BrainAGE-CLIP: A Novel Computational Biomarker for Brain Aging in Mice

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Brain age gap estimation(BrainAGE) has emerged as a powerful biomarker in human neuroimaging, offering insight into deviations from normative aging trajectories and providing a sensitive indicator of neurodegenerative risk, cognitive decline, and disease progression. Extending this paradigm to mice offers unique translational advantages since mice models permit controlled manipulation of genetics, environment, and pathology across the lifespan, thereby enabling mechanistic investigations that are infeasible in humans. However, no mouse BrainAGE models exist in literature. To address the gap, this project developed the first MRI–based mouse BrainAGE pipeline trained on 691 in vivo T1-weighted whole-head scans acquired on a 9.4 T Bruker system across mice aged 0–24 months. The workflow integrates state-of-the-art preprocessing, including N4 bias correction, AI based brain extraction, and age-specific template registration,. Three prediction models were evaluated: a baseline VGG-13 CNN, a VGG transfer learned from human MRI, and a novel CLIP-style BrainAGE model that aligns image embeddings with continuous Fourier-encoded age embeddings through a soft-contrastive loss and auxiliary regression. The CLIP-aligned model achieves the strongest performance, with r=0.922, MAE=1.905 months, and RMSE=2.798 months, demonstrating superior calibration, reduced distributional mismatch (Wilcoxon p=0.557), and improved sensitivity across lifespan extremes. These results support the feasibility of scalable, accurate mouse BrainAGE from routine T1 MRI and demonstrate that cross-species transfer learning and embedding alignment provides substantial gains over standard techniques. This BrainAGE model provides a robust and efficient platform for mice aging research and drug discovery.

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