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Convolutional neural networks for traumatic brain injury classification and outcome prediction

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ABSTRACT

The detection and classification of traumatic brain injury (TBI) by medical professionals can vary due to subjectivity and differences in experience. Thus, a computational approach for detecting and classifying TBI would be invaluable for an objective diagnosis of this injury. In this review paper, various machine learning algorithms used to detect, classify, and predict the severity and outcomes of TBI in a clinical setting are discussed. The most promising of these algorithms is the convolutional neural network (CNN), which is highlighted in the review.

1. Classification of traumatic brain injury

Traumatic brain injury (TBI) is defined as "an alteration in brain function, or other evidence of brain pathology, caused by an external force" by Menon et al. [29]. This broad category of TBI is often partitioned into classes based on injury severity, which include mild, moderate, and severe. After sustaining a mild TBI (mTBI), an individual can experience symptoms such as dizziness, headaches, nausea, and trouble concentrating [41]. In cases of moderate or severe TBI, an individual can experience symptoms such as seizures, aphasia, amnesia, or even coma [41].

1.1. Glasgow coma scale (GCS)

Severity of TBI is often determined using the Glasgow Coma Scale (GCS), which measures a patient's ability to respond to cues from the following three categories: eye opening, verbal response, and motor response [9]. Table 1 provides a detailed description of the three GCS categories and the associated scores. The first category scores eye opening response from 1, indicating no response from the patient, to 4, indicating normal eye opening. The second category scores verbal response from 1, indicating that the patient is not speaking, to 5, indicating the patient is speaking normally. The third category scores physical response from 1, indicating the patient is not moving at all in response to pain, to 6, indicating that the patient is able to move easily and purposefully [9].

The scores from the three GCS categories are summed to determine the injury severity. Patients who score between 13 and 15 on the GCS are classified as having mTBI. However, patients who score between 9 and 12 are classified as having moderate TBI, and those with a score of 8 or lower are classified as having severe TBI. In addition, the GCS may be used to monitor patient recovery. For instance, changes in the GCS for an individual may be an indicator that modifications should be made to their treatment plan [9].

1.2. Brain imaging

Brain imaging techniques commonly used for diagnosis and classification of TBI are Magnetic Resonance Imaging (MRI) and Computerized Tomography (CT). MRI involves the use of magnets and radio waves to create images of the brain's structure, while CT scans are completed by taking X-rays from several angles to check for bleeding, fractures, or other visible injuries [32]. Examples of injuries that can be visualized in CT scans of patients with TBI include contusions, subdural hematoma, or subarachnoid hemorrhage [32]. Although MRI can be used to obtain images with higher sensitivity (e.g. facilitating the identification of smaller contusions and hemorrhagic axonal injury), CT scans are more often used in an initial assessment for TBI because these scans are much quicker to complete than MRI [32].

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Table 1
The Glasgow Coma Scale (GCS).

Response	Scale	Score
Eye opening	Open spontaneously	4
	Open to verbal command or speech	3
	Open to pain	2
	No eye opening	1
Verbal Response	Oriented	5
	Confused conversation	4
	Inappropriate responses	3
	Incomprehensible sounds or speech	2
	No verbal response	1
Motor Response	Obeys commands	6
	Purposeful movement	5
	Withdraws from pain	4
	Abnormal flexion to pain	3
	Extensor response to pain	2
	No motor response	1

Table 2
The Glasgow Outcome Scale (GOS) and Extended Glasgow Outcome Scale (GOSE) (Table based on [33]) .

GOS	GOSE	Description
1 = Dead	1 = Dead	Dead
2 = Vegetative state	2 = Vegetative state	Unaware of self and environment
3 = Severe disability	3 = Lower severe disability	Needs full assistance in activities of daily living (ADL)
	4 = Upper severe disability	Needs partial assistance in ADL
4 = Moderate disability	5 = Lower moderate disability	Independent, but cannot resume work, school, or social activities
	6 = Upper moderate disability	Some disability, but can partly resume work or other activities
5 = Good recovery	7 = Lower good recovery	Minor physical or mental deficits that affect daily life
	8 = Upper good recovery	Full recovery or minor symptoms that do not affect daily life

1.3. *Other tests for assessing TBI severity*

Factors that are considered when determining severity of TBI include

(i) the length of time that the patient was unconscious following the injury and
(ii) the amount of memory loss the patient experienced [32].

Other tests for assessing TBI severity focus on cognitive functions such as orientation, memory, concentration, and recall [32]. These neuropsychological assessments can be given in the form of a test battery meant to capture each cognitive domain of interest and self-report measures for the patient's mood [37]. Additionally, blood tests can be used to determine whether a mild TBI has occurred. For instance, [5] suggested that plasma tau proteins, detectable by blood tests, are released when a mild concussion is sustained. The Centers for Disease Control and Prevention (CDC) defines a concussion to be, "a type of traumatic brain injury-or TBI-caused by a bump, blow, or jolt to the head or body that causes the head and brain to move rapidly back and forth" [2]. In the literature, a concussion is often considered a type of mild traumatic brain injury [27,36,48,49].

2. Outcomes of TBI

A tool that is often used to measure outcomes and recovery after TBI is the Glasgow Outcome Scale (GOS). The scale captures how the TBI affects the patient's ability to function in different aspects of life. For example, the scale takes mental and social well-being into account, as well as assessing physical aspects of the patient's life. The score from the GOS is used to classify an individual's outcome/recovery into one of the following five categories: dead, vegetative state, severe disability, moderate disability, and good recovery [53]. See Table 2 for a description of each category.

The Extended Glasgow Outcome Scale (GOSE) was developed as an extension of the GOS. This scale divides the last three categories of the GOS (i.e. severe disability, moderate disability, and good recovery) into upper and lower categories. This eight category scale was proposed by Jennett et al. [10] in hopes of increasing the sensitivity of the GOS. In 1998, a structured interview was published by Wilson et al. [52] that improved the consistency of the assessment. This interview contained guiding questions to help with assessment of GOS and GOSE and a set of criteria for each category [53]. As a result, the published GOSE along with guiding resources provided a means to standardize the assessment of TBI outcome [53].

The GOS and GOSE are useful for assessing the outcomes of TBI, especially in severe cases. However, studies have also shown that individuals living with TBI are at an increased risk for health conditions and behaviors that are not reflected by the GOS or GOSE. For example, individuals with TBI are at higher risk for diabetes and heart disease, and those who have had a TBI are more likely to engage in risky sexual behavior, substance abuse, and suicidal behaviors [51]. These health conditions and risky behaviors suggests that the GOS and GOSE scores do not always fully reflect the outcomes of TBI or the effects TBI can have on an individual's life. Thus, this highlights some of the limitations of only using the GOS and GOSE to measure TBI outcomes.

2.1. *Machine learning for classification of TBI*

The outcomes of TBI can be life-changing, and the inflammation and chemical changes that occur afterwards can result in even worse injury; therefore, quick diagnosis and early treatment is desirable to reduce these effects [4]. As a result, the use of machine learning algorithms to aid in the detection and classification of TBI could lead to quicker diagnoses and treatments [21]. Also, interpretations of medical images by medical professionals are subjective and may differ from person-to-person based on experience level. Thus, the use of computational methods to extract key information from images and other data, such as presence of contusions or hemorrhaging, may provide a more objective solution for detecting and classifying TBI severity.

Many classical machine learning algorithms such as logistic regression [35], random forest [11,31,46], decision tree [11], naive Bayes [38], k-means clustering [22], and support vector machine (SVM) [26] have been used to detect TBI or signs of TBI, classify severity of TBI, and predict outcomes of TBI. Additionally, decision trees and naive Bayes models have been used for mortality prediction [40]. Logistic regression has also been used for mortality prediction [40] and estimation of probability of intracranial hemorrhage [31]. Random Forest models have been used to classify individuals with and without mTBI using fractional anisotropy features of different structural connections obtained from Network-based statistics [30], and to estimate the probability of intracranial hemorrhage [31] and mortality prediction [40]. SVM models have been used for detection of moderate TBI [16,17], mortality prediction in moderate and severe TBI [40], along with the classification of individuals with and without TBI [6,50].

The accuracy of classical machine learning algorithms in detecting and classifying TBI varies, which makes application of these models in clinical settings challenging. Successfully using clinically relevant models to detect and classify TBI requires machine learning algorithms that are both highly accurate and generalizable [21]. Also, classical machine learning algorithms usually require explicit feature extraction, and they are limited in the complexity of the functions they can model. However, as computers have become more computationally efficient, there has been a shift in focus towards using more computationally expensive deep learning algorithms to classify TBI.

3. Deep learning for classification of TBI

Classical machine learning algorithms usually require input features to be extracted from the data before being fed into the algorithm [20]. However, deep learning algorithms contain input and output layers that perform operations to extract features from the data that are important for a specific task (e.g. image classification or speech recognition) and suppress other features that are not important for the task [20]. Between the input and output layers of a deep learning algorithm, the data passes through several layers called "hidden layers". The hidden layers allow these algorithms to be more flexible and to model more complex functions than classical machine learning algorithms [20].

Fig. 1 depicts a type of deep learning algorithm called an artificial neural network (ANN). An ANN is a type of deep learning algorithm, which has been used to classify the outcomes of TBI patients after 6 months in [8]. In the study by Hale et al. [8], data from GCS, GOS, and CT scans were used to train an ANN to classify the outcomes for patients with TBI as favorable or unfavorable. The ANN model by [8] outperformed the Marshall, Rotterdam, and Helsinki CT classification systems in prediction of the outcomes of pediatric patients with TBI. The Marshall, Rotterdam, and Helsinki CT classification systems are methods commonly used to predict TBI outcomes based on predictive features, such as presence of lesions, from CT scans [23,24,39]. Rau et al. [40] performed a study comparing the performance of ANN, logistic regression, SVM, decision tree, and naive Bayes models in predicting mortality of moderate and severe TBI patients. The machine learning model with the highest accuracy was the ANN model.

Another type of deep learning algorithm that has been used to detect TBI, classify severity of TBI, and predict outcomes of TBI is the convolutional neural network (CNN). Fig. 1B is a depiction of the CNN architecture. CNNs were constructed specifically to learn from data that is in the form of an array or multiple arrays, such as an image [20]. Thus, this makes CNN a better candidate for learning from brain images and other types of data in the form of arrays. Since CNNs can learn directly from images, it is possible to use a CNN for classification without the process of manual feature extraction, which was still necessary for the studies by Hale et al. [8] and Rau et al. [40]. The automatic feature extraction performed by a CNN will save time, and it may allow for the use of predictive features that are not obvious to a human observer. For these reasons, CNNs have potential to be more efficient and accurate than other deep learning models for classification of TBI and prediction of outcomes of TBI. As a result, Section 4 of this review will focus on the use of CNN in TBI research.

4. Convolutional neural networks (CNN)

A convolutional neural network (CNN) is a type of deep learning algorithm that has become increasingly popular, especially for image classification [21], due to this algorithm's ability to find patterns in images.

Fig. 1 B shows a traditional CNN architecture where the first part of the algorithm is composed of convolutional layers and pooling layers, whose purpose is to extract key features from the image [7]. The second part of most CNN algorithms (Fig. 1B) is composed of the fully-connected layers, which serve to perform the classification. The CNN architecture resembles the organization of the visual pathway in the brain [20]. This is due to the fact that the CNN was developed based on the animal visual system [7]. Specifically, the operations of the layers in the CNN were inspired by the functions of simple cells and complex cells in the visual system. The effectiveness of the CNN was proved in the ImageNet Large Scale Visual Recognition Competition in 2012. In this benchmark object category classification challenge, a CNN achieved record breaking accuracy [14,44]. Thus, CNNs have the potential to classify and detect TBI using data from MRI, CT scans, calcium imaging, and electroencephalogram (EEG). Also, CNN models have been used to detect hematomas, cerebral microbleeds, and other lesions that commonly occur with TBI. The sections below detail how CNNs have been used for the classification and/or detection of TBI.

4.1. CNNs with brain images

Koschmieder et al. [13] used a CNN to detect cerebral microbleeds in susceptibility-weighted MRI scans of patients with moderate to severe TBI. Their most effective model achieved 90% detection rate with a low count for false positives in both TBI patients and controls. Also, [43] used a CNN model to segment contusions and lesions from MRIs of brains of patients with mild to severe TBI. To evaluate the performance of their models, they used the Dice Similarity Coefficient (*DSC*), which measures how much the model's segmentation overlaps with the actual segmentation [56]. If A and B are regions in our image, then the Dice Similarity Coefficient of A and B, $DSC(A, B)$ is defined by

$$DSC(A, B) = \frac{2|A \cap B|}{|A| + |B|}.$$

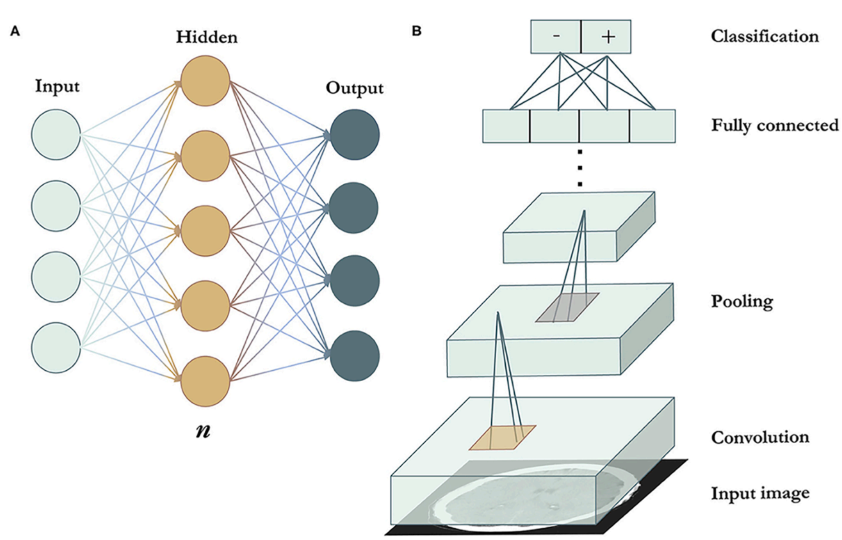

Fig. 1. (A) is a representation of an ANN architecture with one hidden layer. (B) is a representation of a CNN architecture where a convolutional filter is shown in gold and a pooling filter is shown in silver. The final layers are the fully connected and output layers. Figure from Lin and Yuh [21] (Frontiers in Neurology) used under Creative Commons CC-BY license.

This value is in [0,1], and a Dice score close to 1 indicates significant overlap between the regions and an accurate segmentation [56]. Their proposed model achieved a median Dice of 0.75, which was better than the performance for a Random Forest model that was trained to do the same task. These studies suggest that brain MRIs can capture features, such as presence of microbleeds and brain lesions, which is relevant in determining the presence of TBI.

An adaptation of a CNN algorithm that applies sequences of arrays, such as videos or volumetric images, as input is referred to as a 3D-CNN architecture [20]. Mattia et al. [25] used 3D-CNN to classify patients as postanoxic coma patients and controls using structural MRI and functional MRI. Their 3D-CNN model achieved a 96% accuracy, and although their dataset was small, containing data from 63 subjects, their results suggest that functional MRI data offers important information (e.g. functional connectivity [34]) that leads to better performance. Also, the study by [25] showed that 3D-CNN may be useful for classification tasks with brain MRI since their model achieved such high accuracy.

Yao et al. [55] trained a CNN to detect hematomas in patients with TBI using CT images and an image segmentation technique. During the image segmentation process, the CT images are divided into parts (e.g. hematoma or not hematoma) and labeled to identify objects such as regions with brain hematoma and regions without brain hematoma. Their segmentation model using CNN had a high accuracy compared to other models (e.g. the IMPACT model) on the same data. This suggests that CT scans may also be used to detect signs of TBI, such as hematoma, and CNN models are an effective method of detection.

4.2. CNNs with calcium imaging data

Detecting mTBI from MRI and CT scans is challenging because mTBI does not often cause structural changes in the brain that are clearly visible via MRI or CT scans [47]. As a result, some researchers have turned to other types of imaging data to detect mTBI. For instance, calcium imaging has been considered as an alternative for detecting mTBI [12,45]. Calcium imaging is a method of viewing changing concentrations of calcium in the brain, which are linked to electrical activity of neurons [42]. Studies have shown that mTBI may cause changes in functional connectivity in the brain, and these disturbances may be observable through calcium imaging [45].

Calcium imaging data can also be used with the Long-Short Term Memory (LSTM) learning algorithm, which is a type of deep learning algorithm composed of loops of networks that allow information to persist from one network to the next [15]. As a result, it is possible for the LSTM model to capture spatio-temporal features in the calcium imaging data [12]. A CNN-LSTM is a network that uses a CNN to extract features from images that are then fed into a LSTM model. [12] used CNN-LSTM and 3D-CNN on widefield calcium imaging data from mice to classify images as being from a mouse with mTBI or a healthy mouse. The performances of these models were compared to the performances of CNN and SVM on the same data, and the results showed that the CNN-LSTM performed the best, with an average accuracy of 97.24%, followed by 3D-CNN, CNN, and SVM, in that order. [45] also used calcium imaging data to train a CNN. For this study, the calcium images were first used to create functional connectivity networks, which were then represented by images that were used to train the CNN to classify images as coming from a mouse with mTBI or a healthy mouse. This model also achieved a high accuracy of 95%. For both the studies by Koochaki et al. [12] and Salsabilian and Najafizadeh [45], the dataset was quite small, with imaging data coming from less than 10 mice. Their results indicate that a larger scale study should be pursued since their results were promising, but their small dataset means that their results may not be generalizable.

4.3. CNNs with EEG data

Brain imaging equipment to acquire MRI and CT scans can be expensive and the process of acquiring brain scans can be time consuming [18]. Since there are such a high number of patients with TBI, it may be more practical and affordable to collect EEG data from the patient to detect TBI severity. Several studies have shown that the use of EEG to train CNNs for the classification of TBI may be possible [18,19].

The usual input for a CNN is an image [18] and although an EEG does not produce an image, the collected EEG data can be formatted into a matrix for use as input for the CNN. For instance, [18] and [19] let each row of the input matrix for the CNN correspond to a channel of the EEG output. Additionally, each entry of the row corresponds to the amplitude of the EEG wave at a specific time. This method of formatting the EEG data as a matrix allows the CNN model to consider the dependency of the distinct EEG channels, where as other machine learning algorithms (e.g. logistic regression, SVM, ANN, etc.) would consider these to be independent of one another.

Lai et al. [18] used resting-state eye-closed EEG data to train a CNN to classify healthy patients versus patients with moderate TBI, and this method achieved 72.46% accuracy. In 2021, [19] used EEG data to train a CNN with error-correcting output codes SVM (ECOC-SVM) to classify patients as a healthy patient, a patient with mild TBI, or a patient with moderate TBI. The ECOC-SVM is an adapted version of an SVM that allows the model to perform multi-class classification since SVM is a binary classifier by itself [19]. Their model outperformed two previous methods used by Lai et al. [17] and Lai et al. [16], where EEG data was used to train a SVM for a similar task. This model also performed better than the methods used by McNerney et al. [28], which involved the use of EEG data to train a machine learning algorithm called boosting to classify individuals as injured or as controls. A boosting algorithm trains a new classifier at each iteration and then combines the models to create one classifier with higher accuracy [28].

5. Limitations

5.1. Dataset size

Most studies that have used brain imaging or EEG data to train CNNs, or other machine learning algorithms, considered relatively small datasets, such that the results are not statistically significant or generalizable [25]. However, for the results from the CNNs to become generalizable, it is important to have a dataset that is balanced and sufficiently large [1]. Due to privacy concerns and the resources required to collect brain imaging or EEG data, the lack of availability of large datasets is difficult to overcome. However, a possible solution could involve more anonymization of patient data so that it may be made publicly available.

5.2. Data leakage

Another important issue to avoid in any machine learning study is data leakage. Data leakage involves training your model using a feature (or multiple features) that has the result you are trying to predict hidden within itself [3]. For example, if a model is being trained to predict patient diagnosis, then using data about the treatment received in the training data, would lead to data leakage. The treatment received by a patient gives the algorithm information about the diagnosis which would not have been known until after the diagnosis. This leads to models that have reports of high performance during training and testing but fails to generalize.

Data leakage can also occur during cross-validation, which is common practice in many machine learning studies. Yagis et al. [54] determined that cross-validation had a severe affect on the reported performance of many CNN models that were used to classify MRIs from patients with Alzheimer's Disease versus healthy controls and in CNN models that were used to classify patients with Parkinson's Disease versus healthy controls. Specifically, the use of a slice-level training/testing split during cross validation, instead of a subject-level training/testing split, led to significantly inflated accuracy. A slice-level split involves breaking the MRIs into their individual slices and then randomly dividing the slices between training and testing sets such that slices from any subject may be in both the training set and testing set. This leads to data leakage because of the high intra-subject correlation between slices, and the effect of this type of data leakage on the accuracy of the model is even worse when the data set is small. Therefore, in attempts to use CNNs to classify patients with TBI versus healthy controls, a subject-level training/testing split, where subjects are randomly divided into training and testing sets, should be used, and other forms of data leakage should be avoided by carefully preprocessing the data.

6. Conclusion

There is a need to remove the subjectivity when classifying TBI to improve the accuracy of the predicted outcomes. CNN is a viable approach for detecting and classifying TBI to achieve an objective diagnosis of this injury. Many attempts to use classical machine learning methods have shown promise, but they usually involve manual feature extraction, which is time consuming and dependent on human observation. There is evidence that deep learning methods such as the CNN work better than classical machine learning methods for classification of TBI and prediction of outcomes of TBI. Since CNNs are able to perform automatic feature extraction from images (e.g. MRI, CT, and calcium imaging data) and other arrays (e.g. EEG data), this deep learning method is quicker and easier to implement when compared with classical machine learning methods. Furthermore, the structure of CNNs facilitates the classification and predictions of TBI outcome based on spatio-temporal factors, which makes this method better suited to capture important features in 3D images and EEG data obtained from TBI patients. Future work in this area should explore ways of improving the accuracy and generalizability of CNN models in detecting and classifying signs of TBI while avoiding data leakage. More work on developing models that accurately predict the outcomes of TBI would be beneficial in the future as well.

CRediT authorship contribution statement

Laura Zinnel: Writing – original draft. **Sarah A. Bentil:** Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no conflict of interest, nor any known competing financial or personal relationships that could have influenced this paper.

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