(MICCAI 2021)
Self-Supervised Longitudinal Neighbourhood Embedding

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Motivation

Longitudinal MRIs are often used to capture the gradual deterioration of brain structure and function caused by aging or neurological diseases. Analyzing this data via machine learning generally requires a large number of ground-truth labels, which are often missing or expensive to obtain. **Reducing the need for labels**, they propose a self-supervised strategy for representation learning named Longitudinal Neighborhood Embedding (LNE).

Method

LNE explicitly models the similarity between trajectory vectors across different subjects. They do so by building a graph in each training iteration defining neighborhoods in the latent space **so that the progression direction of a subject follows the direction of its neighbors.**

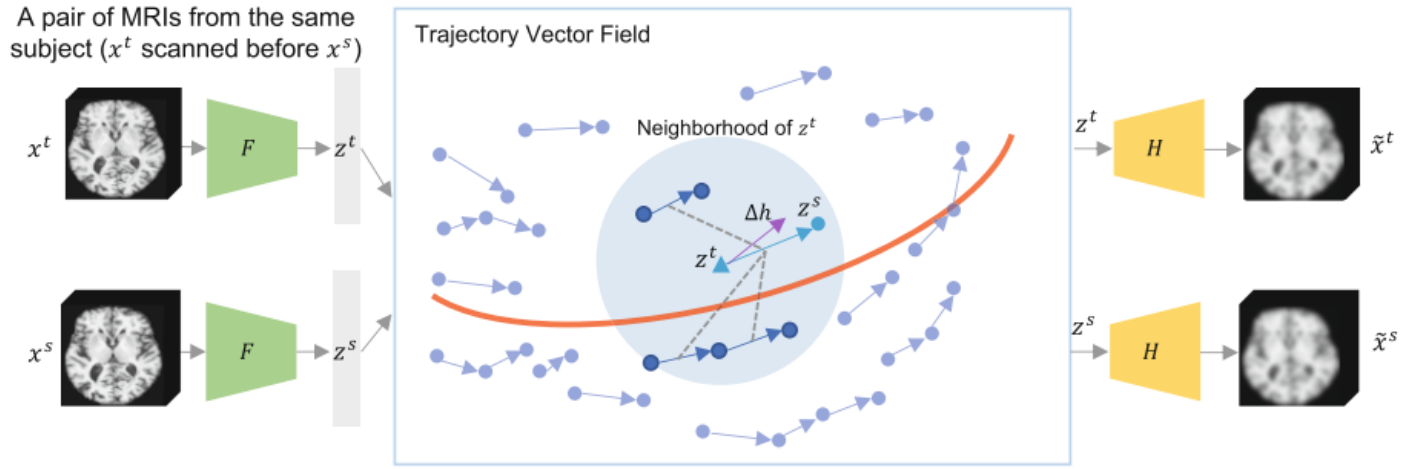
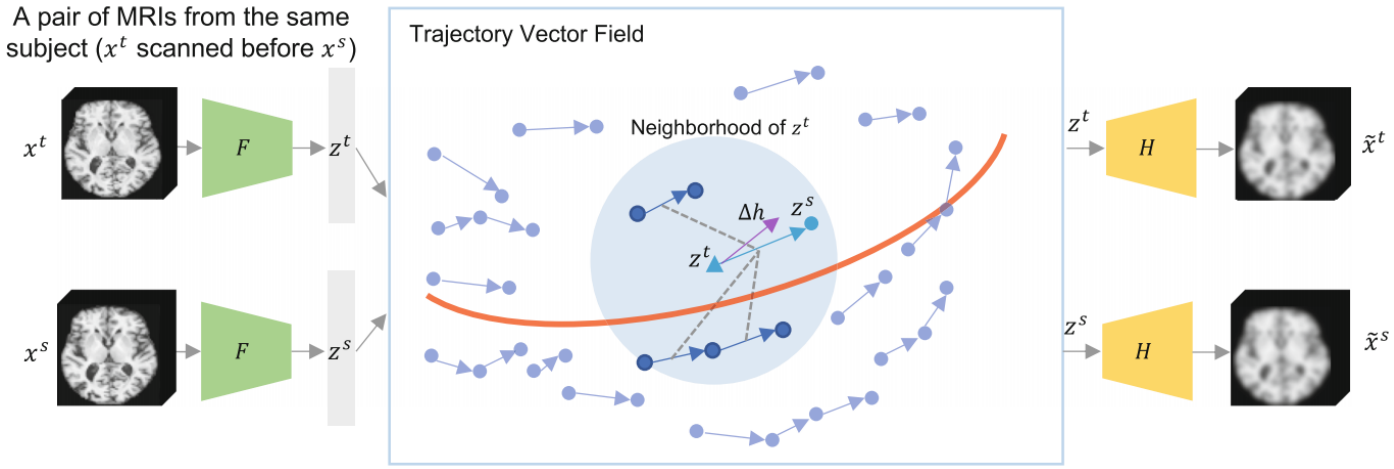


Fig. 1. Overview of the proposed method: an encoder projects a subject-specific image pair (x^t, x^s) into the latent space resulting in a trajectory vector (cyan). We encourage the direction of this vector to be consistent with Δh (purple), a vector pooled from the neighborhood of z^t (blue circle). As a result, the latent space encodes the global morphological change linked to aging (red curve). (Color figure online)

Method



Objective Function.

$$L := \mathbf{E}_{(x^t,x^s)\sim\mathcal{S}} \left(\| x^t - \tilde{x}^t \|_2^2 + \| x^s - \tilde{x}^s \|_2^2 - \lambda \cdot \cos(\theta_{\langle \Delta z, \Delta h \rangle}) \right),$$

1. Pairwise Training Strategy.

i. subject-specific image pairs

$$(x^t, x^s)$$

ii. latent representations

$$z^t = F(x^t),\ z^s = F(x^s)$$

iii. normalized trajectory vector

$$\Delta z^{(t,s)} = (z^s - z^t)/\Delta t^{(t,s)}$$

2. Longitudinal Neighbourhood Embedding.

i. adjacency matrix

$$P_{i,j} = \| z_i^t - z_j^t \|_2$$

$$A_{i,j} := \begin{cases} exp(-\frac{P_{i,j}^2}{2\sigma_i^2}) & j \in \mathcal{N}_i \\ 0, & j \notin \mathcal{N}_i \end{cases}.$$

with $\sigma_i := max(P_{i,j\in\mathcal{N}_i}) - min(P_{i,j\in\mathcal{N}_i})$

ii. longitudinal neighbourhood embedding

$$\Delta h_i := \sum_{j\in\mathcal{N}_i} A_{i,j} D_{i,j}^{-1} \Delta z_j,$$

Experiments

1. Predicting age

Lab data set: 582 MRIs of 274 healthy individuals with the age ranging from 20 to 90. Each subject had 1 to 13 scans with an average of 2.3 scans spanning an average time interval of 3.8 years.

2. Classification

The second data set comprised 2389 longitudinal T1-weighted MRIs (at least two visits per subject) from ADNI, which consisted of 185 NC (age: 75.57 ± 5.06 years), 119 subjects with AD (age: 75.17 ± 7.57 years), 193 subjects diagnosed with sMCI (age: 75.63 ± 6.62 years), and 135 subjects diagnosed with pMCI (age: 75.91 ± 5.35 years). There was no significant age difference between the NC and AD cohorts ($p = 0.55$, two-sample t-test) as well as the sMCI and pMCI cohorts ($p = 0.75$).

Result

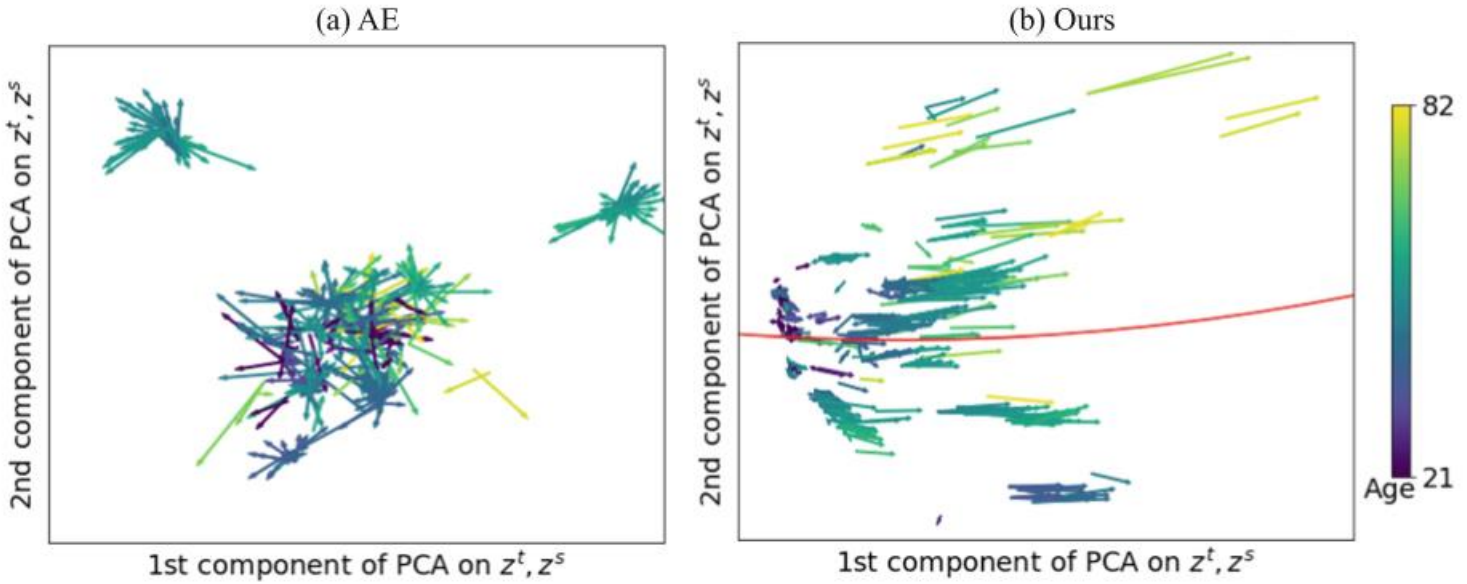


Fig. 2. Experiments on healthy aging: Latent space of AutoEncoder (AE) (a) and the proposed LNE (b) projected into 2D PCA space of z^t and z^s. Arrows represent Δz and are color-coded by the age of z^t. The global trajectory in (b) is fitted by robust linear mixed effect model (red curve). (Color figure online)

Result

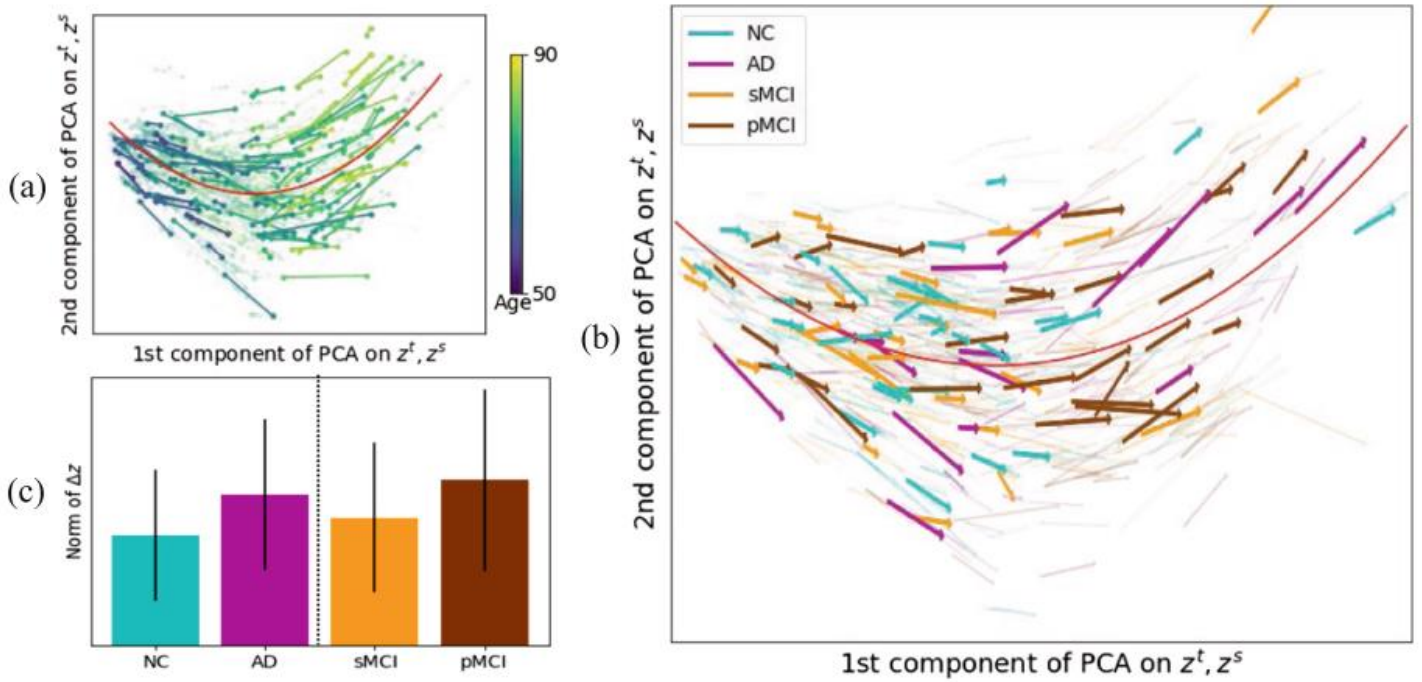


Fig. 3. Experiments on ADNI: (a) The age distribution of the latent space. Lines connecting z^t and z^s are color-coded by the age of z^t; Red curve is the global trajectory fitted by a robust linear mixed effect model. (b) Trajectory vector field color-coded by diagnosis groups; (c) The norm of Δz encoding the speed of aging for 4 different diagnosis groups. (Color figure online)

Result

Table 1. Supervised downstream tasks in frozen or fine-tune scenarios. Left: Age regression on healthy subjects with R2 as an evaluation metric. Right: classification on ADNI dataset with BACC as the metric.

Methods	Health aging (**R2**)		ADNI (**BACC**)			
	Age		NC vs AD		sMCI vs pMCI	
	Frozen	Fine-tune	Frozen	Fine-tune	Frozen	Fine-tune
No pretrain	–	0.72	–	79.4	–	69.3
AE	0.53	0.69	72.2	80.7	62.6	69.5
VAE [12]	0.51	0.69	66.7	77.0	61.3	63.8
SimCLR [6]	0.56	0.73	72.9	82.4	63.3	69.5
LSSL [24]	0.59	**0.74**	74.2	82.1	69.4	71.2
Ours (LNE)	**0.62**	**0.74**	**81.9**	**83.6**	**70.6**	**73.4**

(MICCAI 2021)
Contrastive Learning with Continuous Proxy Meta-Data for 3D MRI Classification

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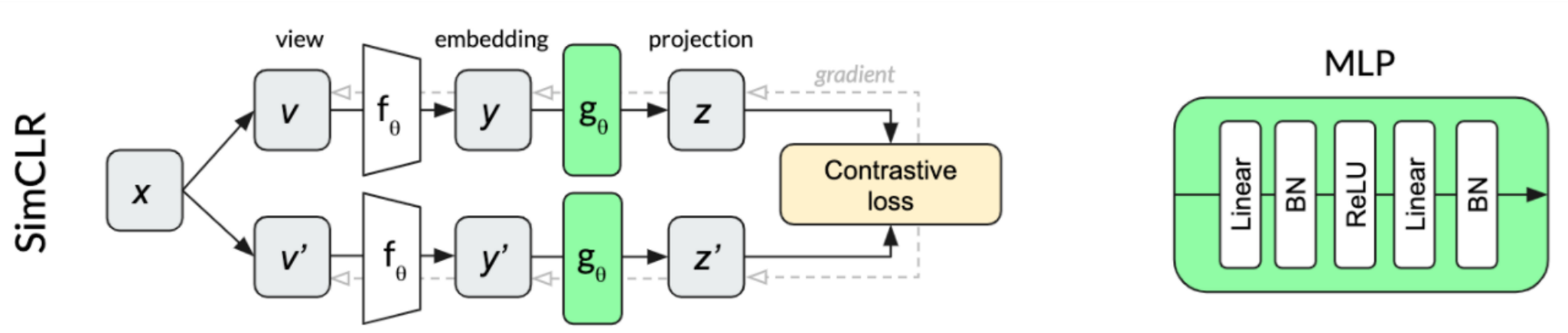
Motivation

Most of recent works do not take advantage of available meta-data, such as participant’s age.

Goal

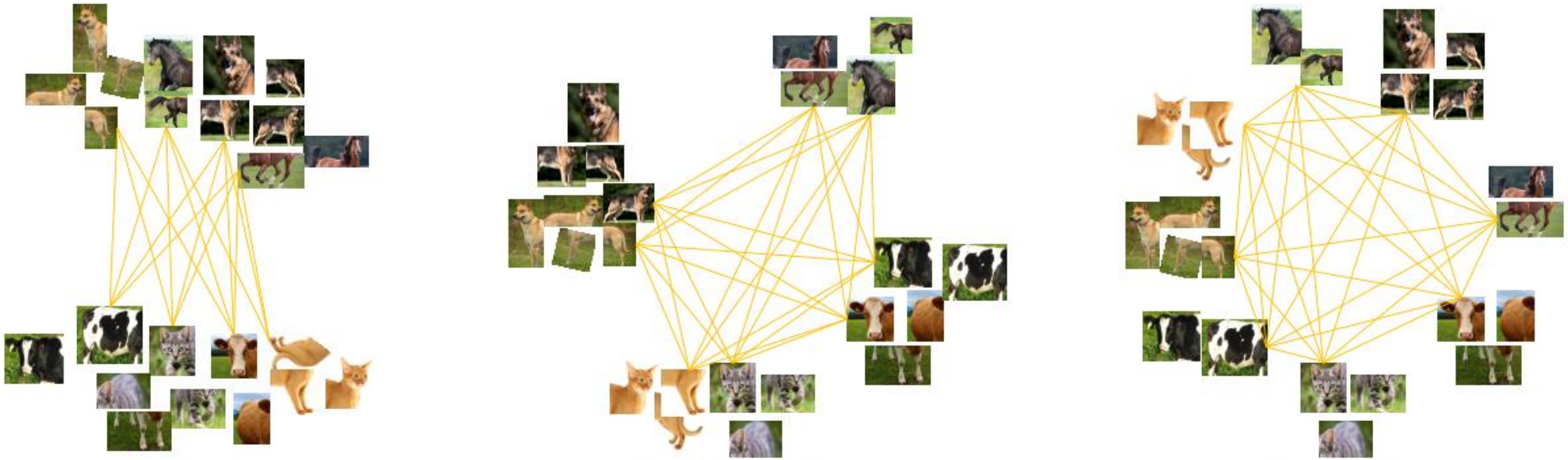
Propose a new **y-Aware InfoNCE loss** inspired from the Noise Contrastive Estimation loss that aims at improving the positive sampling according to the similarity between two proxy meta-data

SimCLR



$$L_N = -\mathbb{E}_X \left[\log \frac{\exp\left(f(x)^T f(x^+)\right)}{\exp(f(x)^T f(x^+)) + \sum_{j=1}^{N-1} \exp\left(f(x)^T f(x_j^-)\right)} \right]$$

Problems



(a) under-clustering (b) ideal clustering (c) over-clustering

Figure 2. Illustration of under-clustering and over-clustering. Each sample pair connected by a yellow line represents a negative pair.

[1] (arXiv 2104) Solving Inefficiency of Self-supervised Representation Learning

Method

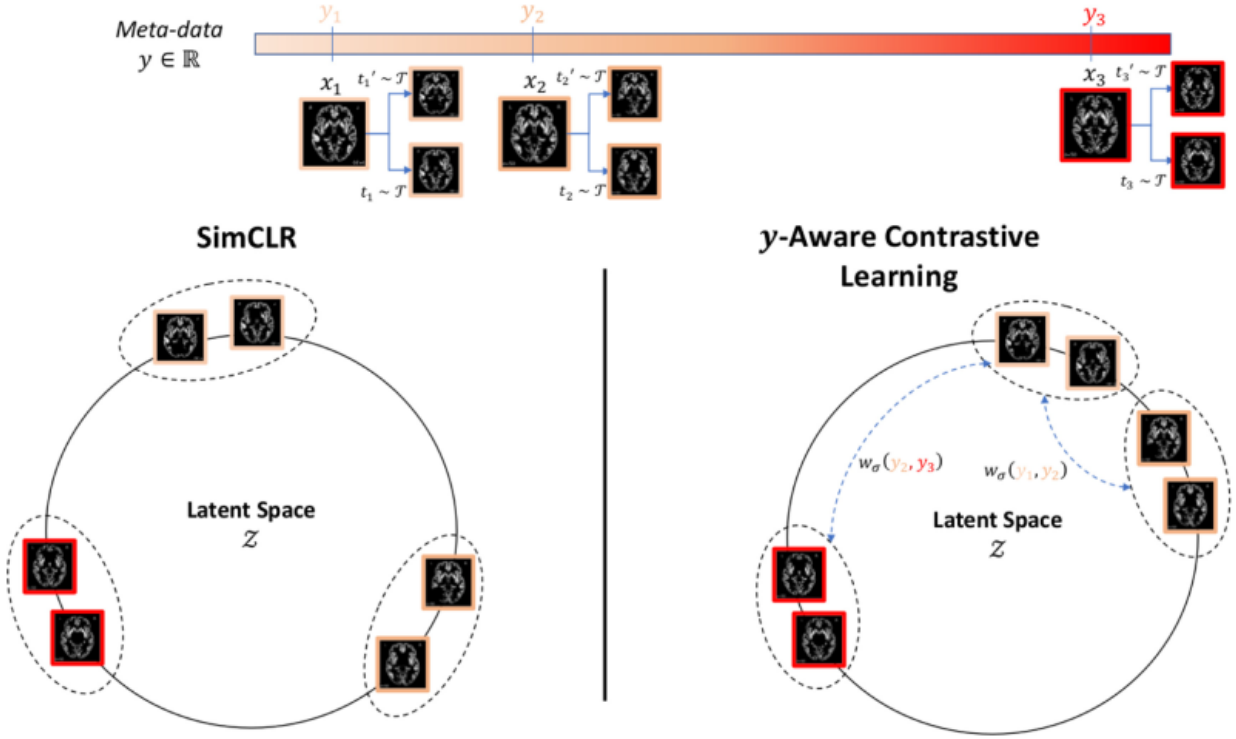


Fig. 1. Differently from SimCLR [5], our new loss can handle meta-data $y \in \mathbb{R}$ by redefining the notion of similarity between two images in the latent space $\mathcal{Z}$. For an image x_i, transformed twice through two augmentations $t_1, t_1' \sim \mathcal{T}$, the resulting views $(t_1(x_i), t_2(x_i))$ are expected to be close in the latent space through the learnt mapping f_θ, as in SimCLR. However, we also expect a different input $x_{k \neq i}$ to be close to x_i in $\mathcal{Z}$ if the two *proxy* meta-data y_i and y_k are similar. We define a similarity function $w_\sigma(y_i, y_k)$ that quantifies this notion of similarity.

InfoNCE loss:

$$\mathcal{L}_{NCE} = -\log \frac{e^{f_\theta(v_1^i, v_2^i)}}{\frac{1}{n}\sum_{j=1}^{n} e^{f_\theta(v_1^i, v_2^j)}}$$

y-Aware InfoNCE loss:

$$\mathcal{L}^y_{NCE} = -\sum_{k=1}^{n} \frac{w_\sigma(y_k, y_i)}{\sum_{j=1}^{n} w_\sigma(y_j, y_i)} \log \frac{e^{f_\theta(v_1^i, v_2^k)}}{\frac{1}{n}\sum_{j=1}^{n} e^{f_\theta(v_1^i, v_2^j)}}$$

Radius Basis Function (RBF) kernel

$$w_\sigma = \exp\left(-\frac{\|\mathbf{x} - \mathbf{x}'\|^2}{2\sigma^2}\right)$$

Experiments

- Datasets

  - **Big Healthy Brains (BHB) dataset** We aggregated 13 publicly available datasets of 3D T1 MRI scans of healthy controls (HC) acquired on more than 70 different scanners and comprising *N* = 10 samples. We use this dataset only to pre-train our model with the **participant's age as the *proxy* meta-data**. The learnt representation is then tested on the following four data-sets using as final task a binary classification between HC and patients.
  - **SCHIZCONNECT-VIP** It comprises *N* = 605 multi-site MRI scans including 275 patients with strict schizophrenia (SCZ：精神分裂) and 330 HC.
  - **BIOBD** This dataset includes *N* = 662 MRI scans acquired on 8 different sites with 356 HC and 306 patients with bipolar disorder (BD：躁郁症).
  - **BSNIP** [25] It includes *N* = 511 MRI scans with *N* = 200 HC, *N* = 194 SCZ and *N* = 117 BD.
  - **Alzheimer's Disease Neuroimaging Initiative (ADNI-GO)** We use *N* = 387 co-registered T1-weighted MRI images divided in *N* = 199 healthy controls and *N* = 188 Alzheimer's patients (AD：阿兹海默). We only included one scan per patient at the first session (baseline).

Result

Evaluation of the representation

Classification is performed using a linear layer on top of the pre-trained frozen encoders.

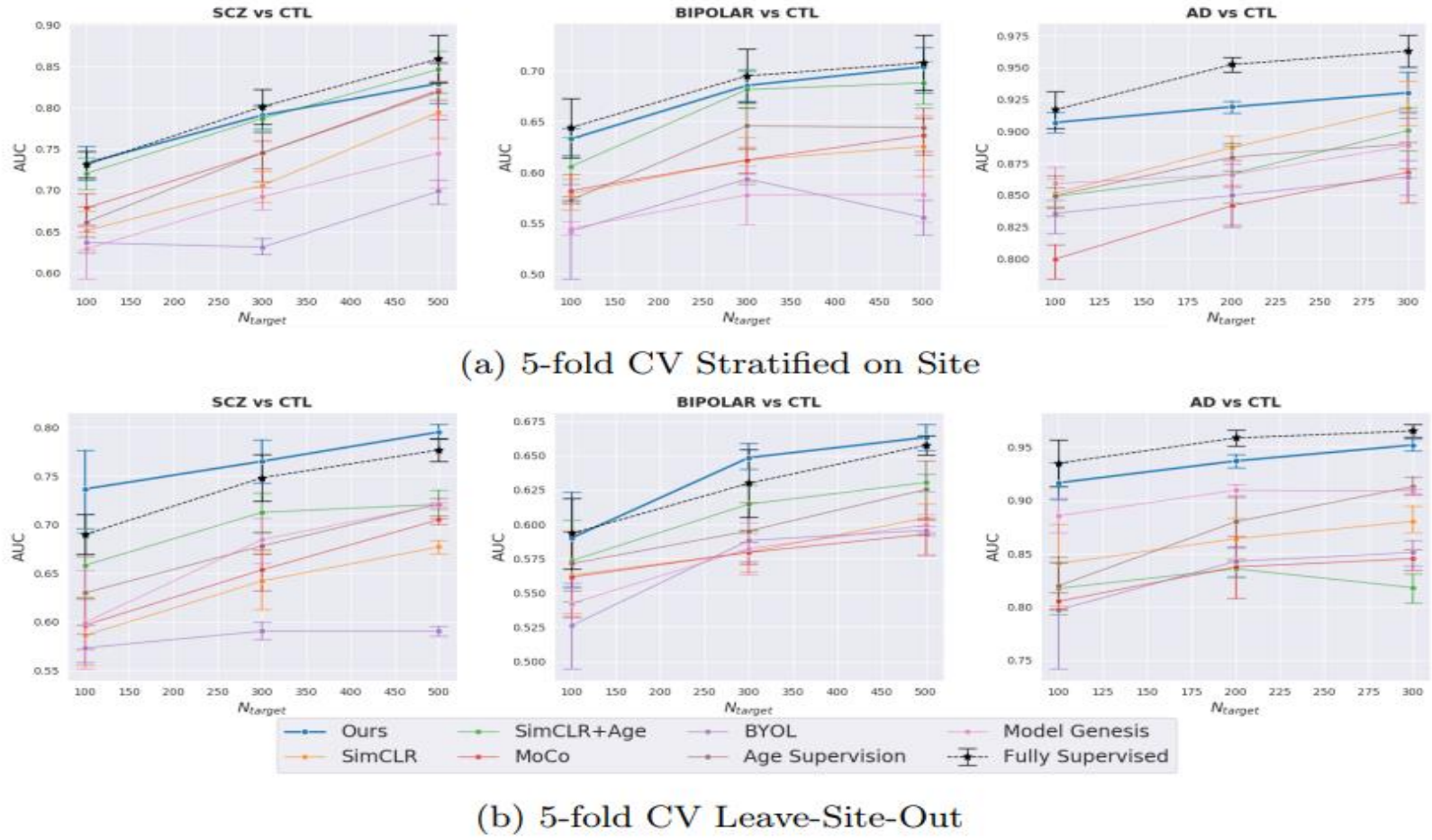


Fig. 2: Comparison of different representations in terms of classification accuracy (downstream task) on three different data-sets (one per column). Classification is performed using a linear layer on top of the pre-trained frozen encoders. (a) Data for training/validation and test come from the the same acquisition sites (b) Data for training/validation and test come from different sites.

Result

Fine-tuning Results

Backbone	Pre-training	SCZ vs HC		BD vs HC		AD vs HC	
		$N_{train} = 100$	$N_{train} = 500$	$N_{train} = 100$	$N_{train} = 500$	$N_{train} = 100$	$N_{train} = 300$
UNet	None	$72.62_{\pm 0.9}$	$76.45_{\pm 2.2}$	$63.03_{\pm 2.7}$	$69.20_{\pm 3.7}$	$88.12_{\pm 3.2}$	$94.16_{\pm 3.9}$
	Model Genesis [29]	$73.00_{\pm 3.4}$	$81.8_{\pm 4.7}$	$60.96_{\pm 1.8}$	$67.04_{\pm 4.4}$	$89.44_{\pm 2.6}$	$95.16_{\pm 3.3}$
	SimCLR [4]	$73.63_{\pm 2.4}$	$80.12_{\pm 4.9}$	$59.89_{\pm 2.6}$	$66.51_{\pm 4.3}$	$90.60_{\pm 2.5}$	$94.21_{\pm 2.7}$
	Age Prediction w/ D.A	$\underline{75.32}_{\pm 2.2}$	$\underline{85.27}_{\pm 2.3}$	$\mathbf{64.6}_{\pm \mathbf{1.6}}$	$\mathbf{70.78}_{\pm \mathbf{2.1}}$	$\underline{91.71}_{\pm 1.1}$	$\underline{95.26}_{\pm 1.5}$
	Age-Aware Contrastive Learning (ours)	$\mathbf{75.95}_{\pm 2.7}$	$\mathbf{85.73}_{\pm 4.7}$	$\underline{63.79}_{\pm 3.0}$	$\underline{70.35}_{\pm 2.7}$	$\mathbf{92.19}_{\pm \mathbf{1.8}}$	$\mathbf{96.58}_{\pm \mathbf{1.6}}$
DenseNet	None	$73.09_{\pm 1.6}$	$85.92_{\pm 2.8}$	$64.39_{\pm 2.9}$	$70.77_{\pm 2.7}$	$92.23_{\pm 1.6}$	$93.68_{\pm 1.7}$
	None w/ D.A	$\underline{74.71}_{\pm 1.3}$	$86.94_{\pm 2.8}$	$64.79_{\pm 1.3}$	$72.25_{\pm 1.5}$	$92.10_{\pm 1.8}$	$94.16_{\pm 2.5}$
	SimCLR [5]	$70.80_{\pm 1.9}$	$86.35_{\pm 2.2}$	$60.57_{\pm 1.9}$	$67.99_{\pm 3.3}$	$91.54_{\pm 1.9}$	$94.26_{\pm 2.9}$
	Age Prediction	$72.90_{\pm 4.6}$	$\underline{87.75}_{\pm 2.0}$	$64.60_{\pm 3.6}$	$72.07_{\pm 3.0}$	$92.07_{\pm 2.7}$	$\underline{96.37}_{\pm 0.9}$
	Age Prediction w/ D.A	$74.06_{\pm 3.4}$	$86.90_{\pm 1.6}$	$\mathbf{65.79}_{\pm 2.0}$	$\underline{73.02}_{\pm 4.3}$	$\mathbf{94.01}_{\pm \mathbf{1.4}}$	$96.10_{\pm 3.0}$
	Age-Aware Contrastive Learning (ours)	$\mathbf{76.33}_{\pm 2.3}$	$\mathbf{88.11}_{\pm 1.5}$	$\underline{65.36}_{\pm 3.7}$	$\mathbf{73.33}_{\pm \mathbf{4.3}}$	$\underline{93.87}_{\pm 1.3}$	$\mathbf{96.84}_{\pm \mathbf{2.3}}$

Table 1: Fine-tuning results using 100 or 500 (300 for AD vs HC) training subjects. For each task, we report the AUC (%) of the fine-tuned models initialized with different approaches with 5-fold cross-validation. For age prediction, we employ the same transformations as in contrastive learning for the Data Augmentation (D.A) strategy. Best results are in **bold** and second bests are underlined.

Thanks for listening