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Machine Learning, Ethics and Brain Death Concepts and Framework

Alok Dabi[1*] and Andrew J Taylor [2]

[1]Assistant Professor, Neurology and Neurosurgery, University of Texas Medical Branch, Texas, USA

[2]Ph.D. Student, Medical Humanities Graduate Program, Institute of Medical Humanities, Graduate School of Biomedical Sciences, University of Texas Medical Branch, Texas, USA

[*]**Corresponding author:** Dabi A, Assistant Professor, Neurology and Neurosurgery, Director Neurosciences Critical Care Program, University of Texas Medical Branch, Galveston, Texas 775555, USA, Tel: 409-772-8053; E-mail: aldabi@utmb.edu

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Abstract

Use of artificial Intelligence and Machine Learning-assisted clinical algorithms that help predict the clinical outcome and influence clinical decisions is rising. In future, it may lead to an ethical confusion when medical decisions influenced by their use lead to 'Death by Neurologic Criteria (DNC) or 'Brain Death.' Therefore, appropriate steps need to be taken preemptively to try and resolve it before it leads to public mistrust about this technological advancement that has immense potential to improve the quality of healthcare while making it more affordable and efficient. This review aims to describe the concept of Machine Learning assisted clinical algorithm, related ethical issues and the framework in which it can be used in relation to DNC cases.

Keywords: ***Deep learning; Machine learning; Brain death; Death by neurologic criteria; Ethics***

1. Introduction

Use of Artificial Intelligence (AI) algorithms has recently seen a steady increase in various aspects of daily life, including smart phone AI assistants like Siri, self-driving cars, web mapping services etc. Not surprisingly, the healthcare has also witnessed the use of Artificial Intelligence, and it is expected to rise exponentially in the near future.

Artificial intelligence is defined as a branch of computer science that attempts to understand and build intelligent entities, often instantiated as software programs. It includes categories like Machine Learning (ML), which is a branch of computer science that uses algorithms to identify patterns in data. Deep Learning (DL) is a subspecialty of Machine Learning, that employs artificial neural networks (NN) with many intervening layers to identify patterns and data [1]. Since its first mention at Dartmouth conference in 1956, AI has come a long way, with an exponential increase in the interest, research and its application in healthcare in the last several years, and with an expected continued rise in many aspects of medicine in future [2].

Deep Learning has been found to be better at the prognostication of the patient outcome than other types of AI programs. DL models have a framework of an input layer (called features), and an output layer (called labels), with intervening hidden layers (sometimes referred as 'the black box' due to their inherent lack of operational transparency and causal insight) [3]. The number of these 'hidden' layers can be a few to over hundred. Each layer can involve thousands of connections, resulting in calculations involving millions to hundreds of millions of parameters. Technological advances have made such calculations possible and relatively affordable. Once trained on labeled data to help identify input-output correlation, these algorithms can then be applied to new data. This format is called 'Supervised machine learning'. In 'Unsupervised machine learning', the algorithm tries to identify patterns in unlabeled data with an aim to find sub-clusters within the original data or detect data outliers or form low-dimensional data representations [1,4] (FIG. 1).

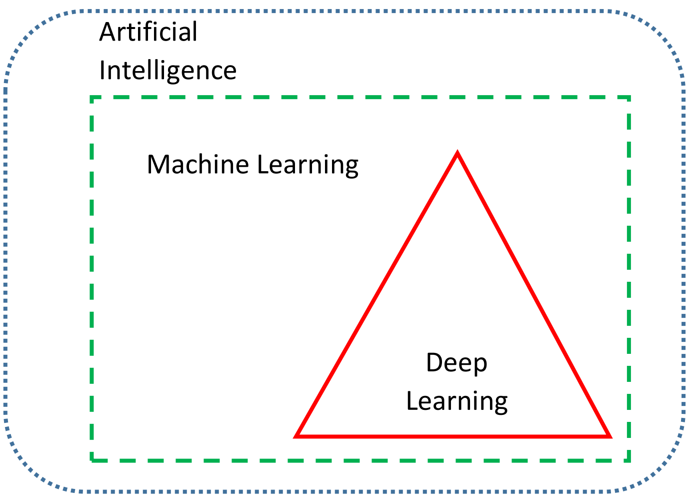

FIG. 1. **Artificial Intelligence, Machine Learning and Deep Learning [5].**

2. Machine Learning Applications in Healthcare

Common applications that include but not limited to are: improved diagnostic modalities, better therapeutic interventions, creation of a smoother workflow in processing of the enormous electronic health record (EHR) data and more accurate clinical prognostication [6]. They can also be used to provide basic clinical triage in areas inaccessible to specialists due to geographic or political isolation [7]. Use of Machine Learning based apps that are trained to detect the mood and mental state of the psychiatry patients by analyzing their speech or facial expressions can be helpful in early detection of potentially treatable psychiatric conditions and therefore help in prevention of certain dangerous outcomes like suicides [8-11].

Deep Learning algorithms have been found to be very effective, even better than human diagnoses in fields like radiology, ophthalmology, dermatology, pathology, which all rely on image-based diagnosis, or in electroencephalogram interpretation, that needs pattern recognition similar to imaging. It has also found use in fields where there is enormous amount of data that can be too overwhelming for human brains to process, for example, genome interpretation or prognostication using the entire hospitals' Electronic Health Record (EHR), or even nationwide EHR data [12,13]. Similarly, the expected data surge generated from the future personal wearable sensors and devices would only be manageable and interpretable with the use of Machine Learning algorithms [1,14].

3. Problems Related to Machine Learning Use in Healthcare

Despite the many benefits of Machine Learning use in healthcare, it does present a unique set of challenges, that need to be overcome before its wider acceptance. As Machine Learning algorithms involve large volumes of high-quality training data, accuracy of this input data is vital. This problem can be resolved by using sophisticated algorithms that can handle 'noisy' data sets without affecting the reliability and accuracy of the prediction models [1].

The "black-box" format of the Machine Learning algorithms makes them intuitively less trustworthy. There is an active research ongoing by the technological companies to make the Machine Learning 'explainable.' This concept now called as "Explainable AI" (xAI) would involve the hidden layers to have human comprehensible 'model' and 'interface' to better understand the underlying technique, its strengths and weaknesses (FIG. 2). This is expected to unveil the 'third-wave AI systems' with applications in Medicine, but also in defense, finance, security and transportation [3,15].

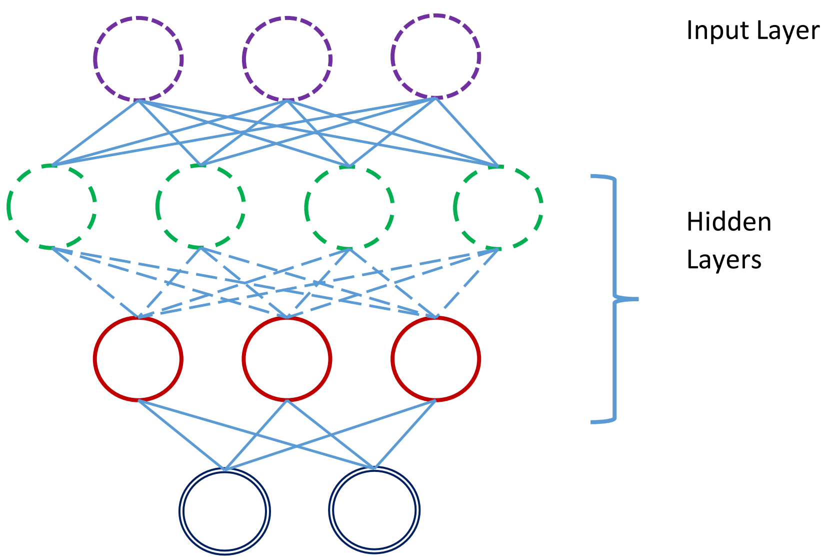

FIG. 2. **Deep Learning architecture with its component layers.**

Many of the ML algorithms generate results that may be too difficult for human interpretation. ML algorithms generate the output data mostly in the form of area-under-the-curve (AUC). Due to this and the basic architecture of these 'black-box' algorithms, it is difficult to compare and validate them in the traditional format of prospective randomized controlled trials. This may be a drawback in their validation and certification, wider application and formulation of official guidelines related to their use unless technological companies and healthcare authorities are able to figure out a practical solution for this problem. Besides, by nature, the ML models are made to improve continuously with time, therefore their certification will potentially need frequent updates. The FDA (Food and Drug Administration) has announced in 2018 to indicate that it may prefer ‘pre-certified’ approach for such software to rectify this problem [1].

AI assisted calculation of clinical data needs to be integrated with other pertinent patient-information (like patient preferences, values, social and cultural norms, faith and belief systems, social support structure, etc.) for full utilization of its potential. Better algorithm designs that can integrate all the relevant inputs can help overcome this obstacle [1].

A smooth integration of the Machine Learning applications in Medicine will also need adaptation on part of the clinicians and patients with the expected change in person-to-person communication format, perceived extra workload from ML generated alerts, additional work up needed due to false positive alarms and concern about missed alert/diagnoses due to false negative ML algorithm results. Once these algorithms are proven to be at par or superior to human clinical decision making, then their acceptability will slowly improve. It is possible that certain subspecialties will adopt these algorithms much earlier than others, example imaging-based or pattern recognition-based fields. Remote areas with lack of physicians are also likely to be early adopters [16].

In the current environment with significant public concern about the consumer privacy, there is concern about the ownership of the enormous amount of healthcare data that is likely to be generated, processed and utilized to make meaningful use of Machine Learning applications. The infrastructure required and the cost of establishing and maintaining such complex computational devices will make it unaffordable to individuals or small healthcare setups. Most likely, the data will be owned by large technological companies, who may potentially decide to distribute and sell it to the third parties for profit. Data hack or leak by rogue individuals or nations may lead to a complex financial and socio-political situation. Having strict policies about ownership with robust data protection strategies can help boost the public confidence in such systems.

Due to the excess cost attached to this, the healthcare setups are at risk of further segregating along the economic lines. Large institutions with big budget may be able to afford them while the smaller clinics and hospitals may lag. This will potentially lead to restructuring of the healthcare with mergers and the collapse of smaller hospitals.

During the initial stages of its use, the Machine Learning algorithms will incur extra cost. The insurance companies are likely to hesitate in bearing this extra financial burden. Once these algorithms are established as part of the ‘standard of care’ (due to their status of being at par or superior to an average clinician), the insurance companies may then impede the clinical decision making if the physician or the patient decides against what the ML algorithm suggests. They may refuse to pay in such situations thus incurring huge costs to the patients and the hospitals.

If there is an unfavorable outcome when ML algorithm assisted clinical decisions are made, then the proportion of responsibility shared between the ML developer, the ML interpreter, the physician and the patient will need to be determined. This can be preemptively dealt with by training the ML- assisted Clinical teams by having mock clinical scenarios and practice runs, possibly even official certification courses (TABLE 1).

TABLE 1. **Machine Learning-assisted algorithmss- Potential problems and proposed solution.**

Machine Learning algorithm – potential problems	Proposed Solutions
Lack of high-quality input data	New sophisticated software that can handle 'noisy data'
'Black Box' format of Deep Learning	Explainable Artificial Intelligence
Difficulty in validation of ML-assisted algorithms	'Pre-certification' of the algorithms by the FDA
Integration with pertinent patient information	Better algorithm design
Human adaptation to ML-assisted healthcare	Medical staff education, training and Certification courses
Ownership and Privacy concern about ML data	Formal regulations by the legislature
Role of Insurance companies and ML-assisted health care financing	Formal regulations by the legislature
Public misperception about the ML-assisted algorithm	Public education via media, internet and social media

4. Brain Death/ Death by Neurologic Criteria

Brain Death {also known as "Death by Neurologic Criteria (DNC)" or "Neurologic criteria for Death"} is defined as 'the clinical state that involves an apneic patient with irreversible coma and absent brainstem reflexes' [17]. It involves 'irreversible cessation of all functions of the entire brain, including the brainstem'. This definition is commonly used in the United States and many European countries, with emphasis on the 'irreversibility' of the coma, where the organism as a 'whole' cannot survive in the absence of artificial life support [18,19].

Physicians invariably and not incorrectly have doubts at some point of time during the decision-making process about the prognostication of 'Death by Neurologic Criteria'. This is highest when the patient is initially admitted, due to the relative lack of clear baseline information with an incomplete understanding of the pathophysiology of the underlying lesion and comorbidities. This doubt also depends on the various diagnostic and therapeutic modalities and interventions available, their utility, risks and expected benefits etc. Expected quality of life and the likely best and the worse possible functional outcomes are important. The physician confusion and doubt about prognostication may also arise due to 'anecdotal' personal experience, personal faith and belief, personality traits, past mistakes, duration of the clinical experience of the individual physician or the collective experience of the team involved, etc. Known and implicit bias by the physicians and their emotional state on that given day may also influence their opinion [20].

In developing nations, additionally the cost of the health care interventions to the family significantly affects the decisions by the family members. This makes it difficult to compare the DNC data from the developing and developed countries [21].

5. Machine Learning Algorithms and their Potential Role in Death by Neurologic Criteria Decisions

The aim for a physician is to improve the clinical outcome of a given patient, and prevent mortality, if possible. Therefore, there is always an attempt to try and predict the chances of mortality, so that the level and urgency of care provided can be escalated if needed. It also helps in efficient allocation of the limited healthcare resources available and to appropriately utilize the palliative care services when indicated.

The Machine Learning models are likely to become better in the next few years at predicting the patients' outcome including mortality of critically ill patients. This paradigm, particularly in the Neurocritical Care units, will be thus predicting the chances of 'death by neurologic criteria (DNC)'. This has the potential to create a state of confusion with ethical and legal dilemmas, including the public, when there is already an element of mistrust and misunderstanding about the DNC. However, this can also be a great opportunity to improve healthcare, if the legislature and the medical fraternity, especially the neurointensivists, develop and apply appropriate policies preemptively regarding AI, ML and DL use in the patient care [22].

Most of the current ML software can predict outcome of patients with ICU (intensive care unit) admission much earlier and better than the standard clinical outcome predictor scales [23,24]. This can be helpful in more efficient allocation of resources, improving the healthcare quality to the patients and reducing the futility of care. It may also be helpful to prepare the patient and/or the family members much earlier about the likely outcome [25]. If warned in time, the palliative care can be initiated for appropriate patients, saving them from unnecessary medical interventions, that may be uncomfortable at the least, and most likely will not impact their long-term outcome in a positive manner [26-28].

Most patients would like to die in their own homes given a choice, yet in the end, almost all die in an institution. A significant proportion of terminal cases may progress to what is called as 'state worse than death'. This is usually described by the patients' or their families as a state of severe disability, with associated social isolation, incontinence, dementia, chronic intractable pain, total dependence for daily care and with a need for advanced technological life-support for sustenance of their lives. Most such patients would choose death over such outcome [29]. Machine learning algorithms can help predict quality of life outcomes much better than the traditional clinical score systems. This can prevent the discomfort that these patients have to go through if they reach such a state [30].

Early prediction of the likelihood of Death by Neurologic Criteria of the donor candidates is vital to coordinate with organ transplant teams. With a uniform, national ML-assisted healthcare software, the physician teams would be able to match prospective donor candidates with patients in need much earlier, if the latter's clinical and genomic data is already uploaded in the healthcare data cloud.

Donor candidate patients for 'Donation by Cardiac Death' (DCD) are a clinical challenge for many intensivists due to the medico-legal parameters regarding the expected time of cardiac arrest post withdrawal of care [31]. With the help of better prognostic ML algorithms, it may be possible to have much better control over the selection of the donor candidate and to appropriately time the withdrawal of active care to improve the yield and the outcome of the organs harvested [32,33]

6. Public Opinion and the Use of Machine Learning Algorithms

The media portrayal of the DNC and the use of ML-assisted algorithm can play a huge role in shaping the public opinion on this vital issue [34,35]. Based on the popular television series in the past, the public perception about post cardiac arrest resuscitation was found to be overoptimistic. This led to unrealistic patient and family expectations about post resuscitation clinical outcome. Similar confusion regarding the ML-assisted algorithms and their use in DNC prediction is avoidable. Pre-emptive formal legislative policy formulation with stress on correct media depiction of this sensitive issue can be very helpful in educating the public. In case of certain media institutions' claim for the need to exercise their 'right of creative freedom', they may be allowed provided they display a disclaimer certificate accepting that their version of Death by Neurologic Criteria is fictional.

If a high profile DNC case and associated media controversy is on-going, it would be helpful for the professional medical societies to reach out to public using different forums (including newspaper, news channels, online and social media outlets etc.) to provide clear, reliable, detailed, medically and legally accurate information in order to educate the masses. This will help in clarifying doubts and improving the public trust and confidence [36,37]. Similar use of these outlets for public education during the current Covid-19 pandemic is a great example of their appropriate use.

7. Conclusions

Death by Neurologic Criteria remains a sensitive issue with potential for significant public and media controversy if mishandled. Use of Machine Learning-assisted clinical algorithms in near future is likely to increase the chances of triggering controversy if their use leads to change in medical decision in a patient, who has a poor outcome. The ethical issues thus arising are likely to have complex social, cultural, religious and financial implications for all those involved. Anticipating and preparing for such possibilities with formulation of official policies by the medical professional societies along with an active public education campaign can help full utilization Machine Learning clinical algorithms.

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