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BrainKilter: A Real-Time EEG Analysis Platform for Neurofeedback Design and Training

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ABSTRACT Neurofeedback targets self-regularized brain activity to normalized brain function based on brain-computer interface (BCI) technology. Although BCI software or platforms have continued to mature in other fields, little effort has been expended on neurofeedback applications. Hence, we present BrainKilter, a real-time electroencephalogram (EEG) analysis platform based on a ''4-tier layered model''. The purposes of BrainKilter are to improve portability and accessibility, allowing different users to choose various options to perform EEG processing, target stimulation-induction through a pipeline, and analyze data online, essentially, to design a protocol paradigm and applicable BCI technology for neurofeedback experiments. The data processing effectiveness and application value of BrainKilter were tested using multiple-parameter neurofeedback training, in which BrainKilter regulated the amplitude of mismatch negative (MMN) signals for healthy individuals. The proposed platform consists of a set of software modules for online protocol design and signal decoding that can be conveniently and efficiently integrated for neurofeedback design and training. The BrainKilter platform provides a truly easy-to-use environment for customizing the experimental paradigm and for optimizing the parameters of neurofeedback experiments for research and clinical neurofeedback applications using BCI technology.

INDEX TERMS BrainKilter, BCI, MMN, neurofeedback, platform, real-time.

I. INTRODUCTION

Bain-computer interfaces (BCI) based on electroencephalogram (EEG) signals seek to transform the user's brain activities into computer commands [1]. The basic neurofeedback procedures have been established for quite a long time, in fact, they and most likely represent even the earliest BCI applications, which targeted the self-normalizing brain function [2]. Although BCIs in other fields have continued to mature and BCI software has expanded and gained strong support, methodological and technical progress with neurofeedback seems to be lagging [3]. From their inception, neurofeedback procedures piqued researchers' interests, who focused on its application for clinical treatment and cognitive modulation. In contrast to general BCI software, neurofeedback software requires a more deliberate experimental design scheme and more precise time control to achieve an effective training outcome [4]. Therefore, an advanced neurofeedback platform will promote neural mechanism for research and clinical applications.

BCI research has been ongoing for nearly 50 years, and the number of BCI software platforms has increased significantly over the past few years [5], [6]. Functional blocks, such as data acquisition, feature extraction, classification, and feedback presentation modules, are some of the major demands BCI researchers place on the software platform. As the complexity of EEG signal analysis has increased, applications for data visualization and processing have been developed. One major problem in BCI neurofeedback software is that all the data processing steps are subjected to a real-time constraint. In addition, BCI applications require portable EEG devices that are suitable for public use and have advantages

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such as low cost and elevated user comfort [7]. The EEG data stream might be transmitted wirelessly (e.g., through Bluetooth communication) to enable for long-term monitoring of daily activities [8]. Moreover, given the variety of neurofeedback protocols that can be administered, being able to autonomously set feedback signal parameters and allow flexible feature selection are required features [9]. However, most commercial neurofeedback training software cannot provide such functions. Therefore, the need for an accessible and portable neurofeedback platform suitable for multiple data processing and experimental design tools, especially for stimulation and feedback paradigms, is gradually gaining importance in neurofeedback training, and the demand for user-friendly systems usable even by nonprogrammers is growing. Neurofeedback systems should help users experiment while progressively controlling the regulatory task and it should provide different sensory modalities corresponding to the user's perception capabilities. Our goal is to assist a variety of users complete neurofeedback tasks based on EEG features, with a particular focus easy and rapid ERP analysis, so that they can flexibly design individual neurofeedback training protocols and to test experimental parameters independently.

In this paper, we first briefly review related works concerning the development of neurofeedback software from the view of the available BCI platforms and commercial software. Next, we introduce the ''4-tier layered model'' architecture of BrainKilter and focus on the Library layer to introduce the neurofeedback experimental design and EEG data processing capabilities. Then, to verify the functionality and usability of our platform, the optimal parameters of MMN as a neurofeedback training protocol were selected based on BrainKilter and performed successfully in healthy individuals. Finally, we discuss our experimental results and summarize the platform features and future development directions.

The main contributions of this paper are summarized as follows:

I. BrainKilter, a real-time EEG analysis platform, that focuses on neurofeedback design and training is proposed. BrainKilter is an easy-to-use tool for designing neurofeedback experiments and training for clinical applications and laboratory research.

II. Parameters of the MMN neurofeedback protocol were optimized based on BrainKilter were successfully used to improve the auditory discrimination ability of healthy subjects by regulating the MMN amplitude based on the optimized scheme.

II. RELATED WORK

Although BCI platforms and frameworks that offer a great number of functions have been available for many years and each has unique features and benefits, they fail to be ideal for neurofeedback applications in various ways. BCILAB, an open-source MATLAB-based toolbox that provides a wide variety of data processing methods, is less focused on clinical or commercial development [10]. BCI2000, a general-purpose software platform for BCI research, supports different data acquisition systems including all major digital EEG amplifiers but provides no valid Bluetooth communication protocol for connecting wearable devices [11]. OpenViBE, a free and open-source platform with a powerful data processing function, has some flaws in its stimulation and feedback paradigms [12]. Pyff is a framework for rapidly developing experimental paradigms, but its outputs are small and lack modification ability from feedback and stimulus application viewpoints [13]. BF++ provides specific protocols such as P300, SSVEP and SMR BCIs [14], but does not provide other important event-related potential (ERP) components, such as mismatch negative (MMN), which is an EEG marker in neurodegenerative disease.

Compared to the BCI platform, commercial neurofeedback software provides a friendlier user experience (https://en.wikipedia.org/w/index.php?title=Comparison_of_neurofeedback_software&oldid=928048377); for example, BioEra can be applied via mobile phones and provides tools to create various types of processing tasks for neurofeedback training. BetterFly helps clinicians control treatment session parameters at a clinic or at the patient's home. BioExplorer allows visualization signal processing and even collects a variety of physiological signals for neurofeedback training in BioTrance [15]. BioGraph Infiniti provides interesting games for neurofeedback, but the collection of EEG data for multiple channels (greater than 8 electrodes) is limited. And most software such as BrainFeedback Pro, BrainMaster, BrainPaint, BWView, Dual Drive Pro, MindReflector, NeuroOptimal, SmartMind, Myndlift, Vilistus, etc. only support a few EEG collection devices or they are limited to devices of the same brand, and for other stimulation device access is restricted. Theses portable and easy-to-use software implementations are capable of meeting the needs of conventional neurofeedback training, such as regulating the EEG frequency band. However, flexible experimental design not limited to the feedback form and real-time ERP processing are not fully available.

Here, we combine the flexibility of the data processing capabilities of the BCI platform with the friendliness of commercial software to develop a new platform suitable for neurofeedback training. The proposed platform improves the flexibility of data processing and facilitates the inclusion of new algorithms through its architectural design and pipelined data processing methods. Simultaneously, by adding multi-element design tools that facilitate designing experimental solutions, it also provides a variety of device communication layers to collect signals and supports a variety of stimulations to meet different neurofeedback training requirements.

III. BrainKilter

BrainKilter is an integrated software program based on BCI technology with a ''4-tier layered model'' that offers experimental design and real-time EEG or ERP data analysis. It provides a set of convenient online debugging tools and meets the demand for routine neurofeedback training.

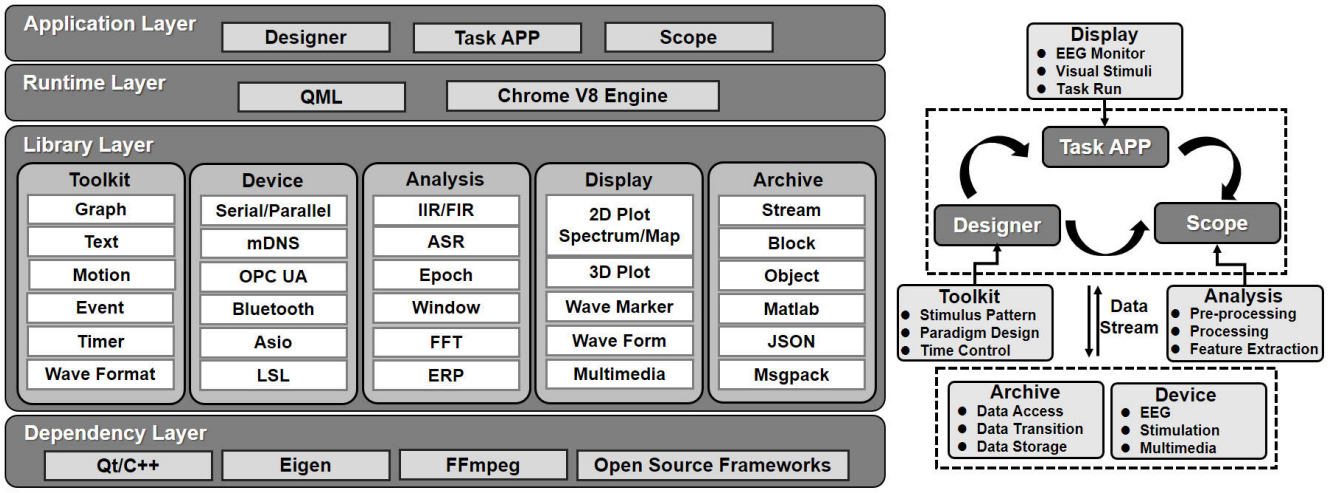

FIGURE 1. The "4-tier layered mode" architecture (a) and function (b) of BrainKilter. (a): QML: Qt Markup Language; mDNS: multicast DNS; OPC UA: OPC Unified Architecture; LSL: Lab Streaming Layer; IIR: Infinite Impulse Response; FIR: Finite Impulse Response; ASR: Artifact Subspace Reconstruction; FFT: Fast Fourier Transform; ERP: Event-Related Potential; JSON: JavaScript Object Notation.

Fig. 1 (a) shows the BrainKilter architecture, and the main BrainKilter interfaces are shown in Fig. 2.

A. APPLICATION LAYER

The application layer contains three modules: Designer, Task APP, and Scope. The neurofeedback protocol design is implemented in Designer, which including training feature selection, feedback modality confirmation and training time setting up. The characteristics of different EEG frequency bands and ERP signal can be chosen as target adjustment feature. The modality of feedback signal is usually set as visual, auditory, tactile or combined modalities. Training time is subdivided into single training session time, interval time and baseline time. The user can control any experimental debugging parameters in Designer. Scope module addresses data preprocessing, data processing, and online or offline feature extraction. Task APP focuses on the operation of the neurofeedback training protocol, where it provides the ability to modify the experimental paradigm parameters and supports a single or double-blind control setup by choosing the feedback signal style, such as one's own neural activity signal or fake signal. It also provides the necessary EEG signal data processing and monitoring features, which are especially suitable for tracking a user's neural states during neurofeedback training and can visualize neural signal features and feedback signals for the user. Baseline and standardized signals can be updated with the neural or cognitive state of the subject each session. Moreover, the neural activity and reward rate of the entire neurofeedback training session are saved, allowing the neurofeedback effect to be evaluated and subsequently, the task difficulty and training time to be modified (Fig.1 (b)).

B. RUNTIME LAYER

All of the functions of BrainKilter run on the Qt Markup Language (QML) engine. Benefiting from the just in time (JIT) acceleration of the Chrome V8 engine, the user can develop new functions using more accessible programming languages, and the owner can compile the code to improve the execution speed.

C. LIBRARY LAYER

Five modules (Toolkit, Device, Analysis, Display, and Archive) are included that offer functionality for experimental design, data reception, data processing, visualization, and data storage, respectively. The Analysis, Toolkit, and Display modules support the Scope, Designer, and Task APP functions, respectively. The Device and Archive modules serve as data stream inputs and outputs, respectively.

1) TOOLKIT

Toolkit focuses on providing a set of drag-and-drop development environments for experimental design. Users can freely create basic graphs, perform text editing, and attach properties such as position, color, zoom, and rotation through the Motion module. To support the entire experimental process design and complete user interactions with the system through mouse and keyboard operations, Toolkit provides an autonomous script editing function, which can consist of experimental logic revision through JavaScript, MATLAB or Python in the Event subsystem. A high-precision timer control function ensures that the time precision is accurate to 1 ms. The waveform designer is primarily responsible for the audible and tactile waveform design.

2) DEVICE

The Device module is used for external device search, matching data protocols, and data signal conversion. The module has been configured with different types of communication protocols, such as multicast Domain Name System (mDNS), Open Platform Communication Unified

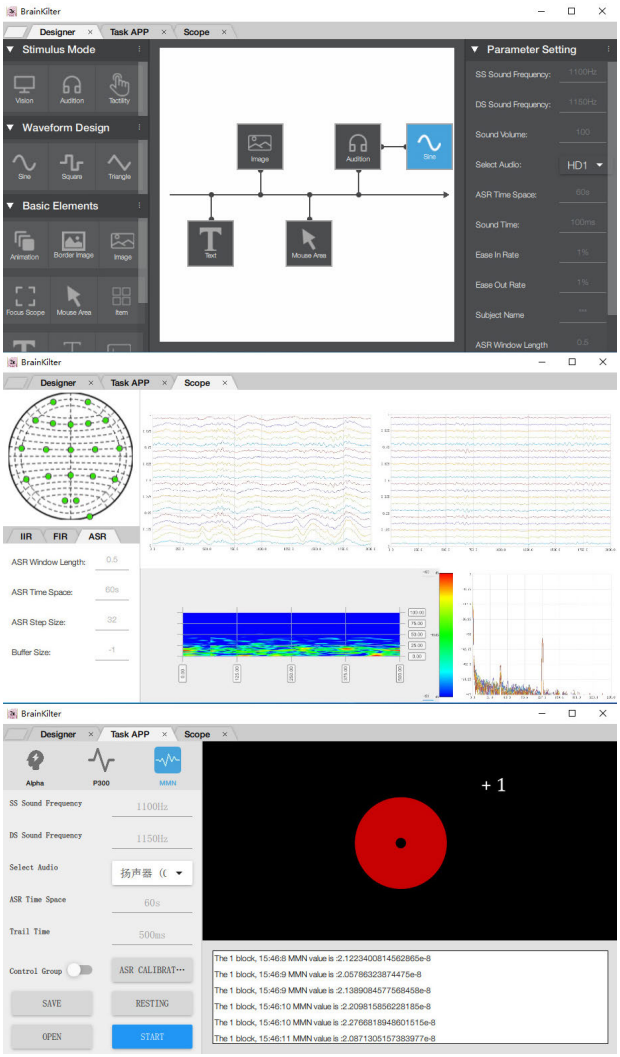

FIGURE 2. The main BrainKilter interfaces (Designer, Scope, and Task APP).

Architecture (OPCUA), Asio, Bluetooth, and Lab Streaming Layer (LSL). The module can maintain stable and reliable connections to different device types, including stimulation devices, multimedia, EEG acquisition, eye tracking, and other sensors, to collect behavioral reactions, neural activity and provide signals for different stimuli.

3) ANALYSIS

The Analysis module performs EEG data analyses with matrix operations based on the Eigen library [16]. The target data processing is completed by a combination of loosely coupled components. Based on the discrete Fourier principle for impedance detection, the high-frequency noise signals can be removed from the EEG data by finite impulse response (FIR) and infinite impulse response (IIR) filters. The IIR filter can be applied to a choice of high pass, low pass, or notch filtering steps, which are commonly utilized to remove muscle and drift artifacts. The FIR filter provides substantial control over filter shaping and linear phase performance (waveform retention over the passband) [17].

The Artifact Subspace Reconstruction (ASR) was designed to detect and remove high-amplitude data components (for example, artifacts stemming from eye blinks, muscle movements, and sensor motion) relative to the artifact-free reference data while recovering the EEG background activity that lies in the subspace spanned by the artifact components [18]. ASR relies on principal components analysis (PCA) and uses a sliding-window, which statistically interpolates the high-variance signal components that exceed a threshold relative to the covariance of the calibration dataset. Each affected EEG time point is then linearly reconstructed from the retained signal subspace based on the correlation structure observed in the calibration data, as shown in Equation (1):

$$S_{clean} = V \times V^T M \times ((V^T M)_{truncated})^{\dagger} \times V^T \times S, \quad (1)$$

where S is the input signal and S_{clean} is the processed signal, V is the eigenvector of the calibration data covariance matrix, and M is the square root of the geometric median of the covariance matrices. This process includes the Moore–Penrose pseudoinverse, which is represented by the symbol "†".

The EEG signal features in the neurofeedback experiment by online short-time Fourier transform, such as the frequency spectrum and time-frequency energy, can be extracted effectively. Epoch data are EEG data segmented by time-locked events or manually configured by the user for real-time ERP processing.

4) DISPLAY

The Display module provides a rich set of visualization components, including 2D Plot for spectrum and topographic maps, and 3D Plot (mainly intended for time-frequency images), Wave Marker for ERP, and the display of sound or vibration frequency waveforms. Multimedia is used to play dynamic images, such as the videos required during neurofeedback experiments.

5) ARCHIVE

The Archive module supports various data structure forms from analyzer output, such as raw data stream, block data with labeled events or key-value data that form objects. It can record, store, and analyze data in BrainKilter. Moreover, it provides an efficient data recording format and can convert data for MATLAB, JavaScript Object Notation (JSON), and even for binary serialization format as Msgpack files.

D. DEPENDENCY LAYER

The dependency layer consists of Qt or C++, Eigen, FFmpeg, and five open-source data frameworks, including Matio, Liblsl, CPython, HDF5, and Zlib, which guarantee proper data calculation and procedural operations.

IV. PLATFORM VALIDATION

To validate and demonstrate the functionality of BrainKilter, an MMN neurofeedback protocol is optimized

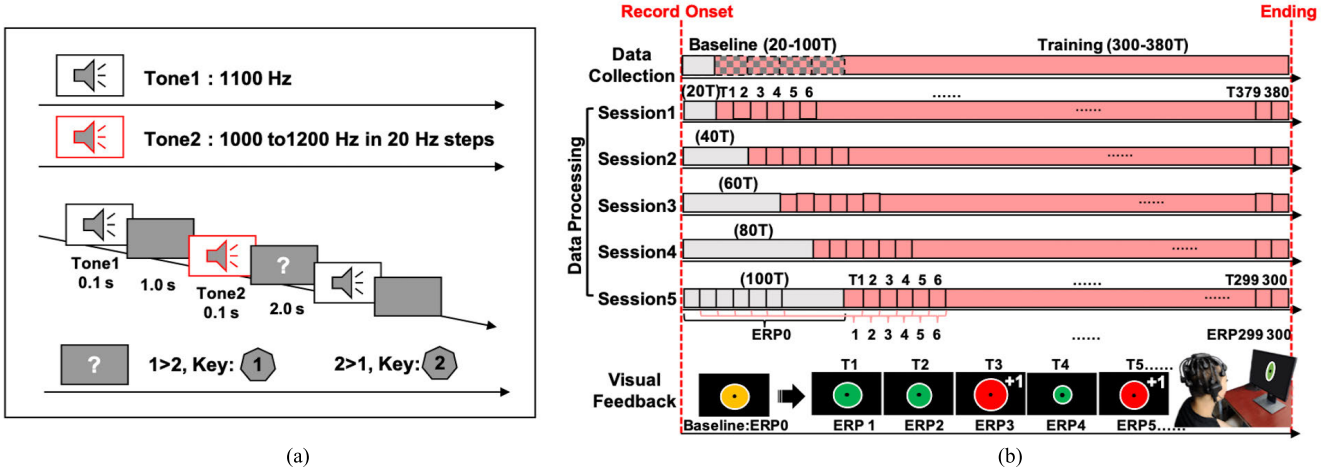

FIGURE 3. DLF test paradigm design (a) and MMN neurofeedback the training protocol design (b). (a): The subject was required to judge within 2.0 seconds whether the second frequency stimulus was more significant than the first frequency stimulus (key 1: Tone 1 > Tone 2, key 2: Tone 2 > Tone 1).

and conducted. MMN is an ERP component that reflects an automatic and pre-attentive form of sensory processing. An MMN wave is automatically generated when a sequence of ''standard'' repetitive stimuli (e.g., p = 0.90) is interrupted by infrequent (e.g., p = 0.10), deviant, ''oddball'' stimuli. MMN neurofeedback experiments have been shown to improve human auditory cortical plasticity and language ability [19]. Previous studies have shown that the use of MMN neurofeedback training can improve a subject's ability to discriminate between two defined frequencies; however, the auditory discriminative abilities of healthy people have not been discussed. MMN steady induction traditionally requires more than 200 stimulation events (containing both standard and deviant) [20]. In the previous neurofeedback protocol, 20 stimulation events were adopted to calculate real-time MMN. The number of events that optimally induce MMN has not been discussed [21]. Here, we discussed different MMN calculation parameters in neurofeedback pretraining and chose the optimal MMN calculation parameters for normal neurofeedback training according to the ERP online data results. The best parameters were the ''personal MMN neurofeedback protocol'' for a 5-day short-term neurofeedback training and before and after a difference limen of frequency (DLF) test, which assessed the effectiveness of the protocol and validated the usability of our platform.

A. SUBJECTS

Twenty-seven healthy volunteers participated in our neurofeedback study. Fifteen (ten males, five females, ages 23.20 ± 1.60 years) were used to optimize the parameters of the neurofeedback protocol. The other twelve subjects were divided into a neurofeedback (NF) group (four males, two females, age 24.00 ± 0.57 years) and a Sham-NF group (four males, two females, age 24.00 ± 1.53 years)) to verify the effectiveness of the protocol. All the subjects were right-handed, with normal hearing ability. None of the volunteers suffered from neurological or psychological disorders or had used medication that could have adversely affected the measurement. All the participants were naive to neurofeedback training procedures and had never participated in previous neurofeedback or auditory training studies. The participants provided written informed consent, and the study was approved by the Medical Research Ethics Committee and Institutional Review Board of XuanWu Hospital.

B. DIFFERENCE LIMEN OF FREQUENCY TEST

The standard procedure for estimating DLF traditionally tested uses a frequency increment detection paradigm in which listeners are instructed to distinguish between a reference tone and a series of comparison tones of higher frequency [22]. In the current paradigm, 1100 Hz was employed as the standard tone, with one set of comparison stimuli that varied from 1000 to 1200 Hz in 20 Hz steps. The detailed experimental paradigm is shown in Fig. 3 (a). Each subject was seated in a shielded room where they listened to the stimuli, which was transmitted by a GSI-61 audiometer and presented binaurally through headphones (TDH 50) at 65-70 dB HL. The signal presentation and subject response were under software control (E-Prime, Psychology Software Tools Inc., Pittsburgh, PA). Each subject received ten sets of trials to familiarize themselves with the sound stimulation procedure before the test. The real test lasted approximately 30 minutes. Participants who participated in the optimization of the parameter performed only the pretraining tests. For those involved in the neurofeedback protocol verification, both the pre- and post-training tests were required.

C. NEUROFEEDBACK TRAINING PROTOCOL

Subjects were seated in an antistatic chair in front of a 23-inch computer screen. Stimuli were presented binaurally via earphones. A Quick-20 dry-wireless headset (Cognionics, San Diego, CA, USA) was used to acquire

the EEG signals [23]; this headset has been used in several previous applications for clinical basic research. Although dry EEG compared with traditional wet EEG is more sensitive to artifacts and noise [24], the ASR algorithm is accurate enough to remove activities from artifacts and eye-related components and sufficiently discriminative to retain signals from brain-related components [25], [26]. BrainKilter was employed to achieve the previously described neurofeedback training, including gathering real-time ERP responses and provide visual feedback stimulus, effectively guaranteeing a robust signal-to-noise ratio. A modification neurofeedback protocol by Chang *et al*. was used in this study [21]. For the auditory stimulus based on an oddball paradigm (standard stimulus: 80%), the standard stimulus is 1100 Hz, and two times the individual's auditory discriminant threshold is used as the deviant stimulus [27]. The individual's auditory discriminant threshold was obtained by the DLF test. The midline electrodes (Fz, Cz, and Pz) were used as training sites. The neurofeedback consisted of 5 sessions; each session contained a baseline period and a training period. To explore the optimal number of ERP events (buffer depths) to calculate the MMN, five types of buffer depths were set up in sessions 1 to 5 during the entire neurofeedback training: that is, the experiments used 20, 40, 60, 80, or 100 trials as baseline and buffer depths, and the sliding window included one trial to update MMN every 0.5 s. The specific parameters are shown in TABLE 1. Overall, 400 trials were conducted, including the baseline and training portion of each session. The experimental design is shown in Fig. 3 (b). Before training, we collected 20-100 EEG signal trials to calculate the baseline MMN.

TABLE 1. The parameters of each session of neurofeedback training.

Session No.	1	2	3	4	5
Buffer Depth (Trial)	20	40	60	80	100
Total (Trial)	400	400	400	400	400
Baseline (Trial)	20	40	60	80	100
Sliding Window (Trial)	1	1	1	1	1
Each Training (Trial)	20	40	60	80	100
Training Times	380	360	340	320	300

The ERP signals from the midline electrodes (Fz, Cz, and Pz) were filtered by an FIR filter of 0.5 Hz to 45 Hz and segmented into 500-ms clean time windows, including a 100 ms prestimulus time as the single-trial baseline for MMN. The MMN component typically peaks approximately 100 ms to 300 ms from the onset of a sudden change in stimulation. The MMN amplitude of the training period was monitored in real time, and we provided the normalization of the MMN as a visual feedback signal to the user in real time. The size of the disc (R_{disc}) (radius: min 14.75 mm to max 177 mm) was calculated according to the MMN amplitude, as shown in Equation (2),

$$R_{disc} = R_{min}(A_{RM}/A_{BM})\sigma \tag{2}$$

where R_{min} is the unit radius of each change of the disc. A_{RM} indicates the amplitude of the real-time MMN. A_{BM} is the amplitude of the baseline MMN, and σ is a parameter of the conversion factor between the pixel value of the disc on the screen and the actual size of the disc to be see. We set the value of σ to 29.5.

During the training period, the subjects attempted to increase the times that the red disc appeared using their own strategies. To ensure that the subjects focused on the visual stimuli, they were instructed to count the red discs during training.

The short-term neurofeedback training experiment was conducted according to the abovementioned protocol using an optimized parameter MMN neurofeedback protocol. However, the subjects in the Sham-NF group regulated the amplitude of MMN based on fake signals, which from the ERP activities of other subjects in the NF group. The training sessions occurred over 5 consecutive days, 10 sessions per day, with 400 trials (including baseline and training) per session and a 30-second rest break between the training and baseline sessions. Before each training session, the baseline and standardized MMN signal of the individual were updated. The average MMN amplitudes of the 1st, 5th, and 10th sessions of one day were used to evaluate the neurofeedback training performances.

D. DATA PROCESSING AND STATISTICAL ANALYSIS

The data processing of the auditory discrimination threshold was performed using the DLF test results based on E-prime. The measured discrimination threshold indicates the sensitivity of participants at perceiving differences between two auditory frequencies. A weighted cumulative Gaussian distribution function f(p) was fitted to the data using maximum-likelihood estimates as shown in Equation (3), where σ is a parameter that describes how steep the curve is and can also be considered as a qualitative measure of the 84% discrimination threshold and standard (1100 Hz). R^2 was used to assess whether each psychometric function could fit in a cumulative Gaussian distribution. The solid curve shows the measured data points using the curve-fitting method [28], [29]:

$$f(p) = 0.5\left[1 + \left(\frac{P - PStd.}{\sigma\sqrt{2}}\right)\right]. \tag{3}$$

The EEG data were processed online in both the MMN parameter optimization experiment and during formal neurofeedback training, and the results were evaluated by offline analysis. The EEG data from all midlines (Fz, Cz, and Pz) were processed online by BrainKilter; this included the raw EEG signal preprocessing, which was subjected to 0.5-45 Hz band-pass FIR filter, and an ASR filter to reject artifacts. Then, the purified EEG signals were processed online by ERP analysis. The EEG data were analyzed offline with EEGLAB, an open source MATLAB toolbox for electrophysiological signal processing [30]. During raw EEG signal preprocessing, the signals underwent 0.5 Hz high-pass and 45 Hz low-pass FIR filters. To reject artifacts, independent

component analysis (ICA) was applied to the EEG signals, and the components responsible for the eye movements and blinks were rejected. The time-frequency analysis, which is based on the wavelet transform, can synchronously provide variations of the EEG signals in both the time and frequency domains [31]. The statistical analyses were conducted using SPSS 19 (SPSS, Chicago, IL, USA). Data are expressed as the mean ± standard error. A pointwise paired t-test was conducted for standard and deviant ERP instances between 100 ms and 300 ms. The two-tailed significance level was set at $p < 0.05$. A one-way ANOVA was combined with post hoc comparisons, including the Bonferroni procedure, was performed to analyze the amplitudes and latencies of the MMN, the reward rates, and the motivation scores after neurofeedback training. Pearson correlations were established to analyze the relationships between the MMN waveforms. A paired t-test was executed for each electrode of each buffer depth to analyze the spectral power of different frequency bands between standard and deviant stimuli. The mean amplitudes of the MMN signals in the 1st to the 5th neurofeedback training days and the auditory frequency threshold of the DLF tests were analyzed by paired sample t-tests within groups and independent sample t-tests across groups. The significance level was set at $p < 0.05$, and the notable significance level was set at $p < 0.01$. The previously described methods of statistical analysis have been verified by other experimental studies [32].

V. RESULTS

A. NEUROFEEDBACK PROTOCOL OPTIMIZATION

1) AUDITORY DISCRIMINATION THRESHOLD

Given the differences in individual auditory discriminative abilities, we assessed each individual's auditory discrimination threshold before training, which helped to customize the neurofeedback protocol for each subject. The results of the auditory discrimination threshold of 15 subjects are shown in SUPPLEMENTAL TABLE 1, in which the mean accuracy is 0.866 ± 0.021, the false alarm rate is 0.005 ± 0.002, and the mean reaction time (ms) is 820.152 ± 45.688. In the neurofeedback training, 1100 Hz was used as the standard stimulus for all individuals, and the individual's double auditory frequency threshold was used as the deviant stimulus.

2) ERP ANALYSIS

We used ERP analysis to obtain a clear MMN response. The real-time MMN waveforms of five buffer depths at the midline electrodes (Fz, Cz, and Pz) of each training result of 15 subjects are shown in Fig. 4. Pointwise paired t-tests between responses to standards and deviants in a 100 ms to 300 ms time window ($p < 0.05$) of each epoch were conducted for the five sessions. From the results, a more pronounced MMN was shown during the neurofeedback training that adopted 20 trials, 60 trials, and 80 trials, respectively, at all three midline electrodes.

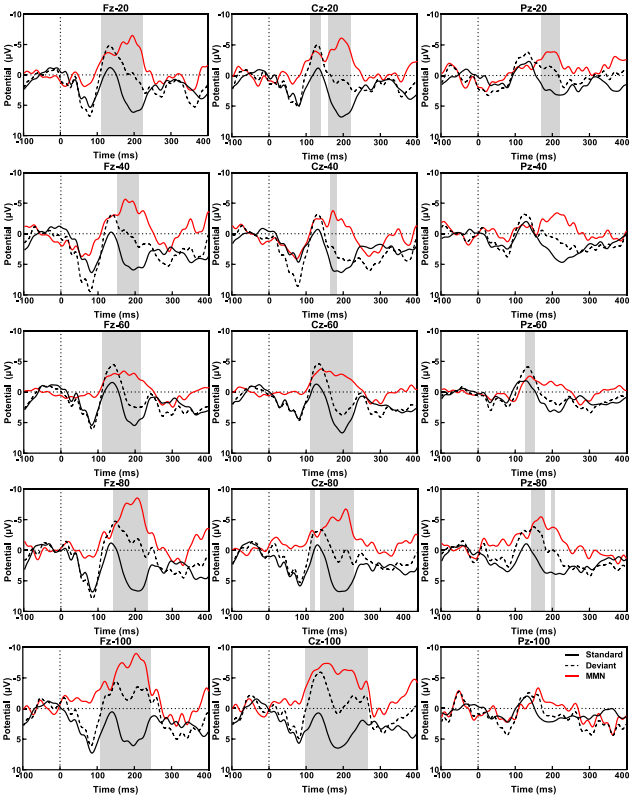

FIGURE 4. Event-related potential (ERP) waveforms of the standard and deviant stimuli of five buffer depths. Mismatch negativity (MMN) waveforms were obtained by subtracting the ERPs in response to standard stimuli from those in response to deviant stimuli. The gray shaded areas show significant differences between the standard and deviant stimuli from 100 ms to 300 ms ($p < 0.05$).

A one-way ANOVA was subsequently conducted for the amplitudes and latencies of the MMN waveform of five buffer depths at the midline electrodes (Fz, Cz, and Pz), as shown in Fig. 5. Bonferroni adjusted alpha levels of 0.005 per test (0.05/10). The results showed that the effect of buffer depth was not significant at Fz for amplitude $F(4,70) = 0.457$, $p > 0.05$ and latency $F(4,70) = 0.681$, $p > 0.05$; at Cz for amplitude $F(4,70) = 1.616$, $p > 0.05$ and latency, $F(4,70) = 1.324$, $p > 0.05$; and at Pz for amplitude $F(4,70) = 0.386$, $p > 0.05$ and latency, $F(4,70) = 0.640$, $p > 0.05$.

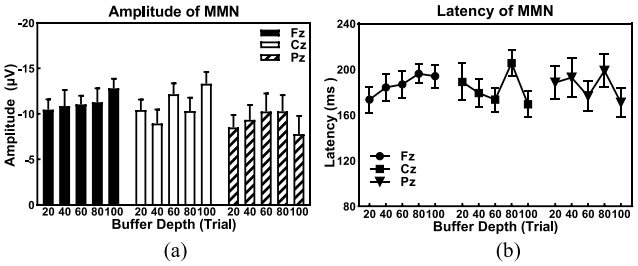

FIGURE 5. Mean amplitudes (a) and latencies (b) of MMN with five buffer depths at the midline electrodes.

As the averages of the amplitude and latency of MMN during training were not affected by the different buffer depths, we investigated whether the buffer depths affected

the stability of the MMN characteristics. Pearson correlations were calculated to explore the correlation between each single training trial MMN and the total MMN. There were strong correlations in 60 trials, 80 trials and 100 trials at three electrodes, with p values < 0.05 and R values > 0.4; however, there were no significant correlations in 20 trials ($p > 0.05$ at Fz, Cz, and Pz) or 40 trials ($p > 0.05$ at Fz, Cz, and Pz) (Fig. 6). Therefore, a buffer depth of 60, 80 or 100 trials may more stably reflect each MMN characteristic during the training.

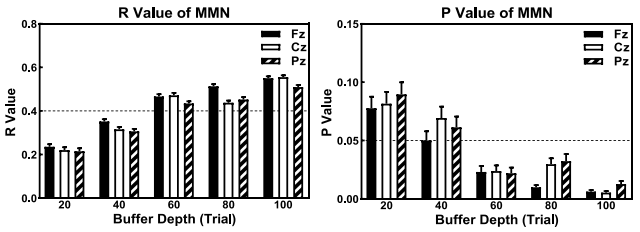

FIGURE 6. MMN correlation analysis between buffer depth (20 trials, 40 trials, 60 trials, 80 trials or 100 trials) and the total trial (400 trials) of the training period at the Fz, Cz, and Pz electrodes. The R value is shown in (a), and the P value is shown in (b).

A one-way ANOVA combined with a post hoc test was executed to analyze the correlation differences in the 60-trial, 80-trial and 100-trial instances, given that the correlations in the 20-trial and 40-trial instances were not significant ($p > 0.05$). Bonferroni adjusted alpha levels of 0.0167 per test (0.05/3). The effects of buffer depth on the R values at three electrodes were significant at Fz: $F(2,42) = 4.645$, $p = 0.015$, Cz: $F(2,42) = 11.248$, $p < 0.01$, and Pz: $F(2,42) = 3.467$, $p = 0.040$. Post hoc significance analyses indicated that 100-trial obtained higher correlations than did the 60-trial at Fz: $p = 0.012$, Cz: $p < 0.01$, and Pz: $p = 0.046$ and 80-trial at Cz: $p < 0.01$ (Fig. 7 (a)). However, no significant difference was found between the 80-trial and 60-trial instances ($p > 0.05$). Moreover, there was no interaction effects of the standard error (SE) of the R values in buffer depths at Fz: $F(2,42) = 1.487$, $p > 0.05$, Cz: $F(2,42) = 1.419$, $p > 0.05$, and Pz: $F(2,42) = 1.115$, $p > 0.05$ (Fig. 7 (b)). Therefore, the stability of the MMN was consistent across those three buffer depths. 100-trial was the most relevant and 60-trial was not significantly different from 80-trial, although they all showed significant correlations.

3) TIME FREQUENCY ANALYSIS

We can better understand MMN from the viewpoint of the frequency domain. Fig. 8 shows the spectral activity of the deviant minus standard stimuli. The powers of the frequency bands (0.5 Hz to 45 Hz) between 100 ms and 300 ms were analyzed by paired t-tests from the theta to the gamma frequencies, considering the inability to obtain the full delta wavelength during this period. A more significant powerful effect of the theta frequency band occurred in 60 trials at Fz: $t = 2.761$, $p = 0.015$, and

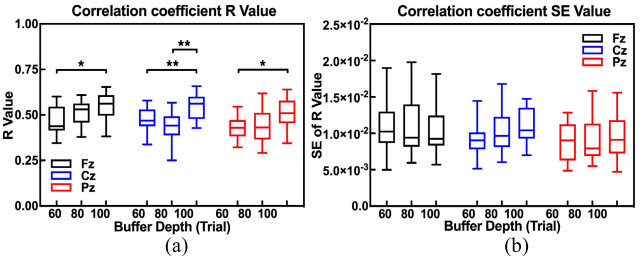

FIGURE 7. Correlation coefficient R value (a) and SE value (b) under three buffer depths at the midline electrodes. *, $p < 0.05$; **, $p < 0.01$.

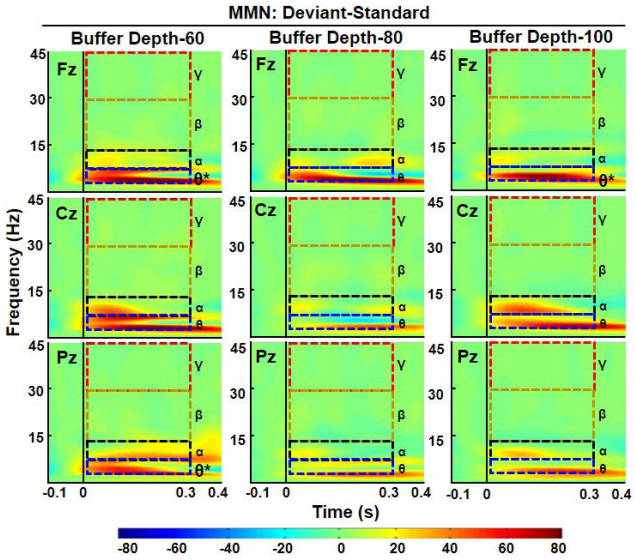

FIGURE 8. Spectral power of different frequencies of the deviant minus standard stimuli under the buffer depth-60, buffer depth-80 and buffer depth-100 at the midline electrodes. Theta: 4 Hz to 8 Hz; alpha: 8 Hz to 13 Hz; beta: 13 Hz to 30 Hz; gamma: 30 Hz to 45 Hz; *, $p < 0.05$.

Pz: $t = 3.009$, $p < 0.01$; in 100 trials at Fz: $t = 2.476$, $p = 0.027$ than in the other frequency bands. However, for the 80 trials, no significant difference occurred between the standard and deviant stimuli from the theta to the gamma bands ($p > 0.05$).

4) OBJECTIVE AND SUBJECTIVE SCORES

Objective rewards and subjective motivation are central components of neurofeedback mechanisms [33]. The reward rate of an individual (R_{indi}) during training refers to the number of red discs (N_{Red}) that appear during training, as shown in Equation (4),

$$R_{indi} = N_{Red}\,(N_{Total} - N_{Base}) \tag{4}$$

where N_{Total} is the total number of trials (400) in each session and N_{Base} is the number of the baseline trials.

Fig. 9 (a) shows that during the different neurofeedback training sessions, the reward rate ranked from high to low was 100 trials, 60 trials, 80 trials, 40 trials, and 20 trials, respectively; however, an ANOVA test showed that the effect of buffer depth on reward rate (objective reward) was not significant, $F(4,70) = 1.858$, $p > 0.05$. To evaluate the subjective motivational perceptions of the participants, we instructed

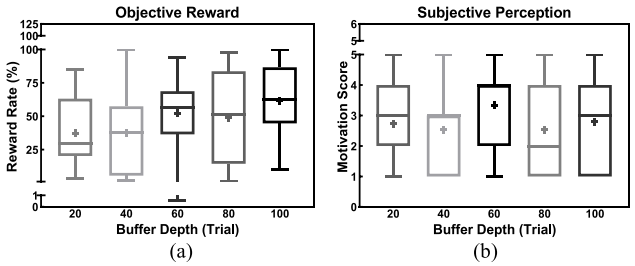

FIGURE 9. Objective reward rate (a) and subjective motivation score of subjective perception (b) after five neurofeedback training sessions.

them to assign a score of 1 to 5 to describe their motivation level (or enhancement level) and the comfort level of the neurofeedback training after each training session (Fig. 9 (b)). Bonferroni adjusted alpha levels of 0.005 per test (0.05/10). Their answers indicated that they considered 60 trials to be the most motivational training parameter; however, the effect of buffer depth on motivation score (subjective perception) was not significant, $F(4,70) = 0.895$, $p > 0.05$.

B. NEUROFEEDBACK TRAINING

Based on the results of the above optimization parameters, here we use the buffer depth of 60 trials for the real-time calculation of MMN parameters in neurofeedback training. The effect of age and education years in the two groups of neurofeedback training was nonsignificant, $t = 0.000$, $p > 0.05$. After five days of neurofeedback training, the auditory discrimination threshold before and after training and the amplitude and latency of MMN on each training day were evaluated.

1) AUDITORY DISCRIMINATION ABILITY

To evaluate the auditory frequency discrimination ability, the individual auditory discrimination thresholds were tested before and after neurofeedback training. After the 5-day training period, subjects in the NF group had a lower threshold ($M = 6.985$, $SD = 3.355$) on the DLF test than they did prior to the training ($M = 13.424$, $SD = 6.985$), $t = 1.987$, $p > 0.05$, while the thresholds in the Sham-NF group remained stable (before: $M = 16.680$, $SD = 8.24$; after: $M = 16.507$, $SD = 6.328$), $t = 0.056$, $p > 0.05$. Importantly, the across group results indicated a significant decrease for subjects in the NF group compared to those in the Sham-NF group, $t = 3.256$, $p < 0.01$, and there was no significant difference between them before the training, $t = 0.598$, $p > 0.05$ (Fig. 10).

2) MMN CHARACTERISTIC ANALYSIS

The MMNs of the subjects in both the Sham-NF group and the NF group were subjected to neurofeedback training by regulating the personal MMN amplitude. A paired T-test was subsequently conducted for the amplitudes and latencies of the MMN at the midline electrodes (Fz, Cz, and Pz) within each group, as shown in Fig. 11. A significant increase in MMN amplitude after five days of NF training compared to their first results at Fz: $t = 4.165$, $p < 0.01$; Cz: $t = 6.741$, $p < 0.01$, and Pz: $t = 4.767$, $p < 0.01$, which occurred in the NF group, while no significant MMN amplitude differences were found in the Sham-NF group, whether at Fz: $t = 1.750$, $p > 0.05$; Cz: $t = -0.609$, $p > 0.05$ or Pz: $t = 0.421$, $p > 0.05$. Independent sample T-test results indicated that the NF group improved the MMN amplitude at the fifth days of training more than did the subjects in the Sham-NF group at Fz: $t = 3.398$, $p < 0.01$, Cz: $t = 3.237$, $p < 0.01$, and Pz: $t = 2.669$, $p = 0.024$. However, the effect of MMN latency was not significant between the first day and the last day within the NF group at Fz: $t = 0.921$, $p > 0.05$; Cz: $t = 2.371$, $p > 0.05$; Pz: $t = 2.204$, $p > 0.05$ and the Sham-NF group at Fz: $t = 0.919$, $p > 0.05$; Cz: $t = -0.170$, $p > 0.05$; Pz: $t = -1.090$, $p > 0.05$ even across the groups on the 5th day at Fz: $t = 0.969$, $p > 0.05$; Cz: $t = 1.923$, $p > 0.05$ and Pz: $t = 1.183$, $p > 0.05$. Therefore, the MMN amplitude significantly improved for the NF group after 5 days of neurofeedback training.

VI. DISCUSSION

BrainKilter provides a new platform consisting of three software modules that can be used for experimental design, online EEG data processing, and neurofeedback training. BrainKilter is intended to be a friendly tool for neurofeedback research in both clinical and commercial environments.

BrainKilter has three primary objectives, one of which is to be portable and accessible. BrainKilter runs on various operating systems, including Windows, Mac, and Linux.

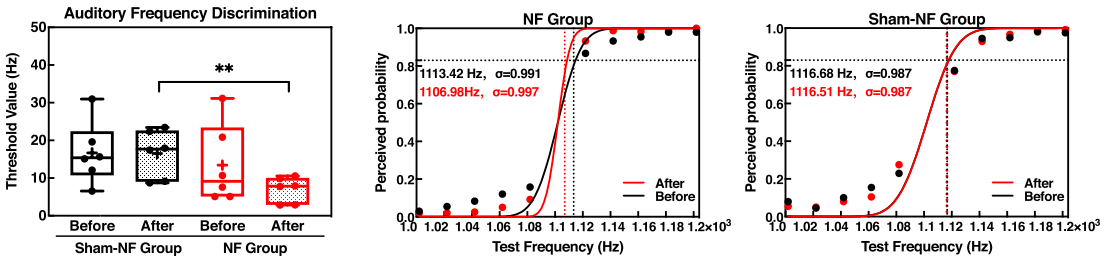

FIGURE 10. The performance of auditory frequency discrimination from frequency discrimination threshold value (a), and threshold fitting curve in NF group (b) and Sham-NF group (c) respectively. Across group, **, $p < 0.01$.

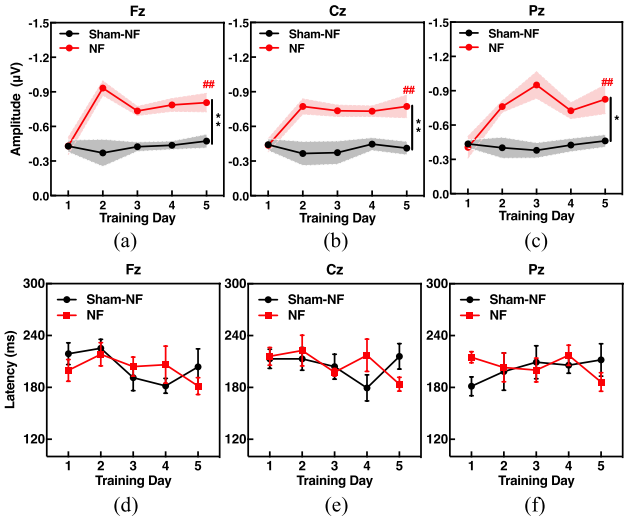

FIGURE 11. The amplitude of MMN at Fz (a), Cz (b), Pz (c) and latency of MMN at Fz (d), Cz (e), Pz (f) during the five neurofeedback training days. Within group, 5th day compared to 1st, ##, $p < 0.01$; Across group, *, $p < 0.05$; **, $p < 0.01$.

It also includes a Device module, which has built-in processing methods for multiple connections, communication protocols, and parsing rules. When the device is connected, the platform will automatically load a configuration file that matches the device by invoking the corresponding processing method to implement data communication with the device. In the future, BrainKilter is expected to support new communication protocols and encapsulation rules directly through configuration files and no processing method preconfiguration will be necessary, which will further enhance its flexibility. Moreover, BrainKilter is designed for different types of users because it provides a platform with a variety of functional tools for data processing and experimental design. For researchers, the functionality to optimize the protocol parameters can facilitate exploration of neurofeedback mechanisms, depending on their neuroscience knowledge. Developers can add new data decoding methods through programming. For users without coding experience, drag and drop capabilities help them to complete the pipeline diagram designs adopted in Toolkit and Analysis to provide a friendly and straightforward method of interaction.

BrainKilter's second goal is to perform online processing of EEG data, which researchers can use to monitor the ongoing dynamics of brain activity as individuals perform different cognitive or behavioral tasks. Using BrainKilter, the combination of different filters and algorithms can satisfy the time-frequency requirements for processing EEG data, and the frequency ranges of different filters, the number and position of the electrodes, the ASR coefficient, and the combination of algorithms can be set autonomously. Furthermore, ASR was adopted in BrainKilter's data preprocessing as an online, real-time capable, component-based method that can effectively remove transient or large-amplitude artifacts. ASR has been proven to be a powerful artifact removal approach and can be applied to automatically clean data for offline data analysis or online real-time EEG applications, such as clinical monitoring and brain-computer interfaces [34]. In previous studies, compared with two other popular methods dedicated to correcting EEG artifacts (ICA and PCA), the ASR method with a suitable coefficient has a significantly better level of artifact correction [35], [36]. Moreover, BrainKilter provides tools for online ERP processing, which solves the critical technical problem of synchronizing stimulus generation and data acquisition. An appropriate sensory stimulus is provided for complex experiments by connecting different devices via the interface. The command-sending process masks the operating system's data buffer, which reduces the delay of the stimulus down to 1 ms. Compared to most of BCI studies that focused on P300, SSVEP, or SMR, MMN as a feedback signal lacks application and clinical research data [37]. Here, we performed a feasible "oddball" paradigm based on standard and deviant stimuli, although MMN is more complicated to monitor and calculate compared to other ERP components. Moreover, although the neuron response time of MMN ranges from 100 ms to 250 ms, we control the reward delay during neurofeedback training within 350 ms under the entire pipeline, which includes a low-order FIR filter, ASR and wireless transmission. Our platform provides filter type selection and parameter setting capabilities that meet the needs of both online neurofeedback training or and offline data processing.

As stimulation and feedback paradigms become increasingly complex and differences in users' anatomical and physiological features demand increasingly individualized NF adjustments, our final goal shows the most important application value: BrainKilter focuses on experimental design mainly through the flexible Toolkit and Display modules, enabling users to design complete experiments without programming, using only element drag-and-drop operations to build experiments and present feedback signals, without requiring scripting. The types and parameters of the stimulus can be edited autonomously. The Display module receives incoming signals from the analysis and translates and forwards them to the users based on the Toolkit parameters. It is also responsible for performing real-time updates and dynamic changes to the feedback signals. The designed experimental protocol runs on the Task APP, and the protocol can be selected, started, paused, and stopped at any time. Users can even modify the parameters during training. Motivation is probably the most crucial property of efficient neurofeedback systems, and experimental tasks should provide the best learning environment for users. For the same neural signal characteristics, the lengths of the different sensory feedback stimulus forms (visual, auditory or tactile), feedback frequency, training cycles, and some other factors will lead to different training results [38]. Because neurofeedback is based on the independent strategies learned by individuals and neurofeedback experiments are often lengthy, personal neurofeedback has gained increasing attention. Hence, we optimized the parameters focused on MMN calculations based on BrainKilter. The auditory MMN

reflects the brain's ability to automatically process auditory information objectively. Considering the differences in individual auditory perception processing ability, the uniform standard and deviant stimuli that are used to induce MMN during neurofeedback training are not sufficiently targeted. Compared to the traditional use of more than 200 trials to obtain a stable and accurate MMN value, being able to operate in real-time is a primary consideration in regulating the dynamic changes of neural activity through neurofeedback. Therefore, we hope to use the minimal number of trials that can obtain a highly stable MMN and accuracy indicator level for a subject. Moreover, we chose the midline electrodes at as the training site because auditory MMN at the Fz and Cz electrodes at the midline is stronger than at other electrodes because the frontal lobe generator exhibits a specific acoustic characteristic dependence and is associated with the frontal lobe and sensory memory [39]. Our results indicated that the MMN was more stable as the buffer depth number of trials increased compared to correlations with the MMN obtained from 400 trials and has a significant correlation with 400 trials from 60 trials and upward at Fz, Cz, and Pz. From the time-frequency analysis, the power of MMN with 60 trials was found to be related to the theta band, which is consistent with previous studies [40]. From a psychological perspective, neurofeedback aims to be a scaffolding system rather than palliation for a missing internal signal; the feedback signal should help subjects identify their own internal signals and promote a sense of agency. If the sense of agency is too low, the neurofeedback protocol will not trigger intrinsic motivation and could negatively affect learning [41]. Our results on MMN neurofeedback pretraining showed that the objective reward rate and subjective motivational experience after neurofeedback training with a buffer depth of 60 was a better choice than the other buffer depths. Moreover, a particular reward rate, of approximately 50% and motivation can promote the activation of the dopamine reward system [9], [42].

Subsequently, we validated the effectiveness of the optimized MMN neurofeedback protocol using a single-blind experiment of healthy people. After 5 short-term training days, the participants in the NF group had significantly enhanced MMN amplitudes but no effect was found regarding latency. A previous study demonstrated the advantages of adjusting the MMN amplitude and latency of MMN based on neurofeedback training by adopting two fixed frequencies as standard and deviant stimuli [21], [43]. However, we adopted an individual's auditory discrimination frequency threshold for the deviant stimuli; therefore, the latency showed a non-significant decline, which may be due to the significant individual differences in deviant stimuli and training that focus only on regulating amplitude. Compared to the results of the DLF test before training, the auditory discrimination threshold of the NF group decreased after neurofeedback training, although there was no significant difference. Considering the short and tight training schedule, longer-term training may have more influence in improving behavioral performance [44]. Therefore, our preliminary MMN neurofeedback results demonstrate that the perception ability of healthy people can be modified. Based on MMN as an important EEG marker of neurological disease and MMN is considered a correlate of pre-attentive processes, which are triggered when the sensory input does not match the echoic memory representation of a prevalent standard stimulus [45], using MMN neurofeedback to improve cognitive ability and as a potential treatment for clinical research is worth exploring.

Above all, the BrainKilter platform provides a truly easy-to-use environment for computerized design and optimization of parameters for neurofeedback experiments and training.

VII. CONCLUSION

In this paper, we presented BrainKilter, a platform for designing neurofeedback experiments and training applications. A personal MMN neurofeedback experiment was subsequently conducted to verify the data processing effectiveness and application value of BrainKilter. Moreover, we discussed parameter optimization for a neurofeedback protocol from the viewpoint of MMN calculations based on BrainKilter that was successfully conducted for healthy individuals. Our platform is continuously updated and improved. Full-function and data-decoding methodological improvements are currently under development. A dynamic statistical analysis function for data features will be able to more effectively screen and analyze quantitative indicators in the new version. Moreover, it is necessary to be able to track the cognitive status of participants in real time. Thus, BrainKilter will enhance the overall user experience and is committed to the research and clinical neurofeedback application of BCI technology.

REFERENCES

[1] C. G. Coogan and B. He, "Brain-computer interface control in a virtual reality environment and applications for the Internet of Things," *IEEE Access*, vol. 6, pp. 10840–10849, 2018.

[2] U. Chaudhary, N. Birbaumer, and A. Ramos-Murguialday, "Brain-computer interfaces for communication and rehabilitation," *Nature Rev. Neurol.*, vol. 12, no. 9, p. 513, 2016.

[3] C. Paret, N. Goldway, C. Zich, J. N. Keynan, T. Hendler, D. Linden, and K. Cohen Kadosh, "Current progress in real-time functional magnetic resonance-based neurofeedback: Methodological challenges and achievements," *NeuroImage*, vol. 202, Nov. 2019, Art. no. 116107.

[4] J. Rogala, K. Jurewicz, K. Paluch, E. Kublik, R. Cetnarski, and A. Wróbel, "The do's and don'ts of neurofeedback training: A review of the controlled studies using healthy adults," *Frontiers Hum. Neurosci.*, vol. 10, p. 301, Jun. 2016.

[5] S. N. Abdulkader, A. Atia, and M.-S. M. Mostafa, "Brain computer interfacing: Applications and challenges," *Egyptian Inform. J.*, vol. 16, pp. 213–230, Jul. 2015.

[6] R. G. Lupu, F. Ungureanu, and C. Cimpanu, "Brain-computer interface: Challenges and research perspectives," in *Proc. 22nd Int. Conf. Control Syst. Comput. Sci. (CSCS)*, May 2019, pp. 387–394.

[7] S. Lee, Y. Shin, S. Woo, K. Kim, and H.-N. Lee, "Review of wireless brain-computer interface systems," in *Brain-Computer Interface Systems: Recent Progress and Future Prospects*. Jun. 2013, pp. 215–238. [Online]. Available: https://www.intechopen.com/books/brain-computer-interface-systems-recent-progress-and-future-prospects/review-of-wireless-brain-computer-interface-systems

[8] C. A. Scholl, Y. M. Chi, M. Elconin, W. R. Gray, M. A. Chevillet, and E. A. Pohlmeyer, "Classification of pilot-induced oscillations during in-flight piloting exercises using dry EEG sensor recordings," in *Proc. 38th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc. (EMBC)*, Aug. 2016, pp. 4467–4470.

[9] A. Gaume, A. Vialatte, A. Mora-Sánchez, C. Ramdani, and F. Vialatte, "A psychoengineering paradigm for the neurocognitive mechanisms of biofeedback and neurofeedback," *Neurosci. Biobehav. Rev.*, vol. 68, pp. 891–910, Sep. 2016.
[10] A. Delorme, T. Mullen, C. Kothe, Z. Akalin Acar, N. Bigdely-Shamlo, A. Vankov, and S. Makeig, "EEGLAB, SIFT, NFT, BCILAB, and ERICA: New tools for advanced EEG processing," *Comput. Intell. Neurosci.*, vol. 2011, pp. 1–12, May 2011, doi: 10.1155/2011/130714.
[11] H. Du, I. Jouny, Y.-C. Yu, and S. Wang, "Exploring P300-based biometric for individual identification based on convolutional neural networks," in *Proc. IEEE Signal Process. Med. Biol. Symp. (SPMB)*, Dec. 2018, pp. 1–3.
[12] J. Lindgren and A. Lecuyer, "OpenViBE and other BCI software platforms," in *Brain-Computer Interfaces 2: Technology and Applications*. Sep. 2016, pp. 179–198. [Online]. Available: https://onlinelibrary.wiley.com/doi/10.1002/9781119332428.ch10
[13] B. Venthur, "Pyff—A Pythonic framework for feedback applications and stimulus presentation in neuroscience," *Frontiers Neurosci.*, vol. 4, p. 179, Oct. 2010, doi: 10.3389/fnins.2010.00179.
[14] L. Bianchi, J. Babiloni, J. Cincotti, D. Mattia, and M. Marciani, "Developing wearable bio-feedback systems: The BF++ framework approach," in *Proc. 1st Int. IEEE EMBS Conf. Neural Eng., Conf.*, Jan. 2004, pp. 607–609.
[15] K. S. Firlik, "Systems and methods for portable neurofeedback," Google Patents 20 100 016 753, Jan. 21, 2010.
[16] A. S. Al-Fahoum and A. A. Al-Fraihat, "Methods of EEG signal features extraction using linear analysis in frequency and time-frequency domains," *ISRN Neurosci.*, vol. 2014, pp. 1–7, Jan. 2014.
[17] A. De Cheveigné and I. Nelken, "Filters: When, why, and how (not) to use them," *Neuron*, vol. 102, no. 2, pp. 280–293, Apr. 2019.
[18] C.-Y. Chang, S.-H. Hsu, L. Pion-Tonachini, and T.-P. Jung, "Evaluation of artifact subspace reconstruction for automatic artifact components removal in multi-channel EEG recordings," *IEEE Trans. Biomed. Eng.*, to be published.
[19] G. A. Light, N. R. Swerdlow, and D. L. Braff, "Preattentive sensory processing as indexed by the MMN and P3a brain responses is associated with cognitive and psychosocial functioning in healthy adults," *J. Cognit. Neurosci.*, vol. 19, no. 10, pp. 1624–1632, Oct. 2007, doi: 10.1162/jocn.2007.19.10.1624.
[20] C. F. Altmann, R. Ueda, S. Furukawa, M. Kashino, T. Mima, and H. Fukuyama, "Auditory mismatch negativity in response to changes of counter-balanced interaural time and level differences," *Frontiers Neurosci.*, vol. 11, p. 387, Jul. 2017, doi: 10.3389/fnins.2017.00387.
[21] M. Chang, H. Iizuka, Y. Naruse, H. Ando, and T. Maeda, "Unconscious learning of auditory discrimination using mismatch negativity (MMN) neurofeedback," *Sci. Rep.*, vol. 4, Oct. 2014, Art. no. 6729, doi: 10.1038/srep06729.
[22] L. Kishon-Rabin, D. A. Roth, B. Van Dijk, T. Yinon, and O. Amir, "Frequency discrimination thresholds: The effect of increment versus decrement detection of frequency," *J. Basic Clin. Physiol. Pharmacol.*, vol. 15, nos. 1–2, pp. 29–40, 2004.
[23] G. Lisi, M. Hamaya, T. Noda, and J. Morimoto, "Dry-wireless EEG and asynchronous adaptive feature extraction towards a plug-and-play co-adaptive brain robot interface," in *Proc. IEEE Int. Conf. Robot. Automat. (ICRA)*, May 2016, pp. 959–966.
[24] F. Marini, C. Lee, J. Wagner, S. Makeig, and M. Gola, "A comparative evaluation of signal quality between a research-grade and a wireless dry-electrode mobile EEG system," *J. Neural Eng.*, vol. 16, no. 5, May 2019, Art. no. 054001.
[25] L. Bonetti, N. Haumann, E. Brattico, M. Kliuchko, P. Vuust, T. Särkämö, and R. Näätänen, "Auditory sensory memory and working memory skills: Association between frontal MMN and performance scores," *Brain Res.*, vol. 1700, pp. 86–98, Dec. 2018.
[26] C.-Y. Chang, S.-H. Hsu, L. Pion-Tonachini, and T.-P. Jung, "Evaluation of artifact subspace reconstruction for automatic EEG artifact removal," in *Proc. 40th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc. (EMBC)*, Jul. 2018, pp. 1242–1245.
[27] D. Restuccia, S. Zanini, M. Cazzagon, I. Del Piero, L. Martucci, and G. D. Marca, "Somatosensory mismatch negativity in healthy children," *Developmental Med. Child Neurol.*, vol. 51, no. 12, pp. 991–998, Dec. 2009.
[28] F. A. Wichmann and N. J. Hill, "The psychometric function: I. Fitting, sampling, and goodness of fit," *Perception Psychophys.*, vol. 63, no. 8, pp. 1293–1313, Nov. 2001.
[29] F. A. Wichmann and N. J. Hill, "The psychometric function: II. Bootstrap-based confidence intervals and sampling," *Perception Psychophys.*, vol. 63, no. 8, pp. 1314–1329, Nov. 2001.
[30] A. Delorme and S. Makeig, "EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis," *J. Neurosci. Methods*, vol. 134, no. 1, pp. 9–21, Mar. 2004.
[31] M. Liu, G. Pei, Y. Peng, C. Wang, T. Yan, and J. Wu, "Disordered high-frequency oscillation in face processing in schizophrenia patients," *Medicine*, vol. 97, no. 6, Feb. 2018, Art. no. e9753.
[32] J. Zhang, "Gender differences in global functional connectivity during facial emotion processing: A visual MMN study," *Frontiers Behav. Neurosci.*, vol. 12, p. 220, Sep. 2018, doi: 10.3389/fnbeh.2018.00220.
[33] R. Sitaram, T. Ros, L. Stoeckel, S. Haller, F. Scharnowski, J. Lewis-Peacock, N. Weiskopf, M. L. Blefari, M. Rana, E. Oblak, N. Birbaumer, and J. Sulzer, "Closed-loop brain training: The science of neurofeedback," *Nature Rev. Neurosci.*, vol. 18, no. 2, pp. 86–100, Feb. 2017.
[34] L. Pion-Tonachini, S.-H. Hsu, C.-Y. Chang, T.-P. Jung, and S. Makeig, "Online automatic artifact rejection using the real-time EEG source-mapping toolbox (REST)," in *Proc. 40th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc. (EMBC)*, Jul. 2018, pp. 106–109.
[35] S. Blum, N. Jacobsen, M. G. Bleichner, and S. Debener, "A Riemannian modification of artifact subspace reconstruction for EEG artifact handling," *Frontiers Hum. Neurosci.*, vol. 13, p. 141, Apr. 2019.
[36] E. Arad, R. P. Bartsch, J. W. Kantelhardt, and M. Plotnik, "Performance-based approach for movement artifact removal from electroencephalographic data recorded during locomotion," *PLoS ONE*, vol. 13, no. 5, May 2018, Art. no. e0197153.
[37] M. Vazquez-Marrufo, "Event-related potentials for the study of cognition," *Event-Rel. Potentials Evoked Potentials*, p. 1, Nov. 2017. [Online]. Available: https://www.intechopen.com/books/event-related-potentials-and-evoked-potentials/event-related-potentials-for-the-study-of-cognition, doi: 10.5772/intechopen.69308.
[38] S. Enriquez-Geppert, R. J. Huster, and C. S. Herrmann, "EEG-neurofeedback as a tool to modulate cognition and behavior: A review tutorial," *Frontiers Hum. Neurosci.*, vol. 11, p. 51, Feb. 2017.
[39] M. I. Garrido, J. M. Kilner, K. E. Stephan, and K. J. Friston, "The mismatch negativity: A review of underlying mechanisms," *Clinical Neurophysiology*, vol. 120, no. 3, pp. 453–463, Mar. 2009.
[40] D. Ko, S. Kwon, G.-T. Lee, C. H. Im, K. H. Kim, and K.-Y. Jung, "Theta oscillation related to the auditory discrimination process in mismatch negativity: Oddball versus control paradigm," *J. Clin. Neurol.*, vol. 8, no. 1, p. 35, 2012, doi: 10.3988/jcn.2012.8.1.35.
[41] M. Sperduti, P. Delaveau, P. Fossati, and J. Nadel, "Different brain structures related to self- and external-agency attribution: A brief review and meta-analysis," *Brain Struct. Function*, vol. 216, no. 2, pp. 151–157, Jun. 2011.
[42] E. S. Bromberg-Martin, M. Matsumoto, and O. Hikosaka, "Dopamine in motivational control: Rewarding, aversive, and alerting," *Neuron*, vol. 68, no. 5, pp. 815–834, Dec. 2010.
[43] M. Chang, H. Iizuka, H. Kashioka, Y. Naruse, M. Furukawa, H. Ando, and T. Maeda, "Unconscious improvement in foreign language learning using mismatch negativity neurofeedback: A preliminary study," *PLoS ONE*, vol. 12, no. 6, Jun. 2017, Art. no. e0178694, doi: 10.1371/journal.pone.0178694.
[44] H. Marzbani, H. R. Marateb, and M. Mansourian, "Neurofeedback: A comprehensive review on system design, methodology and clinical applications," *Basic Clin. Neurosci.*, vol. 7, no. 2, p. 143, 2016.
[45] M. Lindín, K. Correa, M. Zurrón, and F. Díaz, "Mismatch negativity (MMN) amplitude as a biomarker of sensory memory deficit in amnestic mild cognitive impairment," *Frontiers Aging Neurosci.*, vol. 5, p. 79, Nov. 2013.

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