

---

# A Self-Supervised Model for Multi-modal Stroke Risk Prediction

---

**Camille Delgrange**  
Signal Processing Institute  
EPFL University  
Lausanne, Switzerland  
camille.delgrange@alumni.epfl.ch

**Olga Demler**  
Brigham and Women’s Hospital  
Harvard Medical School  
Boston, Massachusetts, USA  
odemler@bwh.harvard.edu

**Samia Mora**  
Brigham and Women’s Hospital  
Harvard Medical School  
Boston, Massachusetts, USA  
smora@bwh.harvard.edu

**Bjoern Menze**  
Department of Quantitative Biomedicine  
University of Zurich  
Zurich, Switzerland  
bjoern.menze@uzh.ch

**Ezequiel de la Rosa**  
Department of Quantitative Biomedicine  
University of Zurich  
Zurich, Switzerland  
ezequiel.delarosa@uzh.ch

**Neda Davoudi\***  
ETH AI Center, Department of Computer Science  
Department of Quantitative Biomedicine  
University of Zurich  
Zürich, Switzerland  
neda.davoudi@ai.ethz.ch

## Abstract

1 Predicting stroke risk is a complex challenge that can be enhanced by integrating  
2 diverse clinically available data modalities. This study introduces a self-supervised  
3 multimodal framework that combines 3D brain imaging, clinical data, and image-  
4 derived features to improve stroke risk prediction prior to onset. By leveraging  
5 large unannotated clinical datasets, the framework captures complementary and  
6 synergistic information across image and tabular data modalities. Our approach is  
7 based on a contrastive learning framework that couples contrastive language-image  
8 pretraining with an image-tabular matching module, to better align multimodal  
9 data representations in a shared latent space. The model is trained on the UK  
10 Biobank, which includes structural brain MRI and clinical data. We benchmark  
11 its performance against state-of-the-art unimodal and multimodal methods using  
12 tabular, image, and image-tabular combinations under diverse frozen and trainable  
13 model settings. The proposed model outperformed self-supervised tabular (image)  
14 methods by 2.6% (2.6%) in ROC-AUC and by 3.3% (5.6%) in balanced accuracy.  
15 Additionally, it showed a 7.6% increase in balanced accuracy compared to the  
16 best multimodal supervised model. Through interpretable tools, our approach  
17 demonstrated better integration of tabular and image data, providing richer and  
18 more aligned embeddings. Gradient-weighted Class Activation Mapping heatmaps  
19 further revealed activated brain regions commonly associated in the literature  
20 with brain aging, stroke risk, and clinical outcomes. This robust self-supervised  
21 multimodal framework surpasses state-of-the-art methods for stroke risk prediction  
22 and offers a strong foundation for future studies integrating diverse data modalities  
23 to advance clinical predictive modeling.

---

\*Corresponding author

## 24 1 Introduction

25 Stroke ranks as the second leading cause of death worldwide, responsible for 11.6% of global  
26 fatalities in 2019. It often results in neurological damage and long-term disability in adults, imposing  
27 significant health and economic challenges [1, 2]. Early detection through predictive models is crucial  
28 in preventing severe outcomes, as cerebrovascular events can cause irreversible brain damage within  
29 hours [3]. The complexity of stroke, driven by multiple risk factors, highlights the importance of  
30 integrating multi-modal data to improve diagnostic accuracy and treatment strategies. Among the  
31 various imaging techniques, Magnetic Resonance Imaging (MRI) stands out as a highly effective  
32 tool, offering high-resolution, non-invasive assessments of structural abnormalities and detailed  
33 visualization of the brain’s vascular network [4].

34 **Uni-modal predictive models** Prior works mainly use convolutional neural networks (CNN) that  
35 can leverage the high-dimensional imaging information for diagnosing patients [5]. Yu et al. applied  
36 deep learning algorithms to extract meaningful imaging features in an increasing order of hierarchical  
37 complexity to make predictions of the infarct volume [6]. Other models that use only clinical data,  
38 often assume linear relationships between traditional risk factors such as age, gender, smoking  
39 status, blood pressure, diabetes, cholesterol levels, and body mass index [7, 8, 9]. Alaa et al. used  
40 AutoPrognosis, an ensemble machine learning approach, to outperform conventional models like  
41 the Framingham score and Cox models [10]. A major limitation of these models is that they don’t  
42 integrate complementary information from other modalities, similar to how clinicians diagnose using  
43 multiple data sources. Biobanks like the UK Biobank (UKB) have become invaluable in this context,  
44 providing vast datasets integrating imaging and clinical information to train machine learning models  
45 for disease prediction [11, 12].

46 **Multi-modal predictive models** Several studies have employed multi-modal data to improve diag-  
47 nostic capabilities by integrating diverse data types [13]. For example, MultiSurv model has shown  
48 success by fusing image and tabular data for cancer survival prediction [14]. multi-modal models  
49 combining image and clinical data have demonstrated better prediction performance for disability  
50 prediction in stroke patients [15, 16]. However, CNNs tend to prioritize image features, and simple  
51 image-tabular CNN concatenation fails to enhance predictive models due to insufficient cross-modal  
52 interactions. To address this, Wolf et al. developed the Dynamic Affine Feature Map Transform  
53 (DAFT), which conditions convolutional feature maps on both image and tabular data, enabling a two-  
54 way information exchange via an auxiliary neural network [17]. While DAFT reduces issues related  
55 to the large number of trainable parameters in standard 3D CNNs and the curse of dimensionality,  
56 it may sacrifice some predictive power compared to deeper models like ResNet. Although recent  
57 models show promise in biomedical prediction tasks, their clinical translation is hindered by limited  
58 annotated datasets, low disease prevalence, and the risk of overfitting. Self-supervised learning (SSL)  
59 is a powerful technique for extracting representative features from unlabeled data, making it valuable  
60 for early disease risk identification.

61 **Self-supervised models** Unlike traditional supervised learning, SSL defines pretext tasks that allow  
62 models to learn meaningful representations from raw data [18]. One prominent SSL technique is  
63 contrastive learning, which trains encoders to generate augmented views of a sample, maximizing  
64 similarity between these views while minimizing similarity with other samples [18]. Popular methods  
65 such as SimCLR [19], BYOL [20], and MOCO [21] have demonstrated success in imaging tasks,  
66 while VIME [22] and SCARF [23] are leading approaches for tabular data. Emerging approaches,  
67 like contrastive language-image pre-training (CLIP) strategy, have evolved from unimodal methods  
68 to integrate diverse modalities. While there was an extensive work done for cardiovascular diseases  
69 prediction [24, 25, 26], stroke risk prediction through volumetric brain images and clinical health  
70 records remains underexplored.

71 We present for the first time, to the best of our knowledge, a self-supervised multi-modal approach  
72 integrating 3D brain MRIs with clinical tabular data for stroke risk prediction. As depicted in Figure 1,  
73 our methodology incorporates cross-modal interactions via CLIP loss [27] and image-tabular matching  
74 (ITM) loss [28, 25]. We demonstrate that our learning strategy outperforms leading (self-)supervised  
75 unimodal methods and that multi-modal image-tabular pre-training leads to better representations and  
76 improved downstream performance. Lastly, we validate the model’s learned features through visual  
77 activation maps, which align with established clinical and neurological findings on stroke-related  
78 brain pathology. Code is available at <https://github.com/CamilleDeLgrange/SSMSRPM>.

## 79 2 Materials and Methods

### 80 2.1 Dataset

81 Our analyses are performed on T2-Fluid Attenuation Inversion Recovery (FLAIR) brain volumes,  
82 and over a subset of clinical information spanning across five categories, extracted from the UKB:  
83 demographics, lifestyle, biomarkers, comorbidities, and medication. The complete list of features  
84 is available in the supplementary materials. Continuous features are standardized using z-score  
85 normalization, while categorical data is one-hot encoded. For our experiments, we use 5000 and 500  
86 samples for training and validation sets respectively for the model pre-training stage. Train, validation,  
87 and test subset for the downstream fine-tuning stage use 278, 93, and 93 samples respectively. The  
88 fine-tuning sets are stratified according to sex, age and stroke diagnosis to account for confounders  
89 to avoid spurious correlations and class imbalance. To handle missing tabular data, we use an  
90 iterative multivariate imputer based on Multivariate Imputation by Chained Equations (MICE)  
91 [29], modelling missing features as a function of existing features over multiple imputation rounds.  
92 Missing categorical data is replaced by the most frequent category. This step is performed after data  
93 normalization, to ensure that the means and standard deviations are calculated only from recorded  
94 values. The 3D brain images are registered to Montreal Neurological Institute brain template (MNI)  
95 space, have uniform dimensions of  $182 \times 218 \times 182$  and a voxel size of  $1mm^3$  and are processed  
96 using the UKB imaging pipeline [30]. Key image-derived phenotypes (IDPs), such as segmented  
97 brain tissue volumes and white matter hyperintensity (WMH) volumes, are extracted and used as  
98 brain IDPs. Brain lesion segmentation is performed using the BIANCA tool to produce 3D binary  
99 lesion masks [31]. Furthermore, lesion segmentation masks are characterized by pyradiomics [32]  
100 through radiomic features such as volume, area, elongation, and sphericity and these features are  
101 used as lesion IDPs.

### 102 2.2 Multi-modal self-supervised framework

103 Our pipeline is split into two sequential steps. First, we pre-train the tabular and imaging encoders  
104 (Figure 1 A) and then we fine-tune them with labels from downstream task (Figure 1 B). Each batch  
105 of data contains pairs of imaging  $x_{j_i}$  and tabular  $x_{j_t}$  samples. These samples are augmented by  
106 random transformations  $t \sim \tau$  from a set of parametric transforms  $\tau$ , such as random cropping and  
107 affine transforms for the images, or random feature corruption for the tabular data. We use an image  
108 augmentation rate of 95% for the model to still occasionally see unaltered data to capture the original  
109 data distribution for transferring the learnt features to the downstream task. The corruption rate of the  
110 tabular data is set to 0.3 as in the original tabular method SCARF [23]. For a given reference point,  
111 known as anchor  $x$ , the positive samples are the ones derived from  $x$  transformations while other  
112 samples in the batch are considered as negative samples. Augmented images  $x_{j_i}$  and tabular data  
113  $x_{j_t}$  are passed through the imaging encoder  $f_{\theta_I}$  and tabular encoder  $f_{\theta_T}$  to generate the embeddings.  
114 These embeddings are propagated through the separate projection heads  $f_{\phi_I}$  and  $f_{\phi_T}$ , and brought  
115 into a shared latent space as projections  $z_{j_i}$  and  $z_{j_t}$ , which are L2-normalized onto a unit hypersphere.  
116 The projections are pulled and pushed in the shared latent space according to the CLIP loss [27],  
117 which maximizes the cosine similarity of projections from the positive samples and minimizes the  
118 similarity of projections from the negative samples in the batch. In contrast to the original InfoNCE  
119 loss used in SimCLR [19], and following the CLIP loss, the projected embeddings similarities are  
120 contrasted between data modalities. An image projection is therefore defined as :

$$z_{j_i} = f_{\phi_I}(f_{\theta_I}(x_{j_i})) \quad (1)$$

121 Considering all N subjects in a batch, the loss for the imaging modality is defined as follows:

$$l_{i,t} = - \sum_{j \in N} \log \frac{\exp(\cos(z_{j_i}, z_{j_t})/\tau)}{\sum_{k \in N, k \neq j} \exp(\cos(z_{j_i}, z_{k_t})/\tau)} \quad (2)$$

122 where  $\tau$  is the temperature parameter. In our experiments, a temperature of 0.1 is selected to work  
123 best, following [19].  $l_{t,i}$  is computed analogously and CLIP loss is defined as follows:

$$\mathcal{L}_{clip} = \lambda l_{i,t} + (1 - \lambda) l_{t,i} \quad (3)$$

124 We choose value of 0.5 for the  $\lambda$  as regularization parameter. The aim is to learn patient-wise  
125 representations invariant to the variation of the image-tabular pairs. Hard negative samples are crucial

126 in contrastive learning as they help the model distinguish between similar samples, preventing trivial  
 127 solutions and enhancing its robustness. We implement a hard negative mining strategy to predict  
 128 whether image-tabular data pairs are positive or negative, using image-tabular matching (ITM) loss.  
 129 In this approach, for each image or tabular representation, we identify an unmatched tabular or image  
 130 representation from the mini-batch. This selection is based on similarity scores computed using the  
 131 CLIP method, which serves as the sampling weight for the negative pairs [25, 28]. A multi-modal  
 132 interaction module is introduced, as shown in Figure 1, which takes the output of the projector  
 133 heads to perform inter-modality learning and generates a multi-modal representation. It uses a  
 134 cross-attention mechanism [33], enabling tabular embeddings to attend to relevant image embeddings.  
 135 The multi-modal interaction module contains two transformer layers, with four attention heads and a  
 136 hidden dimension of 256, each including self-attention, cross-modal attention, an MLP feed-forward  
 137 module and layer normalization [25]. The output of the multi-modal module is a [CLS] token,  
 138 aggregating the information from the entire sequence, used for downstream classification task, where  
 139 the model needs a single feature vector representing the entire input [34]. The [CLS] embedding is  
 140 capturing a joint representation of the image-tabular pair that is fed into the ITM predictor (a linear  
 141 layer) to match the prediction based on a binary cross-entropy loss  $\mathcal{L}_{ITM}$ . Therefore, the complete  
 142 loss is expressed as:

$$\mathcal{L} = (\mathcal{L}_{CLIP} + \mathcal{L}_{ITM})/2 \quad (4)$$

143 **Downstream task predictions** After pre-training, the projection heads were replaced by fully  
 144 connected layers. Extracting the representation before the projector has been shown to improve  
 145 downstream tasks performance [18]. For downstream fine-tuning and binary classification of healthy  
 146 versus stroke (Figure 1 B), we employ ensemble learning to improve model generalization and  
 147 performance by leveraging the rich representations from the image encoder, tabular encoder, and  
 148 the multi-modal transformer interaction module. All pre-trained models are evaluated using linear  
 149 probing (frozen) and fine-tuning (trainable). The frozen models use tuned linear classifiers after the  
 150 feature extractors. The datasets used for model fine-tuning are balanced in each batch of training,  
 151 validation, and test subset. This way, we reduce potential bias due to class-imbalance, as well as  
 152 unstable and slow training due to imbalance batch distributions.

## 153 3 Experiments

### 154 3.1 Benchmarking

155 The herein proposed solution is compared against supervised and SSL strategies, each of them using  
 156 imaging, tabular, and integrated imaging-tabular methodologies.

#### 157 3.1.1 Supervised learning methods

158 To benchmark our proposed method, we implement two state-of-the-art, supervised image-based  
 159 models, namely ResNet50 [21] and DenseNet121 [35], two supervised tabular data approaches,  
 160 namely a two-layer tabular MLP model and a tabular transformer encoder inspired from Du et. al.  
 161 (2024) [25]. We conduct an ablation study using a supervised MLP model with various feature  
 162 combinations to identify the optimal feature set. This process helps us to select the final combination  
 163 of features for improved model performance. The combinations include: *i*) clinical tabular data only,  
 164 spanning the previously mentioned categories (clinical), *ii*) clinical data with brain extracted IDPs  
 165 (clinical + brain IDPs), and *iii*) clinical data, brain IDPs and lesion IDPs (clinical + brain IDPs +  
 166 lesion IDPs). Furthermore, we implement three supervised, multi-modal (imaging-tabular) learning  
 167 models, namely a simple concatenation fusion model (CF) [36], a CF model integrated with the  
 168 tabular transformer encoder inspired by the work from Du et. al. (2024) [25] (CF + Transformer),  
 169 and DAFT model [17]. All models employing an imaging encoder are implemented with ResNet50  
 170 as backbone. DAFT block is integrated within ResNet50 from the third stage onwards. To alleviate  
 171 over-fitting, an early stopping strategy is adopted, with a minimal delta (divergence threshold) of  
 172  $1 \times 10^{-4}$ , a maximal number of epochs of 50, and a patience of 15 epochs.

#### 173 3.1.2 Self-supervised learning methods

174 Our model is compared against leading, self-supervised contrastive solutions, including: *i*) the  
 175 unimodal, image-based SimCLR[19] approach, *ii*) the unimodal, tabular data-based SCARF [23]

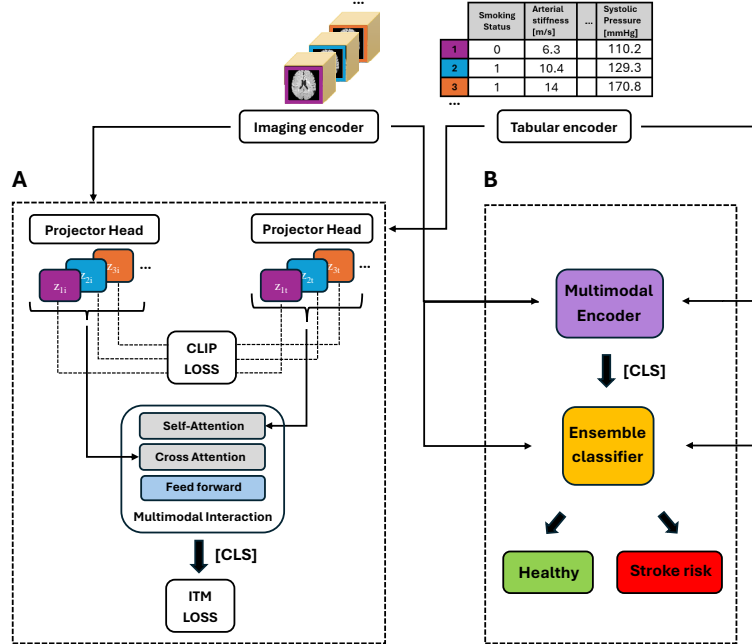


Figure 1: Pipeline for joint imaging and tabular data pre-training (A) and downstream fine tuning (B). CLIP loss is applied on projected data to align the image and tabular representations. Hard negative pairs are mined through CLIP similarities within the batch. A transformer block with self-attention and cross-attention layers is used to cross-attend both modalities, resulting in a multi-modal [CLS] token fed to a classifier and used for further downstream fine tuning. Image-Tabular Matching (ITM) loss evaluates the image-tabular pair matching. In the downstream task, an ensemble classifier is fine-tuned to predict healthy versus stroke from pre-trained imaging, tabular and multimodal encoders.

176 approach, and *iii*) the multi-modal, CLIP method (without ITM loss). The hyperparameters and  
 177 training configurations for all SSL pre-training approaches are adapted for our specific dataset and  
 178 task, and are obtained through hyper-parameter search. All models are pre-trained for 100 epochs  
 179 using an Adam optimizer [37]. The learning rate is warmed up linearly for 10 epochs and decayed  
 180 following a cosine annealing scheduler. For all methods, as in the CLIP+ITM method, the image  
 181 augmentation rate is 95% and the tabular corruption rate 0.3 during pre-training and 80% and  
 182 0.3 during downstream fine tuning. SimCLR is trained using the NTXent objective [19] and the  
 183 temperature parameter is kept to 0.1. Hidden and projected dimensions are respectively 2048 and  
 184 128 for both modalities [19]. The same parameters are used for SCARF [23]. Learning rates are  
 185 chosen with a sweep through a range of learning rates, by tracking the validation loss. Weight decay  
 186 and dropout rate are added depending on the level of overfitting observed at the validation loss. The  
 187 same early stopping strategy is employed as in the supervised learning methods. The downstream  
 188 fine-tuning is using the same parameters as the presented method, using only a single modality  
 189 classifier for unimodal SSL pre-trained methods and a fused representation vector with a single linear  
 190 classifier for the CLIP only model. Trainable models in each SSL unimodal method means that the  
 191 other modality is incorporated during fine-tuning as a full trainable model. The employed batch size  
 192 for all methods is 6. All SSL models are pretrained on a Tesla V100-SXM2 (32GB, 42 CPUs), and  
 193 inference is performed on an NVIDIA GeForce RTX 4090 (24GB, 62 CPUs). Pretraining took  $\sim 24$   
 194 hours, while fine-tuning took less than 1 hour.

### 195 3.2 Interpretability and qualitative analysis

196 Embeddings visualization is done using a two-dimension Uniform Manifold Approximation and  
 197 Projection (UMAP) technique [38], to evaluate the quality of the generated latent space embedding  
 198 after pre-training, using validation samples. Such approach allows to qualitatively assess the latent  
 199 space representation and data distribution after encoding each modality with either a unimodal or

Table 1: Feature selection with supervised MLP results using different combinations of tabular data. ROC-AUC: area under the receiver operating characteristic curve; bAcc (%): balanced Accuracy; Se (%): sensitivity. For each metric, the best-performing method is highlighted in **bold** and the second-best is underlined.

Model	Metrics (%)			
	AUC	bAcc	F1	Se
MLP (clinical)	65.36	<u>61.29</u>	60.87	60.87
MLP (clinical + brain IDPs)	<b>71.37</b>	60.31	<u>65.96</u>	<u>67.39</u>
MLP (clinical + brain IDPs + lesion IDPs)	<u>65.63</u>	<b>62.58</b>	<b>68.69</b>	<b>73.91</b>

200 multi-modal pre-trained model, giving some hints about the successfulness of the learning strategies.  
 201 A latent space embedding size of 2048 dimensions is produced.

202 For qualitative analysis, we generated imaging heatmaps using the Gradient-weighted Class Activation  
 203 Mapping (GradCAM) technique [39] to visualize the regions in each slice that contributed most  
 204 significantly to the model’s predictions across given brain MRI volume. GradCAM [39] heatmaps are  
 205 normalized in the range of 0 to 1 and are upsampled with trilinear interpolation to match the original  
 206 image space. The 7th layer of the ResNet50 encoder is used to allow capturing high-level features  
 207 and spatial structure that is suitable for visualization. The most informative slice (defined as the one  
 208 accounting with the highest heatmap activation scores) for each view in axial, sagittal, or coronal  
 209 plane is generated. We use the 3D GradCAM implementation from MONAI.

210 **3.3 Performance assessment**

211 All models are evaluated through the area under the Receiver Operating Characteristic (ROC) curve.  
 212 Binary classification metrics, namely balanced accuracy, F1-Score, and sensitivity, are included. Clas-  
 213 sification metrics are reported at the Youden-index operating point ( $J = \text{Sensitivity} + \text{Specificity} - 1$ )  
 214 retrieved from the (validation set) ROC curve. The metrics are chosen bearing in mind that potential  
 215 clinical applications of this study could serve as screening and risk stratification tools, where the  
 216 models sensitivity plays an important role to avoid missing positive stroke cases.

217 **4 Results and Discussion**

218 **4.1 Benchmarking**

219 To determine which tabular features to include, we conducted a supervised-learning ablation analysis  
 220 using various combinations of tabular data subgroups. As shown in Table 1, the models that  
 221 incorporate clinical and brain IDPs achieve the highest ROC-AUC scores. However, the method  
 222 that also includes lesion IDPs outperforms in binary classification metrics, such as F1-score and  
 223 sensitivity. To prioritize model robustness while maintaining a smaller feature set, the subsequent  
 224 benchmarking of models using tabular data is performed using only clinical and brain IDPs.

225 A summary of the different models performance is shown in Table 2. It is observed that the proposed  
 226 multi-modal learning strategy outperforms all other methodologies across all considered metrics,  
 227 with the *trainable* model setting performing slightly better than the *frozen* one.

228 When comparing models based on learning approach and data modality, it can be observed that  
 229 the best performing imaging supervised learning strategy is DenseNet121 (ROC-AUC 66.79%). In  
 230 DenseNet architectures, layers are densely connected, which improves feature reuse and gradient  
 231 flow, leading to richer feature representations. However, this dense connectivity increases memory  
 232 overhead during training, particularly with the large inputs used in this study. To optimize the trade-off  
 233 between efficiency and memory usage, we selected ResNet50 as the encoder for SSL pre-training,  
 234 accepting a minor reduction in performance.

235 When comparing SSL strategies, it is evident that fine-tuning both data modalities in multi-modal  
 236 approaches significantly boosts performance. The performance gap is considerable when comparing

237 these multi-modal models with unimodal image-based models, showing that image data alone is  
 238 insufficient for effectively addressing the task. The best performing method is the CLIP+ITM  
 239 model, performing better than all unimodal (tabular and imaging) SSL methods. Interestingly, DAFT  
 240 performs similar to the multi-modal SSL methods in terms of ROC-AUC and balanced accuracy,  
 241 although exhibits poor F1-score and sensitivity results. There is no clear difference in performance  
 242 between trainable and frozen settings across all models. We hypothesize this is because the pre-trained  
 243 models have already developed robust, transferable representations, making fine-tuning less impactful.  
 244 Additionally, the small size of the fine-tuning dataset may limit the effectiveness of further learning  
 245 beyond what was achieved during pre-training. Besides, it could be hypothesized that freezing the  
 246 model may serve as a form of regularization, helping to mitigate overfitting, particularly in this setting  
 247 with limited labeled data.

Table 2: Benchmarking performance results. F and T denote frozen and trainable pre-trained encoders. ROC-AUC: area under the receiver operating characteristic curve; bAcc (%): balanced Accuracy; Se (%): Sensitivity. For each metric, the best-performing method is highlighted in **bold** and the second-best is underlined. The overall best performing method is highlighted in gray.

Model	Tabular	Image	Metrics (%)			
			AUC	bAcc	F1	Se
(a) Supervised Image						
ResNet-50 [40]	-	T	63.25	57.08	60.01	65.22
DenseNet121 [35]	-	T	66.79	66.79	69.90	78.26
(b) Supervised Tabular						
MLP	T	-	71.37	60.31	65.96	67.39
Transformer [25]	T	-	64.38	62.21	47.62	32.61
(c) Supervised multi-modal						
Concat Fuse (CF) [36]	T	T	65.26	60.29	62.63	67.39
Concat Fuse (CF) [w/ Transformer] [36, 25]	T	T	63.48	52.08	66.17	95.65
DAFT [17]	T	T	73.82	63.51	69.57	65.01
(d) SSL Image						
SimCLR [19]	-	F	64.99	52.38	33.33	28.91
SimCLR [19]	-	T	65.59	55.67	43.83	34.78
SimCLR [19]	T	F	72.02	65.56	64.44	63.04
SimCLR [19]	T	T	72.11	65.56	64.44	63.04
(e) SSL Tabular						
SCARF [23]	F	-	71.18	62.42	63.91	67.39
SCARF [23]	T	-	70.35	64.48	62.92	60.87
SCARF [23]	F	T	72.16	62.16	43.48	53.34
SCARF [23]	T	T	72.02	67.85	<u>73.08</u>	78.26
(f) SSL multi-modal						
CLIP [26]	T	T	73.41	61.5	67.24	80.78
CLIP [26]	F	F	73.54	<u>71.00</u>	70.97	71.74
CLIP+ITM [25, 28]	T	T	<u>74.42</u>	<b>71.11</b>	<b>74.22</b>	<b>84.78</b>
CLIP+ITM [25, 28]	F	F	<b>74.75</b>	62.77	67.29	76.60

248 **4.2 Interpretability and qualitative analysis**

249 **4.2.1 Embeddings visualization**

250 Figure 2 shows the UMAP embeddings distribution for unimodal and multi-modal data models. On  
 251 one hand, it can be observed that in Fig. 2 A, there is a clear distinction between (unimodal learnt)  
 252 tabular and imaging data modalities, with data samples clustered by data-type. In this case, the

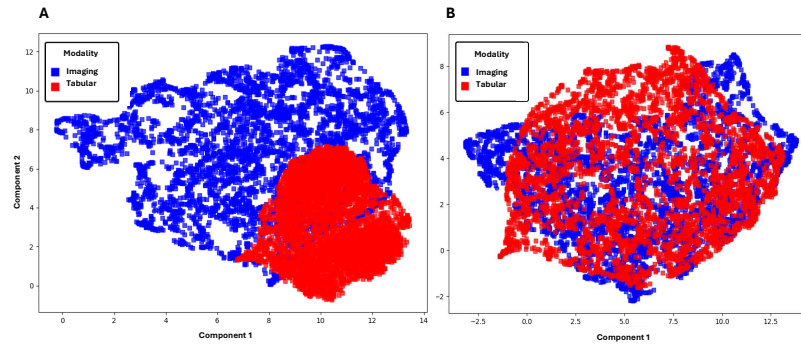


Figure 2: 2D UMAP projections of tabular and imaging embeddings from the validation set, using (A) unimodal pre-trained tabular and imaging encoders and (B) multi-modal pre-trained tabular and imaging encoders.

253 embeddings generated from imaging data and tabular data are significantly different from each other in  
 254 the feature space when generated with a unimodal pre-trained model (i.e., either SCARF or SimCLR).  
 255 The tight clustering of red points suggests that the tabular data embeddings are more homogeneous  
 256 and possibly more concentrated in the feature space compared to the broad representation of brain  
 257 MRI images. Therefore, unimodal-data encoders have learned modality-specific features, without  
 258 capturing interactions between them. On the other hand, in Fig. 2 B the UMAP plot obtained for  
 259 the best performing multi-modal model (CLIP+ITM) is shown. In this case, there is significant  
 260 overlap between the tabular and imaging embeddings, suggesting that the model has found common  
 261 representations for the two different data types, either via shared visual features or via learning  
 262 associated clinical patterns in tabular and brain MRIs. Thus, CLIP+ITM is able to encode the  
 263 underlying patient representation in a common latent space by reducing data augmentation noise.  
 264 Still, there are data-points in the plot having distinct representations within each modality, suggesting  
 265 that the model could not project them to the modality-shared latent space. The broad distribution of  
 266 points across the entire UMAP space suggests that the embeddings capture a wide variety of features  
 267 from both imaging and tabular data, rather than collapsing all data points into a narrow cluster. These  
 268 results expose the enhanced performance of the multi-modal SSL strategy by projecting diverse  
 269 data modalities into a shared embedding space, and thus suggesting a better model starting point for  
 270 downstream analysis.

#### 271 4.2.2 Imaging heatmaps

272 Figure 3 shows results from the GradCAM experiment obtained over predicted samples. When  
 273 inspecting the positive predicted scans (True Positives and False Positives), the model tends to  
 274 highlight anatomical regions surrounding the lateral ventricles and (periventricular) white matter  
 275 areas. Such patterns could be associated to white matter hyperintensities, which are known predictors  
 276 of brain atrophy and age-related brain alterations [41] and also stroke risk predictors in elderly  
 277 individuals [42]. In different studies, correlations have been observed between common age-related  
 278 structural brain changes and brain pathologies [41, 43, 44]. When assessing scans #2 and #4 of  
 279 the true positive patients in Fig. 3, the activation maps are also showing anatomical regions distant  
 280 from the lateral ventricles, showing high activations. Supported from literature, those activations  
 281 could be related to white matter hyperintensities (deep white matter, in this case), often appearing in  
 282 regions of the brain that are not immediately adjacent to the cortical surface, but commonly located in  
 283 subcortical white matter or in deep white matter tracts [41]. Such deep white matter hyperintensities  
 284 are associated with chronic vascular disease and other chronic pathologies (e.g. multiple sclerosis)  
 285 [41]. When evaluating negatively predicted patients (True Negatives and False Negatives), the scans  
 286 are showing less emphasis on the (periventricular) white matter region but instead highlight areas of  
 287 the lower brain (cerebellum, posterior brain) and the cortex. We hypothesize that these areas may



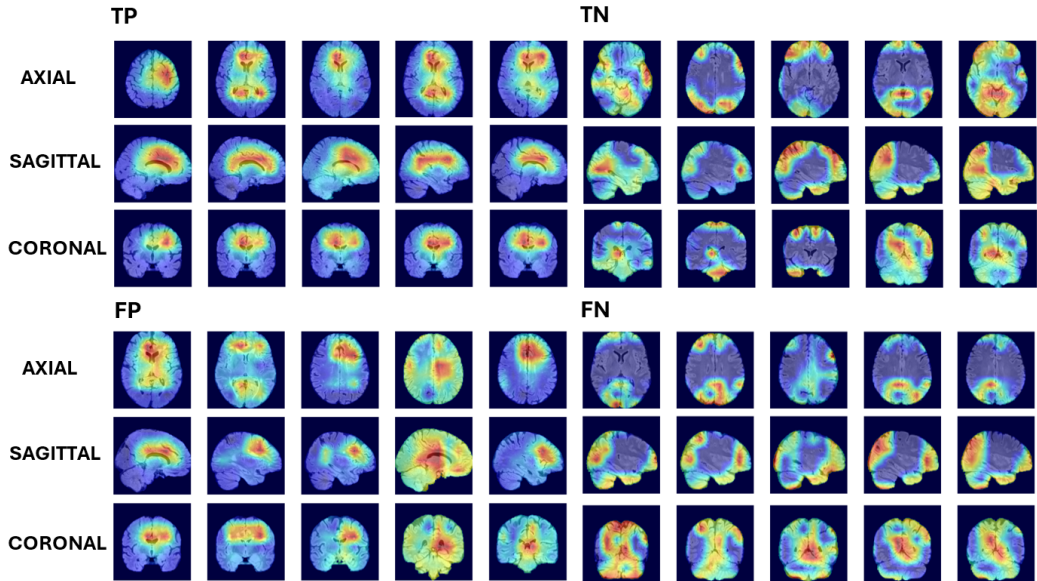


Figure 3: GradCAM-activated brain regions for five patients, categorized as TP (True Positive), TN (True Negative), FP (False Positive), and FN (False Negative). Red (blue) indicates higher (lower) activations.

288 reflect patterns related to normal aging or normal brain atrophy processes, rather than anomalous brain  
 289 conditions. Overall, we can hypothesise from these visualizations that the multi-modal SSL stroke  
 290 risk predictor model focuses on abnormal brain aging patterns for its predictions. We therefore believe  
 291 that future experiments including brain-age and brain structure-age biomarkers could help enhancing  
 292 the models predictability, since they have been shown to be associated with overall cardiovascular  
 293 risk [45], clinical outcome in stroke [46] and overall risk of mortality [47].

294 **Limitations.** Our study is limited by the use of the UK Biobank, whose demographic characteris-  
 295 tics may not fully represent the diversity of global populations, potentially impacting the model’s  
 296 generalizability and clinical utility. Future research should validate our approach using more diverse  
 297 external datasets to improve applicability. Additionally, our test set was constrained by the limited  
 298 availability of pre-stroke imaging samples, as most stroke datasets focus on post-onset cases. Finally,  
 299 the heterogeneity in the time between imaging and stroke onset in the UK Biobank could influence  
 300 model performance, necessitating further experiments to disentangle these effects. Future work could  
 301 also include improving model efficiency by testing further architectures and techniques to reduce  
 302 model parameters (e.g. network pruning).

## 303 5 Conclusion

304 We hereby present an SSL model integrating diverse data modalities for predicting stroke risk. The  
 305 model’s performance is compared against state-of-the-art (self-)supervised models employing both  
 306 unimodal and multi-modal data, including tabular and imaging datasets. A comprehensive set of  
 307 experimental settings is utilized, encompassing different subgroupings of tabular features—such  
 308 as clinical data, brain IDPs, and lesion IDPs—as well as various training regimes that combine  
 309 pre-training and fine-tuning based on data modality.

310 Our results demonstrate that the CLIP model on multi-modal data, combined with an ITM loss,  
 311 outperforms single-modality alternatives. The CLIP+ITM model surpasses the self-supervised tabular  
 312 (image) data SCARF (SimCLR) model by 2.6% (2.6%) in ROC-AUC, and by 3.3% (5.6%) in balanced  
 313 accuracy terms. Our framework also demonstrated an AUROC improvement of 0.93% and 7.6%  
 314 balanced accuracy from the best multi-modal supervised method. Additionally, the proposed model  
 315 produces well-aligned multi-modal representations in a common, data modality-independent space,  
 316 which is unattainable with unimodal tabular or imaging data models. Thus, CLIP-ITM effectively  
 317 leverages complementary and synergistic information from diverse data modalities.

318 Using interpretable GradCAM heatmaps, we identified activated brain regions commonly associated  
319 with brain aging, stroke risk, and clinical outcomes. On one hand, the activated areas indicate that  
320 the model primarily focuses on deep and periventricular white matter hyperintensities for predicting  
321 positive samples, which may be more common and extensive in patients identified as at risk for stroke.  
322 On the other hand, the prediction of negative samples highlights the cerebellum, posterior brain  
323 regions and cortical areas. These results demonstrate the model’s capacity to extract task-specific  
324 features linked to stroke risk, which are well-supported by existing literature.

325 In conclusion, we propose a robust self-supervised multi-modal learning approach for stroke risk  
326 prediction. Our model offers a strong foundation for future studies that aim to integrate multiple data  
327 modalities into prediction models.

## 328 **Acknowledgement**

329 This research has been conducted using the UK Biobank resource under application number 81959  
330 and grants NHLBIR21HL156174, NHLBIK24HL136852, and K24HL136852. This project was  
331 supported by the grant #2023-N-306 of the 1st Joint Call of the Swiss Data Science Center (SDSC)  
332 and the Strategic Focus Area “Personalized Health and Related Technologies (PHRT)” of the ETH  
333 Domain (Swiss Federal Institutes of Technology). N.D. is partially supported by the ETH AI  
334 Center postdoctoral fellowship. B.M., N.D., and E.D. acknowledge support of the Helmut-Horten-  
335 Foundation.

## 336 References

- 337 [1] Liyuan Pu et al. “Projected Global Trends in Ischemic Stroke Incidence, Deaths and Disability-  
338 Adjusted Life Years From 2020 to 2030”. In: *Stroke* 54.5 (May 2023), pp. 1330–1339. ISSN:  
339 15244628. DOI: 10.1161/STROKEAHA.122.040073. URL: <https://www.ahajournals.org/doi/10.1161/STROKEAHA.122.040073>.
- 341 [2] Valery L. Feigin et al. “Global, regional, and national burden of stroke and its risk factors,  
342 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019”. In: *The Lancet*.  
343 *Neurology* 20.10 (2021), pp. 1–26. ISSN: 1474-4465. DOI: 10.1016/S1474-4422(21)00252-  
344 0. URL: <https://pubmed.ncbi.nlm.nih.gov/34487721/>.
- 345 [3] Gagan D. Flora and Manasa K. Nayak. “A Brief Review of Cardiovascular Diseases, Associated  
346 Risk Factors and Current Treatment Regimes”. In: *Current Pharmaceutical Design* 25.38 (Sept.  
347 2019), pp. 4063–4084. ISSN: 13816128. DOI: 10.2174/1381612825666190925163827.  
348 URL: <https://pubmed.ncbi.nlm.nih.gov/31553287/>.
- 349 [4] Valentina Hartwig et al. *Biological effects and safety in magnetic resonance imaging: A review*.  
350 2009. DOI: 10.3390/ijerph6061778. URL: <https://pubmed.ncbi.nlm.nih.gov/19578460/>.
- 352 [5] Huanhuan Zhang and Yufei Qie. *Applying Deep Learning to Medical Imaging: A Review*. Sept.  
353 2023. DOI: 10.3390/app131810521. URL: <https://www.mdpi.com/2076-3417/13/18/10521/html>  
354 <https://www.mdpi.com/2076-3417/13/18/10521>.
- 355 [6] Yannan Yu et al. “Use of deep learning to predict final ischemic stroke lesions from initial  
356 magnetic resonance imaging”. In: *JAMA network open* 3.3 (2020), e200772–e200772.
- 357 [7] Julia Hippisley-Cox et al. “Development and validation of a new algorithm for improved  
358 cardiovascular risk prediction”. In: *Nature Medicine* 30.5 (Apr. 2024), pp. 1440–1447. ISSN:  
359 1546170X. DOI: 10.1038/s41591-024-02905-y. URL: [https://www.nature.com/](https://www.nature.com/articles/s41591-024-02905-y)  
360 [articles/s41591-024-02905-y](https://www.nature.com/articles/s41591-024-02905-y).
- 361 [8] Jaejin An et al. “Recurrent atherosclerotic cardiovascular event rates differ among patients  
362 meeting the very high risk definition according to age, sex, race/ethnicity, and socioeconomic  
363 status”. In: *Journal of the American Heart Association* 9.23 (Dec. 2020). ISSN: 20479980. DOI:  
364 10.1161/JAHA.120.017310. URL: [https://www.ahajournals.org/doi/10.1161/](https://www.ahajournals.org/doi/10.1161/JAHA.120.017310)  
365 [JAHA.120.017310](https://www.ahajournals.org/doi/10.1161/JAHA.120.017310).
- 366 [9] Jia You et al. “Development of machine learning-based models to predict 10-year risk of  
367 cardiovascular disease: a prospective cohort study”. In: *Stroke and vascular neurology* 8.6  
368 (Dec. 2023), pp. 475–485. ISSN: 2059-8696. DOI: 10.1136/SVN-2023-002332. URL:  
369 <https://pubmed.ncbi.nlm.nih.gov/37105576/>.
- 370 [10] Ahmed M. Alaa et al. “Cardiovascular disease risk prediction using automated machine  
371 learning: A prospective study of 423,604 UK Biobank participants”. In: *PLoS ONE* 14.5  
372 (May 2019). ISSN: 19326203. DOI: 10.1371/journal.pone.0213653. URL: <https://pubmed.ncbi.nlm.nih.gov/31091238/>.
- 374 [11] Thomas J. Littlejohns et al. *The UK Biobank imaging enhancement of 100,000 participants: rationale, data collection, management and future directions*. May 2020. DOI: 10.1038/s41467-020-15948-9. URL: <https://www.nature.com/articles/s41467-020-15948-9>.
- 378 [12] UK BioBank. “UK Biobank - UK Biobank”. In: (2021). URL: <https://www.ukbiobank.ac.uk/>.
- 380 [13] Sidong Liu et al. *Multimodal neuroimaging computing: a review of the applications in neuropsychiatric disorders*. Sept. 2015. DOI: 10.1007/s40708-015-0019-x. URL: <https://braininformatics.springeropen.com/articles/10.1007/s40708-015-0019-x>.
- 384 [14] Luís A. Vale-Silva and Karl Rohr. “Long-term cancer survival prediction using multimodal deep learning”. In: *Scientific Reports* 11.1 (June 2021), pp. 1–12. ISSN: 20452322. DOI: 10.1038/s41598-021-92799-4. URL: <https://www.nature.com/articles/s41598-021-92799-4>.
- 388 [15] Adam White et al. “Predicting recovery following stroke: deep learning, multimodal data and feature selection using explainable AI”. In: *arXiv preprint arXiv ...* (Oct. 2023). arXiv: 2310.19174. URL: <https://arxiv.org/abs/2310.19174v1>  
389 <https://arxiv.org/abs/2310.19174v1>  
390 <https://arxiv.org/abs/2310.19174v1>  
391 <https://arxiv.org/pdf/2310.19174>.

- 392 [16] Yongkai Liu et al. “Functional Outcome Prediction in Acute Ischemic Stroke Using a  
393 Fused Imaging and Clinical Deep Learning Model”. In: *Stroke* 54.9 (Sept. 2023), pp. 2316–  
394 2327. ISSN: 15244628. DOI: 10.1161/STROKEAHA.123.044072. URL: [https://www.  
395 ahajournals.org/doi/abs/10.1161/STROKEAHA.123.044072](https://www.ahajournals.org/doi/abs/10.1161/STROKEAHA.123.044072).
- 396 [17] Tom Nuno Wolf, Sebastian Pölsterl, and Christian Wachinger. “DAFT: A universal module to  
397 interweave tabular data and 3D images in CNNs”. In: *NeuroImage* 260 (Oct. 2022), p. 119505.  
398 ISSN: 10959572. DOI: 10.1016/j.neuroimage.2022.119505.
- 399 [18] Randall Balestriero et al. “A Cookbook of Self-Supervised Learning”. In: (2023). arXiv:  
400 2304.12210. URL: <http://arxiv.org/abs/2304.12210>.
- 401 [19] Ting Chen et al. “A simple framework for contrastive learning of visual representations”. In:  
402 *37th International Conference on Machine Learning, ICML 2020 Part F168147-3*. Figure 1  
403 (2020), pp. 1575–1585. arXiv: 2002.05709.
- 404 [20] Jean Bastien Grill et al. “Bootstrap your own latent a new approach to self-supervised learning”.  
405 In: *Advances in Neural Information Processing Systems*. Vol. 2020-Decem. Neural information  
406 processing systems foundation, June 2020. ISBN: 2006.07733v3. arXiv: 2006.07733. URL:  
407 <https://arxiv.org/abs/2006.07733v3>.
- 408 [21] Kaiming He et al. “Momentum Contrast for Unsupervised Visual Representation Learning”.  
409 In: *Proceedings of the IEEE Computer Society Conference on Computer Vision and Pattern  
410 Recognition*. IEEE Computer Society, Nov. 2020, pp. 9726–9735. DOI: 10.1109/CVPR42600.  
411 2020.00975. arXiv: 1911.05722. URL: <https://arxiv.org/abs/1911.05722v3>.
- 412 [22] Rein Houthoofd et al. “VIME: Variational information maximizing exploration”. In: *Advances  
413 in Neural Information Processing Systems*. Vol. 0. Neural information processing systems  
414 foundation, May 2016, pp. 1117–1125. arXiv: 1605.09674. URL: [https://arxiv.org/  
415 abs/1605.09674v4](https://arxiv.org/abs/1605.09674v4).
- 416 [23] Dara Bahri et al. “Scarf: Self-Supervised Contrastive Learning Using Random Feature Cor-  
417 ruption”. In: *ICLR 2022 - 10th International Conference on Learning Representations (2022)*,  
418 pp. 1–24. arXiv: 2106.15147.
- 419 [24] Adityanarayanan Radhakrishnan et al. “Cross-modal autoencoder framework learns holistic  
420 representations of cardiovascular state”. In: *Nature Communications* 14.1 (Dec. 2023). ISSN:  
421 20411723. DOI: 10.1038/s41467-023-38125-0. URL: [/pmc/articles/PMC10140057/  
422 %20/pmc/articles/PMC10140057/?report=abstract%20https://www.ncbi.nlm.  
423 nih.gov/pmc/articles/PMC10140057/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10140057/).
- 424 [25] Siyi Du et al. “TIP: Tabular-Image Pre-training for Multimodal Classification with Incomplete  
425 Data”. In: *arXiv (July 2024)*. arXiv: 2407.07582. URL: [https://arxiv.org/abs/2407.  
426 07582v1](https://arxiv.org/abs/2407.07582v1)<http://arxiv.org/abs/2407.07582>.
- 427 [26] Paul Hager, Martin J. Menten, and Daniel Rueckert. “Best of Both Worlds: Multimodal  
428 Contrastive Learning with Tabular and Imaging Data”. In: *arXiv (2023)*, pp. 23924–23935.  
429 DOI: 10.1109/cvpr52729.2023.02291. arXiv: 2303.14080.
- 430 [27] Alec Radford et al. “Learning Transferable Visual Models From Natural Language Super-  
431 vision”. In: *Proceedings of Machine Learning Research*. Vol. 139. ML Research Press, Feb.  
432 2021, pp. 8748–8763. ISBN: 9781713845065. arXiv: 2103.00020. URL: [https://arxiv.  
433 org/abs/2103.00020v1](https://arxiv.org/abs/2103.00020v1).
- 434 [28] Junnan Li et al. “Align before Fuse: Vision and Language Representation Learning with Mo-  
435 mentum Distillation”. In: *Advances in Neural Information Processing Systems*. Vol. 12. Neural  
436 information processing systems foundation, July 2021, pp. 9694–9705. ISBN: 9781713845393.  
437 arXiv: 2107.07651. URL: <https://arxiv.org/abs/2107.07651v2>.
- 438 [29] Stef van Buuren and Karin Groothuis-Oudshoorn. “mice: Multivariate imputation by chained  
439 equations in R”. In: *Journal of Statistical Software* 45.3 (Dec. 2011), pp. 1–67. ISSN: 15487660.  
440 DOI: 10.18637/jss.v045.i03. URL: [https://www.jstatsoft.  
441 org/index.php/jss/  
article/view/v045i03](https://www.jstatsoft.org/index.php/jss/article/view/v045i03).
- 442 [30] Fidel Alfaro-Almagro et al. “Image processing and Quality Control for the first 10,000 brain  
443 imaging datasets from UK Biobank”. In: *Neuroimage* 166 (2018), pp. 400–424.
- 444 [31] Fidel Alfaro-Almagro et al. “Image processing and Quality Control for the first 10,000 brain  
445 imaging datasets from UK Biobank”. In: *NeuroImage* 166 (Feb. 2018), pp. 400–424. ISSN:  
446 1053-8119. DOI: 10.1016/J.NEUROIMAGE.2017.10.034.
- 447 [32] Joost JM Van Griethuysen et al. “Computational radiomics system to decode the radiographic  
448 phenotype”. In: *Cancer research* 77.21 (2017), e104–e107.

- 449 [33] Ashish Vaswani et al. “Attention is all you need”. In: *Advances in Neural Information Process-*  
450 *ing Systems*. Vol. 2017-Decem. Neural information processing systems foundation, June 2017,  
451 pp. 5999–6009. ISBN: 1706.03762v7. arXiv: 1706.03762. URL: [https://arxiv.org/abs/](https://arxiv.org/abs/1706.03762v7)  
452 [1706.03762v7](https://arxiv.org/abs/1706.03762v7).
- 453 [34] Chao Ye et al. “CT-BERT: Learning Better Tabular Representations Through Cross-Table Pre-  
454 *training*”. In: *Proceedings of the ACM Web Conference 2024 (WWW '24), May 13â•fi17, 2024,*  
455 *Singapore, Singapore 1* (July 2023). DOI: 10.1145/XXXXXXX.XXXXXX. arXiv: 2307.04308.  
456 URL: <https://arxiv.org/abs/2307.04308v1>.
- 457 [35] Gao Huang et al. “Densely connected convolutional networks”. In: *Proceedings - 30th IEEE*  
458 *Conference on Computer Vision and Pattern Recognition, CVPR 2017*. Vol. 2017-Janua.  
459 Institute of Electrical and Electronics Engineers Inc., Aug. 2017, pp. 2261–2269. ISBN:  
460 9781538604571. DOI: 10.1109/CVPR.2017.243. arXiv: 1608.06993. URL: <https://arxiv.org/abs/1608.06993v5>.
- 462 [36] Simeon Spasov et al. “A parameter-efficient deep learning approach to predict conversion  
463 from mild cognitive impairment to Alzheimer’s disease”. In: *NeuroImage* 189 (Apr. 2019),  
464 pp. 276–287. ISSN: 10959572. DOI: 10.1016/j.neuroimage.2019.01.031. URL: <https://pubmed.ncbi.nlm.nih.gov/30654174/>.
- 466 [37] Diederik P. Kingma and Jimmy Lei Ba. “Adam: A method for stochastic optimization”. In:  
467 *3rd International Conference on Learning Representations, ICLR 2015 - Conference Track*  
468 *Proceedings*. International Conference on Learning Representations, ICLR, Dec. 2015. arXiv:  
469 1412.6980. URL: <https://arxiv.org/abs/1412.6980v9>.
- 470 [38] Leland McInnes, John Healy, and James Melville. “UMAP: Uniform Manifold Approximation  
471 and Projection for Dimension Reduction”. In: (2018). arXiv: 1802.03426. URL: <http://arxiv.org/abs/1802.03426>.
- 473 [39] Ramprasaath R. Selvaraju et al. “Grad-CAM: Visual Explanations from Deep Networks via  
474 Gradient-Based Localization”. In: *Proceedings of the IEEE International Conference on*  
475 *Computer Vision*. Vol. 2017-*Octob*. Institute of Electrical and Electronics Engineers Inc., Dec.  
476 2017, pp. 618–626. ISBN: 9781538610329. DOI: 10.1109/ICCV.2017.74.
- 477 [40] Kaiming He et al. “Deep residual learning for image recognition”. In: *Proceedings of the IEEE*  
478 *Computer Society Conference on Computer Vision and Pattern Recognition*. Vol. 2016-Decem.  
479 IEEE Computer Society, Dec. 2016, pp. 770–778. ISBN: 9781467388504. DOI: 10.1109/  
480 CVPR.2016.90. arXiv: 1512.03385. URL: <https://arxiv.org/abs/1512.03385v1>.
- 481 [41] Lukas A. Grajauskas et al. *MRI-based evaluation of structural degeneration in the ageing*  
482 *brain: Pathophysiology and assessment*. Jan. 2019. DOI: 10.1016/j.arr.2018.11.004.
- 483 [42] J-H Park et al. “White matter hyperintensities and recurrent stroke risk in patients with stroke  
484 with small-vessel disease”. In: *European Journal of Neurology* 26.6 (2019), pp. 911–918.
- 485 [43] Hui Guo et al. “MRI assessment of whole-brain structural changes in aging”. In: *Clinical*  
486 *Interventions in Aging* 12 (Aug. 2017), pp. 1251–1270. ISSN: 11781998. DOI: 10.2147/CIA.  
487 S139515. URL: <http://dx.doi.org/10.2147/CIA.S139515>.
- 488 [44] Yong Soo Shim et al. “Pathological correlates of white matter hyperintensities on magnetic  
489 resonance imaging”. In: *Dementia and Geriatric Cognitive Disorders* 39 (Feb. 2015), pp. 92–  
490 104. ISSN: 14219824. DOI: 10.1159/000366411.
- 491 [45] Ann-Marie G De Lange et al. “Multimodal brain-age prediction and cardiovascular risk: The  
492 Whitehall II MRI sub-study”. In: *NeuroImage* 222 (2020), p. 117292.
- 493 [46] Sook-Lai Liew et al. “Association of brain age, lesion volume, and functional outcome in  
494 patients with stroke”. In: *Neurology* 100.20 (2023), e2103–e2113.
- 495 [47] James H Cole et al. “Brain age predicts mortality”. In: *Molecular psychiatry* 23.5 (2018),  
496 pp. 1385–1392.

## 497 **NeurIPS Paper Checklist**

### 498 **1. Claims**

499 Question: Do the main claims made in the abstract and introduction accurately reflect the  
500 paper's contributions and scope?

501 Answer: [Yes]

502 Justification: Yes- both quantitative and qualitative experiments were conducted to support  
503 the claims of this work.

504 Guidelines:

- 505 • The answer NA means that the abstract and introduction do not include the claims  
506 made in the paper.
- 507 • The abstract and/or introduction should clearly state the claims made, including the  
508 contributions made in the paper and important assumptions and limitations. A No or  
509 NA answer to this question will not be perceived well by the reviewers.
- 510 • The claims made should match theoretical and experimental results, and reflect how  
511 much the results can be expected to generalize to other settings.
- 512 • It is fine to include aspirational goals as motivation as long as it is clear that these goals  
513 are not attained by the paper.

### 514 **2. Limitations**

515 Question: Does the paper discuss the limitations of the work performed by the authors?

516 Answer: [Yes]

517 Justification: Yes, the limitations are discussed after the results in page 8.

518 Guidelines:

- 519 • The answer NA means that the paper has no limitation while the answer No means that  
520 the paper has limitations, but those are not discussed in the paper.
- 521 • The authors are encouraged to create a separate "Limitations" section in their paper.
- 522 • The paper should point out any strong assumptions and how robust the results are to  
523 violations of these assumptions (e.g., independence assumptions, noiseless settings,  
524 model well-specification, asymptotic approximations only holding locally). The authors  
525 should reflect on how these assumptions might be violated in practice and what the  
526 implications would be.
- 527 • The authors should reflect on the scope of the claims made, e.g., if the approach was  
528 only tested on a few datasets or with a few runs. In general, empirical results often  
529 depend on implicit assumptions, which should be articulated.
- 530 • The authors should reflect on the factors that influence the performance of the approach.  
531 For example, a facial recognition algorithm may perform poorly when image resolution  
532 is low or images are taken in low lighting. Or a speech-to-text system might not be  
533 used reliably to provide closed captions for online lectures because it fails to handle  
534 technical jargon.
- 535 • The authors should discuss the computational efficiency of the proposed algorithms  
536 and how they scale with dataset size.
- 537 • If applicable, the authors should discuss possible limitations of their approach to  
538 address problems of privacy and fairness.
- 539 • While the authors might fear that complete honesty about limitations might be used by  
540 reviewers as grounds for rejection, a worse outcome might be that reviewers discover  
541 limitations that aren't acknowledged in the paper. The authors should use their best  
542 judgment and recognize that individual actions in favor of transparency play an impor-  
543 tant role in developing norms that preserve the integrity of the community. Reviewers  
544 will be specifically instructed to not penalize honesty concerning limitations.

### 545 **3. Theory Assumptions and Proofs**

546 Question: For each theoretical result, does the paper provide the full set of assumptions and  
547 a complete (and correct) proof?

548 Answer: [NA]

549 Justification: There is no theoretical assumption or proof in this work.

550 Guidelines:

- 551 • The answer NA means that the paper does not include theoretical results.
- 552 • All the theorems, formulas, and proofs in the paper should be numbered and cross-
- 553 referenced.
- 554 • All assumptions should be clearly stated or referenced in the statement of any theorems.
- 555 • The proofs can either appear in the main paper or the supplemental material, but if
- 556 they appear in the supplemental material, the authors are encouraged to provide a short
- 557 proof sketch to provide intuition.
- 558 • Inversely, any informal proof provided in the core of the paper should be complemented
- 559 by formal proofs provided in appendix or supplemental material.
- 560 • Theorems and Lemmas that the proof relies upon should be properly referenced.

#### 561 4. Experimental Result Reproducibility

562 Question: Does the paper fully disclose all the information needed to reproduce the main ex-

563 perimental results of the paper to the extent that it affects the main claims and/or conclusions

564 of the paper (regardless of whether the code and data are provided or not)?

565 Answer: [\[Yes\]](#)

566 Justification: Yes, all the experimental parameters as well as all the models architecture

567 details are given in sections 2 and 3. The code will be published open source for full

568 reproducibility in the camera-ready version.

569 Guidelines:

- 570 • The answer NA means that the paper does not include experiments.
- 571 • If the paper includes experiments, a No answer to this question will not be perceived
- 572 well by the reviewers: Making the paper reproducible is important, regardless of
- 573 whether the code and data are provided or not.
- 574 • If the contribution is a dataset and/or model, the authors should describe the steps taken
- 575 to make their results reproducible or verifiable.
- 576 • Depending on the contribution, reproducibility can be accomplished in various ways.
- 577 For example, if the contribution is a novel architecture, describing the architecture fully
- 578 might suffice, or if the contribution is a specific model and empirical evaluation, it may
- 579 be necessary to either make it possible for others to replicate the model with the same
- 580 dataset, or provide access to the model. In general, releasing code and data is often
- 581 one good way to accomplish this, but reproducibility can also be provided via detailed
- 582 instructions for how to replicate the results, access to a hosted model (e.g., in the case
- 583 of a large language model), releasing of a model checkpoint, or other means that are
- 584 appropriate to the research performed.
- 585 • While NeurIPS does not require releasing code, the conference does require all submissions
- 586 to provide some reasonable avenue for reproducibility, which may depend on the
- 587 nature of the contribution. For example
  - 588 (a) If the contribution is primarily a new algorithm, the paper should make it clear how
  - 589 to reproduce that algorithm.
  - 590 (b) If the contribution is primarily a new model architecture, the paper should describe
  - 591 the architecture clearly and fully.
  - 592 (c) If the contribution is a new model (e.g., a large language model), then there should
  - 593 either be a way to access this model for reproducing the results or a way to reproduce
  - 594 the model (e.g., with an open-source dataset or instructions for how to construct
  - 595 the dataset).
  - 596 (d) We recognize that reproducibility may be tricky in some cases, in which case
  - 597 authors are welcome to describe the particular way they provide for reproducibility.
  - 598 In the case of closed-source models, it may be that access to the model is limited in
  - 599 some way (e.g., to registered users), but it should be possible for other researchers
  - 600 to have some path to reproducing or verifying the results.

#### 601 5. Open access to data and code

602 Question: Does the paper provide open access to the data and code, with sufficient instruc-  
603 tions to faithfully reproduce the main experimental results, as described in supplemental  
604 material?

605 Answer: [No]

606 Justification: The code will be released in the camera-ready version to fully reproduce all  
607 the experimental results as described. The data is from the UK Biobank and is therefore not  
608 publicly available.

609 Guidelines:

- 610 • The answer NA means that paper does not include experiments requiring code.
- 611 • Please see the NeurIPS code and data submission guidelines ([https://nips.cc/  
612 public/guides/CodeSubmissionPolicy](https://nips.cc/public/guides/CodeSubmissionPolicy)) for more details.
- 613 • While we encourage the release of code and data, we understand that this might not be  
614 possible, so “No” is an acceptable answer. Papers cannot be rejected simply for not  
615 including code, unless this is central to the contribution (e.g., for a new open-source  
616 benchmark).
- 617 • The instructions should contain the exact command and environment needed to run to  
618 reproduce the results. See the NeurIPS code and data submission guidelines ([https:  
619 //nips.cc/public/guides/CodeSubmissionPolicy](https://nips.cc/public/guides/CodeSubmissionPolicy)) for more details.
- 620 • The authors should provide instructions on data access and preparation, including how  
621 to access the raw data, preprocessed data, intermediate data, and generated data, etc.
- 622 • The authors should provide scripts to reproduce all experimental results for the new  
623 proposed method and baselines. If only a subset of experiments are reproducible, they  
624 should state which ones are omitted from the script and why.
- 625 • At submission time, to preserve anonymity, the authors should release anonymized  
626 versions (if applicable).
- 627 • Providing as much information as possible in supplemental material (appended to the  
628 paper) is recommended, but including URLs to data and code is permitted.

## 629 6. Experimental Setting/Details

630 Question: Does the paper specify all the training and test details (e.g., data splits, hyper-  
631 parameters, how they were chosen, type of optimizer, etc.) necessary to understand the  
632 results?

633 Answer: [Yes]

634 Justification: Yes, every detail is shared concerning the pretraining and training splits,  
635 hyperparameters and optimizers used in sections 2 and 3.

636 Guidelines:

- 637 • The answer NA means that the paper does not include experiments.
- 638 • The experimental setting should be presented in the core of the paper to a level of detail  
639 that is necessary to appreciate the results and make sense of them.
- 640 • The full details can be provided either with the code, in appendix, or as supplemental  
641 material.

## 642 7. Experiment Statistical Significance

643 Question: Does the paper report error bars suitably and correctly defined or other appropriate  
644 information about the statistical significance of the experiments?

645 Answer: [NA]

646 Justification: Error bars or confidence intervals are not really applicable in this con-  
647 text/case/experiments. Train/test splits and model initialization are precised.

648 Guidelines:

- 649 • The answer NA means that the paper does not include experiments.
- 650 • The authors should answer "Yes" if the results are accompanied by error bars, confi-  
651 dence intervals, or statistical significance tests, at least for the experiments that support  
652 the main claims of the paper.



- 653 • The factors of variability that the error bars are capturing should be clearly stated (for  
654 example, train/test split, initialization, random drawing of some parameter, or overall  
655 run with given experimental conditions).
- 656 • The method for calculating the error bars should be explained (closed form formula,  
657 call to a library function, bootstrap, etc.)
- 658 • The assumptions made should be given (e.g., Normally distributed errors).
- 659 • It should be clear whether the error bar is the standard deviation or the standard error  
660 of the mean.
- 661 • It is OK to report 1-sigma error bars, but one should state it. The authors should  
662 preferably report a 2-sigma error bar than state that they have a 96% CI, if the hypothesis  
663 of Normality of errors is not verified.
- 664 • For asymmetric distributions, the authors should be careful not to show in tables or  
665 figures symmetric error bars that would yield results that are out of range (e.g. negative  
666 error rates).
- 667 • If error bars are reported in tables or plots, The authors should explain in the text how  
668 they were calculated and reference the corresponding figures or tables in the text.

## 669 8. Experiments Compute Resources

670 Question: For each experiment, does the paper provide sufficient information on the com-  
671 puter resources (type of compute workers, memory, time of execution) needed to reproduce  
672 the experiments?

673 Answer: [Yes]

674 Justification: The details for compute resources are elaborated in section 3.1.2.

675 Guidelines:

- 676 • The answer NA means that the paper does not include experiments.
- 677 • The paper should indicate the type of compute workers CPU or GPU, internal cluster,  
678 or cloud provider, including relevant memory and storage.
- 679 • The paper should provide the amount of compute required for each of the individual  
680 experimental runs as well as estimate the total compute.
- 681 • The paper should disclose whether the full research project required more compute  
682 than the experiments reported in the paper (e.g., preliminary or failed experiments that  
683 didn't make it into the paper).

## 684 9. Code Of Ethics

685 Question: Does the research conducted in the paper conform, in every respect, with the  
686 NeurIPS Code of Ethics <https://neurips.cc/public/EthicsGuidelines?>

687 Answer: [Yes]

688 Justification: Yes, data anonymisation was preserved according to UKB guidelines and  
689 societal impact was maximized in the context of this research work. No participant was  
690 harmed and they were all volunteers to the UKB.

691 Guidelines:

- 692 • The answer NA means that the authors have not reviewed the NeurIPS Code of Ethics.
- 693 • If the authors answer No, they should explain the special circumstances that require a  
694 deviation from the Code of Ethics.
- 695 • The authors should make sure to preserve anonymity (e.g., if there is a special consid-  
696 eration due to laws or regulations in their jurisdiction).

## 697 10. Broader Impacts

698 Question: Does the paper discuss both potential positive societal impacts and negative  
699 societal impacts of the work performed?

700 Answer: [Yes]

701 Justification: Yes, the discussion and conclusion elaborate on the potential benefits of  
702 anticipating stroke events in healthy populations.

703 Guidelines:

- 704 • The answer NA means that there is no societal impact of the work performed.
- 705 • If the authors answer NA or No, they should explain why their work has no societal
- 706 impact or why the paper does not address societal impact.
- 707 • Examples of negative societal impacts include potential malicious or unintended uses
- 708 (e.g., disinformation, generating fake profiles, surveillance), fairness considerations
- 709 (e.g., deployment of technologies that could make decisions that unfairly impact specific
- 710 groups), privacy considerations, and security considerations.
- 711 • The conference expects that many papers will be foundational research and not tied
- 712 to particular applications, let alone deployments. However, if there is a direct path to
- 713 any negative applications, the authors should point it out. For example, it is legitimate
- 714 to point out that an improvement in the quality of generative models could be used to
- 715 generate deepfakes for disinformation. On the other hand, it is not needed to point out
- 716 that a generic algorithm for optimizing neural networks could enable people to train
- 717 models that generate Deepfakes faster.
- 718 • The authors should consider possible harms that could arise when the technology is
- 719 being used as intended and functioning correctly, harms that could arise when the
- 720 technology is being used as intended but gives incorrect results, and harms following
- 721 from (intentional or unintentional) misuse of the technology.
- 722 • If there are negative societal impacts, the authors could also discuss possible mitigation
- 723 strategies (e.g., gated release of models, providing defenses in addition to attacks,
- 724 mechanisms for monitoring misuse, mechanisms to monitor how a system learns from
- 725 feedback over time, improving the efficiency and accessibility of ML).

## 726 11. Safeguards

727 Question: Does the paper describe safeguards that have been put in place for responsible  
 728 release of data or models that have a high risk for misuse (e.g., pretrained language models,  
 729 image generators, or scraped datasets)?

730 Answer: [NA]

731 Justification: The paper poses no such risk.

732 Guidelines:

- 733 • The answer NA means that the paper poses no such risks.
- 734 • Released models that have a high risk for misuse or dual-use should be released with
- 735 necessary safeguards to allow for controlled use of the model, for example by requiring
- 736 that users adhere to usage guidelines or restrictions to access the model or implementing
- 737 safety filters.
- 738 • Datasets that have been scraped from the Internet could pose safety risks. The authors
- 739 should describe how they avoided releasing unsafe images.
- 740 • We recognize that providing effective safeguards is challenging, and many papers do
- 741 not require this, but we encourage authors to take this into account and make a best
- 742 faith effort.

## 743 12. Licenses for existing assets

744 Question: Are the creators or original owners of assets (e.g., code, data, models), used in  
 745 the paper, properly credited and are the license and terms of use explicitly mentioned and  
 746 properly respected?

747 Answer: [Yes]

748 Justification: All references to data (UK Biobank), codes, and models are referenced  
 749 accordingly.

750 Guidelines:

- 751 • The answer NA means that the paper does not use existing assets.
- 752 • The authors should cite the original paper that produced the code package or dataset.
- 753 • The authors should state which version of the asset is used and, if possible, include a
- 754 URL.
- 755 • The name of the license (e.g., CC-BY 4.0) should be included for each asset.

- 756 • For scraped data from a particular source (e.g., website), the copyright and terms of  
757 service of that source should be provided.
- 758 • If assets are released, the license, copyright information, and terms of use in the  
759 package should be provided. For popular datasets, [paperswithcode.com/datasets](https://paperswithcode.com/datasets)  
760 has curated licenses for some datasets. Their licensing guide can help determine the  
761 license of a dataset.
- 762 • For existing datasets that are re-packaged, both the original license and the license of  
763 the derived asset (if it has changed) should be provided.
- 764 • If this information is not available online, the authors are encouraged to reach out to  
765 the asset's creators.

### 766 13. **New Assets**

767 Question: Are new assets introduced in the paper well documented and is the documentation  
768 provided alongside the assets?

769 Answer: [NA]

770 Justification: Code, documentations and pre-trained models checkpoints will be released for  
771 camera-ready version.

772 Guidelines:

- 773 • The answer NA means that the paper does not release new assets.
- 774 • Researchers should communicate the details of the dataset/code/model as part of their  
775 submissions via structured templates. This includes details about training, license,  
776 limitations, etc.
- 777 • The paper should discuss whether and how consent was obtained from people whose  
778 asset is used.
- 779 • At submission time, remember to anonymize your assets (if applicable). You can either  
780 create an anonymized URL or include an anonymized zip file.

### 781 14. **Crowdsourcing and Research with Human Subjects**

782 Question: For crowdsourcing experiments and research with human subjects, does the paper  
783 include the full text of instructions given to participants and screenshots, if applicable, as  
784 well as details about compensation (if any)?

785 Answer: [NA]

786 Justification: The paper does not involve crowdsourcing. We use the data from human  
787 participants that were already collected by UK Biobank.

788 Guidelines:

- 789 • The answer NA means that the paper does not involve crowdsourcing nor research with  
790 human subjects.
- 791 • Including this information in the supplemental material is fine, but if the main contribu-  
792 tion of the paper involves human subjects, then as much detail as possible should be  
793 included in the main paper.
- 794 • According to the NeurIPS Code of Ethics, workers involved in data collection, curation,  
795 or other labor should be paid at least the minimum wage in the country of the data  
796 collector.

### 797 15. **Institutional Review Board (IRB) Approvals or Equivalent for Research with Human 798 Subjects**

799 Question: Does the paper describe potential risks incurred by study participants, whether  
800 such risks were disclosed to the subjects, and whether Institutional Review Board (IRB)  
801 approvals (or an equivalent approval/review based on the requirements of your country or  
802 institution) were obtained?

803 Answer: [NA]

804 Justification: The paper does not involve crowdsourcing. We use the data from human  
805 participants that were already collected by UK Biobank.

806 Guidelines:

807  
808  
809  
810  
811  
812  
813  
814  
815  
816

- The answer NA means that the paper does not involve crowdsourcing nor research with human subjects.
- Depending on the country in which research is conducted, IRB approval (or equivalent) may be required for any human subjects research. If you obtained IRB approval, you should clearly state this in the paper.
- We recognize that the procedures for this may vary significantly between institutions and locations, and we expect authors to adhere to the NeurIPS Code of Ethics and the guidelines for their institution.
- For initial submissions, do not include any information that would break anonymity (if applicable), such as the institution conducting the review.