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Can Artificial Intelligence Diagnose Transient Global Amnesia Using Electroencephalography Data?

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Background and Purpose This study aimed to determine the ability of deep learning using convolutional neural networks (CNNs) to diagnose transient global amnesia (TGA) based on electroencephalography (EEG) data, and to differentiate between patients with recurrent TGA events and those with a single TGA event.

Methods We retrospectively enrolled newly diagnosed patients with TGA and healthy controls. All patients with TGA and the healthy controls underwent EEG. The EEG signals were converted into images using time-frequency analysis with short-time Fourier transforms. We employed two CNN models (AlexNet and VGG19) to classify the patients with TGA and the healthy controls, and for further classification of patients with recurrent TGA events and those with a single TGA event.

Results We enrolled 171 patients with TGA and 68 healthy controls. The accuracy and area under the curve (AUC) of the AlexNet and VGG19 models in classifying patients with TGA and healthy controls were 70.4% and 71.8%, and 0.718 and 0.743, respectively. In addition, the accuracy and AUC of the AlexNet and VGG19 models in classifying patients with recurrent TGA events and those with a single TGA event were 71.1% and 88.4%, and 0.773 and 0.873, respectively.

Conclusions We have successfully demonstrated the feasibility of deep learning in diagnosing TGA based on EEG data, and used two different CNN models to distinguish between patients with recurrent TGA events and those with a single TGA event.

Keywords deep learning; electroencephalography; transient global amnesia.

INTRODUCTION

Transient global amnesia (TGA) is a clinical syndrome characterized by the sudden onset of anterograde amnesia, sometimes with a partial retrograde component, which may last up to 24 h.[1] TGA often affects people aged 50–80 years with an annual incidence rate of 10 per 100,000 population, while that in the population older than 50 years is 32 per 100,000.[2,3] Although several pathogeneses of TGA have been suggested, such as migraines, ischemia, epileptic seizures, venous congestion, metabolic stress, and psychological disturbances,[4,5] the exact mechanism of TGA remains unclear.

Electroencephalography (EEG) findings are often found to be normal during or after TGA events,[6,7] while a transient amnesia event can occur due to epileptic seizures, which is known as transient epileptic amnesia (TEA).[8] TEA should be differentiated from TGA during the diagnosis because some patients with TEA need acute treatment or secondary prevention via antiseizure medication. Although temporal focal slow-wave activity can be seen in patients with TGA on EEG, it is generally impossible to diagnose TGA using EEG findings.[6,9] Instead, TGA is diagnosed based on clinical findings, and some diagnostic criteria relating to clinical

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history have been suggested.[10] However, in clinical practice, medical history records are often restricted when a family member or observer does not accompany the patient. In addition, TGA is sometimes subsequently diagnosed as TEA after frequent recurrences of symptoms because epileptiform discharge is not often observed in patients with TEA on EEG.[11]

Machine learning is a class of artificial intelligence (AI) that uses algorithms that can independently learn through training using raw data, rather than through explicit programming.[12] Deep learning is a subfield of machine learning.[13] Unlike traditional machine learning, deep learning does not require a human to specify the knowledge that the computer needs.[14] With the increasing utilization of AI in various fields of medical science, researchers have used it to study neurology, such as in seizure detection and epilepsy diagnosis, and to identify REM-sleep behavior disorder.[15-20] However, no previous studies have used deep learning to diagnose TGA.

The aim of this study was to determine the ability of deep learning using convolutional neural networks (CNNs) to diagnose TGA based on EEG data, and to differentiate between patients with recurrent TGA events and those with a single TGA event. We expected that deep-learning model would be able to distinguish between patients with TGA and healthy controls based on EEG findings, and between those with recurrent TGA events and with a single TGA event.

METHODS

Participants

This was a retrospective study that was approved by the Institutional Review Board of our hospital (IRB No. 2020-08-009). Informed consent from the participants was waived. We enrolled patients with TGA using the following criteria: 1) newly diagnosed with TGA at our hospital between March 2010 and March 2021 according to clinical criteria,[10] 2) no structural lesions in brain magnetic resonance imaging (MRI), except hippocampal dot lesions on diffusion-weighted imaging (DWI), and 3) EEG performed at the time of TGA diagnosis, as part of the routine care provided to patients with TGA. All of the patients with TGA underwent EEG after ictal periods of TGA. We additionally classified the patients with TGA into two groups: patients with recurrent TGA events (two or more TGA events) and those with a single TGA event (the first TGA event). If a patient had EEG data for both their first and second TGA attacks, they were assigned to the recurrent-TGA-events group. We also used the EEG data from age- and sex-matched healthy controls who had no previous medical or neurological disease history. These EEG data had been previously collected for research purposes in a previous study of healthy subjects.[21]

EEG acquisition and preprocessing

All EEG recordings were carried out using the same type of EEG machine (TWin® EEG, Astro-Med, Inc.; West Warwick, RI, USA) at our hospital. They were conducted using gold electrodes attached by trained personnel using electrode paste. The 23 electrodes (Fp1, Fp2, F7, F8, T1, T2, T3, T4, T5, T6, O1, O2, F3, F4, C3, C4, P3, P4, Cz, Pz, Oz, A1, and A2) were placed using the international 10–20 system. The electrode impedance was kept below 5 kΩ. The sampling frequency was 200 Hz, and EEG recordings lasted at least 30 min. Data were high- and lowpass filtered at 0.5 and 55.0 Hz, respectively.

Deep learning models

The EEG was referenced to the average montage and exported in the European Data File format. We opened the EEG data using Curry SBA® software (version 8.0.3.26, Compumedics; Charlotte, NC, USA). We selected a recording time of 10 s for the EEG, which showed normal background activities and no artifacts or epileptiform discharges. The EEG signals were converted into an image using time-frequency analysis with short-time Fourier transforms with the following settings: average wavelet of all the channels, resolution=1.28 s, minimum frequency = 0 Hz, maximum frequency=12.5 Hz, and medium spectrogram size. We saved the images as figure files for transfer learning (Fig. 1).

Deep learning was conducted using MATLAB (version R2020b, the MathWorks, Inc.; Natick, MA, USA). We employed the CNN models AlexNet and VGG19 to classify the patients with TGA and healthy controls, and the patients with recurrent TGA events and those with a single TGA event. We loaded a pretrained network and replaced final layers to learn features specific to our data set. We divided the participants at a 7:3 ratio for the network training and testing phases, respectively. The image input sizes for the AlexNet and VGG19 models were was 227×227 and 224×224, respectively. We also performed image data augmentation, which randomly flipped the image along the vertical axis and translated up to 30 pixels horizontally and vertically. We specified the training options as following: stochastic gradient descent with momentum solvers, 1×10^{-4} initial learning rate, six as the maximum epochs, and a minibatch size of ten. Finally, we calculated the classification accuracy of the test set. We presented one example of a saliency map as Supplementary Fig. 1 (in the online-only Data Supplement).

Statistical analysis

When comparing the demographic and clinical characteristics between groups, the chi-squared test or Fisher's exact test was used for categorical variables, and the independent samples *t*-test or Mann-Whitney test was used for continuous vari-

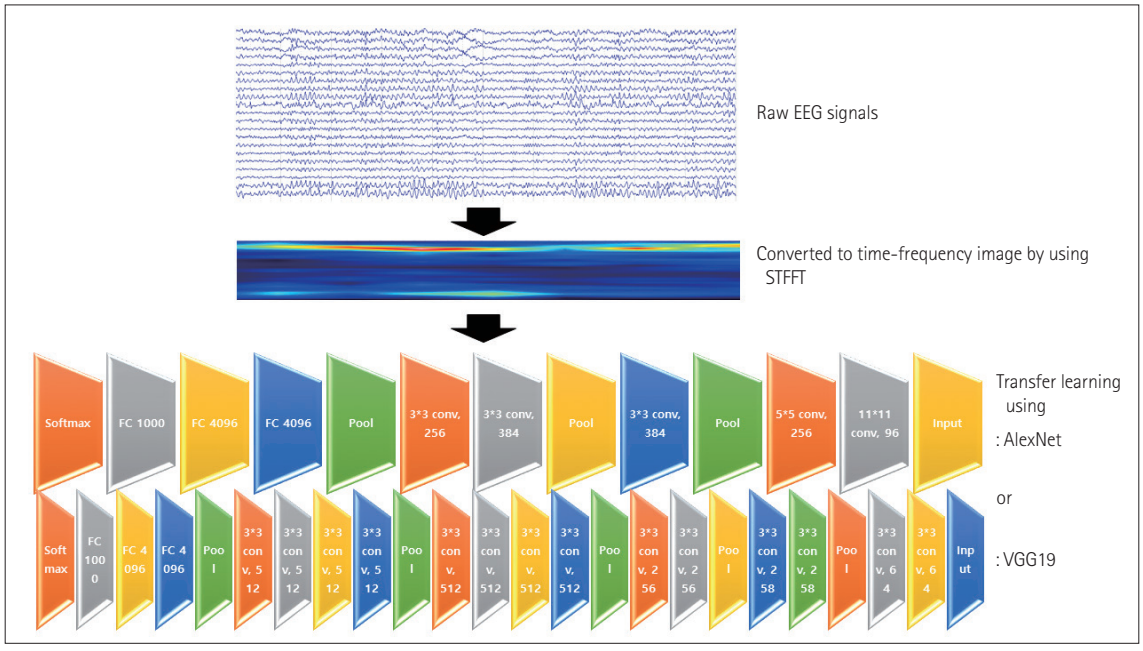

Fig. 1. Analysis process based on EEG using transfer learning with convolutional neural networks (AlexNet and VGG19 models). EEG, electroencephalography; STFFT, short-time Fourier transforms.

Table 1. Demographic and clinical characteristics of the participants

	Patients with TGA (*n*=171)	Healthy controls (*n*=68)	*p*
Age (yr)	61.7±8.1	60.1±10.5	0.208
Sex, male	51 (29.8)	20 (29.4)	0.949
	Patients with recurrent events (*n*=20)	**Patients with a single event (*n*=151)**	***p***
Age (yr)	60.6±9.5	61.8±7.9	0.522
Sex, male	8 (40.0)	43 (28.4)	0.291
EEG abnormalities	1 (5.0)	11 (7.2)	1.000
EEG time from ictal onset, days	6 (2–17)	5 (1–14)	0.534
Hippocampal dot lesions on DWI	3 (15.0)	36 (23.8)	0.377
Duration of amnesia, h	4 (1.0–6.0)	4 (2.5–7.0)	0.320
Precipitation factor	10 (50.0)	79 (52.3)	0.845
Emotional stress	6	47	
Physical activity	2	14	
Temperature change	2	18	
Past medical history	12 (60.0)	59 (39.1)	0.075
Hypertension	5	34	
Dyslipidemia	5	14	
Diabetes	3	11	
Others	1	12	

Data are mean±SD, *n*, *n* (%), or median (interquartile range) values.
DWI, diffusion-weighted imaging; EEG, electroencephalography; TGA, transient global amnesia.

ables. All of the statistical analyses were performed using MedCalc® statistical software (version 20.01, MedCalc Software; Ostend, Belgium). We set $p<0.05$ to indicate significance.

RESULTS

Participants

We enrolled 171 patients with TGA and 68 healthy controls. Table 1 lists the demographic and clinical characteristics of the patients with TGA and health controls. The mean age and sex distribution did not differ significantly between these

two patient groups (61.7 vs. 60.1 years old, p=0.208; 51/171 vs. 20/68 males/females, p=0.949; respectively). Of the 171 patients with TGA, 20 had recurrent TGA events and 151 had a single TGA event. The demographic factors of age and sex, and the clinical characteristics of EEG abnormalities (focal slowing), EEG time from ictal symptom onset, presence of

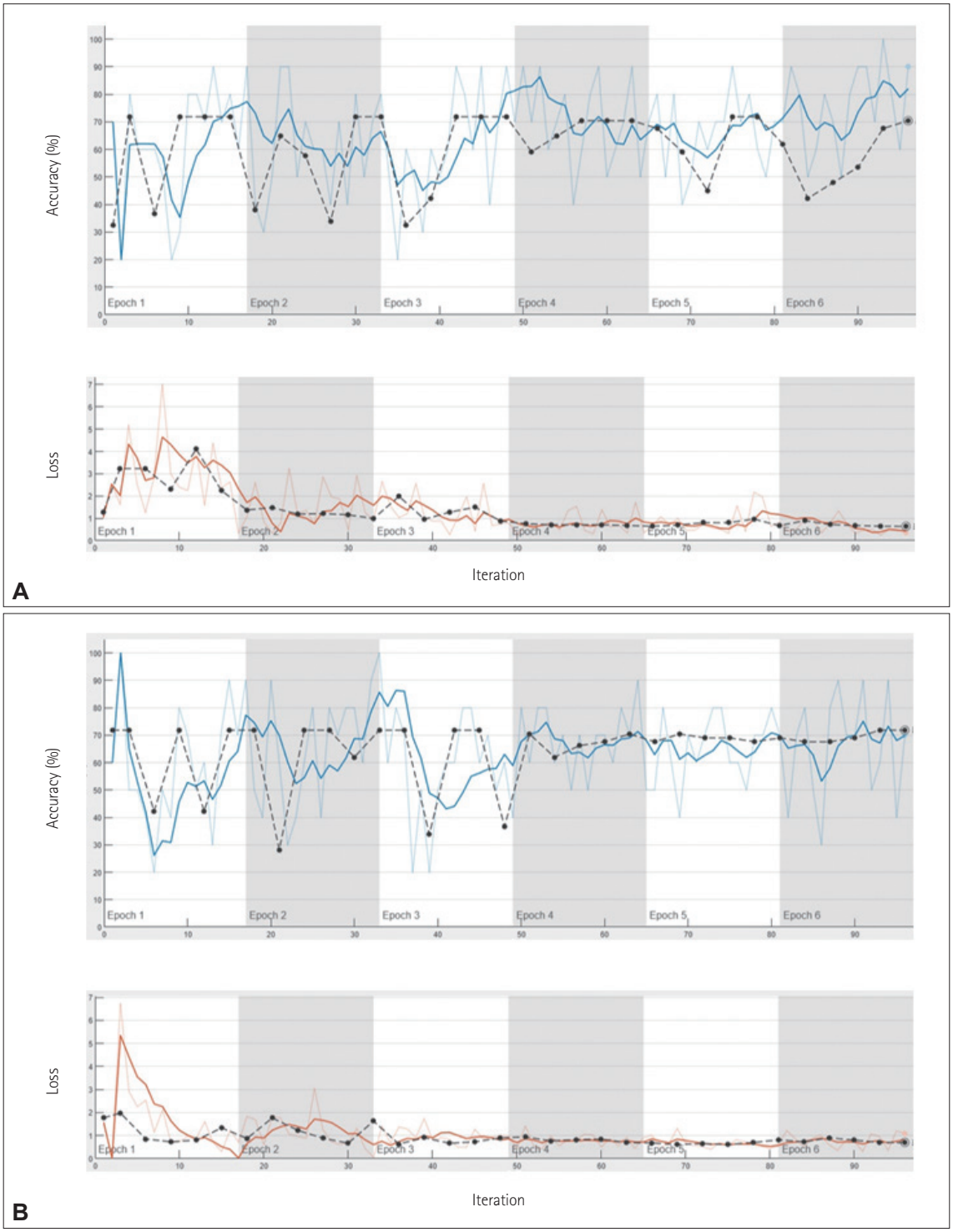

Fig. 2. Progress plots for accuracy and loss values in classifying patients with TGA and healthy controls (A), and in classifying patients with recurrent TGA events and those with a single event (B) using the AlexNet model. Blue and red lines represent training, and black dotted lines represent validation. TGA, transient global amnesia.

hippocampal dot lesions on DWI, duration of amnesia, presence of precipitating factors, and past medical history did not differ between the groups.

Classification accuracy of the AlexNet and VGG19 CNN models

Fig. 2 shows the classification performances of the AlexNet models. The accuracy of the AlexNet models in classifying

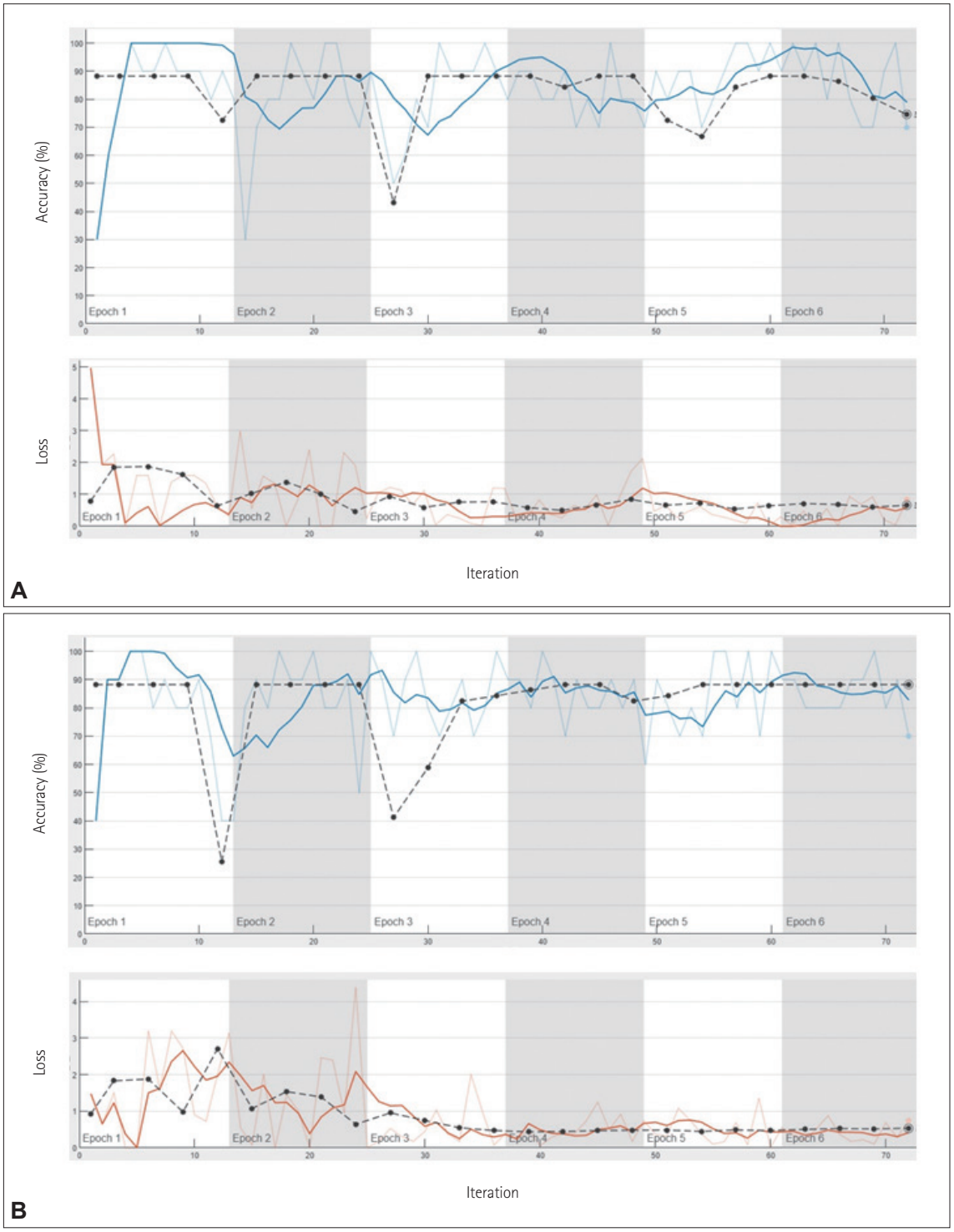

Fig. 3. Progress plots for accuracy and loss values in classifying patients with TGA and healthy controls (A), and in classifying patients with recurrent TGA events and those with a single event (B) using the VGG19 model. Blue and red lines represent training, and black dotted lines represent validation. TGA, transient global amnesia.

patients with TGA and healthy controls was 70.4% (Fig. 2A), with sensitivity, specificity, positive predictive, negative predictive, and area under the curve (AUC) values of 68.6%, 75.0%, 87.5%, 48.3%, and 0.718, respectively. In addition, the accuracy of the AlexNet models in classifying patients with recurrent TGA events and those with a single TGA event was 71.1% (Fig. 2B), with sensitivity, specificity, positive predictive, negative predictive, and AUC values of 68.8%, 85.7%, 96.8%, 30.0%, and 0.773, respectively.

Fig. 3 shows the classification performances of the VGG19 models. The accuracy of the VGG19 models in classifying patients with TGA and healthy controls was 71.8% (Fig. 3A), with sensitivity, specificity, positive predictive, negative predictive, and AUC values of 66.6%, 80.0%, 89.7%, 50.0%, and 0.743, respectively. In addition, the accuracy of the VGG19 models in classifying patients with recurrent TGA events and those with a single TGA event was 88.4% (Fig. 3B), with sensitivity, specificity, positive predictive, negative predictive, and AUC values of 88.8%, 85.7%, 97.5%, 54.5%, and 0.873, respectively. Table 2 lists the confusion matrix of the test data set.

DISCUSSION

This study has demonstrated the feasibility of deep learning in diagnosing TGA based on EEG data, and for distinguishing between patients with recurrent TGA events and those with a single TGA event using two different CNN models.

Deep learning has been an emerging technique in the field of neuroscience.[22] It has been applied to various neurological disorders, such as Alzheimer's disease, epilepsy, brain tumors, Parkinson's disease, infectious central nervous system diseases, and other degenerative diseases.[23] Most of these studies used brain imaging data, including that from CT, MRI, or PET.[24] However, some studies in the field of epilepsy research have used EEG data.[15,16,25] One of these studies successfully demonstrated using a deep-learning model to detect seizures based on EEG data, with an accuracy of 99.46%.[26] Another study on seizure prediction through feature extraction from EEG data also found high sensitivities between 91.8% and 96.6%.[27] Another on seizure prediction and warnings that utilized a wearable device with a deep-learning classifier based on intracranial EEG data produced a sensitivity of 69%.[28] The present study was the first to use deep learning based on EEG data in patients with TGA. Because the ictal period of TGA is short, we often encounter patients with TGA in the postictal period and receive their history from the attendant. Moreover, there are practically no biomarkers for TGA diagnosis other than hippocampal dot lesions on DWI.[29] Since TGA generally follows a benign course, it is important to distinguish it from other diseases. This study was therefore expected to facilitate the diagnosis and management of patients with TGA.

The accuracy of diagnosing TGA based on EEG data using CNN was 70%–80% in this study, which could be interpreted as a disappointing result. Several factors can be considered that would explain these results. One study found that the ability of deep learning is highly dependent on the total sample size.[23] Moreover, most studies have found a positive correlation between the overall accuracy of deep learning and the sample size. Our results could therefore be attributed to the relatively small sample. Another possibility was the use of light CNN models. The AlexNet model is a deep CNN model that won the 2012 ImageNet Large Scale Visual Recognition Challenge (ILSVRC) with a top-5 error rate of 15.3%.[30] The network consists of five convolutional, max-pooling, and dropout layers, and three fully connected layers. The VGG19 model is a variant of VGGNet, which was created in 2014 and consists of 19 layers.[31] The accuracy of VGG19 is generally known to be higher than that of AlexNet, which was also confirmed in our study. Both of these CNN models are simple and so are easy to use and have the advantage of short analysis times, but their accuracies are relatively low. We believe that the accuracy could have been improved if a different analysis model was used, such as NASNet-Large or DenseNet201.

This study has also demonstrated the feasibility of deep learning in classifying patients with recurrent TGA events and those with single TGA event, which had higher accuracy than classifying patients with TGA and healthy controls. There have been a few studies that identified the factors associated with

Table 2. Confusion matrix of the test data set

	AlexNet model	
	Patients with TGA	**Healthy controls**
Predicted patients with TGA	35	5
Predicted healthy controls	16	15
	AlexNet model	
	Patients with a single event	**Recurrent TGA events**
Predicted patients with TGA	31	1
Predicted healthy controls	14	6
	VGG19 model	
	Patients with TGA	**Healthy controls**
Predicted patients with TGA	35	4
Predicted healthy controls	16	16
	VGG19 model	
	Patients with a single event	**Patients with recurrent TGA events**
Predicted patients with TGA	40	1
Predicted healthy controls	5	6

TGA, transient global amnesia.

TGA event recurrence: earlier age at first TGA event, history of migraine or depression, previous head trauma injury, and family history of dementia.[32,33] We also previously demonstrated differences in the brain networks of patients with recurrent TGA events and those with a single TGA event.[34] We used cerebral blood flow (CBF) based on arterial spin-labeling MRI to analyze the functional brain network. Although the CBF did not differ significantly between the two groups, the eccentricity of the functional network was higher in patients with recurrent TGA events than in those with a single TGA event. In this study, we also found an association between TGA recurrence and EEG data, although all of the EEG presented normal background activity upon visual inspection. This might indicate that there is a relationship between the brain network alterations and EEG findings in patients with TGA. Furthermore, we recently demonstrated that the glymphatic system function differed significantly according to TGA event recurrence,[35] being higher in patients with recurrent TGA events than in those with a single event. These previous findings along with the present results suggest that the pathophysiology of patients with recurrent TGA events differ from that of patients with one TGA event. Further studies are needed to confirm this assumption.

This study was the first to demonstrate the feasibility of using deep learning to diagnose TGA based on EEG findings, and to distinguish between patients with recurrent TGA events and those with a single TGA event. It suggested that AI is a technology that can help to diagnose and identify neurological diseases. However, there were some limitations. First, this was a retrospective study conducted at a single center with a small sample. Larger data sets are needed to improve the ability to assess deep learning. Second, we only used routine EEG recordings from clinical practice, and not high-resolution EEG recordings. High-resolution EEG with at least 32 electrodes has being widely used in many recent studies for precise localization and spatial analyses.[36] Third, our EEG data were obtained during the postictal period, not during actual TGA events. The ictal EEG recordings presumably reflect more abnormality than postictal state EEG recordings. Fourth, we applied two CNN models in this study (AlexNet and VGG19) whose accuracies are relatively low. We presumed that the accuracy could be improved by using another updated model, such as deep CNN with a range of different architectures, which is designed for decoding imagined or executed tasks from raw EEG data.[37] Fifth, we did not use CNN models to differentiate TGA from other causes of amnesia, such as TEA. Further studies with larger samples and high-resolution EEG may be needed to confirm the usefulness of deep-learning models in managing patients with TGA.

We have successfully demonstrated the feasibility of deep learning in diagnosing TGA based on EEG findings, and distinguishing between patients with recurrent TGA events and those with a single TGA event using two different CNN models. In the future, AI is expected to be useful for discovering and analyzing EEG features that humans cannot identify by themselves.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2023.19.1.36.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

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Author Contributions

Conceptulation: all authors. Data curation: Young Deok Seo, Dong Ah Lee. Formal analysis: Kang Min Park. Methodology: Kang Min Park. Supervision: Kang Min Park. Validation: Young Deok Seo, Dong Ah Lee. Visualization: Kang Min Park. Writing—original draft: Young Deok Seo, Kang Min Park. Writing—review & editing: all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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None

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