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A Multimodal Deep Learning Approach for Huntington's disease Detection Using MRI and Genetic Data

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Abstract - Huntington's disease (HD) is a progressive neurodegenerative condition, and early identification using medical imaging is essential for prompt care. This study uses HD Predictor, a recognized medical image classification system that uses MRI imaging and numerical data to improve diagnostic accuracy. The HD Predictor architecture comprises two main pathways: image and metadata processing. In image processing, ResNet-50's last fully connected (FC) layer is replaced with a 128-neuron layer to extract deep features. The metadata processing branch uses a compact feed forward neural network to examine the CAG value via a 16-neuron layer to gather genetic data. Concatenating and processing the obtained information in a final classification layer determines if the brain sample is impaired or healthy.

The Cross Entropy loss function is best for multi-class classification. The Adam optimizer, with a learning rate of 0.0001, helps update weights, while the ReduceLROnPlateau scheduler adapts the learning rate to validation findings to increase stability. Training over 30 epochs improves the model's decision-making. By using MRI images and CAG repeat data, HD Predictor outperforms image-based categorization methods. This study emphasizes multimodal data fusion in medical imaging and offers an effective Huntington's disease detection approach.

Keywords - Huntington's disease, medical image classification, MRI, deep learning, ResNet-50, multimodal learning, CAG repeats, feature fusion, neurodegenerative disorders, healthcare AI.

INTRODUCTION-

Huntington's disease (HD) is an uncommon, hereditary neurological condition resulting from a mutation in the huntingtin (HTT) gene. It results in increasing cognitive deterioration, motor impairments, and psychological disorders, all of which significantly affect quality of life. For prompt intervention, efficient treatment planning, and ongoing patient care, early HD detection is essential [1]. MRI can detect structural and functional brain abnormalities, improving neurodegenerative disease diagnosis. Nonetheless, conventional diagnosis frequently depends on the visual evaluations of radiologists, which may be subjective and susceptible to inaccuracies. Advancements in AI and deep learning facilitate automated, precise picture processing, enhancing reliability and diminishing reliance on manual interpretation.

Deep learning, particularly convolutional neural networks (CNNs), has demonstrated significant efficacy in the analysis of medical pictures[2]. ResNet-50 is a robust model capable of extracting intricate characteristics and addressing challenges such as the vanishing gradient via residual connections. Nevertheless, a classification based on images alone is unable to capture the complexities of Huntington's disease since genetic influences are also highly important in the onset and development of the disease. The most important marker is the repeat length of the CAG in the HTT gene, and the longer the length of repetition, the earlier the onset of disease. In reaction to this, our study introduces HD Predictor, a deep learning platform that will combine MRI images with genetic data. The model contains two main branches: one of them is an image processing branch, using a modified ResNet-50 where the last fully connected layer is swapped by a 128-neuron layer to provide better feature extraction, and another branch is a metadata branch that analyzes CAG repeat lengths that are done using a 16-neuron feed-forward network [3].The results of both are combined and relayed to a final classification layer to determine whether a sample belongs to a healthy or HD-affected person. HD Predictor combines the information provided by the gene with that of imaging, therefore enabling it to deliver more accurate and reliable predictions than those models that solely rely on the latter. Proper training of the model enhances the categorization performance. We employ the Cross Entropy loss function, which is optimal for classification tasks, in conjunction with

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the Adam optimizer at a learning rate of 0.0001 to facilitate efficient weight updates and prevent convergence to suboptimal local solutions[4]. A ReduceLROnPlateau scheduler autonomously decreases the learning rate if validation accuracy fails to enhance during three successive epochs, therefore enhancing training stability. This mitigates overfitting and facilitates consistent convergence. Over 30 epochs, the model learns to improve its decision-making. MRI scans and genetic data, notably CAG repeat length, are used to improve HD Predictor over CNN models that just use imaging. A multimodal technique that captures structural brain patterns and genetic markers improves Huntington's disease identification. Data fusion in medical imaging improves diagnostic precision, as shown here[5].

BACKGROUND

Medical image classification with deep learning has gained a lot of attention in recent years, especially for neurodegenerative diseases (NDs) including Alzheimer's, Parkinson's, and Huntington's disease. Many previous studies have proven that using convolutional neural network (CNN) models is effective to accumulate such relevant imaging data for disease detection. Resnet-50 is commonly used in depth wise feature extraction for its efficiency in learning high-level abstraction in medical images by solving the vanishing-gradient problem through shortcut connections[6].

1. Deep Learning in Medical Image Classification

The use of deep learning for medical image classification has made this possible, automatically classifying neurodegenerative diseases with quite high accuracy [7]. In this study, we used HD Predictor, a deep learning framework for analyzing MRI data to identify Huntington's disease. We apply a convolutional neural network named ResNet-50, which is a state-of-the-art model, to learn complex patterns from the images and improve the accuracy of the classification. Nevertheless, relying purely on imaging can miss important genetic signals. In response, HD Predictor combines characteristics from the MRI with CAG repeat length, significantly improving the prediction. This ability to leverage deep learning on multiple types of data demonstrates a powerful utility in more accurate and comprehensive illness identification that traditional single-source approaches cannot achieve.

2. Effectiveness of ResNet-50

ResNet 50: The most widely used deep learning architecture, famous for the extraction of important features from complex medical image data [8]. Methods: A modified ResNet-50 is applied to MRI data inside an HD predictor. One of the most common challenges in training deep networks is the vanishing gradient problem, which reduces the effectiveness of learning. ResNet-50 implements residual connection functionalities to enable the model to learn deep hierarchical features without forgetting its performance. It outperforms competitors in identifying subtle changes in brain structure vital to the detection of neurodegenerative diseases, which is particularly useful for this kind of approach. To achieve this, HD Predictor modifies the original network by replacing the last fully connected layer with a 128-neuron layer, thereby maximizing the network's ability to differentiate between healthy individuals and those with neurodegenerative diseases.
Nevertheless, imaging alone is not a complete demonstration of how the disease progresses. To overcome this, HD Predictor combines such image qualities with ResNet-50 with CAG repeat length data and makes use of multimodal learning to achieve better classification performance. The integrative method increases the specificity of the HD detection, proving the ResNet-50 with a genetic information combination to be an effective tool in accurate medical diagnosis.

3. MRI-Based Classification Models

It can be stated that MRI-based classification models are critical to neurodegenerative illness diagnosis by means of structural abnormalities in brain imaging. In this research the authors demonstrate how HD Predictor can be used to tell the difference between normal and affected individuals by using MRI images. Individual methods of diagnosis used historically usually include manual radiology diagnostic assessments that are subjective and biased to human error. Recently, samples of deep learning, like the convolutional neural networks (CNNs) and, in particular, the ResNet-50 model, have significantly increased the accuracy rates of classifications due to their ability to automatically learn important features in brain images. Nevertheless, analysis based on MRI data will be insufficient to reveal crucial genetic information that affects disease progression. In order to deal with this issue, HD Predictor integrates imaging properties with CAG repeat length, which is a genetic determinant of Huntington disease. The combination of imaging and genetics gives a broader picture of the condition and is more accurate in predicting it, and the science offers a better standard of diagnosis compared to the current MRI-based procedure.

4. Significance of Genetic Markers in Huntington's Disease

Genetic markers play a crucial role in identifying and understanding the progress of Huntington disease (HD). Huntington genetic biomarker is mainly the CAG repeat length in the HTT gene. Usually, people have less than 36 repeats, meaning they are not at risk. However, when this barrier was overcome, Huntington's disease (HD) usually appeared. Repeated infections are closely related to the earlier symptoms and the rate of speedier and more intense disease progress. Therefore, the integration of genetic data in predictive analyses is significant in improving the accuracy of

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the diagnosis and in earlier detection. This paper shows that HD Predictor extends MRI-based deep learning with the CAG repeat length to increase the accuracy of the disease detection. Structural brain abnormalities related to HD are clearly found with MRI scans but do not explain the genetic basis of HD. Relying entirely on imaging at times may lead to a misdiagnosis, but especially during the early stages of HD, the brain degeneration may be minimal or even insignificant. To deal with this, HD Predictor uses a fully connected network to analyze the CAG repeat values through a 16-neuron layer, hence earning meaningful genetic information. These are combined with the characteristics of an edited ResNet-50 that analyzes MRI data. This is a multimodal fusion that substantially increases the accuracy of diagnosis, being a more comprehensive and timely diagnosis of Huntington's disease[9].

METHODOLOGY

The article proposes the procedure of HD Predictor, a deep learning-based mechanism that incorporates the analysis of MRI and genetic information in the most appropriate way to determine HD. The model consists of two major components: the branch, which concerns the analysis of MRI images, and the branch that covers the management of genetic metadata. The two branches are then combined so that the system can make more accurate and reliable predictions.

1. Dataset Preparation

The information consists of MRIs of healthy and Huntington's disease patients. Raw/rigid images are further improved using preprocessing skills including intensity balancing, skull-stripping and noise-reduction. The genetic data are the lengths of repeats CAG linked to each individual MRI image. This numerical characteristic can be considered as a key biomarker towards HD classification. Data Augmentation: MRI images are augmented using methods such as rotation, flipping and contrast enhancement so as to reduce overfitting and encourage generalization.

Model Architecture-

HD Predictor model combines image and information analysis in order to more precisely categorize Huntington s disease.

Image Processing Branch: A modified ResNet-50 model will be used to derive complex features of MRI data in this branch. The traditional fully connected (FC) layer is substituted by a 128-neuron layer; thus, the network can give attention to the structural abnormalities that characterize HD.

Metadata Processing Branch: This branch examines CAG repeat length which is a critical predictive genetic factor in Huntington disease using a simple fully connected network comprising of 16 neurons. This set up allows the model to trace the major numerical trends which are closely intertwined to the progression and advancement of the disease. Fusion and Classification: The features that have been extracted on each branch are fused together and passed through a final classification layer which indicates whether an individual is healthy or affected by HD.

$$X_1 = \sigma(I * W^{(1)} + b^{(1)})$$

$$X_2 = Pool_{(2,2,2)}(X_1)$$

$$X_3 = \sigma(X_2 * W^{(2)} + b^{(2)})$$

$$X_4 = Pool_{(2,2,2)}(X_3)$$

$$X_5 = \sigma(X_4 * W^{(3)} + b^{(3)})$$

$$X_6 = Pool_{(2,2,2)}(X_5)$$

$$F = Flatten(X_6)$$

$$Z_0 = F \oplus M$$

$$Z_1 = \sigma(Z_0 W^{(4)} + b^{(4)})$$

$$Z_2 = \sigma(Z_1 W^{(5)} + b^{(5)})$$

$$\hat{y} = \sigma\_sigmoid(Z_2 W^{(6)} + b^{(6)})$$

$$\hat{y} = \sigma\_sigmoid(\ \sigma(\ (F \oplus M)\ W\text{^}(4) + b\text{^}(4)\ )\ W\text{^}(5) + b\text{^}(5)\ )\ W\text{^}(6) + b\text{^}(6)$$

The neural network representation provides a clear and simple representation of the flow of data in the model. It outlines all steps, starting with the input of MRI scans, genetic information and proceeding to feature extraction, fusion and classification. This illustration makes the understanding and interpretation of the complex structure to be easy.

1. Training and Optimization:

The training of HD Predictor is designed to make the learning curve short and flat, convergence stable, and generalization strong, and at the same time minimize the risk of overfitting. Different optimization models are used with the aim of improving the performance of the classification area in the identification of Huntington's disease. The 3D CNN first examines MRI scans and genetic data and predicts spatial patterns using microscopic-sized kernels. The pooling layers make complex processing less demanding, retaining the important characteristics, and successively more abstract filters extract additional abstract attributes. The picture feature elements are squashed and combined with CAG repeat length, which is refined through the fully connected layers, and it is transported via a sigmoid layer to provide correct predictions. same time, a high level of encryption to protect the data in the process. This assists in avoiding illegal access, altering of data, and identity theft [5].

Layer	Type	Kernel / Units	Stride / Pool Size	Activation	Output Shape
Input (MRI Volume)	3D Image Input	–	–	–	(D × H × W × C)
Input (Meta data)	Vector Input	–	–	–	(M,)

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Conv3D-1	Convolution	3×3×3, 32 filters	(1,1,1)	ReLU	(D,H,W,32)
MaxPooling 3D-1	Pooling	–	(2,2,2)	–	(D/2,H/2,W/2,32)
Conv3D-2	Convolution	3×3×3, 64 filters	(1,1,1)	ReLU	(D/2,H/2,W/2,64)
MaxPooling 3D-2	Pooling	–	(2,2,2)	–	(D/4,H/4,W/4,64)
Conv3D-3	Convolution	3×3×3, 128 filters	(1,1,1)	ReLU	(D/4,H/4,W/4,128)
MaxPooling 3D-3	Pooling	–	(2,2,2)	–	(D/8,H/8,W/8,128)
Flatten	Flatten	–	–	–	(F,)
Concatenate	Fusion (Image+Meta)	–	–	–	(F+M,)
Dense-1	Fully Connected	128 units	–	ReLU	(128,)
Dense-2	Fully Connected	64 units	–	ReLU	(64,)
Output Layer	Fully Connected	1 unit	–	Sigmoid	(1,)

Table1: Parameters of the proposed 3D CNN for Huntington's disease Detection

Loss Function

The Cross Entropy Loss function is used to train the model, which is quite effective in the binary classification-based visualization of the HD-affected and healthy individuals. This loss also measures the distance between the probability distributions predicted by the model and the actual labels, thereby helping the model to adjust its decision boundaries more effectively during training.

Optimizer

The model utilizes the Adam (Adaptive Moment Estimation) optimizer to effectively update weight using a learning rate of 0.0001. Adam combines the benefits of Stochastic Gradient Descent (SGD) and momentum-based learning, and it accordingly offers the benefits of variable learning rates during the training process. This facilitates the model's quick learning process, preventing it from becoming mired in local suboptimal solutions.

Learning Rate Adjustment

A ReduceLROnPlateau scheduler is used when training to adjust the learning rate based on validation performance. In case validation accuracy does not improve within three consecutive epochs, the learning rate is reduced to set weight updates more accurately and prevent overfitting. This stabilizes converged models, and the variance of loss values is reduced[11].

Batch Size and Epochs

The model is trained during 30 epochs and increasingly trained to extract features and accurately classify. The value of the batch size is selected to use the memory adequately and not to exacerbate learning too much.

1. Evaluation Metrics:

To evaluate the efficacy of HD Predictor in identifying Huntington's disease (HD), many assessment measures are employed to offer a comprehensive perspective on its performance[12].

Accuracy: Aid in determining the overall precision of predictions by determining the ratio of the number of fine-grained correctly classified samples to the number of samples.

Precision: Refers to that proportion of accurately classified positive cases (HD) to all the cases that were predicted to be positive. The increased accuracy reduces falsely made decisions, therefore providing more reliability in diagnosis.

Recall (Sensitivity): Reflects the ability of the model in precise identification of the real cases of HD. Increased memory reduces the risk of ignoring patients, which is necessary during medical diagnosis.

F1-Score: The idea is to compute a single score that is a combination of precision and recall, so it is especially favorable in the cases of class imbalances.

ROC-AUC Analysis: The Receiver Operating Characteristic - Area Under the Curve (ROC-AUC) assesses the model's capacity to distinguish between HD and non-HD instances. An elevated AUC score signifies superior discriminating ability.

Results

Huntington's disease (HD) is a hereditary condition that leads to the progressive degeneration and death of nerve cells in certain regions of the brain. The illness targets regions of the brain responsible for regulating voluntary movement, in addition to other areas. Individuals afflicted with Huntington's disease exhibit involuntary movements and atypical bodily postures, including difficulties in behavior, emotion, cognition, and personality. Symptoms of Huntington's Disease often manifest in middle-aged individuals (adult HD). They may also manifest in children, however this occurrence is uncommon. The condition deteriorates progressively [13].

More Likely to Get Huntington's Disease

When a parent possesses Huntington's disease (HD), each offspring has a 50% probability of acquiring the chromosome 4 variant that harbors the HD mutation. If a kid does not inherit the HD mutation, they will not acquire the disease and

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cannot transmit it to subsequent generations. When Huntington's disease manifests in the absence of a familial background, it is referred to as sporadic Huntington's disease. Huntington's disease (HD) is induced by a mutation in the gene encoding the protein Huntingtin. The detection induces the repetition of the DNA building units known as cytosine, adenine, and guanine (CAG) much above their typical frequency. The majority of individuals possess less than 27 CAG repeats in their HD gene, so they are not susceptible to the illness. Individuals with CAG repeats in the intermediate range (27 to 35) are unlikely to manifest the condition; nonetheless, they may transmit it to subsequent generations. Individuals with Huntington's disease may possess 36 or more CAG repeats[14].

Huntington's Disease Diagnosed and Treated

Generally now from this points onwards study related to building the model will be discussed, due to a lot of parameters are studied while diagnosing Huntington's Disease.

1. Neurological Exam and Medical History.

2. Diagnostic Imaging.

3. Genetic Tests.

Diagnostic Imaging: In some cases, especially if a person's family history and genetic testing are inconclusive, the physician may recommend brain imaging, such as CT(Computed Tomography) scan or more like MRI(Magnetic Resonance Imaging). As the disease progresses, these scans typically reveal shrinkage in parts of the brain and enlargement of fluid-filled cavities called ventricles. These changes do not necessarily indicate HD and still have normal findings on a CT or MRI scan.

Latest updates on Huntington's Disease Imaging Research:

Scientist are using imaging technology to learn how HD affects the chemical systems of the brain, characterize neurons that have died, view changes in the volume and structure of the brain in people with HD, and to understand how HD affects the functioning of different brain regions[15].

Dataset on Huntington's Disease:

Previously we have developed a 3 Dimensional neural network for Huntington's Disease Detection. But due to unavailability of dataset for human in HD we were unable to construct the neural network for human. To find out the dataset web scraping methods were used to find the dataset of Huntington's disease. The data were in the form of csv files and 2D images of HD affected Human Brain and normal Human Brain.

The sample contents of csv files are as follows:

File Name	Subject ID	Brain Type	CAG
Affected1	M1517	Axial	64
Affected2	M1506	Axial	55
Affected3	M1450-85	Axial	56

Table2: Comparison CAG With respect to sample

The dataset is a synthetic dataset created by us due to unavailability of the dataset. To request access for the dataset from the Australian Research Centre the mails and their reply have been attached with this report.

The dataset also contains 2D images of Affected and Unaffected Human brain with following samples:

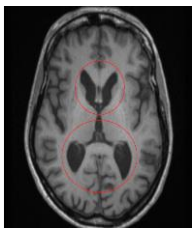

Fig. 1 Affected

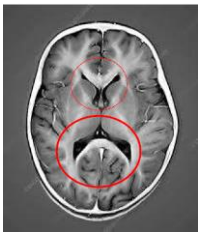

Fig. 2 Not Affected

As we can see from the images we get valuable insights about HD. In the normal human we can see that the highlighted gaps are very less as compared to HD affected Human. From these observations we can conclude there important observations in the images to detect Huntington's Disease so we used these MRI images to detect Huntington's Disease. Now looking at the csv data file there are labels for the images such as the type of Brain MRI image mostly the type is Axial in the synthetic dataset[9][16].

The most important column in the dataset file is the CAG as described in the above case study it is the block of DNA if adenine, cytosine and guanine. Now as we observe the dataset the CAG repeats for normal humans are fewer than 27 and the risk of HD increases as the CAG repeats increases more and more.

Neural Network Model Report:

The HD Predictor model is a deep learning framework designed for binary classification of brain images into affected and non-affected categories. The model builds upon the well-established ResNet-50 architecture, a powerful convolutional neural network (CNN) pre-trained on the ImageNet dataset. Unlike standard image classification models, this implementation enhances predictive accuracy by incorporating an additional metadata feature: the CAG repeat count, which is associated with Huntington's disease. The inclusion of metadata allows the model to leverage not only image-based information but also numerical biomarkers, potentially

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improving classification performance. The dataset consists of high-definition brain images and labelled with metadata. Each image is associated with a unique identifier, a brain type classification (either “affected” or “healthy”), and a numerical CAG value. To handle variations in image formats, the dataset loader dynamically verifies and locates images with extensions such as jpg. In cases where the expected filename does not match exactly, the program intelligently searches for variations to prevent missing data errors.

Pre-processing:

A very important part of getting the data ready for model training is preprocessing. Random scaling, cropping images to 224×224 pixels, flipping them horizontally, and random rotations of up to 15 degrees are among the changes used for the training set. These augmentations enhance the dataset's diversity, facilitating improved generalization of the model to novel, unobserved inputs. For validation and test sets, photos are shrunk to 256 pixels, center-cropped to 224×224 pixels, then normalized using ImageNet's mean and standard deviation. This uniform preprocessing guarantees dependable assessment and allows the model to excel across various input conditions.

Design of Neural Network:

The HD Predictor model comprises two primary pathways: an image processing branch and a metadata processing branch. The image branch employs a modified ResNet-50, substituting the last fully connected (FC) layer with a 128-neuron layer to extract intricate characteristics from MRI scans. The metadata branch is a straightforward fully connected network that analyzes the CAG repeat value via a 16-neuron layer, yielding significant genetic information. The attributes from both branches are subsequently amalgamated and processed via a conclusive classification layer, which ascertains whether the brain sample is from a healthy or diseased individual. Integrating imaging and genetic data improves model predictions over image-only techniques[17].
The HD Predictor model operates via two primary pathways: one for picture analysis and another for genetic information processing. The image branch employs a modified ResNet-50, substituting the final fully connected layer with a 128-neuron layer to extract intricate characteristics from MRI scans. Within the genetic branch, the CAG repeat number is processed by a smaller fully connected network with 16 neurons that pull out important data. Following their combination, these two feature sets are sent through a final classification layer that determines if the brain sample is impacted or healthy. Imaging plus genetic data improves model accuracy and reliability.

Training the Neural Network:

During training, the model processes batches of thirty-two images simultaneously. After each epoch, the model's validation accuracy is used to assess its learning. To maximize outcomes, the model with the highest validation accuracy is saved. This check pointing method mitigates over fitting and guarantees the availability of the most dependable model for final testing and evaluation.

Testing the Model:

Upon completing the training of a model, it is essential to evaluate its performance on novel, unseen data. We use a separate test dataset. The model is transitioned to evaluation mode, ensuring that layers such as batch normalization and dropout function appropriately, hence yielding a more accurate assessment. Classification accuracy, the percentage of correct test data predictions, measures its performance. This final accuracy score provides us with a solid notion of how effectively the model will function when applied to circumstances that occur in the actual world.
A primary benefit of this method is its utilization of metadata, particularly the CAG repeat count. Combining brain imaging data with numerical information, the HD Predictor model classifies Huntington's disease better than image-only methods. The model employs ResNet-50, a robust deep learning architecture recognized for its proficiency in extracting intricate features from photos. Methods such as learning rate scheduling and data augmentation enhance the model's robustness and its capacity to manage novel inputs[18].

Nonetheless, certain limits exist. The existing paradigm depends exclusively on accuracy to evaluate performance, which may be insufficient for medical applications because the repercussions of false positives and false negatives can vary significantly. Subsequent iterations of the model would gain from the incorporation of other metrics such as precision, recall, F1-score, and ROC-AUC.
Another issue is data imbalance, when one class dominates. This may result in model bias. Employing methodologies like as resampling or cost-sensitive loss functions may rectify this issue. The HD Predictor model is a potential method for classifying Huntington's disease. The integration of ResNet-50 with CAG repeat counts results in elevated accuracy. Future endeavors should concentrate on evaluating the model's fairness, employing more sophisticated neural architectures for data handling, and including a broader array of performance indicators to enhance the model's reliability and interpretability.

CONCLUSION

An innovative deep learning tool called HD Predictor is highly improving the detection of Huntington disease. This new method improves upon previous methods by combining

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genetic testing, specifically the presence of CAG repeats in the HTT gene, with MRI brain scan analysis. This is game-changing in that it combines the benefits of both imaging and genetic markers, making it more effective than when either is used individually. The HD Predictor uses a version of the ResNet-50 model to analyze brain images and a small neural network for analysis of genetic information. It is designed to show and fuse the most important elements of both sources, therefore increasing its precision in forecasting. To aid the course of effective learning, the model uses the cross-entropy loss function, the Adam optimizer, and an adaptive learning rate schedule in the training process. The results prove how powerful this combination is. The model can supplement genetic data in order to diagnose conditions such as Huntington neurodegenerative disease. The HD Predictor also represents an important step of medical AI, showing that combining multiple data sets can also allow for earlier and more accurate diagnosis. This could possibly help in the care of patients and treatment options for individuals with Huntington's disease.

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