**Table 1. Brain age prediction performance across cohorts.** Summary of model performance metrics across typically developing and clinical populations. Results demonstrate strong performance in the HCP-Development discovery cohort and robust generalization across three independent validation cohorts of typically developing individuals. Prediction accuracy and mean absolute error (MAE) in clinical populations (ADHD and ASD) are comparable to those observed in typically developing children. N represents sample size; MAE represents mean absolute error in years; correlation represents Pearson's r between predicted and chronological age.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Population** | **Dataset** | **N** | **Age Range (year)** | **Accuracy (r²)** | **MAE (year)** | **p-value** |
| **Typically Developing** | | | | | | |
| Discovery | HCP-Development | 632 | 8–22 | 0.823 | 1.40 | < 0.001 |
| Validation | NKI-RS | 369 | 6–21 | 0.847 | 1.43 | < 0.001 |
| CMI-HBN | 117 | 6–21 | 0.793 | 1.25 | < 0.001 |
| ADHD-200 | 289 | 7–21 | 0.738 | 1.55 | < 0.001 |
| **Clinical Populations** | | | | | | |
| ADHD | ADHD-200 | 201 | 7–21 | 0.703 | 1.40 | < 0.001 |
| CMI-HBN | 654 | 6–21 | 0.749 | 1.32 | < 0.001 |
| ASD | ABIDE | 353 | 6–21 | 0.903 | 0.97 | < 0.001 |
| Stanford | 154 | 7–18 | 0.673 | 1.09 | < 0.001 |

**Table 2. Brain-behavior relationships across populations**. Relationships between brain features and behavioral measures in typically developing and clinical populations. Results show significant associations between xAI-derived brain features and multiple clinical measures, including inattention, hyperactivity, and autism symptom severity. For typically developing individuals, relationships are expressed as spearman correlation values between actual behavior score and predicted behavior from principal components regression models. For clinical populations (ADHD and ASD), correlations (r) are reported between brain features and disorder-specific measures. All reported relationships are statistically significant (*p* < 0.05), demonstrating the clinical relevance of the identified brain features.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Population** | **Dataset** | **Behavioral Measure** | **Correlation (r)** | **p-value** |
| TD | NKI-RS | Hyperactivity | 0.645 | < 0.001 |
| Inattention | 0.669 | < 0.001 |
| ADHD | ADHD-200 | Hyperactivity | 0.397 | < 0.001 |
| Inattention | 0.392 | < 0.001 |
| CMI-HBN | Hyperactivity | 0.391 | < 0.001 |
| Inattention | 0.411 | < 0.001 |
| ASD | ABIDE | ADOS Total | 0.525 | < 0.001 |
| ADOS Social | 0.490 | < 0.001 |
| ADOS Communication | 0.529 | < 0.001 |
| Stanford | SRS Total | 0.308 | = 0.002 |

TD = Typically Developing; ADOS = Autism Diagnostic Observation Schedule

**Table 3: Top 20% Shared regions among TD cohorts**

|  |  |  |  |
| --- | --- | --- | --- |
| **Brain Regions** | **Subdivision** | **(ID) Region Label** | **Count** |
| **Middle Temporal Gyrus** | A35/36c, caudal area 35/36 | (112), PhG\_R\_6\_2 | 490 |
| **Prefrontal Cortex** | A8vl, ventrolateral area 8 | (24), MFG\_R\_7\_5 | 487 |
| **Thalamus** | Otha, occipital thalamus | (241), Tha\_L\_8\_6 | 487 |
| **PCC, Precuneus** | A5m, medial area 5(PEm) | (149), Pcun\_L\_4\_2 | 486 |
| **Prefrontal Cortex** | IFJ, inferior frontal junction | (17), MFG\_L\_7\_2 | 486 |
| **Precentral Gyrus** | A4hf, area 4(head and face region) | (54), PrG\_R\_6\_1 | 478 |
| **Inferior Temporal Gyrus** | A37vm, ventromedial area37 | (92), ITG\_R\_7\_2 | 474 |
| **Striatum** | dCa, dorsal caudate | (227), Str\_L\_6\_5 | 472 |
| **Prefrontal Cortex** | IFS, inferior frontal sulcus | (32), IFG\_R\_6\_2 | 468 |
| **Middle Temporal Gyrus** | A28/34, area 28/34 (EC, entorhinal cortex) | (115), PhG\_L\_6\_4 | 467 |
| **Middle Temporal Gyrus** | A35/36c, caudal area 35/36 | (111), PhG\_L\_6\_2 | 464 |
| **Inferior Temporal Gyrus** | A20r, rostral area 20 | (94), ITG\_R\_7\_3 | 458 |
| **Inferior Parietal Lobe** | A39rd, rostrodorsal area 39(Hip3) | (138), IPL\_R\_6\_2 | 450 |
| **Inferior Parietal Lobe** | A39c, caudal area 39(PGp) | (135), IPL\_L\_6\_1 | 450 |
| **Thalamus** | Otha, occipital thalamus | (242), Tha\_R\_8\_6 | 438 |
| **Precentral Gyrus** | A4t, area 4(trunk region) | (60), PrG\_R\_6\_4 | 430 |
| **Thalamus** | rTtha, rostral Temporal thalamus | (238), Tha\_R\_8\_4 | 418 |
| **Superior Temporal Gyrus** | A38l, lateral area 38 | (78), STG\_R\_6\_5 | 406 |
| **Superior Parietal Lobule** | A7ip, intraparietal area 7(hIP3) | (126), SPL\_R\_5\_1 | 404 |
| **PCC, Precuneus** | dmPOS, dorsomeidal parietooccipital  sulcus(PEr) | (151), Pcun\_L\_4\_3 | 398 |
| **Striatum** | dlPu, dorsolateral putamen | (230), Str\_R\_6\_6 | 391 |
| **Precentral Gyrus** | A4t, area 4(trunk region) | (59), PrG\_L\_6\_4 | 390 |
| **Paracentral Lobule** | A4ll, area 4, (lower limb region) | (67), PCL\_L\_2\_2 | 383 |
| **Cingulate Gyrus** | A23v, ventral area 23 | (182), CG\_R\_7\_4 | 378 |
| **Striatum** | dlPu, dorsolateral putamen | (229), Str\_L\_6\_6 | 376 |
| **Inferior Temporal Gyrus** | A37vl, ventrolatral area37 | (108), FuG\_R\_3\_3 | 375 |
| **Superior Parietal Lobule** | A7pc, postcentral area 7 | (130), SPL\_R\_5\_3 | 372 |
| **Postcentral Gyrus** | A2, area 2 | (160), PoG\_R\_4\_3 | 364 |
| **Cingulate Gyrus** | A23v, ventral area 23 | (181), CG\_L\_7\_4 | 362 |
| **PCC, Precuneus** | dmPOS, dorsomeidal parietooccipital  sulcus(PEr) | (152), Pcun\_R\_4\_3 | 351 |

**Table 4: Top 20% Shared regions among ADHD cohorts**

|  |  |  |  |
| --- | --- | --- | --- |
| **Brain Regions** | **Subdivision** | **(ID) Region Label** | **Count** |
| **Middle Temporal Gyrus** | A35/36c, caudal area 35/36 | (112), PhG\_R\_6\_2 | 494 |
| **PCC, Precuneus** | A5m, medial area 5(PEm) | (149), Pcun\_L\_4\_2 | 492 |
| **Middle Temporal Gyrus** | A35/36c, caudal area 35/36 | (111), PhG\_L\_6\_2 | 487 |
| **Prefrontal Cortex** | IFS, inferior frontal sulcus | (32), IFG\_R\_6\_2 | 483 |
| **Thalamus** | Otha, occipital thalamus | (242), Tha\_R\_8\_6 | 483 |
| **Inferior Temporal Gyrus** | A20r, rostral area 20 | (94), ITG\_R\_7\_3 | 481 |
| **Precentral Gyrus** | A4hf, area 4(head and face region) | (54), PrG\_R\_6\_1 | 481 |
| **Middle Temporal Gyrus** | A28/34, area 28/34 (EC, entorhinal cortex) | (115), PhG\_L\_6\_4 | 479 |
| **Prefrontal Cortex** | A8vl, ventrolateral area 8 | (24), MFG\_R\_7\_5 | 476 |
| **Prefrontal Cortex** | A11l, lateral area 11 | (45), OrG\_L\_6\_3 | 466 |
| **Striatum** | dCa, dorsal caudate | (227), Str\_L\_6\_5 | 465 |
| **Inferior Parietal Lobe** | A39rd, rostrodorsal area 39(Hip3) | (138), IPL\_R\_6\_2 | 462 |
| **Precentral Gyrus** | A4t, area 4(trunk region) | (60), PrG\_R\_6\_4 | 458 |
| **Inferior Parietal Lobe** | A39c, caudal area 39(PGp) | (135), IPL\_L\_6\_1 | 453 |
| **Striatum** | dlPu, dorsolateral putamen | (230), Str\_R\_6\_6 | 449 |
| **Superior Temporal Gyrus** | A38l, lateral area 38 | (78), STG\_R\_6\_5 | 442 |
| **PCC, Precuneus** | dmPOS, dorsomeidal parietooccipital  sulcus(PEr) | (151), Pcun\_L\_4\_3 | 434 |
| **Inferior Temporal Gyrus** | A37vm, ventromedial area37 | (92), ITG\_R\_7\_2 | 434 |
| **Thalamus** | Otha, occipital thalamus | (241), Tha\_L\_8\_6 | 428 |
| **Thalamus** | rTtha, rostral Temporal thalamus | (238), Tha\_R\_8\_4 | 420 |
| **Precentral Gyrus** | A4ul, area 4(upper limb region) | (57), PrG\_L\_6\_3 | 417 |
| **Striatum** | GP, globus pallidus | (222), Str\_R\_6\_2 | 408 |
| **Inferior Parietal Lobe** | A40rd, rostrodorsal area 40(PFt) | (139), IPL\_L\_6\_3 | 404 |
| **Superior Parietal Lobule** | A7ip, intraparietal area 7(hIP3) | (126), SPL\_R\_5\_1 | 398 |
| **Inferior Temporal Gyrus** | A20r, rostral area 20 | (93), ITG\_L\_7\_3 | 398 |
| **Superior Parietal Lobule** | A7pc, postcentral area 7 | (130), SPL\_R\_5\_3 | 394 |
| **Postcentral Gyrus** | A2, area 2 | (160), PoG\_R\_4\_3 | 392 |
| **Paracentral Lobule** | A4ll, area 4, (lower limb region) | (67), PCL\_L\_2\_2 | 389 |
| **Postcentral Gyrus** | A1/2/3ulhf, area 1/2/3(upper limb, head and face region) | (155), PoG\_L\_4\_1 | 371 |
| **PCC, Precuneus** | A5m, medial area 5(PEm) | (150), Pcun\_R\_4\_2 | 355 |

**Table 5: Top 20% Shared regions among ASD cohorts**

|  |  |  |  |
| --- | --- | --- | --- |
| **Brain Regions** | **Subdivision** | **(ID) Region Label** | **Count** |
| **Prefrontal Cortex** | A8vl, ventrolateral area 8 | (24), MFG\_R\_7\_5 | 496 |
| **Prefrontal Cortex** | IFS, inferior frontal sulcus | (32), IFG\_R\_6\_2 | 496 |
| **PCC, Precuneus** | A5m, medial area 5(PEm) | (149), Pcun\_L\_4\_2 | 490 |
| **PCC, Precuneus** | dmPOS, dorsomeidal parietooccipital  sulcus(PEr) | (151), Pcun\_L\_4\_3 | 489 |
| **Inferior Parietal Lobe** | A39rd, rostrodorsal area 39(Hip3) | (138), IPL\_R\_6\_2 | 485 |
| **Prefrontal Cortex** | A9l, lateral area 9 | (6), SFG\_R\_7\_3 | 483 |
| **Striatum** | dCa, dorsal caudate | (227), Str\_L\_6\_5 | 482 |
| **Middle Temporal Gyrus** | A35/36c, caudal area 35/36 | (111), PhG\_L\_6\_2 | 478 |
| **Inferior Parietal Lobe** | A39c, caudal area 39(PGp) | (135), IPL\_L\_6\_1 | 475 |
| **Middle Temporal Gyrus** | A35/36c, caudal area 35/36 | (112), PhG\_R\_6\_2 | 468 |
| **Middle Temporal Gyrus** | A28/34, area 28/34 (EC, entorhinal cortex) | (116), PhG\_R\_6\_4 | 467 |
| **PCC, Precuneus** | dmPOS, dorsomeidal parietooccipital  sulcus(PEr) | (152), Pcun\_R\_4\_3 | 451 |
| **Inferior Temporal Gyrus** | A37vm, ventromedial area37 | (92), ITG\_R\_7\_2 | 448 |
| **Thalamus** | Otha, occipital thalamus | (242), Tha\_R\_8\_6 | 437 |
| **Striatum** | dlPu, dorsolateral putamen | (230), Str\_R\_6\_6 | 427 |
| **Superior Parietal Lobule** | A7ip, intraparietal area 7(hIP3) | (126), SPL\_R\_5\_1 | 425 |
| **Striatum** | dCa, dorsal caudate | (228), Str\_R\_6\_5 | 412 |
| **Thalamus** | Otha, occipital thalamus | (241), Tha\_L\_8\_6 | 410 |
| **Cingulate Gyrus** | A23d, dorsal area 23 | (176), CG\_R\_7\_1 | 406 |
| **Superior Temporal Gyrus** | A38l, lateral area 38 | (78), STG\_R\_6\_5 | 403 |
| **Inferior Temporal Gyrus** | A37vl, ventrolatral area37 | (108), FuG\_R\_3\_3 | 394 |
| **Paracentral Lobule** | A4ll, area 4, (lower limb region) | (67), PCL\_L\_2\_2 | 380 |
| **Precentral Gyrus** | A4t, area 4(trunk region) | (59), PrG\_L\_6\_4 | 377 |
| **Superior Parietal Lobule** | A7pc, postcentral area 7 | (130), SPL\_R\_5\_3 | 375 |
| **Precentral Gyrus** | A4hf, area 4(head and face region) | (54), PrG\_R\_6\_1 | 359 |
| **Occipital Gyrus** | msOccG, medial superior occipital gyrus | (207), sOcG\_L\_2\_1 | 356 |
| **Superior Temporal Gyrus** | A38m, medial area 38 | (69), STG\_L\_6\_1 | 354 |
| **Precentral Gyrus** | A4t, area 4(trunk region) | (60), PrG\_R\_6\_4 | 350 |
| **Cingulate Gyrus** | A23v, ventral area 23 | (181), CG\_L\_7\_4 | 327 |
| **Inferior Temporal Gyrus** | A20r, rostral area 20 | (94), ITG\_R\_7\_3 | 325 |

**Table 6. Brain age prediction performance across cohorts using conventional machine learning approaches.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Population** | **Dataset** | **Accuracy (r²) of Conventional Machine Learning Approaches** | | | | | | |
| **linSVR** | **KNN** | **DT** | **LR** | **RC** | **LASSO** | **RF** |
| TD | HCP-Development | 0.939 (0.00) | 0.538  **(**1e-107**)** | 0.799  **(**2e-221**)** | 0.938  (0.00) | 0.938  (0.00) | 0.668  (5e-153) | 0.871  (2e-282) |
| NKI-RS | 0.667  (9e-90) | 0.291  (3e-29) | 0.274  (2e-27) | 0.667  (1e-89) | 0.667  (1e-89) | 0.459  (7e-51) | 0.406  (2e-43) |
| CMI-HBN | 0.504  (2e-19) | 0.245  (1e-08) | 0.073  (3e-03) | 0.503  (2e-19) | 0.503  (2e-19) | 0.355  (1e-12) | 0.254  (6e-09) |
| ADHD-200 | 0.196  (2-15) | 0.060  (2e-05) | 0.075  (2e-06) | 0.195  (2e-15) | 0.195  (2e-15) | 0.133  (1e-10) | 0.168  (3e-13) |
| ADHD | CMI-HBN | 0.444  (4e-85) | 0.181  (5e-30) | 0.102  (6e-17) | 0.442  (1e-84) | 0.442  (1e-84) | 0.267  (7e-46) | 0.233  (2e-39) |
| ADHD-200 | 0.138  (2e-07) | 0.033  (1e-02) | 0.020  (5e-02) | 0.138  (2e-07) | 0.138  (2e-07) | 0.125  (7e-07) | 0.074  (2e-04) |
| ASD | ABIDE | 0.272  (4e-28) | 0.046  (2e-05) | 0.025  (2e-03) | 0.270  (7e-28) | 0.270  (7e-28) | 0.101  (2e-10) | 0.093  (1e-09) |
| Stanford | 0.118  (2e-05) | 0.036  (2e-02) | 0.001  (7e-01) | 0.118  (2e-05) | 0.118  (2e-05) | 0.035  (2e-02) | 0.012  (2e-01) |