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Tablet-based EEG diagnostics for epilepsy patients in the West African Republic of Guinea

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Abstract

Background: Epilepsy is most common in lower income settings where access to EEG is generally poor. A low-cost tablet-based electroencephalography (EEG) device may be valuable, but the quality and reproducibility of the EEG output are not established.

Methods: A tablet-based EEG was deployed in a heterogeneous epilepsy cohort in the Republic of Guinea (2018–2019), consisting of a tablet wirelessly connected to a 14-electrode cap. Participants underwent EEGs twice, separated by a variable time interval. Recordings were scored remotely by experts in clinical neurophysiology on data quality and clinical utility.

Results: There were 149 participants (41% female, median age 17.9 years; 66.6% ≤21 years; mean seizures per month 5.7+/−standard deviation 15.5). The mean duration of EEG1 was 53 minutes+/−12.3 and EEG2 was 29.6+/−12.8. The mean quality scores of EEG1 and EEG2 were 6.4 (range 1(low)-10(high); both medians 7.0). Forty-four (29.5%) participants had epileptiform discharges (EDs) at EEG1 and 25 (16.7%) at EEG2. EDs were focal/multifocal (rather than generalized) in 70.1% of EEG1 and 72.5% of EEG2 interpretations. Thirty-nine (26.1%) were recommended for neuroimaging after EEG1 and 22 (14.7%) after EEG2. Of participants without EDs at EEG1 (n=53, 55.8%), 7 (13.2%) had EDs at EEG2. Of participants with detectable EDs on EEG1 (n=23, 24.2%), 12 (52.1%) did not have EDs at EEG2.

Conclusions: The tablet-based EEG has a reproducible quality level on repeat testing and is useful for the detection of EDs. The incremental yield of a second EEG in this setting was ~13%. The need for neuroimaging access was evident.

Keywords

Electroencephalography; Seizure; Diagnosis; Africa; mHealth; Epilepsy

Introduction:

Smart technology including tele-medicine has potential to aid diagnostic care worldwide. In high-income countries, electroencephalography (EEG) recordings are a standard of care for the characterization of clinical 'ictal' and also 'non-ictal' events, to aid epilepsy diagnosis and classification, and to facilitate the selection of appropriate treatment [1–3]. More than 80% of the 50 million people with epilepsy (PWE) worldwide live in low- and middle-income countries [4]. This large group of PWE face challenges in both the diagnosis and treatment of epilepsy. There are significant barriers to implementing EEG diagnostic services in low- and middle-income countries: expensive equipment; few trained clinical

physiologists, clinical neurophysiologists and neurologists; and intermittent electrical power supply streams.

By 2024, there will be an estimated 7.1 billion smartphone owners worldwide, one fifth of whom are expected to reside in low-income countries [5]. Smartphones and computer tablets could be used for economical EEG data attainment and remote interpretation via use of electrode caps which are mobile-compatible. Compared to standard EEG technology, this is emerging as a lower-cost, portable, and user-friendly option. Previous work by our group demonstrated that a mobile software app with an off-the-shelf headset called the **S**martphone **B**rain **S**canner-**2** (SBS2), has a moderate sensitivity and high specificity for the detection of epileptiform abnormalities and that the use of this platform enables patients who otherwise would not have access to specialist input, access to expert clinical epilepsy or EEG support [6,7]. Here we report a new longitudinal cohort of PWE in the West African Republic of Guinea across all ages. Our paper extends previous work to focus on the quality of the EEGs in this setting by comparing sequential EEGs. The clinical utility of a repeat second EEG is understood with standard EEG[8]; however, for mobile technologies and digital health, the utility is not currently well described. We also aimed to study the impact of improved temporal lobe coverage by amendment to the EEG electrode placement compared to prior reports.

Methods:

Ethics Approvals:

This study was approved by the Ignace Deen Hospital's Ethics Review Committee and the Partners Healthcare Inc. Institutional Review Board. Each participant or next of kin proxy, in the case of children or cognitively impaired adults, provided individual written consent.

Study site and participant enrolment:

We recruited 155 participants, across all ages (youngest 8 months) in the Republic of Guinea (total population 12.41 million in 2019)[9]. Participant enrolment and data collection took place at the Ignace Deen Hospital in Conakry, the capital city (8/29/2018 – 6/1/2019). PWE or those who had a suspected seizure disorder of any age were eligible for enrolment and were recruited based on physician, health care worker, or self-referral. The study team conducted local and national television and radio interviews to publicize the study to a wide audience. Eligibility was assessed prior to enrolment by study physicians from Ignace Deen Hospital and Massachusetts General Hospital and research coordinators who performed structured clinical interview assessments. People who reported two or more unprovoked lifetime seizures were eligible for enrolment. Patients with only febrile seizures were excluded. Each enrolled participant was remunerated for both study visits.

Equipment:

The SBS2 is a software and hardware application for EEG that operates on mobile devices[10]. The software is available under Massachusetts Institute of Technology License and the hardware platform is available under CERN Open Hardware License (https://github.com/SmartphoneBrainScanner). Data processing tasks are supported by the software

framework including data acquisition, filtering, recording, and real-time artifact removal. Operating Systems including Windows, OSX, Linux, and Android are compatible with the software. Our raw EEG data collection was carried out using Windows tablets. Data were obtained with a sampling rate of 128 Hz, and wirelessly transmitted to the tablet. Five sizes of EasyCap™ EEG caps were available (range 40 cm to 56 cm) and were selected individually for each participant. The electrodes were positioned at F3, F4, F7, F8, C3, C4, P3, P4, T3, T4, T9, T10, O1, O2, Fz, Cz, Pz, Fpz, A1, and A2. F7, F8, T3, T4, T9 and T10 electrodes were added in this study to ensure temporal lobe coverage (Figure 2). The reference electrode and ground electrodes were FCz and AFz respectively. At the beginning of each EEG recording, the electrodes impedance was below 5 kΩ.

Data acquisition:

Each participant was assessed using a specific epilepsy focused questionnaire and underwent an SBS2 EEG (EEG1) at baseline and repeat SBS2 EEG (EEG2) later. All first EEGs were performed in August or September 2018. The date of follow-up EEG varied between subjects due to staff limitations, ability to contact patients, and patient capacity to take time to attend a follow-up appointment. Small groups of participants were re-called every two weeks between November 2018 and June 2019. Time between EEGs thus ranged from two to ten months.

Each participant was supine on a hospital bed and asked to minimize their movement and close their eyes throughout the recording. Individual recordings aimed to analyze the awake state primarily and also natural sleep if this occurred during the recording period. EEG1 was planned to have a target duration of 1 hour. The EEG2 recordings were planned to last a minimum of 20 minutes and no longer than 30 minutes. Recordings were completed during the daytime in a dedicated study room at the Ignace Deen Hospital in Conakry.

Study staff, including house-staff neurology residents, medical students, research coordinators, and nurses from both Guinea and the U.S.A. performed SBS2 EEG recordings. Study staff underwent a 1-hour training session prior to administration of the SBS EEG on participants. Specific study staff were eligible to collect data if they had medical experience with neurological patients, were approved by the human ethics board, and were trained in administration of the SBS2 EEG. EEG files were coded by participant number and stored on encrypted, password-protected computers and external hard drives. Files were transferred securely to readers using a web-based file sharing application.

Data interpretation was possible via a secure web-based reading platform, crowdEEG (http://crowdeeg.ca) [6,7]. The crowdEEG platform provides a centralized portal for remote EEG interpretation by neurophysiologists, ensuring consistent montage and filter options as well as a fully integrated and customizable input template. The platform organizes and manages data in a patient-centric manner. One patient can be associated with multiple EEG files. EEGs can be assigned to multiple readers independently or to the same reader more than once to support inter-rater variability studies.

EEG Interpretation:

Pediatric and adult neurologists and clinical neurophysiologists from the U.S.A., U.K., and Canada interpreted the SBS2 data. Readers were blind to clinical details with the exception of age and, when applicable, names of anti-epileptic drugs (AEDs). Readers interpreting EEG2 were blind to the results of EEG1 and vice versa. Readers were randomly assigned EEGs to interpret via the CrowdEEG online reading platform. Readers were instructed to categorize the EEGs and record their interpretation on a standardized online recording source attached to each EEG.

Recordings were classified as normal or abnormal overall, and abnormalities were classified according to whether there were epileptiform discharges (EDs) and their localization. EDs were determined at the discretion of the reader and further categorized as focal or generalized when present.

Quality scores were assigned by individual readers with a range from one (worst quality, uninterpretable) to ten (best quality, easily readable without artifact) [6]. Readers were able to enter notes further explaining their interpretation. The reader was required to enter whether Stage 2 non-REM sleep (NREM) was recorded, whether a repeat EEG study was recommended and whether neuroimaging was recommended. Each SBS2 recording was read once. All EEG interpretation occurred on desktop computers, and viewing montages were selected according to the preference of the interpreting physician.

Five different montages were available including common average reference, Anterior-posterior (AP) bipolar, Transverse bipolar, Ear reference and Pz reference. Filter options included (low pass [70 Hz, 30 Hz, 15 Hz, off], high pass [10 Hz, 3 Hz, 1 Hz, 0.5 Hz, off], and a notch [60 Hz, 50 Hz, off]). The gain could be globally adjusted or adjusted for individual channels. The crowdEEG platform incorporates a study report template, allowing readers to enter observations while reading.

Exclusion criteria:

Participants whose EEG1 or EEG2 duration was less than five minutes were excluded. This five-minute minimum duration was chosen due the need to have a sufficiently long recording to make an interpretation by readers in this setting.

Statistical methods;

Descriptive statistics were calculated for participant age, number of seizures per month, proportion treated with AEDs, EEG quality score, and duration of recording time. Statistical analyses were carried out using the Cohens Kappa (κ) test and 95% confidence intervals of the point estimates (CI 95%) using the Python 2.7.14 program. Epileptiform discharges (EDs) were scored and compared between EEG1 and EEG2 and disaggregated as focal or generalized. Participants for whom at least one EEG was not scored for EDs were excluded from the comparison of EEG1 and EEG2.

Results:

Participants:

Five (3.3%) participants were excluded from the analysis because the SBS2 recording was five minutes or less and one (0.6%) additional patient was excluded as the inter-EEG interval for this participant was less than two days (due to a calendar scheduling error). 149 remaining participants with two SBS2 EEGs were therefore available for further analysis (41% female (n=61), mean age 17.9 years). Most (n=112, 72%) of the cohort was 21 years or younger at time of enrolment.

All participants in the final analyses completed two SBS2 EEGs between 2018 and 2019. One hundred and one (68%) participants with two EEGs were currently treated with at least one AED (Table 1).

Tablet-based electroencephalograms:

The mean duration of EEG1 was 53+/−12.3 minutes and the mean duration of EEG2 was 29.6+/−12.8 minutes.

EEG quality:

The mean quality score of EEG1 was 6.4 (median 7.0), and the mean quality score from EEG2 was 6.4 (median 7.0) (Figure 1).

Of the total EEGs performed, 106 (35.6%) were recommended for repeat testing. Twenty-five (8.3%) were recommended to be repeated for the same patients after both EEG1 and EEG2 and had a mean quality score of 3.5. Participants recommended for one repeat EEG (n=106, 35.6%) had a lower mean score (4.7) than those who were not recommended for a repeat EEG at all (mean score 6.4).

Twenty-five (8.3%) participants had no useable EEG after two repeat tests due to excessive muscle artefact, excessive sweat artefact, and/or malfunctioning EEG channels. Eighteen (72%) participants without a useable EEG were 21 years of age or younger, including four (16%) participants 1 year old or younger. Seventy-one (47.6%) of the EEG1 recordings and 86 (57.7%) of the EEG2 recordings had at least one EEG channel malfunctioning or artefactual during part of the test. Thirty (20.1%) participants achieved Stage 2 NREM sleep during EEG1 and fifteen (10.1%) participants achieved this during EEG2.

Diagnostic findings:

Of those without EDs at EEG1 (n=53, 55.8%), seven (13.2%) had EDs at EEG2. Of those with detectable EDs on EEG1 (n=23, 24.2%), 12 (52.1%) did not have EDs at EEG2 (κ=0.250, 95% CI, 0.058, 0.442) (Table 2). It was not compulsory to score each EEG and therefore some of the reports included qualitative descriptions only (n=54, 36%). On EEG1 70.1% of participants were identified to have focal or multi-focal epileptiform discharges compared to 27.3% with generalised EDs. One additional participant (2.3%) was identified during EEG1 to have EDs; however the type was unclear due to artifact. On EEG2, 72.5% of participants were identified to have focal EDs and 27.5% with generalised EDs.

Neuroimaging follow-up:

Neuroimaging was recommended for 39 (26.1%) participants after EEG1 and 22 (14.7%) participants after EEG2.

Discussion:

We demonstrate the reproducible quality provided by the SBS2 device on repeat EEG testing in a new epilepsy cohort in the Republic of Guinea. The clinical utility of repeat EEG testing using standard EEG technology is known [11–12], however for mobile technologies and digital health, particularly in low-income settings, this has yet to be established.

EEGs recorded at the onset of a disease process prior to treatment are valuable at the first presentation to help establish the diagnosis. They are also useful in the re-evaluation of patients with long-standing epilepsy for comparative purposes. Repeat EEGs need to be interpreted in the correct clinical context with a thorough clinical assessment, review of medical records, and in conjunction with the previous EEG study. The isolated findings of a new EEG taken out of context may be misleading; for example, it may be normal in a treated patient with generalized epilepsy or may show modified frontal epileptiform fragments [12, 13]. However, a recent EEG may identify subclinical or subtle clinical events in a patient thought to have controlled seizures. Repeat standard EEG testing is therefore indicated in several scenarios, most commonly the following situations: when a patient is seizure-free and treatment reduction may be considered; when seizures are not adequately controlled; when alteration in AEDs is required (for example in relation to pregnancy); or when there has been a recent convulsion after a long seizure-free period [12]. We employ a pragmatic, real-world scenario in which to test this hypothesis where skilled personnel are not the data collectors.

EEG quality:

Despite the challenges of carrying out an EEG in the humid, crowded, environment in Guinea, we demonstrate that the quality across both SBS2 EEGs were comparable and -although not perfect - were of medium to high quality on our rating scale. Myogenic artefact and sweat artefact - presenting on the EEG as either high frequency activity (>20Hz) or low frequency activity (<1Hz) respectively - likely secondary to the hot, humid, environment in Guinea were instigators for the need to repeat the EEG. The majority of participants without a useable EEG were children. Myogenic artefact is a particular issue in this group [13]. The lack of video alongside the EEG is a limitation of the SBS2 and its interpretation. This would help to distinguish certain artefacts as well as aid in semiological assessment when relevant.

Diagnostic findings:

A significantly lower proportion of EDs was detected on EEG2 compared to EEG1 overall however the proportion of focal EDs compared to generalised EDs was comparable. Notably the majority of participants were initiated on AEDs in the interval between EEG1 and EEG2. AED availability is problematic and sporadic in Guinea and participants had intermittent access to these. Thus, the impact AED treatment had on subsequent EEG testing

is difficult to assess. It is known that treatment with some AEDs may decrease the frequency of EDs on the EEG [14,15] and also that over the disease course, EDs seen on the EEG can be modified [1]. These are two potential confounding factors affecting our results. However, it would be unethical not to treat the participants with antiepileptic drugs and this was considered a necessary limitation of our study design. In addition, half the number of patients obtained Stage 2 NREM sleep in EEG2 compared to EEG1 and it is well described that sleep activates EDs [16]. Lastly, the mean duration of recording of EEG1 compared to EEG2 was approximately 50% greater, potentially increasing the likelihood of ED detection in EEG1. This was done for pragmatic purposes to reflect the real-world context in which Guinean health care workers practice. Each of these factors could influence our results. Thus a second EEG provided marginal added value. The first EEG was likely long enough in duration and was sufficient to support epilepsy classification and diagnosis for most PWE. We recommend that one SBS2 EEG of at least 50 minutes in duration is adequate to support diagnosis in the majority of cases. This recommended duration has been made to account for technical challenges (i.e. potential malfunctioning channels) and the high rate of myogenic and sweat artefacts encountered in the Guinean setting.

Clinical follow-up:

Our study reveals the unmet need for neuroimaging among Guinean PWE. The need for neuroimaging can sometimes be identified from the clinical history but clear focal changes on EEG in the absence of a clear focal seizure or focal seizure onset history can also prompt neuroimaging. Neuroimaging was suggested in cases where focal EDs were identified. Despite neuroimaging recommendations following EEG1, participants did not obtain imaging prior to EEG2, generally because they could not afford it. In some cases, this inter-EEG interval was as long as ten months.

Our study inadvertently highlights the need for improved access to MRI brain scanners in this region and we raise the question as to whether portable, compact, low-cost MRI scanners could be utilized effectively in tandem with portable EEG. Imaging procedures are presently referred to neighboring countries. There is one 0.3 Tesla MRI brain scanner in Guinea which costs about 200 USD per scan. This cost approximates one-quarter of the average gross national income per capita per year for a Guinean citizen (860 USD, 2018) [17].

Promise of Portable EEG:

The SBS2 software allows acquisition of real-time EEG data on standard Android mobile smartphones and tablets with a good spatial resolution and frame rates in excess of 40 frames per second[7]. The high specificity and reduced sensitivity of this system was demonstrated by our group previously. The specificity for EDs is comparable to that of Xltek® standard EEG technology [6,7]. Handheld devices hold promise because they enable low-cost capture, processing, and transmission of EEG data in regions where a standard EEG machine would be financially inaccessible. Together with the development of mobile-compatible electrode caps, a unique opportunity to establish a complete EEG system which is portable, affordable and user-friendly is emerging. There are multiple such systems but

none that depend on smartphones: others have recently shown that commercially available, wearable EEG devices can be used for diagnostic purposes and have preserved quality [18].

It was evident from our review of these participants' remote EEGs, that many have florid EDs, with numerous seizures captured even on a brief EEG recording, as well as some participants with epileptic encephalopathies which are currently poorly treated or untreated. EEG diagnostics, together with accurate semiological history taking, aids the clinician in determining epilepsy classification. Moreover, the classification of epilepsy as focal or generalized has an impact on treatments prescribed and subsequent seizure control for the patient [19].

We emphasize here the pressing need for access to these diagnostics in this population. In Sub-Saharan Africa there is currently estimated to be one neurologist for every 500,000 people and some countries still do not have a single practicing neurologist [20]. We have demonstrated the reproducible quality and utility of the SBS2 tablet-based EEG in this setting as one possible option.

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Data Availability Statement:

Data will be provided upon reasonable request by qualified investigators, subject to ethics board approvals.

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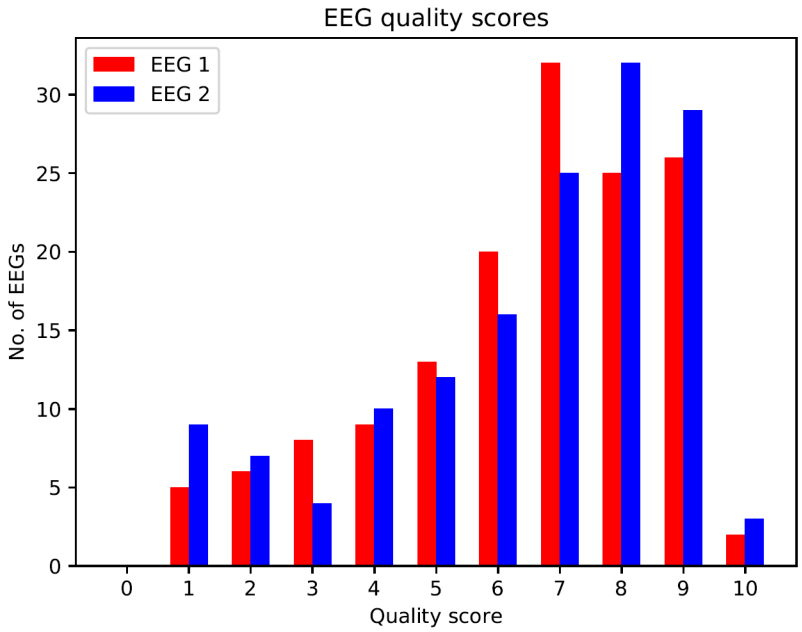

Figure 1: Histogram of EEG1 and EEG2 quality scores

Quality scores are rounded down to the nearest integer bin; for example, 4.5 is binned as 4.

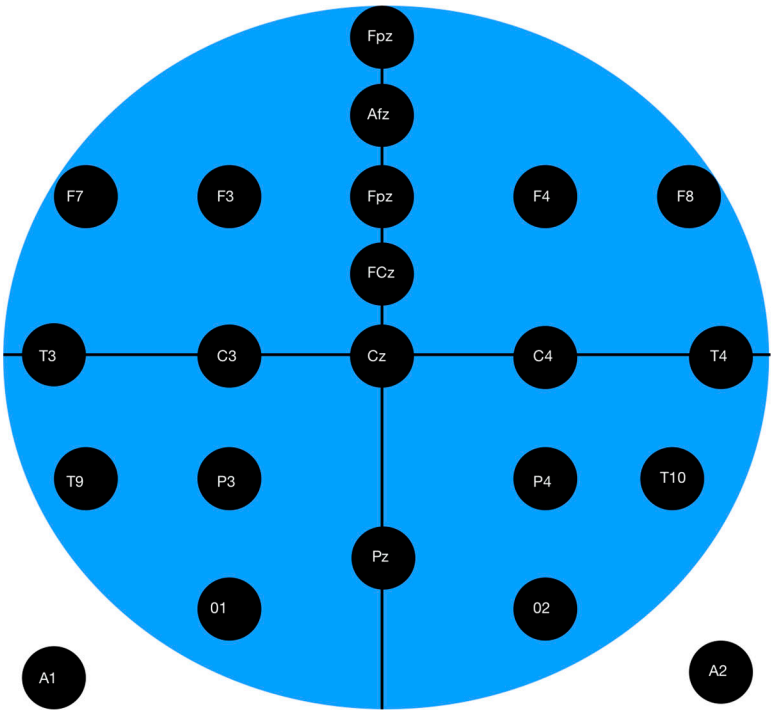

Figure 2:
SBS2 schematic demonstrating electrode positions, including the ground (# - AFz) and reference electrodes (* Cz).

Table 1:

Clinical Characteristics of Participants (n=149 participants)

	n (%)	
Seizure characteristics		
Loss of consciousness	123 (83)	
Fall with convulsions	116 (78)	
Fall without convulsions	5 (3)	
Starring spells	76 (51)	
No seizures in previous month	51 (34)	
Experienced seizure lasting >5 min.[a]	65 (44)	
Ever used an AED	130 (87)	
Regularly using AED	87 (58)	
AEDs used	Currently	Previously
Phenobarbital	28 (19)	22 (15)
Carbamazepine	38 (26)	25 (17)
Sodium Valproate	30 (20)	17 (11)
Levetiracetam	14 (9)	13 (9)
Clonazepam	1 (0.6)	2 (1)
Clobazam	1 (0.6)	0
Diazepam	1 (0.6)	0
Other[b]	7 (5)	3 (2)
Prior diagnostic tests		
CT	57 (38)	
MRI	5 (3)	
Injuries		
Burn	14 (9)	
Fracture	14 (9)	
Head trauma	21 (14)	
Road accident	1 (0.6)	
Other[c]	76 (51)	
Medical History		
Closed head injury	20 (13)	
Stroke	8 (5)	
Cerebral Infection	8 (5)	
Alcohol use	5 (3)	

[a] 57 participants were not administered this question because they were not accompanied by an adult witness.

[b] 7 participants had taken an AED of unknown name and dose. 1 took lamotrigine. 2 took gabapentin.

[c] Includes 72 participants who reported cutaneous wounds due to seizures.

Table 2:

Comparison of the Presence of Epileptiform Abnormalities between Two Separate EEGs (n=95 participants)

		EEG 2		Cohen's Kappa	
		No epileptiform abnormalities	**Epileptiform abnormalities**	**Cohen's Kappa**	**95% CI**
EEG 1	**No epileptiform abnormalities**	53	7	0.250	[0.058, 0.442]
	Epileptiform abnormalities	23	12		