Participants were categorized into IC-CoDE Impaired and Intact groups according to the IC-CoDE taxonomy. The study evaluated the sensitivity and specificity of various MoCA cutoffs and used Spearman correlations to explore relationships between MoCA total scores and clinical and demographic factors, as well as between MoCA domain scores and individual neuropsychological tests.

RESULTS

The distribution of MoCA total and domain scores between the IC-CoDE intact and impaired groups were shown in Figures 1A and 1B. Significant differences were observed in the MoCA total score (Cohen's d = 2.77) and several domains: visuospatial/executive (Cohen's d = 0.935), naming (Cohen's d = 0.475), language (Cohen's d = 0.981), delayed recall (Cohen's d = 1.55), and orientation (Cohen's d = 0.336), with the IC-CoDE impaired group scoring lower. No differences were found in the attention (Cohen's d = 0.697) or abstraction (Cohen's d = 0.589) domains. Figure 1C shown that the bi-domain/ generalized phenotype had lower MoCA total scores compared to the intact phenotype ($H = 4.08$, $p < 0.001$). Discriminant function analysis (DFA) indicated that MoCA domains correctly classified 78% of cases according to the IC-CoDE taxonomy, with 23.5% of IC-CoDE impaired patients and 21.2% of IC-CoDE intact patients misclassified, resulting in an overall 40% impairment classification rate. Of the patients with a MoCA total score below 24, 63.2% were classified as IC-CoDE impaired, including 26.4% with generalized impairment, 21.1% with bi-domain impairment, 15.8% with single domain impairment, and 36.8% were classified as IC-CoDE intact. Among patients with a MoCA score below 23, 81.9% were classified as IC-CoDE impaired, including 36.4% with generalized impairment, 36.4% with bi-domain impairment, 9.1% with single domain impairment, and 18.2% were classified as IC-CoDE intact. Higher education, fewer antiepileptic drugs, and fewer errors on the ADAS-Cog were moderately associated with higher MoCA total scores. Additionally, higher letter fluency scores were linked to better scores on

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the abstraction domain, higher animal fluency scores correlated with better language domain scores, higher auditory naming scores were associated with lower naming domain scores, and better memory domain scores were related to improved performance across all memory measures (word list memory, story memory, and visual memory).

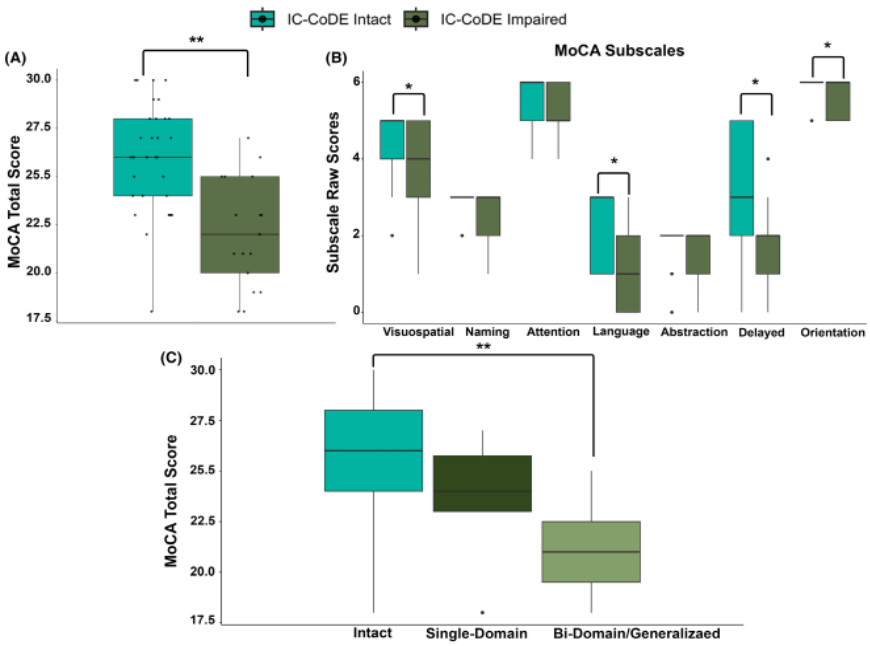

Figure 1. (A, B) MoCA domain and overall score differences between the IC-CoDE intact and impaired groups. (C) The distribution of MoCA total scores according to the phenotype of IC-CoDE. One asterisk indicates significance <0.05, while two asterisks indicate significance <0.001.

DISCUSSION

Overall, patients in this cohort had lower MoCA total scores compared to a large sample of cognitively healthy older adults. In older adults with epilepsy, Pirscoveanu et al. reported that scores on the MoCA were lower in older adults with epilepsy compared to healthy controls.[4] About one-third of our cohort was categorized as impaired according to the IC-CoDE taxonomy, a rate consistent with previous research on older adults with epilepsy,[5] in comparison, 54% of patients were classified as abnormal using the MoCA cutoff of <26. This cutoff demonstrated an overall accuracy of 72%, correctly identifying about 88% of those classified as impaired by the IC-CoDE taxonomy. However, it also failed to exclude 36.4% of cognitively intact patients, leading to false-positive errors, where cognitive impairment was inaccurately classified.

CONCLUSION

This study offered a preliminary validation of the MoCA as an effective screening tool for older adults with epilepsy, helping to identify those who may need more extensive neuropsychological evaluation. The findings suggest that a lower cutoff (e.g., < 24) was more effective in detecting cognitive impairment in this population compared to the commonly recommended cutoff. Additionally, the study showed a significant alignment between MoCA domains and standard neuropsychological assessments. It is essential to conduct similar research in other regions globally to confirm these findings.

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Case report on Neurocysticercosis as a Hidden Contributor to Acquired Epilepsy

INTRODUCTION

This case study highlights the importance of neuroimaging, particularly in poor nations, when examining individuals with neurological disorders like epilepsy. The impact of NCC on public health can be minimised by avoiding and treating it with early diagnosis and appropriate treatment.

Neurocysticercosis (NCC) is a neglected tropical disease affecting the central nervous system (CNS), caused by the larvae of the pork tapeworm (Taenia solium).[1] It is the most widespread parasitic infection of the brain globally, particularly in regions with inadequate sanitation and limited access to clean water.[2] NCC represents a major public health issue globally, especially in developing countries.[2] Despite its significant effects on individuals and communities, NCC is frequently underreported and misdiagnosed. It is a major contributor to preventable epilepsy cases worldwide, accounting for approximately 30% of all epilepsy cases in endemic regions. Although the precise mechanism of NCC-induced seizures is not fully understood, it is thought to be related to the inflammatory response triggered by cyst degeneration. Advances in diagnostic techniques, antiparasitic medications, anti-inflammatory therapies, and minimally invasive surgical options have greatly enhanced the prognosis for patients with NCC.[3] This case report details a Nigerian woman from a rural area who presented with stroke-like symptoms and had a decade-long history of recurring seizures and headaches. Neuroimaging revealed a diagnosis of NCC. This case highlights the critical role of neuroimaging and suggests that NCC should be considered as a differential diagnosis in patients with neurological symptoms from endemic areas. Early detection and timely treatment are crucial for improving patient outcomes.

CASE PRESENTATION

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A 44-year-old woman came to the neurology clinic with a three-day history of left limb weakness and difficulty walking. She did not have symptoms like altered consciousness, fever, vomiting, neck stiffness, or pain. She had been diagnosed with right focal unaware epilepsy with bilateral tonic-clonic seizures ten years ago, but no neuroimaging was performed at that time. Despite being prescribed carbamazepine 200 mg twice daily, her irregular adherence led to monthly seizures. She also experienced recurrent headaches. Two months before her clinic visit, she had episodes of memory impairment and slurred speech, which resolved within a few days. She struggled to recall names and recent events. The patient lived in an area with poor sanitation, consumed pork, and was exposed to free-roaming pigs. On examination, she had left hemiparesis, with muscle strength of 4/5 in her left arm and leg, left facial nerve palsy, and a Glasgow coma score of 15. Fundoscopy and other systemic evaluations were mostly normal. The initial assessment suggested a likely ischemic stroke in the right hemisphere. A non-contrast CT scan revealed multiple oval-shaped hypodense lesions in both cerebral hemispheres, with the largest lesions measuring 2.04×1.35 cm in the right frontal lobe, 2.03×1.46 cm in the left frontal lobe, and 1.77×1.60 cm in the right parietal lobe, as well as multiple small calcific densities (Figure 1). No infarction was noted. The imaging findings were consistent with neurocysticercosis (NCC). Laboratory tests showed normal results except for an elevated erythrocyte sedimentation rate. Due to a lack of testing resources, serological tests for parasitic infections were not performed. The patient was treated with oral dexamethasone (4 mg twice daily) for 10 days, oral albendazole (400 mg twice daily) for 30 days, oral carbamazepine CR (200 mg twice daily), and oral folic acid (5 mg daily). She also received physical therapy for her limb weakness. At her three-month follow-up, she showed significant improvement with no seizures, headaches, or memory issues. She is still under follow-up, though a follow-up neuroimaging procedure has been delayed due to financial constraints.

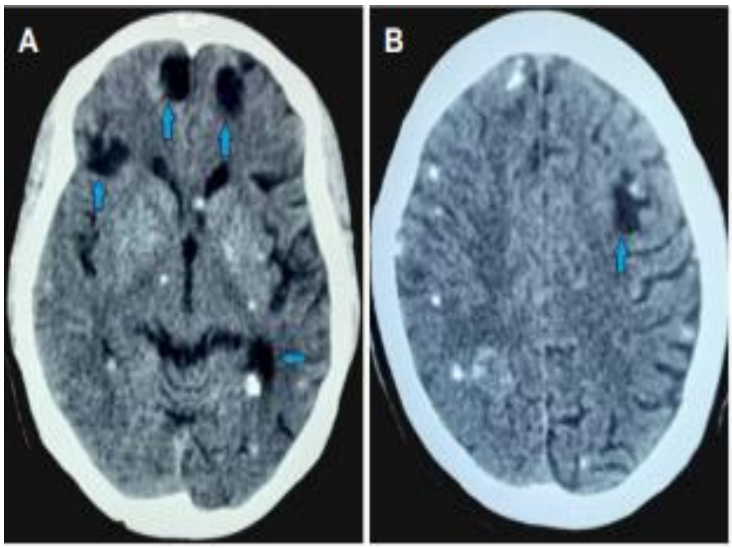

Figure 1. An axial segment of a non-contrast brain CT scan reveals the following: (A) many hypodense, oval-shaped lesions in both cerebral hemispheres, with the greatest lesions located in the left frontal, right parietal, and right frontal lobes (blue arrows). Both hemispheres also contain several tiny calcific concentrations. (B) An oval-shaped, hypodense lesion with many small-sized calcific densities in both cerebral hemispheres (blue arrow). CT - computed tomography.

DISCUSSION

The exact mechanism of epileptogenesis in neurocysticercosis (NCC) remains uncertain, but potential explanations involve local inflammation and reactive gliotic scarring.[4] Diagnosing neurocysticercosis (NCC) can be difficult due to its symptoms overlapping with other

neurological disorders, and standard neuroimaging might not always identify cysticerci. However, recent imaging advancements have enhanced NCC diagnosis. MRI is particularly effective at identifying scolex and active non-calcified cysts, while CT scans are better suited for detecting calcified cysts.[5] Analyzing cerebrospinal fluid can be helpful in diagnosing neurocysticercosis, as elevated antibody levels and increased leukocyte counts suggest an active infection.[6] The patient's history of epilepsy and recurrent headaches indicated a potential underlying neurological issue. The delay in diagnosis resulted from the absence of previous neuroimaging, which could have facilitated earlier detection. Ultimately, the diagnosis was confirmed with a CT scan during her current evaluation.

CONCLUSION

This case highlighted the critical role of neuroimaging in evaluating neurological disorders such as epilepsy, particularly in developing countries. Timely diagnosis and appropriate treatment are essential for managing NCC effectively and mitigating its public health impact.

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