1. Introduction

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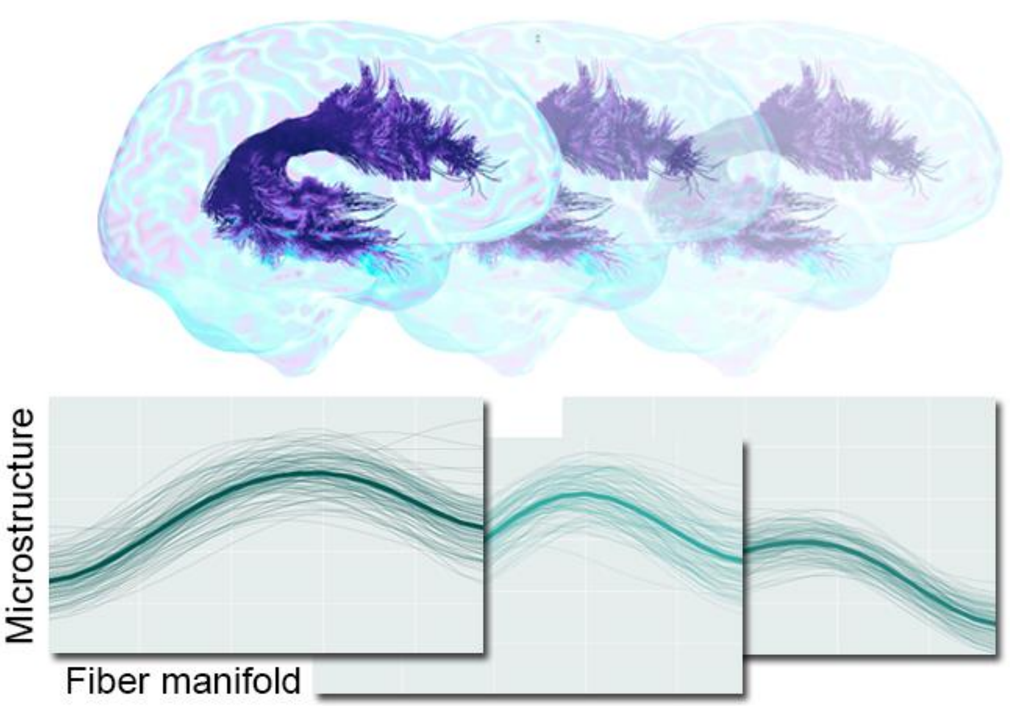
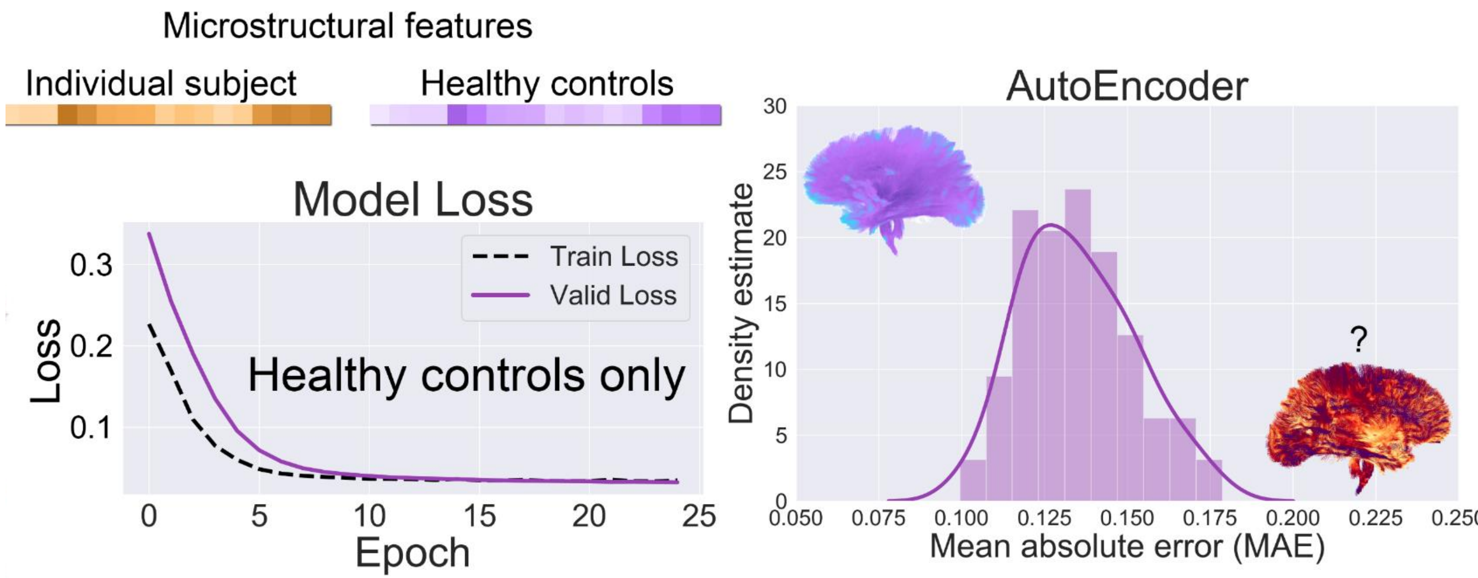
There is an urgent need for a paradigm shift from group-wise comparisons[1] (N vs M) to individual diagnosis (1 vs M) in diffusion MRI (**dMRI**) to enable the analysis of rare cases and clinically-heterogeneous groups[2].

Autoencoders[3] have the great potential to detect anomalies in neuroimaging data[4].

Tractometry



Anomaly detection



[1] Jones, Derek K., and Mara Cercignani. *NMR in Biomedicine* 23.7 (2010): 803-820.
[2] Marquand, AF., et al. *Biological psychiatry* 80.7 (2016): 552-561
[3] Hinton, Geoffrey E., and Ruslan R. Salakhutdinov. *science* 313.5786 (2006): 504-507.
[4] Zimmerer, D et al. MIDL 2019

2.1 Methods

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Dataset

90 typically developing children (**TD**, 8-18 years)

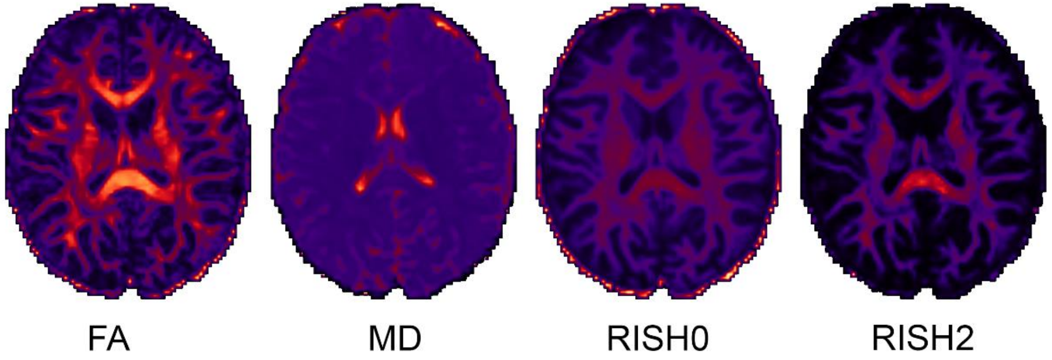
8 children with copy-number variants (**CNV**, 8-15 years)

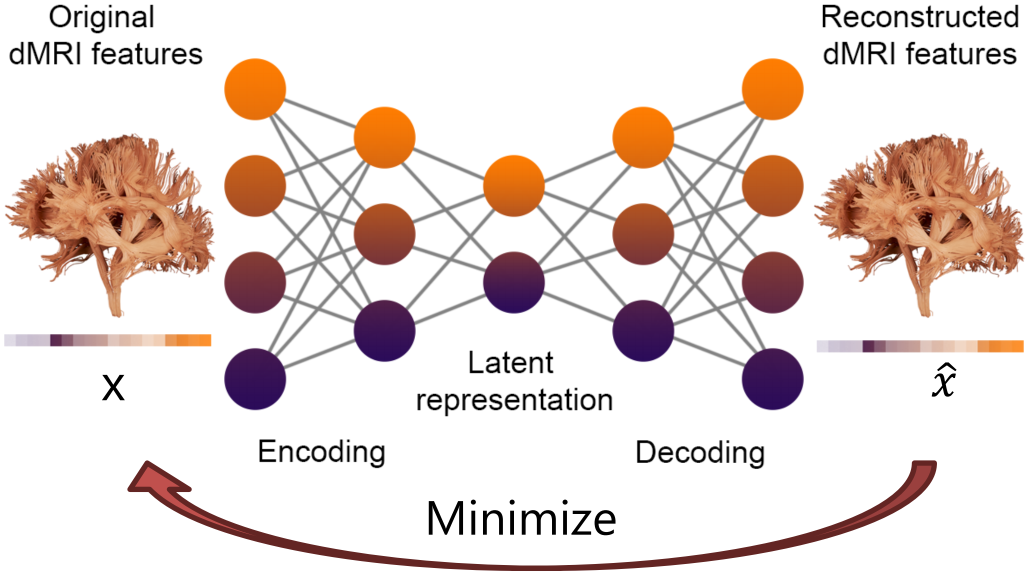
Preprocessed[5] as in *Chamberland et al. 2019*

2×2×2 mm^3 isotropic voxels and
30 diffusion directions at b = 500 s/mm^2,
30 … at b = 1200 s/mm^2,
60 … at b = 2400 s/mm^2,
60 … at b = 4000 s/mm^2,
*60 … at b = 6000 s/mm^2 (Siemens 3T **Connectom** scanner @**300 mT/m**)*

Tractometry

- Automated tract segmentation using TractSeg[6]
- Tractometry[7-9] using **FA**, **MD**, **RISH0** and **RISH2**[10]
- Tract profiles → feature vector
  - n = 26 tracts × 20 locations = 520 features for each subject.





[5] Chamberland, M, et al. *NeuroImage* 200 (2019): 89-100.
[6] Wasserthal, J, et al. *NeuroImage* 183 (2018): 239-253.
[7] Bells, S. et al. *In Proc ISMRM 2011.*
[8] Cousineau, M. et al. *NeuroImage: Clinical* 16 (2017): 222-233.
[9] Yeatman, JD., et al. *PloS one* 7.11 (2012).
[10] Mirzaalian, H. et al. NeuroImage 135 (2016): 311-323.

2.2 Methods

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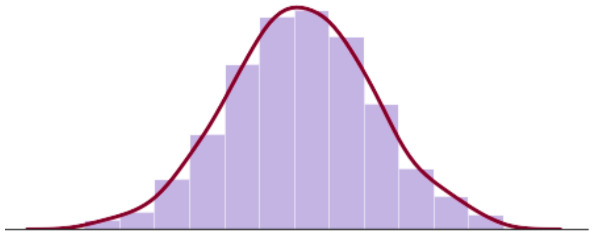
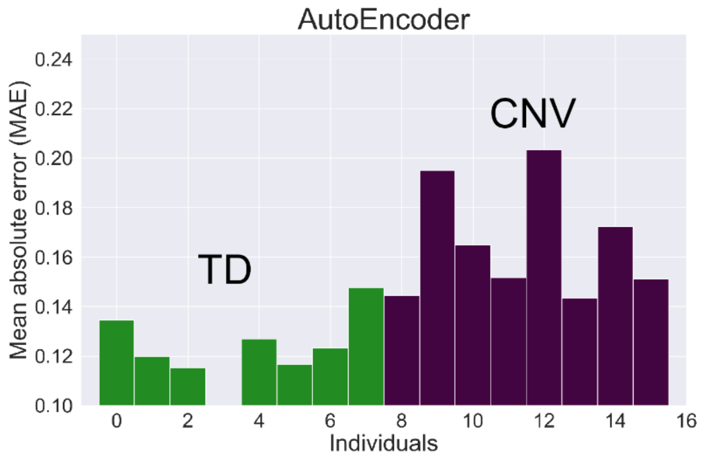
Evaluation

- Validation set (n = 16) → **CNV** (n = 8) + a random subset of **TD** (n = 8).
- The rest of the **TD** (n = 82) data was used to establish a **normative** distribution.
- Anomaly score → mean absolute error (**MAE**) over all features.
- CV shuffle repeat 100 times → derive a mean anomaly score per subject.



$$MAE = \frac{1}{n}\sum_{j=1}^{n}|y_j - \hat{y}_j|$$



Using the subject labels, we report the mean ROC area under the curve (**AUC**) across the iterations and compared the results with traditional Z-score[9] and PCA[11] approaches.

Z vs **M** vs **MAE**

Univariate Z-score | PCA + Mahalanobis Distance | Autoencoder + Mean Absolute Error

[9] Yeatman, JD., et al. *PloS one* 7.11 (2012).
[11] Taylor, PN, et al. *Neurology* (2020).

3. Results

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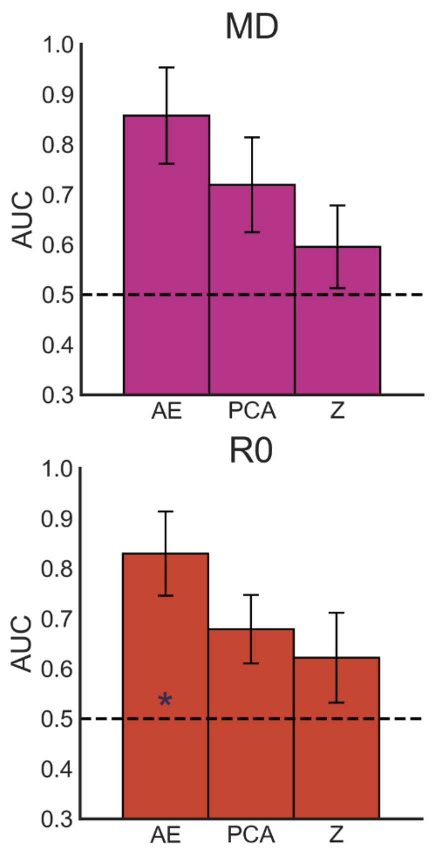

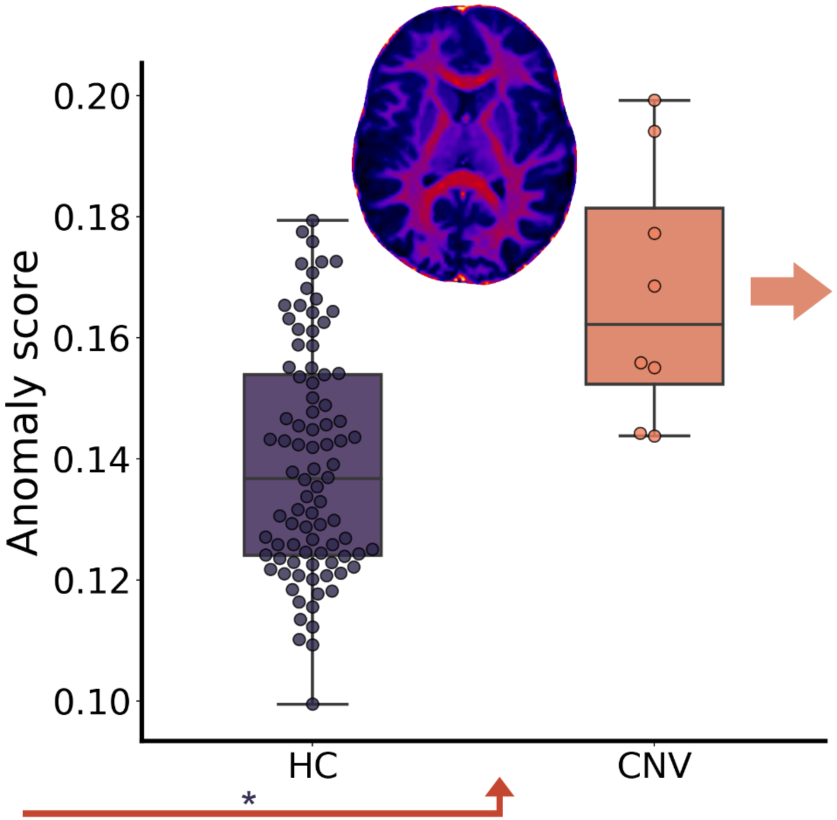

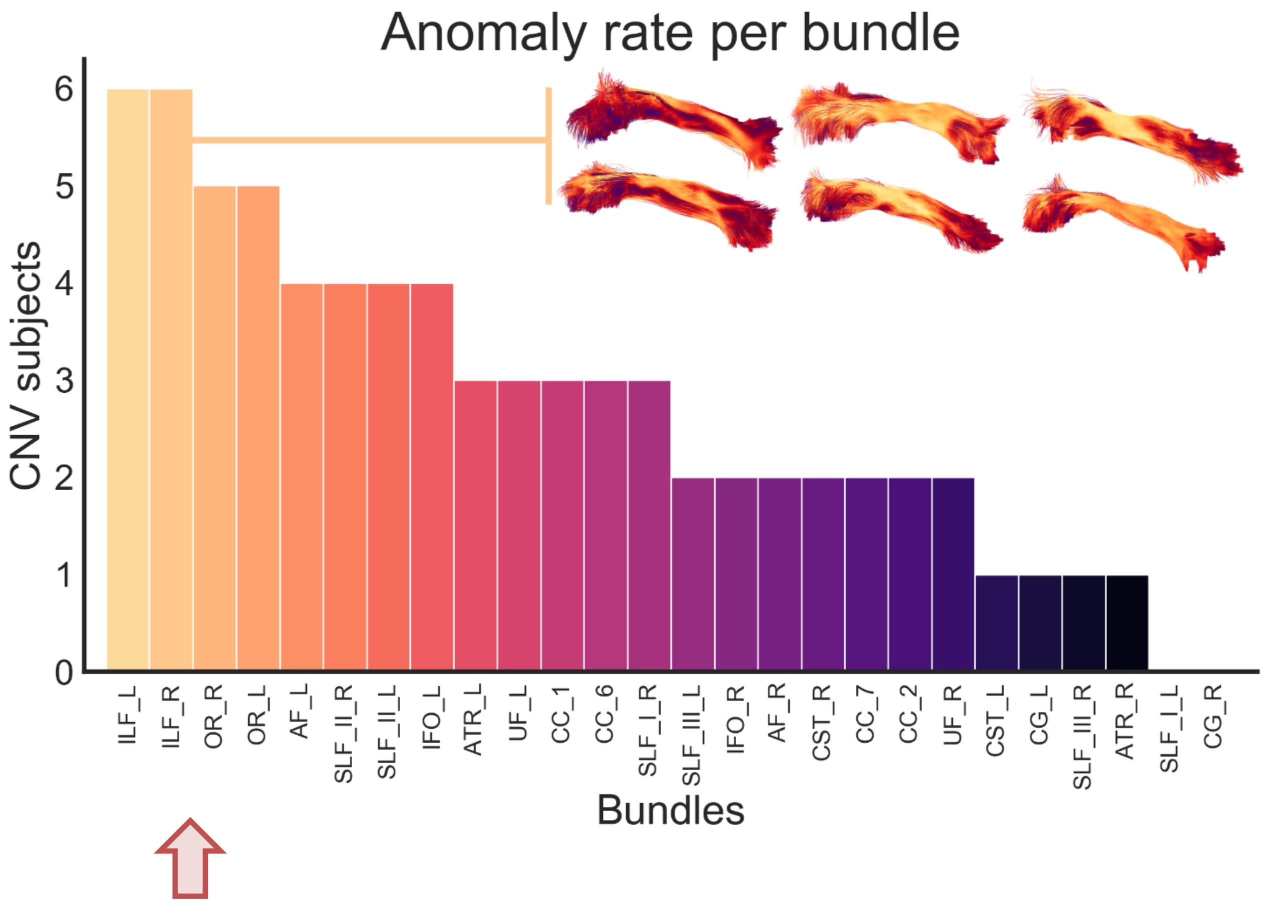

For all four microstructural metrics, the autoencoder approach was better at identifying CNV subjects as outliers, providing substantially higher sensitivity-specificity trade-offs.

Anomalies mostly occurred along the **ILF** and **OR** bundles (bilateral).

4. Feature inspection

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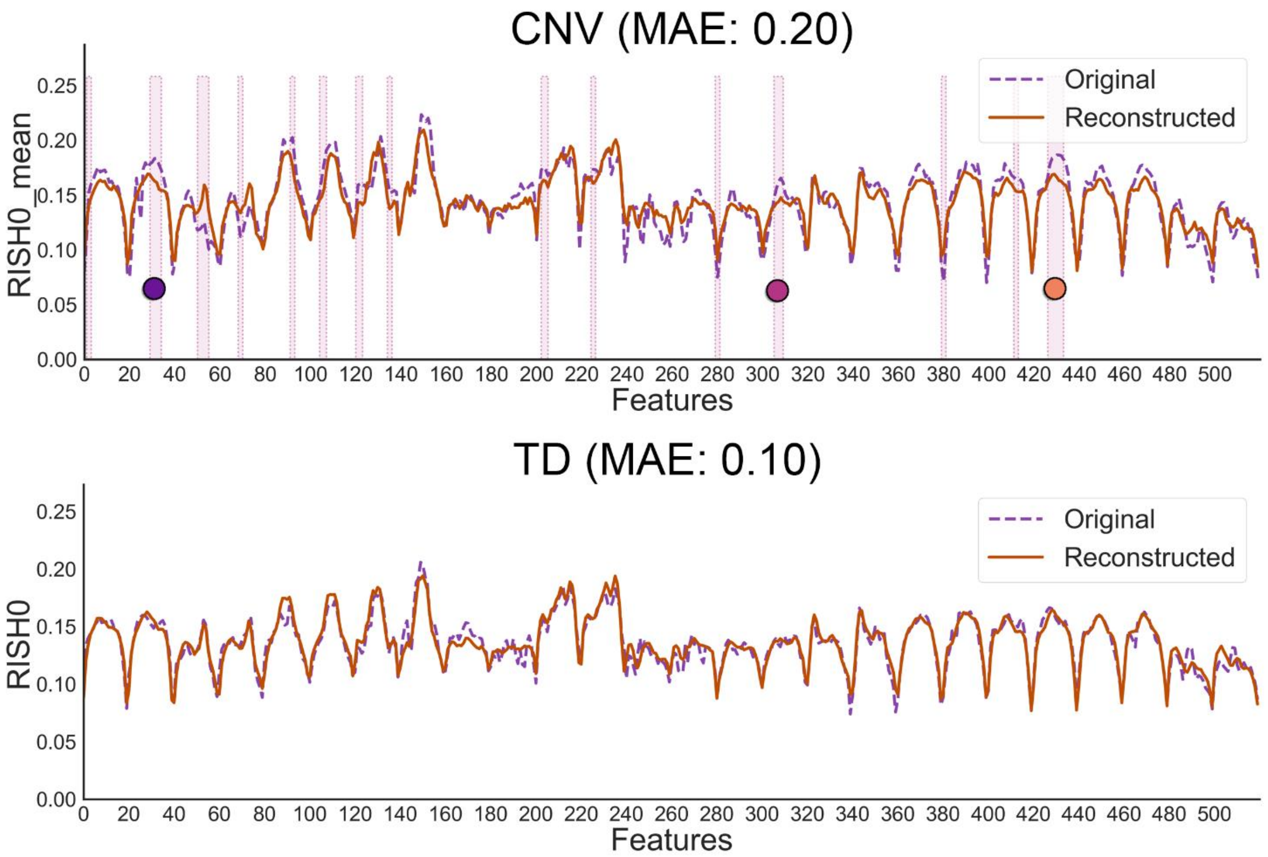

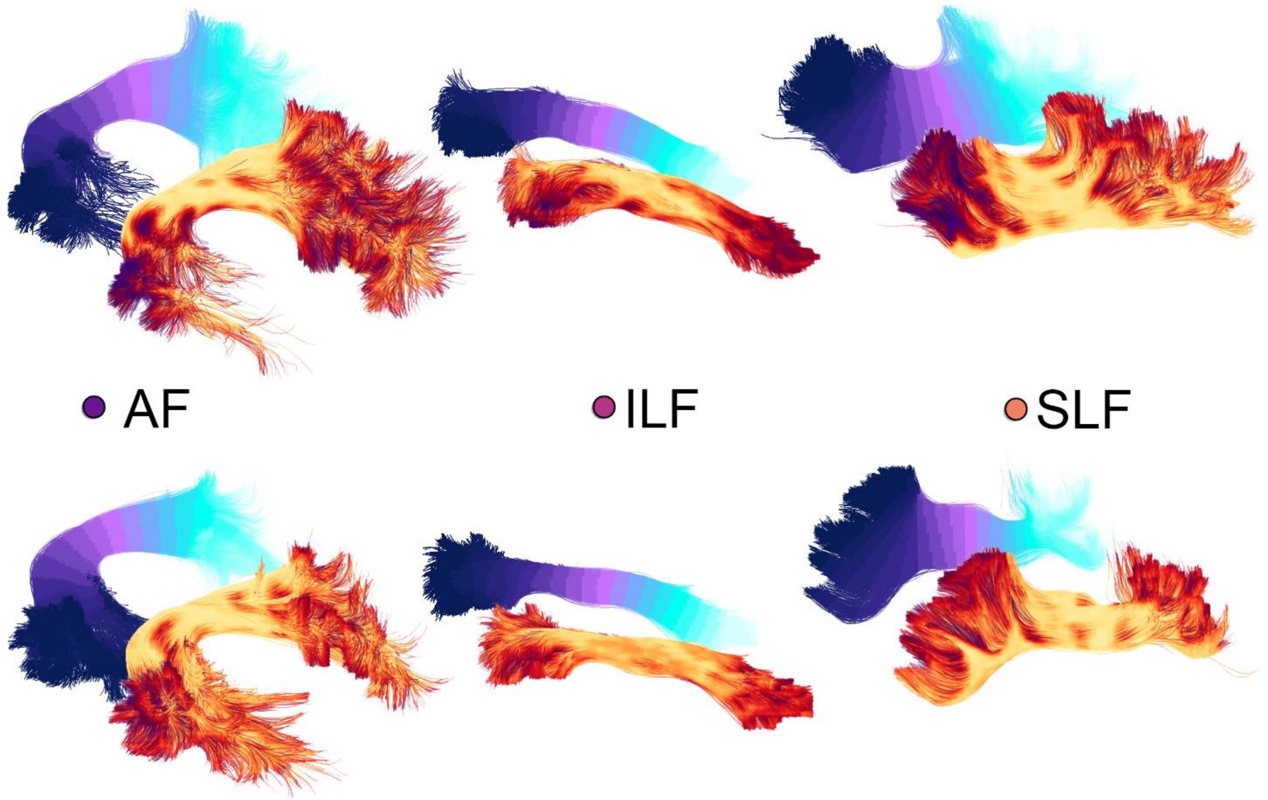

A key advantage of using deep autoencoders for anomaly detection over traditional PCA-derived approach is their unique ability to interpret anomaly scores based on **feature** inspection.

Peer-reviewed short paper (@MIDL2020): arxiv.org/abs/2005.11082