

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

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

Methods: 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 EEG twice (EEG1 and EEG2), separated by a variable time interval. Recordings were scored remotely by experts in clinical neurophysiology as to data quality and clinical utility.

Results: There were 149 participants (41% female; median age 17.9 years; 66.6% ≤21 years of age; mean seizures per month $5.7 \pm \text{SD } 15.5$). The mean duration of EEG1 was 53 ± 12.3 min and that of EEG2 was 29.6 ± 12.8 min. The mean quality scores of EEG1 and EEG2 were 6.4 [range, 1 (low) to 10 (high); both medians 7.0]. A total of 44 (29.5%) participants had epileptiform discharges (EDs) at EEG1 and 25 (16.8%) had EDs at EEG2. EDs were focal/multifocal (rather than generalized) in 70.1% of EEG1 and 72.5% of EEG2 interpretations. A total of 39 (26.2%) were recommended for neuroimaging after EEG1 and 22 (14.8%) after EEG2. Of participants without EDs at EEG1 ($n = 53$, 55.8%), seven (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: Tablet-based EEG had a reproducible quality level on repeat testing and was 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.

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Introduction

Smart technology including telemedicine has the 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 mobile-compatible electrode caps. Compared with 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 Smartphone Brain Scanner-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 article extends previous work to focus on the quality of the EEG in this setting by comparing sequential EEG. The clinical utility of a repeat second EEG is understood with standard EEG [8]; however, the utility is not currently well described for mobile technologies and digital health. We also aimed to study the impact of improved temporal lobe coverage by amendment to the EEG electrode placement compared with previous reports.

Methods

Ethical approval

This study was approved by the Ignace Deen Hospital’s Ethics Review Committee and the Partners Healthcare Inc. (Somerville, MA, USA) 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 (29 August 2018 to 1 June 2019). PWE or those who had a suspected seizure disorder of any age were eligible for enrolment and were recruited based on referral by a physician or healthcare 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 before enrolment by study physicians from the Ignace Deen Hospital and Massachusetts General Hospital and research coordinators who performed structured clinical interview assessments. Subjects 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 Easy-Cap™ (Herrsching, Germany) EEG caps were available (range 40–56 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 (Fig. 1). The reference electrode and ground electrodes were FCz and AFz, respectively. At the beginning of each EEG recording, the electrode impedance was below 5 kΩ.

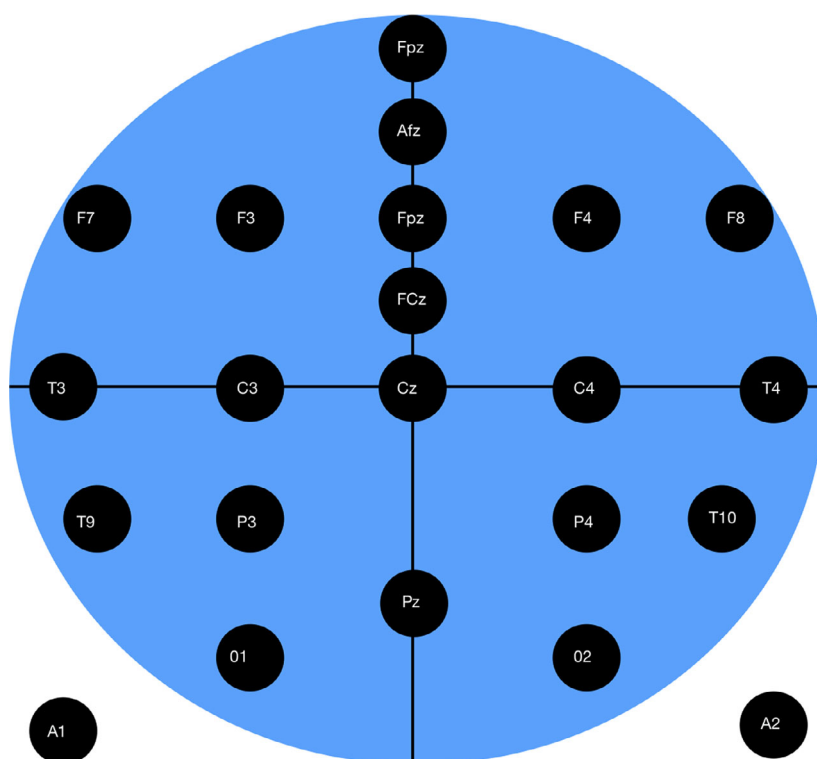


Figure 1 Smartphone Brain Scanner-2 schematic demonstrating electrode positions, including the ground (AFz) and reference (Cz) electrodes. [Colour figure can be viewed at wileyonlinelibrary.com]

Data acquisition

Each participant was assessed using a specific epilepsy-focused questionnaire and underwent SBS2 EEG (EEG1) at baseline and repeat SBS2 EEG (EEG2) later. All EEG1 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 recalled every 2 weeks between November 2018 and June 2019. Time between EEG1 and EEG2 thus ranged from 2 to 10 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 h. The EEG2 recordings were planned to last between 20 and 30 min. Recordings were completed during the daytime in a dedicated study room at the Ignace Deen Hospital.

Study staff, including house-staff neurology residents, medical students, research coordinators and nurses from both Guinea and the USA, performed SBS2 EEG recordings. Study staff underwent a 1-h training session before administration of the SBS2 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. EEG can be assigned to multiple readers independently or to the same reader more than once to support inter-rater variability studies.

Electroencephalography interpretation

Pediatric and adult neurologists and clinical neurophysiologists from the USA, UK and Canada interpreted the SBS2 data. Readers were blind to clinical details with the exception of age and, when applicable, names of antiepileptic drugs (AEDs). Readers interpreting EEG2 were blind to the results of EEG1 and

vice versa. Readers were randomly assigned EEG to interpret via the crowdEEG online reading platform. Readers were instructed to categorize the EEG 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 1 (worst quality, uninterpretable) to 10 (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-rapid eye movement sleep 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 bipolar, transverse bipolar, ear reference and Pz reference. Filter options included low pass (70, 30, 15 Hz, off), high pass (10, 3, 1, 0.5 Hz, off) and a notch (60, 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 <5 min were excluded. This 5-min minimum duration was chosen due to 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 Cohen's κ test and 95% confidence intervals of the point estimates using the Python 2.7.14 program (Python Software Foundation, Wilmington, DE, USA). 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 ≤ 5 min and one (0.6%) additional patient was excluded as the inter-EEG interval was <2 days (due to a calendar scheduling error). A total of 149 remaining participants with two SBS2 EEG 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 of age at time of enrolment.

All participants in the final analyses completed two SBS2 EEG between 2018 and 2019. A total of 101 (67.8%) participants with two EEG were currently being treated with at least one AED (Table 1).

Tablet-based electroencephalography

The mean duration of EEG1 was 53 ± 12.3 min and the mean duration of EEG2 was 29.6 ± 12.8 min.

Electroencephalography quality

The mean quality score of EEG1 was 6.4 (median 7.0) and the mean quality score of EEG2 was 6.4 (median 7.0) (Fig. 2).

Of the total EEG performed, 106 (35.6%) were recommended for repeat testing. A total of 25 (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 (mean score 6.4).

A total of 25 (8.3%) participants had no useable EEG after two repeat tests due to excessive muscle artifact, excessive sweat artifact and/or malfunctioning EEG channels. A total of 18 (72%) participants without a useable EEG were ≤ 21 years of age, including four (16%) participants ≤ 1 year old. A total of 71 (47.6%) of the EEG1 recordings and 86 (57.7%) of the EEG2 recordings had at least one EEG channel malfunction or artifact during part of the test. A total of 30 (20.1%) participants achieved Stage 2 non-rapid eye movement sleep during EEG1 and 15 (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%)

Table 1 Clinical characteristics of participants (*n* = 149)

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%)
Previous diagnostic tests		
CT Head	57 (38%)	
MRI brain	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%)	

CT, computed tomography; MRI, magnetic resonance imaging. Data are given as *n* (%). ^aA total of 57 participants were not asked this question because they were not accompanied by an adult witness. ^bSeven participants had taken an antiepileptic drug (AED) of unknown name and dose. One participant took lamotrigine. Two participants took gabapentin. ^cIncludes 72 participants who reported cutaneous wounds due to seizures.

did not have EDs at EEG2 ($\kappa = 0.250$; 95% confidence intervals, 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 as having focal or multifocal EDs compared with 27.3% with generalized EDs. One additional participant (2.3%) was identified during EEG1 as having EDs; however, the type was unclear due to artifact. On EEG2, 72.5% of participants were identified as having focal EDs and 27.5% as having generalized 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.

The EEG recorded at the onset of a disease process before treatment is valuable at the first presentation to help establish the diagnosis. It is also useful in the re-evaluation of patients with long-standing epilepsy for comparative purposes. Repeat EEG needs to be interpreted in the correct clinical context with a thorough clinical assessment and 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, e.g. 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 (e.g. 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.

Electroencephalography quality

Despite the challenges of carrying out EEG in the humid, crowded environment in Guinea, we demonstrate that the quality across both SBS2 EEG1 and EEG2 was similar and, although not perfect, was of medium to high quality on our rating scale. Myogenic artifact and sweat artifact [presenting on the EEG as either high-frequency activity (>20 Hz) or low-frequency activity (<1 Hz), respectively], probably secondary to the hot, humid environment in Guinea, were instigators for the need to repeat the EEG. The majority of participants without useable EEG were children. Myogenic artifact 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 artifacts as well as aid in semiological assessment when relevant.

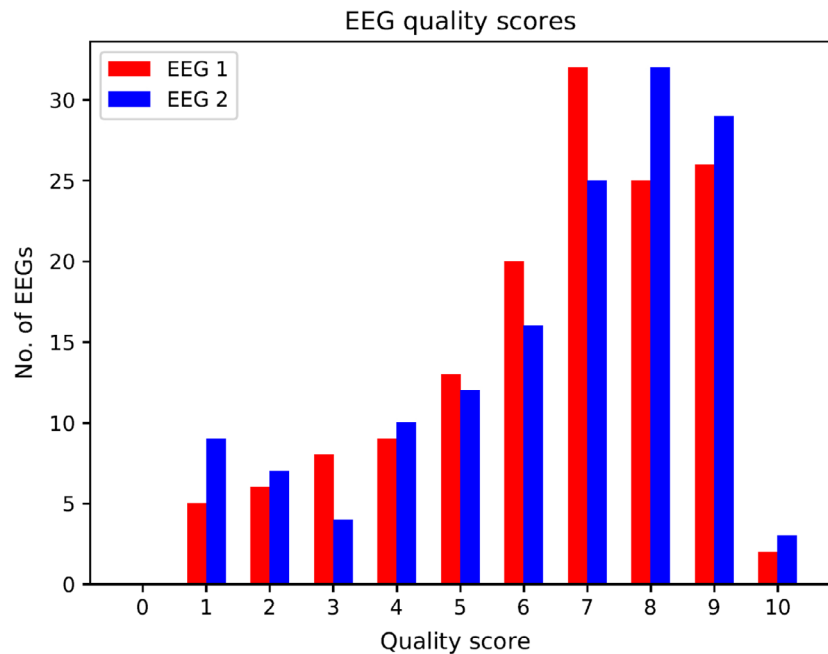


Figure 2 Histogram of electroencephalography (EEG1 and EEG2) quality scores. Quality scores are rounded down to the nearest integer bin, e.g. 4.5 is binned as 4. [Colour figure can be viewed at wileyonlinelibrary.com]

Table 2 Comparison of the presence of epileptiform abnormalities between two separate electroencephalography (EEG) recordings ($n = 95$ participants)

	EEG2		Cohen's κ	95% CI
	No epileptiform abnormalities	Epileptiform abnormalities		
EEG1				
No epileptiform abnormalities	53	7	0.250	0.058–0.442
Epileptiform abnormalities	23	12		

CI, confidence intervals.

Diagnostic findings

A significantly lower proportion of EDs was detected on EEG2 compared with EEG1 overall; however, the proportion of focal EDs compared with generalized EDs was similar. It is notable that 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 them. Thus, the impact that 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 AEDs and this was considered a necessary limitation of our study design. In addition, half of the patients attained Stage 2 non-rapid eye movement sleep in EEG2 compared with EEG1 and it is well described that sleep activates EDs [16]. Lastly, the mean duration of recording of EEG1 compared with 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 healthcare workers practice. Each of these factors could influence our results. Thus, a second EEG provided marginal added value. The first EEG was probably of long enough duration and was sufficient to support epilepsy classification and diagnosis for most PWE. We recommend that one SBS2 EEG of at least 50 min 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 artifacts 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 before EEG2, generally because they could not afford it. In some cases, this inter-EEG interval was as long as 10 months.

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

Promise of portable electroencephalography

The SBS2 software allows acquisition of real-time EEG data on standard Android smartphones and tablets with a good spatial resolution and frame rates in excess of 40 frames/s [7]. The high specificity and reduced sensitivity of this system were demonstrated by our group previously. The specificity for EDs is similar to that of Xltek® (Natus Medical Inc., Pleasanton, CA, USA) 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 that 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 EEG that many have florid EDs, with numerous seizures captured on even a brief EEG recording, as well as some participants with epileptic encephalopathies that 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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Disclosure of conflicts of interest

F. Mateen and T. Lehn-Schioler hold shares in the company BrainCapture. All other authors declare no financial or other conflicts of interest.

Data availability statement

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

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