Stroke Risk Stratification Using Neural Networks

Shrikant Pawar

Abstract Current primary stroke preventive strategies seem insufficient in light of the increased prevalence of stroke, the steady or increasing death rates from cardiovascular illnesses, and the expanding list of stroke risk factors. A class of computer algorithms known as machine learning (ML) can learn from data without having to be explicitly programmed. To predict stroke and its effects, a number of physiological and clinical indicators have been used. A cyber-physical stroke rehabilitation system (CP-SRS) as well as the modified Rankin Scale (mRS90) and National Institutes of Health Stroke Scale (NIHSS24) have both been predicted using ANN models. The results of this study indicate that neural networks might create a new and efficient way to categorize stroke patients' risk.

Keywords Neural network · Stroke · Prediction

1 Introduction

Stroke is the world's largest cause of death and disability, with a lifetime risk of 25% [1]. Ischemic heart disease, according to the World Health Organization is one of the main cause of deaths worldwide. The second and third most frequent causes of mortality are stroke and COPD, respectively. 89% of DALYs and 86% of fatalities worldwide in low- and middle-income countries are caused by stroke. Given the increasing prevalence of stroke, the steady or rising death rates from cardiovascular diseases, and the growing list of stroke risk factors, current primary stroke prevention methods look insufficient. Machine learning (ML) refers to a data-learning classes

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S. Pawar (✉)
Department of Computer Science, Claflin University, Orangeburg, SC 29115, USA
e-mail: spawar@claflin.edu

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of computer algorithms without being explicitly programmed. Several early studies [2–6] have used machine learning to predict stroke lesions. A number of physiological and clinical parameters have been used to predict stroke and its effects. Lin et al. [7] developed a hybrid artificial neural network with a tenfold cross-validation to achieve a 0.94 AUC in both ischemic and hemorrhagic stroke using preadmission and inpatient data. When follow-up information was added, the prediction's accuracy rose to 0.97 AUC. They screened 206 clinical variables with little performance loss to identify 17 important features from the ischemic stroke dataset and 22 critical traits from the hemorrhagic stroke dataset [7]. Support vector machines have also been utilized to forecast motor and cognitive recovery during rehabilitation therapy during the early stage of stroke, as well as to evaluate the cost-benefits of thrombolysis and thrombectomy therapy during the acute stage of stroke [8, 9]. For high-risk undiagnosed family members of familial hypercholesterolemia, random forest (RF) has also been employed to speed up early diagnosis and rapid intervention [10]. RF for imputation and automated hyperparameter optimization (AutoHPO) has been utilized to predict stroke, with an ACC of 71.6% and a sensitivity of 67.4% [11]. Other classification techniques include spiking neural networks (SNNs) for personalized modeling of spatio-temporal data (SSTD) and event prediction, artificial neural networks (ANNs) for early atherosclerosis diagnosis and to determine whether a perfusion deficit exists and where it will be located on CT perfusion images, and kNN to find a gene expression pattern that is distinct in peripheral blood that may aid in the early identification of a stroke [12–15]. Additionally, ANN models have been developed to forecast the modified Rankin Scale (mRS90) and National Institutes of Health Stroke Scale (NIHSS24) as well as to validate the cyber-physical stroke rehabilitation system (CP-SRS) [16, 17]. The findings of the present study suggest that neural networks may develop a novel and effective method for classifying the risk of stroke patients.

2 Materials and Methods

2.1 Study Design and Subjects

This study used data from Lee et al. [18]'s observational cohort study based on electronic health records. From January 2012 to December 2015, this observational cohort study using electronic health records was conducted in a tertiary referral hospital. The tertiary stroke center's treatment met the standards set forth by the Brain Attack Coalition, and the stroke unit also held certification from the Korean Stroke Association. With a population of around four million, the regional emergency medical center provides care to the southern portion of Gyeonggi Province in South Korea, and its emergency room (ER) sees about 89,000 patients yearly

[18–20]. All patients' stroke diagnoses were made according to three categories: true stroke, ischemic stroke, hemorrhagic stroke, and non-emergent vs. emergent large vessel occlusion. After reviewing the ER file, imaging results, and laboratory test results for potential differential diagnoses, the conclusive stroke diagnosis was made. When the neurologic evaluation and imaging data from CT and/or magnetic resonance imaging, including diffusion weighted images, were in agreement, a true stroke was recognized. True stroke and ischemic stroke are two different types of transient cerebral ischemia event. When the clinical data was consistent with non-vascular etiologies, stroke mimics were discovered. A significant arterial occlusion and hemorrhagic stroke were both confirmed by the initial CT angiography. The internal carotid artery, the M1 or M2 portion of the middle cerebral artery, or the basilar artery are all examples of ELVO [21, 22]. In the end, 11 variables were taken into consideration for training, including infarct lateral, infarct site, gender, age, seizure absent, starting glucose, systolic blood pressure, diastolic blood pressure, pulse rate, body temperature, and arterial oxygen saturation (SaO_2). The supplementary file section has a download link for the data used. A total of 900 males and 660 females had their data collected. Table 1 gives the distribution of the various variables. On average, ages, initial glucose, systolic blood pressure, diastolic blood pressure, pulse rate, body temperature, and SaO_2 for males were 61.83, 149.90, 147.94, 85.52, 83.17, 36.47, and 99.55, while for females, it ranged from 66.62, 144.55, 147.20, 85.48, 83.31, 36.52, and 99.32, respectively.

3 Training and Testing

In this study, we used a three-layer multilayer perceptron (MLP) model, consisting of an input layer with 11 independent variables, a hidden layer with a set number of neurons that were tuned by training, and an output layer that shows the likelihood of the principal outcome. By iteratively updating the weights between the neurons, a backpropagation technique was utilized to minimize the loss function and maximize the model's ability to predict the primary outcome. Between predicted and actual values, there is discrepancy, which is represented by the loss function. In view of the relatively small sample size, training of neural networks was performed using backpropagation [23] with a 3, 5, and tenfold splits for training and testing/validation data. Different constant learning rates (lr's) in range of 0.00001–0.19 were tested to find the optimal lr with minimization of the loss function, with higher lr's the accuracy was seen to decrease (Fig. 1). A steady accuracy (0.89) seen with lr's 0.00001–0.01 was eventually selected for final training. Data normalization was necessary for continuous independent variables in order to locate the best solution faster. In order to scale variable data, the max–min technique was used [24]. The study cohort included an uneven distribution of patients who had or did not have a

Table 1 Distribution of different training variables

	Age			Initial glucose			Systolic blood pressure			Diastolic blood pressure		
	Mean	Min.	Max.	Mean	Min.	Max.	Mean	Min.	Max.	Mean	Min.	Max.
Male ($n = 900$)	61.83537	15	94	149.9021	30	1065	147.9455	60	300	85.5228	33	140
Female ($n = 660$)	66.62424	18	99	144.5591	32	518	147.2045	70	263	85.48333	36	687
	Pulse rate			Body temperature			SaO_2					
	Mean	Min.	Max.	Mean	Min.	Max.	Mean	Min.	Max.			
Male ($n = 900$)	83.1733	32	180	36.48022	34.4	40.2	99.55061	50	100			
Female ($n = 660$)	83.31152	33	162	36.52424	31.4	40	99.32879	50	100			

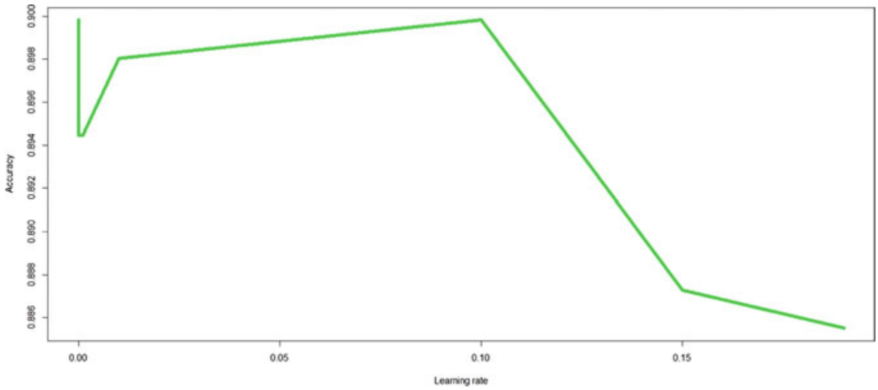

Fig. 1 Different tested learning rates and their accuracies

primary outcome. This might skew predictions in favor of the non-recurrence group. As a result, we randomly chose a 1:1 matched number of patients for training and testing who did not have a primary outcome and those who did. We choose to generate 13 different networks, each for prediction of stroke, hemorrhagic stroke, ischemic stroke, and stroke outcomes like affection of one side face, one side arm, one side leg, asymmetry, not ambulating, not able to speak, not able to grasp, visual disturbance, abnormal sensation, and mental change. Evaluation was performed using accuracy, precision, sensitivity, specificity, and fscore metrics on validation set. The training code can be accessed from the supplementary section.

4 Results

From total 1560 patients, 1153 subjects had stroke, 895 had ischemic type, 259 had hemorrhagic type, 473 had one side face affected, 965 had one side arm affected, 840 had one side leg affected, 1163 had asymmetry, 587 were not ambulating, 762 were not able to speak, 243 were not able to grasp, 22 had visual disturbances, 218 had abnormal sensation, and 349 had mental changes. Approximately, 74% subjects were affected with stroke, and this number matched with remaining non-stroke subjects is a reasonable training size to generate neural network on. With only stroke outcome, infarct size and diastolic blood pressure constituted maximal weights on trained network (Fig. 2). For predicting all other outcomes, stroke outcome was considered as an additional input variable on trained network. For only hemorrhage outcome, stroke and age; for only ischemic outcome stroke; for only abnormal sensation outcome stroke, infarct site, body temperature; for only asymmetry outcome infarct site, systolic blood pressure; for only mental change outcome, body temperature and

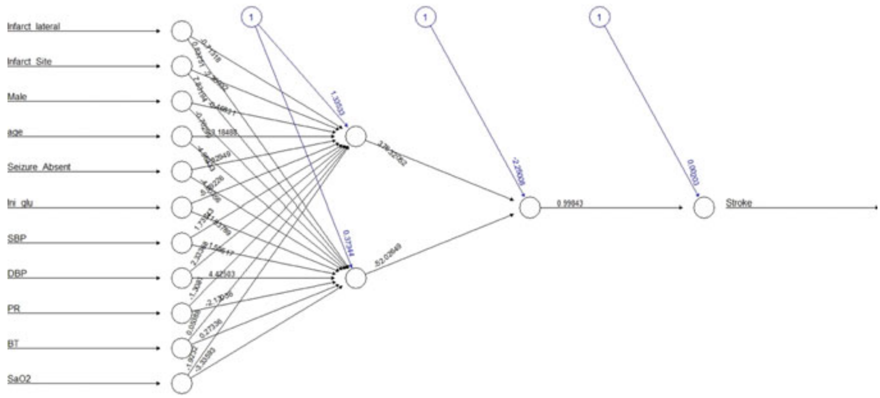

Fig. 2 Trained network for only stroke outcome

SaO_2; for only not able to grasp outcome, infarct lateral, gender, initial glucose, body temperature and SaO_2; for only not able to speak outcome, age, diastolic blood pressure, body temperature, and stroke; for only non-ambulating outcome, diastolic blood pressure, infarct lateral; for only one side arm outcome, gender, age, and SaO_2; for only one side face outcome, body temperature, age, and stroke; for only one side leg outcome, infarct lateral, and gender; and for only visual disturbance outcome, infarct lateral and body temperature contributed maximal weights (Fig. 3). A three, five, and tenfold validation metrics are provided in Table 2 for only stroke outcome. Surprisingly, with only 1560 subjects, we were able to achieve a stroke prediction accuracy of 0.89, sensitivity of 0.95, specificity of 0.70, f score of 0.92, and precision of 0.90. With other sub-outcomes, visual disturbances followed by abnormal sensation, mental changes, not able to grasp, and hemorrhagic had maximal accuracies (Table 3). Prediction of ischemic stroke had minimal accuracy. Several other variables like nutrition, seizures, cardiac evaluation, etc., not considered in this training constitute risk factors for ischemic stroke [25]. This may be one of the reasons for poor ischemic stroke prediction accuracy when compared to other outcomes.

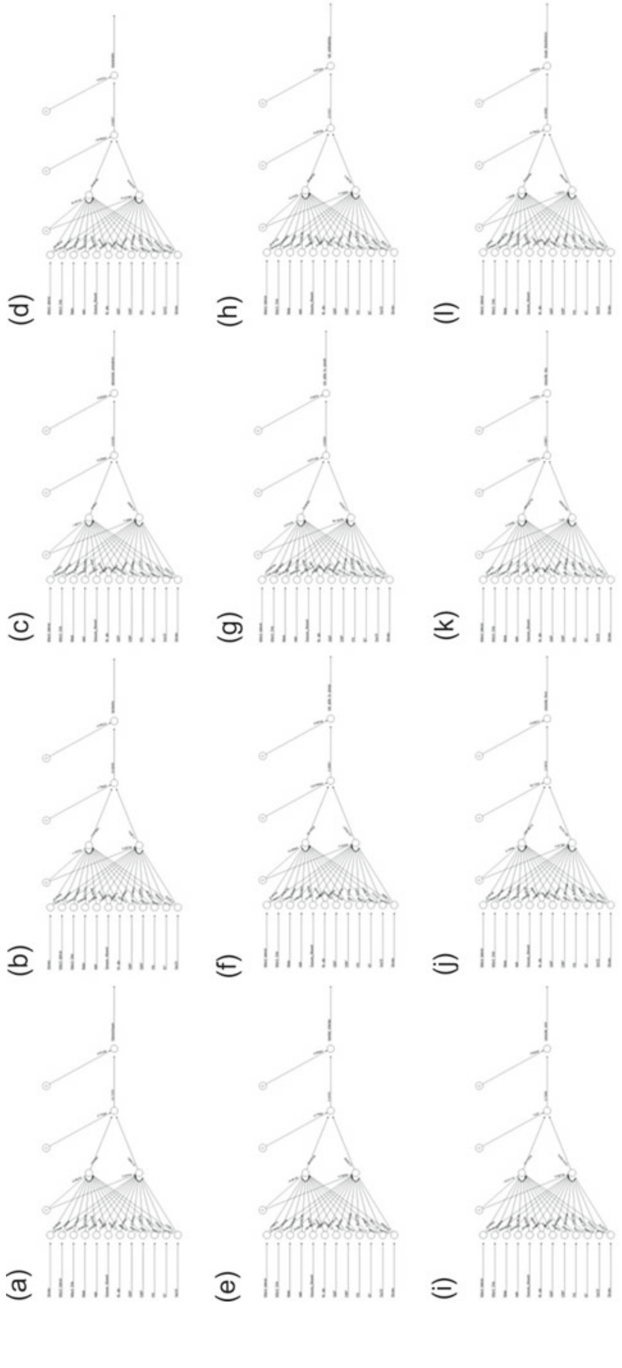

Fig. 3 Trained networks for 12 outcomes

Table 2 Three, five, and tenfold validation evaluation metrics for stroke prediction

Metric	Threefold stroke	Fivefold stroke	Tenfold stroke
Sensitivity	0.95	0.94	0.94
Specificity	0.70	0.71	0.74
f score	0.92	0.93	0.93
Precision	0.90	0.91	0.92
Accuracy	0.89	0.89	0.89

5 Discussion

There are some flaws in the current study. The data comes from a retrospective single-center study with an uneven set-in view of patient numbers with and without the main outcome. To balance the two groups, the no-recurrence occurrences were randomly down-sampled. It is possible that this process will discard training-related data. Additionally, we only used imaging characteristics that could be reliably detected during routine imaging exams and clinical variables that are simple to access in clinical practice, whereas subsequent relevant studies could accommodate more imaging characteristics and clinical variables that may affect the risk of stroke patients.

Table 3 Threefold validation evaluation metrics for 12 outcome predictions

Metric	Hemorrhagic	Ischemic	One-sided face	One-sided arm	One-sided leg	Asymmetry	Not ambulatory	Not able to speak	Visual disturbances	Abnormal sensation	Mental change	Not able to grasp
Sensitivity	0.32	0.51	0.42	0.70	0.61	0.83	0.45	0.50	0.50	0.30	0.57	0.04
Specificity	0.89	0.31	0.71	0.54	0.59	0.41	0.66	0.55	0.99	0.85	0.86	0.84
f score	0.41	0.42	0.06	0.73	0.67	0.78	0.42	0.41	0.50	0.06	0.46	0.03
Precision	0.59	0.36	0.03	0.76	0.75	0.74	0.39	0.35	0.50	0.03	0.39	0.03
Accuracy	0.71	0.40	0.70	0.65	0.60	0.69	0.59	0.53	0.99	0.84	0.82	0.73

6 Conclusion

The contemporary stroke service system has greatly decreased the incidence of stroke relapse in these individuals by making prompt attention and management for stroke patients more accessible. However, some patient subgroups continue to have a high risk of having a future debilitating stroke and may be difficult to identify using traditional risk prediction scores. Therefore, a more precise and complex risk prediction system is needed. Our method has an advantage over conventional statistical techniques or risk prediction scores because it reflects complex relationships between continuous and categorical independent variables and the outcome and quantifies the weights of independent variables in relation to their influence on the outcome.

Competing Interests The authors declare that they have no competing interests.

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Supplementary Files
The data utilized can be downloaded from here: https://github.com/spawar2/Neural-Networks-Stroke/blob/main/pone.0231113.s002.xlsx

The training code can be accessed here: https://github.com/spawar2/Neural-Networks-Stroke/blob/main/Neural-Networks-Stroke.R

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