

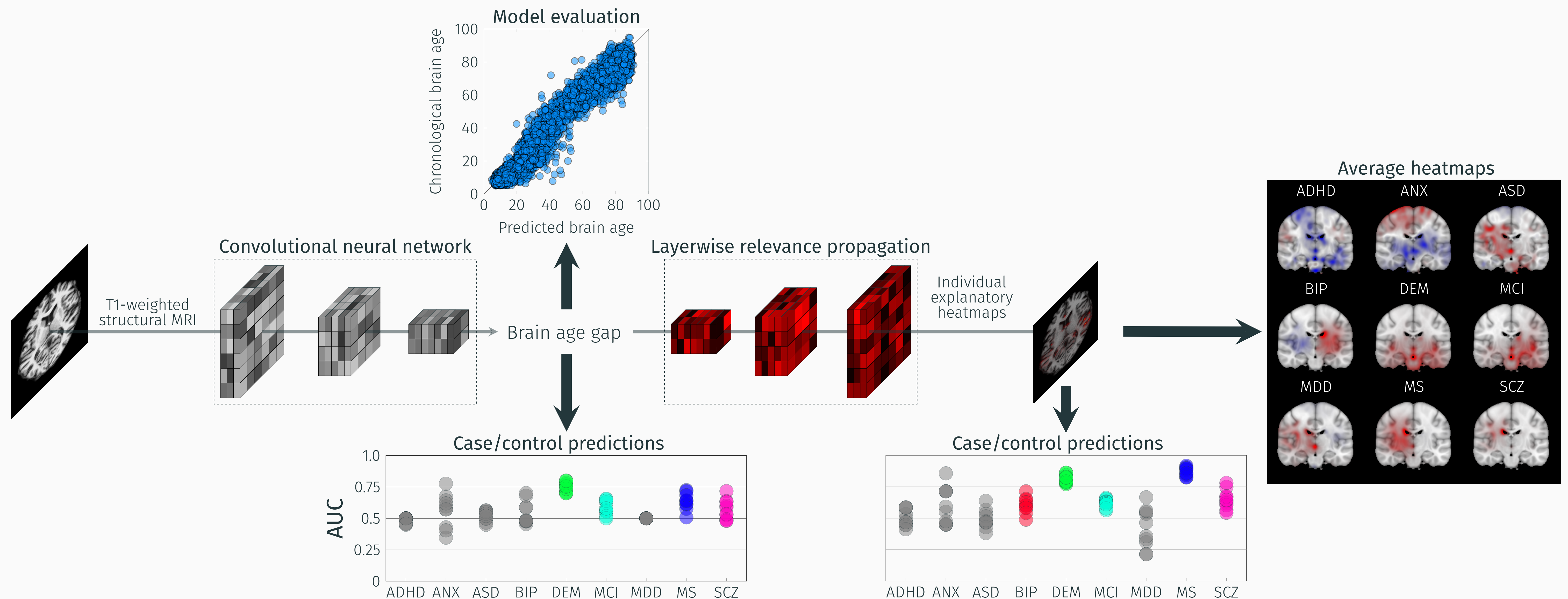
# Increasing the sensitivity of brain age modelling with explainable artificial intelligence

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## Introduction

The brain age gap (BAG), a neuroimaging-derived measure encoding the difference between the apparent and chronological age of the brain, has revealed older-appearing brains in patients with various conditions<sup>1</sup>. Although this phenomena is evident at the group-level, the abstract nature of BAG limits its utility for individualized clinical decision-making. Explainable artificial intelligence (XAI) can unveil concrete and precise visual patterns in the individual patient causing deviations in BAG, that are plausibly more clinically useful than the singular measure.

## Methods

We trained a convolutional neural network to predict BAG using 80,007 structural magnetic resonance images from 67,881 participants. On top of the model we implemented layer-wise relevance propagation, a post-hoc XAI technique for explaining decision made by a model. This allowed us to procure heatmaps highlighting regions underlying a deviating BAG in individual participants. Finally, we investigated how these regions differed between participants, and whether their content could support clinical decision-making across nine conditions (Table 1).

## Results

Our model achieved satisfactory predictive performance in a held-out dataset (mean absolute error=4.51) from unknown scanners. Singular BAGs from our model allowed us to meaningfully discriminate patients from controls (mean AUC>0.5 in a nested cross-validation,  $p<0.05$ ) for four out of nine diagnoses (DEM, MCI, MS, SCZ). The heatmaps yielded significantly improved predictions (mean  $AUC_{map}>mean AUC_{BAG}$ ,  $p<0.05$ ) for five out of nine diagnoses (BIP, DEM, MCI, MS, SCZ). Except MCI and DEM, the highlighted regions varied notably between conditions.

## Conclusion

Combining brain age models with XAI increases its utility for personalized clinical decision-making.

## References

1. Franke, K. & Gaser, C. Ten Years of BrainAGE as a Neuroimaging Biomarker of Brain Aging: What Insights Have We Gained? *Frontiers in Neurology*, 2019
2. Martin S.A. et al. Interpretable machine learning for dementia: A systematic review. *Alzheimer's Dementia*, 2023